

The Politics of **CANCER**

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REVISED AND EXPANDED EDITION

Samuel S. Epstein

M.D.

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SAMUEL S. EPSTEIN, M.D., is Professor of Occupational and Environmental Medicine at the School of Public Health, University of Illinois at the Medical Center, Chicago. He has been Chief of the Laboratories of Environmental Toxicology and Carcinogenesis at the Children's Cancer Research Foundation in Boston, Senior Research Associate in Pathology at Harvard Medical School, and Swetland Professor of Environmental Health and Human Ecology at Case Western Reserve University Medical School. An authority on toxic and carcinogenic hazards due to chemical pollutants, he is the author of over two hundred scientific publications and four books; has served as consultant to various Congressional committees, federal agencies, and organized labor; and is president of the Rachel Carson Trust and chairperson of the Commission for the Advancement of Public Interest Organizations.

THE POLITICS OF CANCER

**SAMUEL S. EPSTEIN,
M.D.**

REVISED AND EXPANDED EDITION

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To my parents

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Foreword

No word in the English language is more chilling than cancer. It's hard to imagine anyone not wanting "war" waged against this disease. Yet those closely associated with the National Cancer Program and our regulatory efforts to control cancer-causing chemicals have found it increasingly difficult to agree on how that war should be fought.

The chemical causation of cancer was hardly mentioned eight years ago when Congress was debating the National Cancer Attack Act. Most Americans and members of Congress were impressed with the optimism voiced by physicians and clinical research spokesmen. There was widespread belief that there could be major breakthroughs in the treatment of cancer victims in a matter of years, possibly in the form of a Salk-type vaccine. Such an approach made some sense in the '60s, when it was commonly believed that much cancer was caused by a virus.

But at least since 1970, it has been generally accepted that the majority of all cancer is caused by chemicals and environmental factors—what we touch, breathe, eat, drink, work with, or otherwise absorb. Some of these factors occur naturally in the environment; most do not. They are put there by man.

Those same factors also cause other damage. For example, recent research relating to birth defects suggests that many cancer-causing chemicals also cause heritable mutations. In 1974, vinyl chloride, which had already been linked to liver cancer, was also tied to lung and brain cancer and birth defects. Most scientists believe that reversing such extensive damage is far beyond the scope of current technology.

For that reason, those involved in formulating the government's cancer research policy have become adamant about the need to

better understand the risks of cancer-causing chemicals and to prevent exposure to them.

But such efforts have faced serious obstacles. One problem has been the orientation of many individuals who have played a dominant role in shaping our national cancer policy. For the most part, they are surgeons, radiologists, chemotherapyists, and well-intentioned survivors of cancer. However, these people usually fail to have a basic understanding of the concept of cancer as an environmentally induced disease. In some instances, they fear that a major new emphasis in the National Cancer Program toward the environment will reduce visibility and funding for other research efforts. Thus, for one reason or another, there has been considerable resistance against moving the study of environmental causes of cancer from the back burner of the National Cancer Program.

Another obstacle has been the large expenditures required to eliminate these environmental hazards. Most Americans probably would favor the elimination of a clearly established cancer hazard, regardless of the cost. But some people in both government and industry, including some top economists in the current (Carter) administration, feel that "economic considerations" should be given greater weight, despite clear evidence that additional cancer deaths will result.

The trump card of a few opponents of tighter governmental regulation of cancer-causing chemicals is that evidence of carcinogenicity is rarely 100 percent conclusive. There is usually some element of doubt as to whether a particular chemical causes cancer. Thus, while initial tests with animals will strongly suggest a cancer link in humans, conclusive proof of that link often is years or even decades away. Regulatory action to protect workers and the general public from further exposure to a potential hazard may add millions of dollars to the cost of producing needed products, and the possibility would remain that further research might conceivably show that the chemical does not cause cancer. In either case, the stakes are enormous.

To err on the side of "economic considerations" could mean millions of lives. An extreme example of these costs can be seen in the case of asbestos. Prior to World War II, there was already considerable scientific evidence that asbestos posed serious health problems. In fact, Henry Johns, one of the co-founders of the

Johns-Manville Corp., the major asbestos supplier in the United States, died apparently of asbestosis.

During the 1930s, the German government agreed to pay compensation claims to workers who had been exposed to asbestos and were suffering from respiratory diseases. American and other scientific literature at that time contained numerous descriptions of asbestos-induced diseases, yet during and after World War II we continued to use asbestos in shipbuilding and other industries with virtually no controls. A study recently released by the Department of Health, Education and Welfare shows that approximately 2 million asbestos-related cancer deaths will occur during the next thirty to thirty-five years as a result of exposures that have already occurred. That means about 60,000 deaths per year from now until the year 2013—more than the combined death rate from all automobile, airplane, ship, and railroad accidents.

Failure to heed the early warning signs about asbestos has cost us continuing suffering and deaths. And the economic consequences of our failure have also been monstrous: increased medical bills, lost income and productivity, higher Medicaid and Medicare costs, and additional Social Security and SSI payments. Together, these cost Americans billions of dollars each year, and will continue to do so in the coming few decades.

So the cost of erring on the side of “economic considerations” is high, but erring on the side of stopping possibly harmful exposures can also be expensive. Redesigning our factories and manufacturing processes, developing safe chemical substitutes, and monitoring chemical concentrations is not cheap. Cost estimates of controlling worker exposure to cancer-causing coke emissions, for example, range from \$150 million to \$1 billion. The cost of controlling worker exposure to arsenic is estimated at \$100 million to \$225 million. Private industry has also recently claimed that it will cost more than \$88 billion to control exposure to all workplace carcinogens.

In at least two instances, those of benzidine dyes and dry-woven asbestos textiles, carcinogens have been virtually eliminated in the United States because of health problems which apparently could not be resolved cheaply enough to permit American factories to continue competing with the international market. So with these cases, the profits—together with the health problems—have been, in one sense, exported. Imports of these two

products from Taiwan, Mexico, India, Rumania, and other countries have steadily increased.

Our errors, however, have seldom if ever been on the side of worker health. We have now identified, for instance, dozens of chemicals that probably are carcinogenic, but there is no regulation of their use, and hundreds of thousands of workers are being exposed to them daily.

Take trichloroethylene, for example. Congressmen don't even have to leave their offices to see workers using this chemical to clean carpets. It is also widely used in dry cleaning, and as an industrial solvent. We know it is similar to vinyl chloride in its chemical structure, and that when fed to rats or mice, they develop liver cancer. Most scientists would conclude from these data that the odds are good that this chemical also causes cancer in humans. Yet our response to finding out more about trichloroethylene has been to wait for more "conclusive evidence" that human beings would die from this exposure. Regulations have not been issued, and workers have not even been warned about the danger. The majority of those working with trichloroethylene are as ignorant today of the potential danger from this chemical as the shipyard workers were decades ago of the potential hazards they faced from asbestos.

Many difficult decisions will have to be made in the years ahead about how we live with the new chemical hazards in our environment. There is a point where questions like these become political and ethical, as well as scientific. Those questions should not be resolved without broad-based public understanding and participation. This discussion has not yet taken place, and it will not until the scientific questions have been more thoroughly understood.

Dr. Epstein's book clearly explains the scientific problems involved in environmentally induced cancer and carcinogenesis. Equally important, it analyzes the wide range of political and social considerations involved in our failure to regulate carcinogens and stem the growing tide of cancer. I hope that by reading this book more citizens will understand and become involved in the complex and difficult decisions that lie ahead.

CONGRESSMAN DAVID OBEY (D-Wisc.)

Preface

If one thousand people died every day of cholera, swine flu, or food poisoning, an epidemic of major proportions would be at hand and the entire country would mobilize against it. Yet cancer claims that many lives daily, often in prolonged and agonizing pain, and most people believe they can do nothing about it. Cancer, they think, strikes where it will, with no apparent cause. Some take out a cancer insurance policy, all hope not to be one of its victims.

But cancer has distinct, identifiable causes. It is not just another degenerative disease associated with aging. It can largely be prevented, but this requires more than just scientific effort or individual action. The control and prevention of cancer will require a concerted national effort. This book is offered as a contribution to that essentially political process.

There are four basic axioms of cancer causation which will be continually referred to:

1. *Cancer is caused mainly by exposure to chemical or physical agents in the environment.* To be sure, there are genetic aspects to cancer, and some cancers are suspected to be caused by viruses, but these factors account for only a small fraction of all cases.* Just as germs cause infections, so do certain chemical and physical agents, *carcinogens*, cause cancer.† While some carcinogens,

* There is little or no evidence that chemical carcinogens cause cancer by activating latent viruses in human cells.

† The relation of carcinogens to cancer is pragmatic and has been established by observation of human and animal populations, and not by prior understanding of the biological mechanisms involved. To be sure, a great deal is known about the biochemical, immunological, and other effects of many carcinogens at the cellular level. It now seems that the carcinogenic action of certain chemicals is due to their direct interaction with

such as arsenic, asbestos, aflatoxins, and ionizing radiation, occur naturally, there is increasing recognition of the dangers of synthetic petrochemical carcinogens, such as vinyl chloride and bischloromethylether, which have been introduced into the workplace and environment in growing numbers over the last few decades.

2. The more of a carcinogen present in the human environment, hence the greater the exposure to it, the greater is the chance of developing cancer from it.

3. Although environmental carcinogens are the predominant causes of human cancer, the incidence of cancer in any population of animals or humans exposed to a carcinogen may be influenced by a variety of factors. The development of cancer is of course profoundly influenced by genetic, endocrine, immunological, viral, biochemical and possibly even psychological factors. Additionally, there are a wide range of other external factors which can increase individual sensitivity to a given carcinogen or carcinogens. Among these are excesses or deficiencies in certain dietary components, exposure to other carcinogens which enhance the effects of a particular carcinogen, and exposure to *promoting* (or *co-carcinogenic*) agents which, while not carcinogenic in themselves, may enhance the effect of an already present carcinogen.‡ These factors do not themselves cause cancer, but they can and do affect when a certain carcinogen will trigger cancer in an individual and how rapidly or slowly the course of the clinical symptoms and the disease will progress.

4. There is no known method for measuring or predicting a "safe" level of exposure to any carcinogen below which cancer will not result in any individual or population group. That is, there is no basis for the threshold hypothesis which claims that exposure

cellular genes. Large research programs and institutions have been built upon studies yielding such information. However, the promise of improved treatment and prevention of cancer based upon this knowledge of the mechanism of carcinogenesis has not yet been fulfilled.

‡ For example, alcohol, which does not itself appear to cause cancer, other than possibly in the liver, increases the risk of cancer of the mouth, larynx, and esophagus, particularly in tobacco smokers. The "fertile ground" concept expresses the possible influence of such factors on the response of the host to any specific carcinogen.

to relatively low levels of carcinogens is safe and therefore justifiable.

This book has been shaped by the author's longstanding scientific involvement in toxicology and carcinogenesis, including several of the case studies discussed in this book. (It does not deal with nuclear radioactivity, a potent source of carcinogens, which would require a book in itself. Certainly, issues raised in this book apply directly to the dangers of radiation, but the solutions to the problems posed by nuclear materials are different than those that apply to chemicals.) *The Politics of Cancer* is also based on the author's support of attempts to control human exposure to carcinogenic and other toxic chemicals, including many of those discussed in the following pages. In these efforts, he has worked with Congressional committees and regulatory agencies, and also with public interest groups and organized labor.

Chapter One

The Impact of Cancer

A Bittersweet Example

On March 9, 1977, an agency of the federal government, the U. S. Food and Drug Administration (FDA), proposed a ban on the use of saccharin, an artificial sweetener in foods. The public responded loudly. In outrage, citizens demanded that the government withdraw the proposal. Congress and the agency were barraged with thousands of letters, cables, and phone calls. The diet-soda generation had risen in arms.

Hearings were held. The news media were flooded with reports. The soft-drink industry paid for full-page advertisements in leading national newspapers to protest the FDA decision. Industry lobbies, responding to and organizing public opinion, gathered in strength.

Much of the controversy surrounding the saccharin ban arose from the public's sudden awareness and astonishment that this regulatory decision was based solely on the results of animal feeding tests. Further, the public was surprised that these tests were

carried out using what seemed to be excessively high quantities of saccharin. In the case of the most recent study, rats had been fed concentrations of saccharin equivalent to a daily dose of 800 cans of diet soda. Predictably, comedians and editorial cartoonists had a field day. Johnny Carson joked that Canadian researchers who fed rats large quantities of saccharin in their coffee went broke paying for the coffee. The nation simultaneously laughed and stormed over the FDA decision.

Some people, though, weren't laughing. Public health activists were concerned that the standard scientific practices which had been used in the study of saccharin, in particular the use of rodents to test for cancer, were under attack. In turn, they were concerned that public misconception about the nature of this scientific research might cause legislative backlash and weaken the government's power to limit exposure to other chemicals suspected of causing cancer. This was not an idle concern. The scientific community lined up on opposite sides and issued conflicting statements about the saccharin question with the same vigor as the public. Statisticians, toxicologists, cancer researchers, environmental scientists, physicians, and chemists all joined in the fray.

Two quotations illustrate how far apart apparently informed scientific opinions could be. In March, 1977, Guy Newell, Jr., then acting director and now deputy director of the National Cancer Institute (NCI), testified: "Based on human data, we do not believe saccharin is a potent carcinogen for humans, if it is one at all."¹ David Rall, director of the National Institute of Environmental Health Sciences, a sister institute of the NCI, clearly disagreed with Newell:

It may be that drinking just a couple of bottles [of a diet cola] a day may be risky for some people. FDA certainly should get saccharin out of diet pop. . . . When one looks at the data that have been accumulated from animal experiments over the years, there is plenty of reason to doubt that saccharin is safe. . . . In practically all of the studies that have been done including those in which animals were fed saccharin at much lower doses than in the Canadian study, you find tumors in more of the saccharin-fed animals than in the controls.

Such diversity of opinion among scientists fed the public's concern and confusion. After all, how could the lay press and the nation be expected to make a decision on an issue about which the nation's leading scientists couldn't agree? What's more, why couldn't they agree? Isn't science by nature exact?*

The fact is, much cancer research at its present stage of development must focus on statistical trends and tendencies in animal and human populations to link, in a causal chain, a particular agent or agents with a particular type of cancer. As was so clearly seen with saccharin, the ultimate judgment whether a substance causes cancer in humans is not always easy. The public has found, and scientists have had to admit, that there are many subjective and judgmental decisions being made about cancer—its causes, prevention, and control. Many of these judgments, particularly when regulation comes under discussion, have little to do with pure science. The economic impact of banning a substance or requiring its strict control, the technological feasibility of substituting new processes, the desirability of low-calorie foods in the nation's diet—all these topics are implicit in the saccharin issue. In short, the science of the saccharin decision is clearly mixed up with non-scientific considerations. Even the very basis of the research into saccharin's carcinogenicity is mixed up with economics and politics.

It is vital that the public learn where the science of cancer ends and social policy considerations begin. Further, it is important to realize that the basis of many so-called "scientific" decisions are in fact economic considerations, and not science. When regulatory judgments are made and laws are passed (or not passed) which touch on our lives and welfare, we must understand the real basis of the decision-making process.

Cancer is a problem which touches each of us in some way. We and our families are daily exposed to agents that cause cancer (called carcinogens), often unknowingly, while we breathe, eat, drink, work, and sleep. Moreover, we usually have no knowledge of what we are being exposed to. In order for us to respond to the

* The popular notion that science is strictly a logical process has largely been abandoned by philosophers of science, yet the idea still retains an iron grip on the public mind.

cancer threat, we must all be equipped with the basic information needed to demand preventive policies and actions. If action is to be effective, it must be based on information and directed within the realistic limits of the political system.

The Impact of Cancer

The Human Costs

Cancer is now a killing and disabling disease of epidemic proportions.[†] More than 53 million people in the United States (over a quarter of the population) will develop some form of cancer, from which approximately 20 percent of the U.S. population will die.² It is estimated that 765,000 new cancer cases will be diagnosed in 1979,[‡] and there will be 395,000 cancer deaths. Cancer deaths this year alone were about five times higher than the total U.S. military deaths in all the Vietnam and Korean war years combined.

Cancer strikes not only the elderly, but also other age groups, including infants. Among males, cancer is the second leading cause of death for all age groups except 15–34 years, where it is exceeded by violent deaths, accidents, homicide, and suicide (Table 1.1). Among females, cancer is the leading cause of death

[†] The impact of cancer is often expressed in terms of mortality or of incidence rates. (Cancer incidence data comes from the NCI; mortality data from the National Center for Health Statistics.) The mortality rate is the number of people in a particular population who die of cancer in a given time period, usually specified as a number per 100,000 population. The incidence rate is the number of new cases per year in the population, again usually per 100,000 population. Incidence rates are a more meaningful measure of the impact of cancer than are mortality, which also reflect curability. The longer the survival or the greater the cure rate for a given cancer, the more the incidence rate will exceed the mortality rate. Skin cancer, for example, has the highest incidence rate of all cancers, but because the chances of catching and curing the disease at an early stage are good, its mortality rate is small. Lung cancer, on the other hand, occurs less often than skin cancer, but once detected its prognosis is poor; hence its mortality rate approaches its incidence rate.

[‡] This figure excludes about 300,000 new cases of non-melanoma skin cancer and carcinoma-in-situ.

for ages 35–54 years and the second leading cause for all other ages up to 75.

Black males, as a group, experience the highest incidence of cancer in the United States, while black females experience the lowest; whites are intermediate between these two, with males higher than females.³ Strong racial variations exist for cancer at almost every body site. For instance, blacks have three to four times as much cancer of the esophagus as whites, twice as much cancer of the cervix, and prostate, and higher rates of cancer of the stomach, pancreas, and lung.⁴

The most common sites of fatal cancer are the lung and large bowel in men, and the breast and large bowel in women (See Tables 1.2 and 1.3 and Figure 1.1). Virtually every other organ in the body is also a potential site for cancer's attack. Leukaemia is the leading cause of fatal cancer in children.

A high and unmeasurable cost is the fear of contracting cancer oneself. Such fears are particularly well founded in individuals or groups at "high risk" of developing cancer from past exposures to carcinogens: hundreds of thousands of workers currently or previously exposed to occupational carcinogens; women treated with estrogens for "menopausal symptoms"; and pre-menopausal women who have received repeated breast x-rays (mammography).

The Financial Costs

Obviously, cancer also places an enormous economic and social burden on the cancer victim, on the victim's family, and on society. It is a disease which can begin unobtrusively and linger on for years. Specialized treatment is often necessary. The total direct cost of treatment for an individual case continues to increase, with current estimates averaging \$20,000 and ranging between \$5,000 and \$30,000.⁵ Indirect costs to the family are often much greater still, including loss of earnings from premature disability and death and the depletion of family financial resources. Dollar costs aside, the agony of watching a loved one die is an incalculable emotional burden.

Total national costs from cancer, both direct and indirect, were

Table 1.1 *Top Three Causes of Death in 1971*

Age in Years	Sex	Most Frequent Causes of Death						Percent of All Deaths*
		First	Percent of All Deaths*	Second	Percent of All Deaths*	Third	Congenital malformation	
1-14	M	Accidents	49	Cancer	12	Congenital malformation	7	7
	F	Accidents	38	Cancer	12	Congenital malformation	8	
15-34	M	Accidents	48	Homicide	13	Suicide	9	8
	F	Accidents	30	Cancer	13	Suicide	8	
35-54	M	Heart disease	34	Cancer	18	Accidents	11	7
	F	Cancer	33	Heart disease	18	Stroke	7	
55-74	M	Heart disease	43	Cancer	22	Stroke	8	11
	F	Heart disease	38	Cancer	26	Stroke	11	
75+	M	Heart disease	46	Cancer	14	Stroke	14	11
	F	Heart disease	50	Stroke	18	Cancer	11	

Source: *Vital Statistics of the United States, 1971*. Vol. II, Mortality, Pt. A, U.S. DHEW, Public Health Service, 1975.

* Percent of all deaths for the given age group and sex.

Table 1.2 U. S. Mortality for the Three Leading Cancer Sites in Major Age Groups by Sex in 1975

Rank	Under 15		15-34		35-54		55-74		75+	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
1	Leukaemia	Leukaemia	Leukaemia	Breast	Lung	Breast	Lung	Breast	Lung	Colon and rectum
2	Brain and nervous system	Brain and nervous system	Brain and nervous system	Leukaemia	Colon and rectum	Lung	Colon and rectum	Colon and rectum	Prostate	Breast
3	Lympho- and reticulo-sarcoma	Bone	Testis	Brain and nervous system	Pancreas	Colon and rectum	Prostate	Lung	Colon and rectum	Lung

Source: American Cancer Society, "1978 Cancer Facts and Figures," New York, 1977.

Table 1.3 *Estimates of New Cancer Cases and Cancer Deaths in 1979*

Site	No. of Cases*	Deaths*
Lung	112,000	98,000
Colon-rectum	112,000	52,000
Breast	107,000	35,000
Uterus	53,000†	11,000
Mouth	24,000	9,000
Skin	14,000‡	6,000
Leukaemia	22,000	15,000

Source: American Cancer Society, "1979 Cancer Facts and Figures," New York, 1978.

* Figures rounded to the nearest 1,000.

† If carcinoma in situ is included, cases total over 98,000.

‡ Estimated new cases of non-melanoma over 300,000.

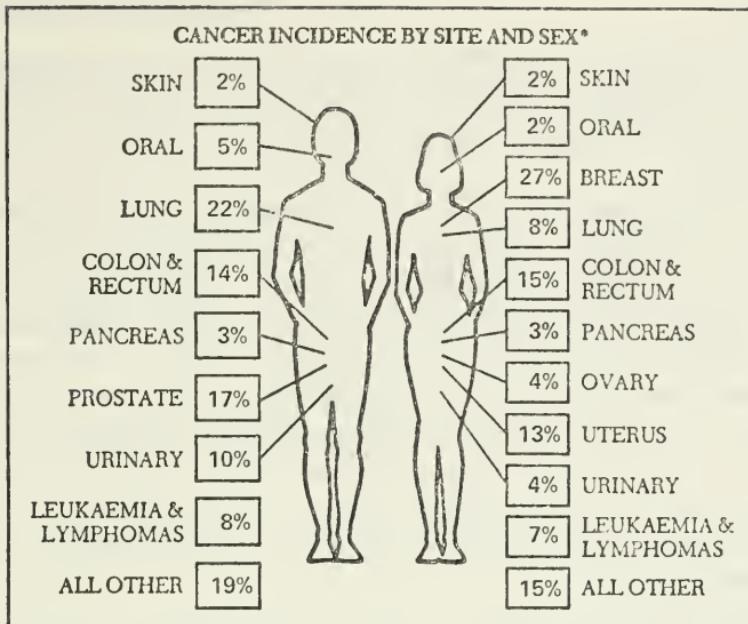
Incidence estimates are based on rates from NCI SEER Programs, 1973-76.

estimated by HEW in 1971 to be about \$15 billion annually. Projections for 1978 are in the region of \$30 billion.*⁶

The Static Cure Rate of Cancer

Many cancers are lethal, even when diagnosed early and treated with the best modern techniques. Our ability to treat cancer effectively has not markedly increased on an overall basis over the last four or so decades. Even the improvements in cancer cure rates which were achieved from the mid-1930s to the mid-1950s, from an approximate overall 20 percent to a 33 percent five-year survival rate, seem to have been due not so much to the

* These figures underestimate the true costs, which are still largely unrecognized. For example, a recent National Occupational Hazards Survey by the National Institute for Occupational Safety and Health estimated that the costs of surveillance of workers exposed to just those few carcinogens currently regulated by the Department of Labor are as high as \$8.5 billion. (The results of this survey are summarized in an NIOSH document, "The Right to Know," July, 1977.)



*Excluding non-melanoma skin cancer and carcinoma in situ of uterine cervix.

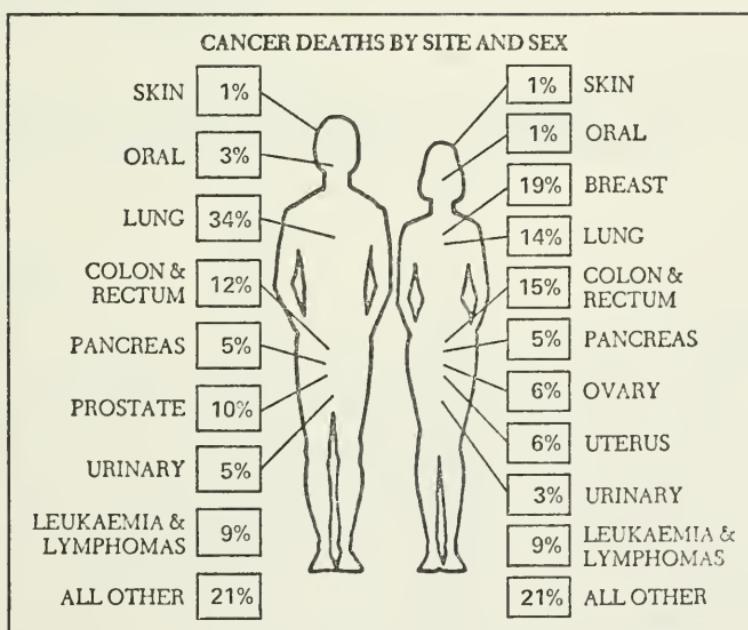


Figure 1.1 Estimates of Cancer Incidence and Deaths by Site and Sex in 1979

Source: American Cancer Society, "1979 Cancer Facts and Figures," New York, 1978.

early detection or specialized treatment of cancer with drugs or radiation therapy as largely to advances in general surgical and postoperative procedures, particularly blood transfusion and antibiotics.

Modern figures on cancer survival rates are not encouraging, in spite of common claims to the contrary. When the percentage of people who have survived for five years after cancer diagnosis and treatment in the period 1970–73 are compared to similar figures for 1960–63, it can be seen (Table 1.4) that with the exception of cancer of the prostate, and some relatively uncommon cancers such as Hodgkin's disease, acute lymphocytic leukaemia in children, (and also choriocarcinoma and Wilm's tumor), where in some instances prolonged regressions, if not cures have been achieved, no substantial overall progress has been made in treating cancer.⁷

Table 1.4 Five-Year Survival Rates for Cancer* (Whites)

Type of Cancer	Sex	5-Year Survival Rates %	
		1950–1959	1965–1969
Lung	M	7	8
	F	11	12
Breast	F	60	64
Cervix	F	59	56
Uterus (Body)	F	71	74
Prostate	M	47	56
Colon	M	42	43
	F	46	46
Stomach	M	12	12
	F	13	14
Hodgkin's disease	M	31	52
	F	38	56
Childhood leukaemia*	M	1	4
	F	2	8

Source: M. H. Myers, NCI, May 1979.

* These data are composite of results from three participants in the SEER program: Connecticut Tumor Registry; Registry of the University of Iowa; and Registry of the Charity Hospital of New Orleans. Results reflect rates with a standard error of less than 5 percent.

Particularly for the major cancer killers, such as lung, breast, and colon, the odds of a cure have not improved much over the last two decades. The prognosis for lung cancer, the most common fatal type among men, remains poor; only about one of ten victims survives for five years after diagnosis. Victims of Hodgkin's disease now have about a 60 percent five-year survival rate, but Hodgkin's disease represents only about 1 percent of all cancers. Table 1.4 reflects the best available data on historical trends in cancer patient survival from the NCI Cancer Surveillance Epidemiology and End Results (SEER) program.⁸ (Results are much less encouraging than those claimed by the American Cancer Society on the basis of the same NCI Data.) This is the case despite the vast sums of money spent over the last 30 years, despite the high priorities for cancer research set by Congress, despite devotion of an entire federal agency (the National Cancer Institute) to the cancer problem, and in the face of continuing misleading and optimistic reassurances by the American Cancer Society.

The Increasing Incidence of Cancer

The Facts

Cancer is the plague of the twentieth century. In 1900, pneumonia and influenza headed the list of the ten leading causes of death in the United States, followed by tuberculosis, infectious gastrointestinal diseases, and heart disease. Cancer, number eight, caused less than 4 percent of all deaths (Table 1.5). By 1976, cancer was the second leading cause of death after heart disease, accounting for about 20 percent of all deaths. Cancer is now the only major killing disease whose incidence is on the increase.†

† The death rate from cardiovascular disease is now on the progressive decline, having dropped 20 percent from 1968 to 1975, when the annual toll (994,513) fell below one million for the first time in more than a decade. The death rate from cirrhosis of the liver and crimes of violence, including suicide, are also on the increase, but these are minor killing diseases compared with cancer.

Table 1.5 *The Ten Leading Causes of Death in the U.S. in 1900 and in 1976*

Rank	Cause of Death	1900	
		Crude Death Rate per 100,000 Population	Percent of Total Deaths
<i>All causes</i>		1,719.1	100.0
1	Influenza and pneumonia	202.2	11.8
2	Tuberculosis	194.4	11.3
3	Gastroenteritis	142.7	8.3
4	Diseases of heart	137.4	8.0
5	Cerebral hemorrhage	106.9	6.2
6	Chronic nephritis	81.0	4.7
7	Accidents	72.3	4.2
8	Cancer	64.0	3.7
9	Certain diseases of infancy	62.6	3.6
10	Diphtheria	40.3	2.3

Source: "Facts of Life and Death," National Center for Health Statistics, Public Health Service Publication no. 600, 1970, Table 12.

To some extent, this increase in cancer mortality reflects the increased longevity which has occurred in the U.S. population during this century. Living longer increases the chances of developing cancer. However, there is also a greater cancer risk in each specific age group.⁹ Thus a fifty-year-old man today is more likely to die of cancer than was a fifty-year-old man in 1950. It has been recently calculated, by Marvin Schneiderman, Assistant Director for Field Studies and Statistics of the NCI, that between 9.5 percent and 27 percent of the increase in the death rate from cancer over the past few decades is due to the increased cancer risk of specific age groups. The increased cancer death rate, therefore holds true despite the factor of age.[†] Standardized cancer death

† This conclusion is based on the calculation of death rates for a standard population with a fixed percentage of people in each age category. Statisticians can then adjust the data to reflect a hypothetical constant age distribution and thus compensate for differences in aging.

1976

Rank	Cause of Death	Crude Death Rate per 100,000 Population	Percent of Total Deaths
	<i>All causes</i>	889.5	100.0
1	Diseases of heart	337.1	37.9
2	Cancer	175.8	19.8
3	Stroke	87.9	9.9
4	Accidents	46.9	5.3
5	Influenza and pneumonia	28.7	3.2
6	Diabetes mellitus	16.1	1.8
7	Cirrhosis of liver	14.7	1.6
8	Arteriosclerosis	13.9	1.5
9	Suicide	12.5	1.4
10	Diseases of infancy	11.6	1.3

Source: American Cancer Society, "1979 Cancer Facts and Figures," New York, 1978.

rate data, adjusted for age and based on the total U.S. population, also show an overall and progressive increase of about 11 percent over the last four decades.

Table 1.6 shows how the standardized cancer incidence rates (the number of newly detected cases per 100,000 population each year) have changed over the thirty-two-year period ending in 1969. These data were collected by the NCI during its periodic National Cancer Surveys and are adjusted to reflect changes in regions surveyed and, especially, changing age structures of the populations, i.e., to discount the effects of aging of the population. These are the most accurate nationwide data available on cancer incidence, and they reflect the general trend observed more recently in regional and local tumor registries, such as those of the states of Connecticut and California. As Table 1.6 indicates, there have been substantial increases between 1937 and 1969 in the incidence of cancer of a wide range of organs in males and females,

Table 1.6 Changes in Age-Standardized Cancer Incidence from 1937 to 1969

Cancer Site	Group*	Percent Changes		Net Change 1937- 1969
		1937- 1947	1947- 1969	
Esophagus	WM	6	-28	Down
	WF	19	-18	Up
	BM	62	101	Up†
	BF	57	89	Up†
Stomach	WM	-23	-59	Down
	WF	-30	-67	Down
	BM	3	-48	Down
	BF	3	-56	Down
Colon	WM	17	26	Up
	WF	16	-1	Up
	BM	5	90	Up†
	BF	37	129	Up†
Rectum	WM	16	-22	Down
	WF	25	-29	Down
	BM	59	3	Up
	BF	62	-27	Up
Pancreas	WM	33	22	Up
	WF	12	21	Up
	BM	132	30	Up†
	BF	88	127	Up†
Lung	WM	115	133	Up†
	WF	63	108	Up†
	BM	202	234	Up†
	BF	71	213	Up†
Breast	WF	10	4	Up
	BF	9	25	Up
Ovary	WF	16	-10	Up
	BF	80	16	Up
Prostate	WM	17	23	Up
	BM	63	55	Up†
Bladder	WM	22	21	Up
	WF	8	-26	Down
	BM	25	118	Up†
	BF	44	-43	Up

both black and white. Of the thirty-four categories of cancer type by sex and race listed in the left-hand columns of Table 1.6, the incidence of cancer has increased in about two-thirds of them (twenty-four categories). In half of these (twelve categories) the incidence rate has increased by more than 75 percent. Similar substantial increases have occurred for malignant melanoma and thyroid cancer in white males and for lymphoma in black males and females.

These major increases in cancer incidence up to 1969 have been maintained progressively and more recently have become even more marked for certain sites.

As can be seen from Table 1.7, the increase in cancer incidence from 1970 to 1975 involves not only the lung but a wide range of organs in both sexes and racial groups and therefore cannot be largely due to smoking. In fact, the overall increase in total cancer incidence for all sites is comparable to that when cancer of the lung is excluded (see Table 1.8).

The differences between the increased incidence rates for cancer of all sites and all sites excluding the lung reflect the relative increase in the incidence of lung cancer compared to all other cancers. For white males, lung cancer and all other cancers are increasing at about the same rate, whereas in black males, lung cancer is now increasing less rapidly. For white and black females, lung cancer is increasing more rapidly than all other cancers, reflecting the increase in smoking by females.

The rate of increase in the incidence and mortality of cancer seems to be sharper in blacks, particularly males, than in whites. Esophageal and bladder cancers are on the increase in blacks, although they are declining among whites. Cancer of the breast is also increasing among blacks at a time when it has leveled off among whites. Cancers of other sites including prostate, pancreas, lung, and ovary are also on the increase in blacks.

Source: S. J. Cutler and S. S. Devesa, "Trends in Cancer Incidence and Mortality in the USA," in R. Doll and I. Voldopija, eds., *Host Environment Interactions in the Etiology of Cancer in Man*, International Agency for Research on Cancer, Lyon, France, 1973, pp. 15-34.

* WM=white male; WF=white female; BM=black male; BF=black female.

† Total increase exceeds 75 percent.

Table 1.7 Changes in Standardized Cancer Incidence (for Some Major Sites) from 1970 to 1975

Cancer Site	Annual Percent Changes in Incidence Rates, 1970-1975*			
	WM†	BM	WF	BF
Lung	1.0	0.7	8.5	11.6
Bladder	2.4	8.2	3.2	10.0
Rectum	0.3	4.5	2.3	9.9
Colon	0.8	4.9	1.0	4.9
Melanoma (skin)	6.0	36.6‡		
Cervix			-6.5	-6.1
Uterus			9.0	12.0
Breast			2.3	8.9
All sites	0.9	2.3	2.2	6.1

Source: NCI, Third National Cancer Survey, 1969-1971, and Cancer Surveillance Epidemiology and End Results (SEER) Program.

* The 1975 standardized overall cancer incidence rate (per 100,000) is 359.8 for white males; 413.2 for black males; 299.8 for white females; and 329.1 for black females.

† WM=white male; BM=black male; WF=white female; BF=black female

‡ Estimate unreliable as based on small number of cases.

Table 1.8 Changes in Cancer Incidence Rates from 1970 to 1975

Group	Average Percent Increase in Incidence Rates, 1970-1975			
	Cancers of All Sites		Cancers of All Sites except Lung	
	Annual	5-Year	Annual	5-Year
White male	0.9	4.7	0.9	4.6
Black male	2.3	11.9	2.7	14.3
White female	2.2	11.6	1.8	10.2
Black female	6.1	34.6	5.7	32.2

Source: As for Table 1.7. NCI, Third National Cancer Survey, 1969-1971; SEER Program; and statement of M. A. Schneiderman before the U. S. Department of Labor, Occupational Safety and Health Administration, OSHA Docket 090, April 4, 1978.

The actual probability, at today's death rates, of a person born today getting cancer by the age of eighty-five is 27 percent for both men and women. This is up from 19 percent for men and 22 percent for women in 1950.¹⁰

It is clear that there has been a real and absolute increase in cancer incidence and mortality during this century which cannot be explained away by increased life span or by smoking. A significant acceleration in the long-term upward trend of cancer mortality is now underway. The increase offers additional support for the conclusion by most independent experts that cancer is environmental in origin and that the recent increase in the incidence of cancer is due to industrial pollutants.

Attempts to Deny the Facts

Many industry groups have tried to argue away this increase in cancer. Their arguments were summarized in an anonymous January, 1978, report by the American Industrial Health Council, an organization recently created by the chemical industry to fight effective regulation of carcinogens in the workplace:

If we use the turn of the century as a time against which to compare today's cancer problem, there has indeed been an increase in the incidence of cancer . . . but the increase is predominantly attributable to (1) greater longevity (the incidence of cancer increases with age), and (2) pandemic cigarette smoking.¹¹

The American Industrial Health Council attempts to support its arguments with graphs that show a decrease in cancer death rates when lung cancer (which in the general population is largely due to smoking) is excluded. The council argues that cancer is on the decline, that its present incidence can largely be attributed to smoking and diet, and that industrial chemicals are responsible for no more than 5 percent of all cancers in the United States. However, it is easy to see from industry data that two sites have accounted for most of the decrease, stomach and cervix, and that this decrease has been more than matched by increases at other sites. The lower rate of cervix cancer is due in part to widespread Pap screening programs which detect and treat precancerous con-

ditions, not to the disappearance of its possible environmental causes.* The decline in stomach cancer is still unexplained. As is obvious from Tables 1.7 and 1.8, smoking is not a significant cause of the increased incidence of cancer in the past decade.

The industry position is based on oversimplification of a complex statistical problem. Cancer is probably not one disease but a spectrum of diseases with common features but different—though proximate—causes. Cancer strikes different parts of the population with different force. Any attempt to represent the effect of cancer with a single summary statistic for many cancer sites lumped together necessarily masks the real situation. As Table 1.6 shows, the incidence of many different types of cancer has risen dramatically in recent decades. There is also growing evidence incriminating the role of industrial chemicals as major causes of cancer. Further confirmation of this was provided by a September 15, 1978, blue-ribbon HEW report, "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors," prepared by ten leading experts in the NCI, the National Institute of Environmental Health Sciences, and the National Institute for Occupational Safety and Health. The report conservatively estimates (with detailed epidemiological and statistical evidence) that up to about 38 percent of total cancer mortality over the next three decades will be associated with asbestos and five other "high-exposure" carcinogens (arsenic, benzene, chromium, nickel oxides, and petroleum fractions). These estimates, however, exclude the effects of radiation and a wide range of other known occupational carcinogens. Furthermore, these estimates fail to consider the effect of occupational carcinogens on the general community (community cancer), due to their discharge or escape from industrial plants and hazardous waste disposal sites.

Environmental Causes of Cancer

An informed consensus has gradually developed that most cancer is environmental in origin and is therefore preventable. The

* The decrease in cervix cancer rates is less real than apparent, as a large portion of older women (perhaps as many as 30–50 percent in some areas of the country) have had hysterectomies.

striking increase in cancer death rates in this century cannot be accounted for by aging alone and cannot be due to genetic changes in the population, which would take generations to propagate throughout the population. Furthermore, a series of epidemiological studies have concluded that environmental factors cause from 70 percent to 90 percent of all cancers. Such estimates are derived from a comparison of cancer incidence and mortality in different countries all over the world.¹² Countries at low risk for a given type of cancer are assumed to establish the background rate for that cancer type. A higher cancer rate in other countries is then attributed to environmental factors peculiar to them. Genetic differences between countries or regions are largely discounted in view of evidence that groups which migrate from one country to another tend to develop cancers at the sites and rates prevalent in their adopted countries.¹³

Striking geographical variations in the incidence and mortality of a wide range of specific organ cancers (sometimes as much as 2,000 percent) are now well recognized, and in some instances the environmental causes for its excess rates in certain regions have been discovered.¹⁴ The high incidence of cancer of the mouth in Asia, representing some 35 percent of all Asiatic cancers (in contrast to less than 1 percent of European and North American cancers), is clearly due to the common habit of chewing betel nuts and tobacco leaves. The high incidence of liver cancers in the Bantu and in Guam is well recognized and is likely to be due to dietary contamination with aflatoxin, a potent fungal carcinogenic toxin, and to eating cycad plants containing naturally occurring (azoxylglucoside) carcinogens, respectively. The high incidence of cancer of the esophagus in Zambians drinking a homemade alcoholic brew (*kachasu*) and in residents of the Calvados area of France incriminates strong alcoholic spirits, possibly contaminated with carcinogens such as nitrosamines.

Environmental factors incriminated as causes of human cancer encompass a wide range of influences including background and man-made radiation, smoking, naturally occurring plant, fungal, bacterial, and chemical carcinogens, and industrial chemical carcinogens contaminating air, water, food, consumer products, and the workplace. While it is known that smoking is associated with up to 80,000 lung cancer deaths each year, there is no reliable

method for calculating the numbers of deaths caused by other classes of carcinogens. For instance, it has been claimed, particularly by the chemical industry, that industrial chemicals are a relatively trivial cause of cancer, accounting for only about 5 percent of all cancers in adult males.¹⁵ This figure is based on estimates of the effects of those workplace chemicals *known* to cause cancer. But in view of the very limited number of epidemiological studies that have been carried out in the workplace there is every reason to suspect that many other industrial chemicals are carcinogenic, but not yet so identified. Also, there is no way of currently determining how many workers are unknowingly exposed to industrial carcinogens, so figures based on known workplace carcinogens will seriously underestimate the carcinogenic hazards of industrial chemicals.[†] Two or more carcinogens, furthermore, can interact synergistically and thus greatly increase the carcinogenic effects over those induced by either carcinogen alone. For example, the incidence of lung cancer among asbestos workers who smoke cigarettes is many times greater than either that of non-smoking asbestos workers or of smokers among the general population.¹⁶ The additional lung cancers due to synergistic effects would not have occurred in the absence of the occupational exposure to asbestos.

The Cancer Maps

Cancers caused by industrial chemicals are not restricted to the workers immediately exposed to them. These chemicals are discharged or escape from plants handling them into the air, water,

[†] The majority of industries has not been evaluated for cancer and other chronic effects. This alone makes it impossible to estimate the number of cancers that are industrially related. Furthermore, it seems premature to assume that the effects of more recently introduced industrial chemicals can be gauged through current cancer rates. It must also be stressed that the majority of epidemiological studies so far undertaken in the workplace have been in larger industries which are likely to be less hazardous than the innumerable small plants manufacturing, handling, or processing carcinogenic chemicals under even more poorly controlled conditions.

and soil of the surrounding communities, and also to hazardous waste disposal sites of distant communities. (Workers also carry them home on contaminated clothes to their families.) Examination of overall cancer death rates on a state and county basis, using the recently published maps of the National Cancer Institute showing the geographical distribution of overall cancer mortality rates and rates for most major sites in men and women between 1950 and 1969, clearly shows excess rates for people living in industrialized areas, particularly in the vicinity of petrochemical plants.^{17‡} While some of the excess cancers in males are due to exposures within the plant, the excess female cancers are most likely due to contamination of the community air or water by carcinogens originating from the plant. In a growing number of instances, chemical monitoring has demonstrated the presence of occupational carcinogens such as asbestos, vinyl chloride, benzene, arsenic, benzidine, Kepone and nitrosamines in the air outside plants.

An additional major source of community exposure to carcinogens that is becoming belatedly recognized are hazardous waste disposal sites and the innumerable sites where hazardous wastes have been improperly dumped, such as municipal landfills, industrial dumps, and abandoned mines. Recent EPA estimates indicate that as much as 90 percent of hazardous wastes continue to be improperly discarded, in some cases in the immediate vicinity of populated areas.

More recent NCI cancer-mortality data for 1969 to 1971 generally confirms previous findings in the NCI maps of markedly higher overall cancer-mortality rates in urbanized and industrialized states than in rural and agricultural states. The most striking recent change is the marked increase in rates in many southern and southwestern states, presumably corresponding to their rapid industrialization during the previous two decades. Additionally, rates in New York have edged up, and now rank with those of New Jersey.

The extent and importance of proximity of residence to industry, and possibility of exposure to industrial chemical carcinogens,

‡ The pattern of distribution for each cancer site and sex and ethnic group tends to be distinctive.

as a substantial factor in causes of cancer in the general public is becoming increasingly recognized. Table 1.9 lists the five states with the highest overall cancer death rates for both men and women during the period 1950-69 and contrasts these with the five states with the lowest rates. As can be seen, the five highest rates, both for men and women, are all found in the northeast in some of the country's most heavily industrialized states. In contrast, the states with the lowest cancer death rates are in predominantly rural western and southern states, where there is relatively little industry. The combined cancer death rate for the five highest states is 45 percent greater than that for the five lowest among males, and 38 percent greater among females. These large differences between urban industrial and rural environments, taken in the aggregate, point strongly to an important role of industrial pollution, possibly together with pollution from non-industrial sources, such as automobiles. One would be hard pressed to explain away differences of this large magnitude on the basis of possible differences in smoking, medical care, lifestyle patterns, or other such factors. New Jersey and Wyoming, for instance, have almost identical per capita tobacco sales (New Jersey's sales are 2 percent higher), but New Jersey's female cancer death rate is 36 percent higher than that of Wyoming.*

* The chemical industry has attempted to explain away the high cancer rates in New Jersey on a variety of grounds. The most bizarre of these are contained in a pamphlet, "A Rational View of Cancer in New Jersey," by Harry B. Demopoulos, a pathologist at New York University Medical Center, which was widely circulated by the New Jersey Chamber of Commerce, although apparently never submitted for publication to a scientific journal. Demopoulos argues, with lack of any supporting evidence, that the high cancer mortality rates in New Jersey are the result of average incidence rates coupled with below-average cure rates due to the large number of foreign-trained doctors in the state. Demopoulos also asserts that most workplace exposures in New Jersey are fully controlled, that asbestos is a "weak carcinogen" (although there is overwhelming evidence that it is one of the most potent known carcinogens), that vinyl chloride is a weak carcinogen (although this produces malignant tumors in animals at the lowest level, 1 ppm, yet tested, and in exposed workers at levels below 10 ppm), that cigarette smoking is the cause of *all* lung cancer (ignoring substantial evidence that a wide range of occupational carcinogens, including asbestos, are unequivocally incriminated as causes of lung cancer), that high fat diets are the cause of *all* colon cancer (when the farthest that current hypotheses go is that such a diet may be a contributory or promoting factor in some cases).

Differences in cancer mortality rates among states and counties are even more striking when specific types of cancer rates are compared. As Table 1.10 shows, the excess rates for lung, bladder, and colon-rectal cancers are much greater for females living in New Jersey than in Wyoming or North Carolina. Similar but less marked excesses are also seen for breast cancer, a cancer not generally considered to result from exposure to industrial chemicals. When comparisons are extended to the United States as a whole, the strongest association in any county between cancer death rates and the location of petrochemical plants are found for bladder cancer.

Use of only the state-by-state data masks much of the association between industrialization and excess cancer mortality rates. All states contain some areas that are urbanized and industrialized, and other areas that are predominantly rural. The cancer maps show that, within any given state, there are much higher cancer mortality rates in industrialized than in rural counties. For example, the state of Maryland has the highest male lung cancer mortality rate in the nation, 27 percent above the U.S. average. However, the rate for Garrett County in Maryland is 35 percent below the U.S. average, ranking it in the bottom third of all U.S. counties. Similarly, the rate for the state of Montana is 18 percent below the U.S. average, while Deer Lodge County, Montana, has a rate 71 percent above the U.S. average, ranking it near the top of all U.S. counties. Standardized mortality rates for almost all cancers are higher in predominantly urban than in predominantly rural counties (Table 1.11). Even the county-by-county data may mask large differences. For example, three districts in Los Angeles County with a high concentration of petrochemical industries, and for which high levels of the carcinogen benzo[a]pyrene have been measured in the air and soil, have lung cancer rates in white males 40 percent above those in the remainder of the country.¹⁸

There are some apparent exceptions to the overall association between industrialization and excess cancer rates, which reflect a wide range of factors. For instance, there are certain urban counties in the not yet highly industrialized state of Florida that have high cancer rates comparable to those in heavily industrialized New Jersey counties. This most probably reflects migration to Florida of retired senior citizens who have lived and worked for

Table 1.9 States with the Five Highest and the Five Lowest Cancer Mortality Rates

	Five Highest States		Five Lowest States		Difference between Highest & Lowest
	State	Mortality Rate*	State	Mortality Rate	
<i>Males</i>					
New Jersey	205.01	Utah	133.13		
Washington, D.C.	203.75	New Mexico	136.30		
Rhode Island	203.17	Wyoming	138.93		
New York	199.24	Idaho	139.02		
Connecticut	195.68	North Carolina	140.11		
All five	200.36	All five	138.51		45%
<i>Females</i>					
New York	148.01	Utah	102.06		
New Jersey	147.92	North Carolina	106.97		
Rhode Island	143.37	Arkansas	108.03		
Washington, D.C.	141.73	Wyoming	109.09		
Maine	140.46	Idaho	110.15		
All five	147.37	All five	107.09		38%

Source: Based on T. J. Mason and F. W. McKay, "U.S. Cancer Mortality by County, 1950-1969," DHEW Publication (NIH) 74-615, Washington, D.C., 1973.

* Age-adjusted annual mortality rate for all cancers per 100,000 population.

Table 1.10 Comparison of Cancer Death Rates: New Jersey, Wyoming, and North Carolina, White Females*

Cancer Death Rates	State			Excess Rate for New Jersey (%)
	New Jersey	Wyoming	North Carolina	
Overall	147.9	109.1	107.0	36
Lung	7.2	4.4	4.5	64
Bladder	2.9	1.6	2.1	81
Leukaemia	5.7	4.8	5.6	19
Colon and rectum	21.7	12.4	10.9	71
Pancreas	6.3	5.1	5.2	24
Breast	30.6	21.1	19.3	45

Source: Based on T. J. Mason and F. W. McKay, "U.S. Cancer Mortality by County, 1950-1969," DHEW Publication (NIH) 74-615, Washington, D.C., 1973.

* Age-adjusted annual mortality rate per 100,000 population.

Table 1.11 Ratios of Cancer Mortality Rates in Urban Counties Compared to Rates in Rural Counties*

White Males			White Females		
Cancer	Site	Ratio	Cancer	Site	Ratio
Esophagus		3.08	Esophagus		2.12
Bladder		2.10	Lung		1.64
Lung		1.89	Breast		1.61
All malignant neoplasms		1.56	Bladder		1.58
Stomach		1.45	All malignant neoplasms		1.36

Source: R. Hoover, T. Mason, F. W. McKay, and J. F. Fraumeni, Jr., "Geographic Pattern of Cancer Mortality in the United States," in *Persons at High Risk of Cancer: An Approach to Cancer Etiology and Control*, ed. J. F. Fraumeni, Jr. (New York: Academic Press, 1975), pp. 343-60.

* Based on NCI 1950-69 data in 970 counties (of which 957 were "entirely" rural and 13 entirely urban).

most of their lives in the heavily industrialized northeast. Similarly, the high cancer rates in the non-industrialized city of San Francisco probably reflects contiguity with the three adjacent counties of Alameda, Contra Costa, and San Mateo, which all have heavy concentrations of petro-chemical industries, and steel fabricating plants.

While it is not possible to use cancer maps to determine the precise factors responsible for the striking differences in overall cancer rates and in rates for cancer of specific organs among counties all over the United States, the location of large petrochemical plants in counties with excess rates—with the strong likelihood of pollution of nearby communities—is the most plausible explanation. Calculations based on figures such as those in Tables 1.9 and 1.10 suggest that such industrial pollution may be a cause of 30 to 40 percent of cancers in the general population, but it would be unwise to interpret these figures except in a general way, as they may also reflect an incremental role of non-industrial sources of air pollution. It is clear, however, that industrial chemicals are major causes of cancer in the general population as well as the workforce.

The New Era of Petrochemical Carcinogens

The recognition that environmental agents are the major cause of cancer, and the identification of the specific causal roles that many of them play, has led to an increased concern about the carcinogenic and other toxic effects of the many new chemicals which are being produced and dispersed into the environment. A measure of this concern and evidence that the petrochemical industry itself can no longer cope with the risks of its own operations is the industry's skyrocketing insurance premiums, with renewals sometimes fifty times higher than old rates. We are living in a new era of organic chemicals, not just familiar ones, but exotic ones which have never previously existed on earth, and to which no living thing has previously had to adapt. Organic chemicals containing carbon, hydrogen, and chlorine (or other halogens) are rarely, if ever, found in nature. Organochlorines are non-degradable or poorly degradable, persist in the environment and in the body, and are fat soluble and have accumulated and concentrated in the food chain. As a class, it also contains a disproportionately high number of carcinogens (several of which will be discussed in the case studies that follow). Literally thousands of new organic chemicals are being released into the environment, and not in lots of a few pounds or gallons but by the millions and billions of pounds and gallons. The intricate biochemical defenses that living beings throughout evolution have developed to cope with their environment are now being constantly violated by foreign materials introduced into the environment in petroleum products, synthetic organic chemicals, and organic pesticides (Table 1.12).

Petroleum Products Petroleum first achieved commercial importance in 1859, but significant quantities were not produced until the development of the internal combustion engine in the late nineteenth century. The growing use of gasoline led to the devel-

opment in 1913 of large-scale hydrocarbon cracking processes, which for the first time made available large quantities of low-molecular-weight hydrocarbons, the starting material for the production of many organic compounds.¹⁹ After World War II, catalytic cracking made possible yet another dramatic increase in hydrocarbon production from petroleum sources. The age of chemical solvents had begun. The growth of refining capacity is traced in Table 1.13.

Synthetic Organic Chemicals Prior to 1900, the great bulk of all organic raw materials was derived from coal tar, and, to a lesser extent, from the distillation of wood. In 1931, the U. S. National Bureau of Standards and the American Petroleum Institute began a systematic study of petroleum hydrocarbon synthesis and uses. This culminated after World War II in a fundamental shift of organic chemical production to the petroleum industry, which, along with increased hydrocarbon production from catalytic cracking of petroleum, gave birth to a new petrochemical industry. Petrochemicals are the quintessence of the "process industry," in which a small number of primary constituents from crude oil are converted into a large number of intermediate chemicals and a still larger number of large scale end products.† A disproportionately large number of recognized carcinogens fall into just three families of widely used petrochemicals: aromatic amines, in the form of dyes and synthetic intermediates, particularly epoxy compounds and hydrazines; chlorinated olefins, as monomers and pesticides; and alkyl halides, as solvents and degreasing agents. Benzene provides a good example of the exponential growth of a petrochemical product. Its production in the United States rose from 125 million gallons in 1940 to 410 million in 1955 to 1.5 billion in 1976.

Insecticides Large-scale use of insecticides began in the 1870s, when the potato beetle was spreading rapidly eastward across the

† As Barry Commoner stresses, the petrochemical industry is the most capital-intensive of all manufacturing industries, producing only about \$.80 of value added per dollar of capital invested, as compared with about \$3.64 in the case of a typical natural competitor, the leather industry. The economy of scale in the petrochemical industry allows it to successfully invade large, well-developed markets, such as the clothing industry, which exhibit a high elasticity of demand.

United States. Inorganic pesticides, calcium arsenate and copper sulfate, for example, were used to control pests and fungi, and they dominated these agricultural markets until World War II.

Table 1.12 Rate of Increase in Production from 1945 to 1970 of Selected Groups of "New" Chemicals

Chemical	Percent Increase
Synthetic fibers	5,980
Plastics	1,960
Nitrogen fertilizers	1,050
Synthetic organic chemicals	950
Organic solvents	746

Source: Barry Commoner, *The Closing Circle*, N.Y., Knopf, 1971.

Table 1.13 Growth in U. S. Crude Refining Capacity from 1900 to 1960

Year	Capacity (millions of barrels, daily)
1900	0.50
1931	3.91
1952	7.70
1960	10.36

Source: Kirk and Othmer, eds., *Encyclopedia of Chemistry and Technology*, 15:3 (1968); and W. L. Nelson, *Petroleum Refinery Engineering*, N.Y., McGraw-Hill, 1936.

Organic pesticides, which were expensive and variable in supply, were limited to a few natural products, such as rotenone, nicotine, and pyrethrum. The inorganics, however, tended to leave toxic residues which accumulated in the soil until levels were reached which made further growing of crops unprofitable. In 1939, when DDT was developed for widespread use, synthetic organic insecticides began to gain importance. After the war, many other chlorinated organic pesticides were developed, such as chlordane, toxaphene, dieldrin, and aldrin. As will be seen in chapter 7, many of these compounds, which have been released into the environment in mammoth quantities (DDT at 2.75 million pounds per month in 1945), are highly persistent and carcinogenic.

As is apparent, the end of World War II marked a turning point

in the growth of the chemical industry. American enterprise, with its enormous productive capacity, had to create new products at an unparalleled pace in order to keep its large plants and refineries operating. It set to work aggressively developing "needs" for new types of goods and services.[‡] As a by-product of this prodigious effort, more new chemicals to be used in making these goods were created, which in turn required the creation of new markets to produce them on a large, and hence economically profitable, scale. Table 1.12 shows the rate of production of a variety of chemical substances which had not existed on the face of the earth until a few decades ago.

This productive spiral continues to accelerate, dipping occasionally only to wait for markets to stabilize, for new products to catch on, or for capital to become available. Figure 1.2 shows the trend in production for various classes of synthetic organic chemicals over the past sixty years. As can be seen, the total U.S. production of synthetic organic chemicals increased from about 1 billion pounds in 1940 to 300 billion pounds by 1976. Annual growth rates of 15 percent or more are not uncommon for the organic chemical industries, at a time when the rest of the economy is advancing by only 4 or 5 percent per year.

This pattern of growth applies not just to a handful of chemicals but to tens of thousands of them. As of November, 1977, the Chemical Abstracts Service computer registry of chemical compounds contained over four million distinct entries. What's more, the registry is growing at the rate of about 6,000 compounds per week. While most of these are exotic laboratory curiosities which will never reach the market, the Chemical Abstracts Service has submitted to the Environmental Protection Agency a list of some 33,000 chemicals in its files which it now believes to be in common use.²⁰

With the exception of special-purpose legislation and regulation relating to a relatively small number of chemical products, there were virtually no regulatory controls over industrial chemicals, the majority of which have never been tested for carcinogenesis and other toxic effects, until the advent of toxic substances legislation

[‡] These innovations supplant pre-existing markets and products, and establish a type of economic imperialism for the petrochemical industry, leaving consumers with little option but to surrender old products, most of them natural, in favor of synthetic replacements.

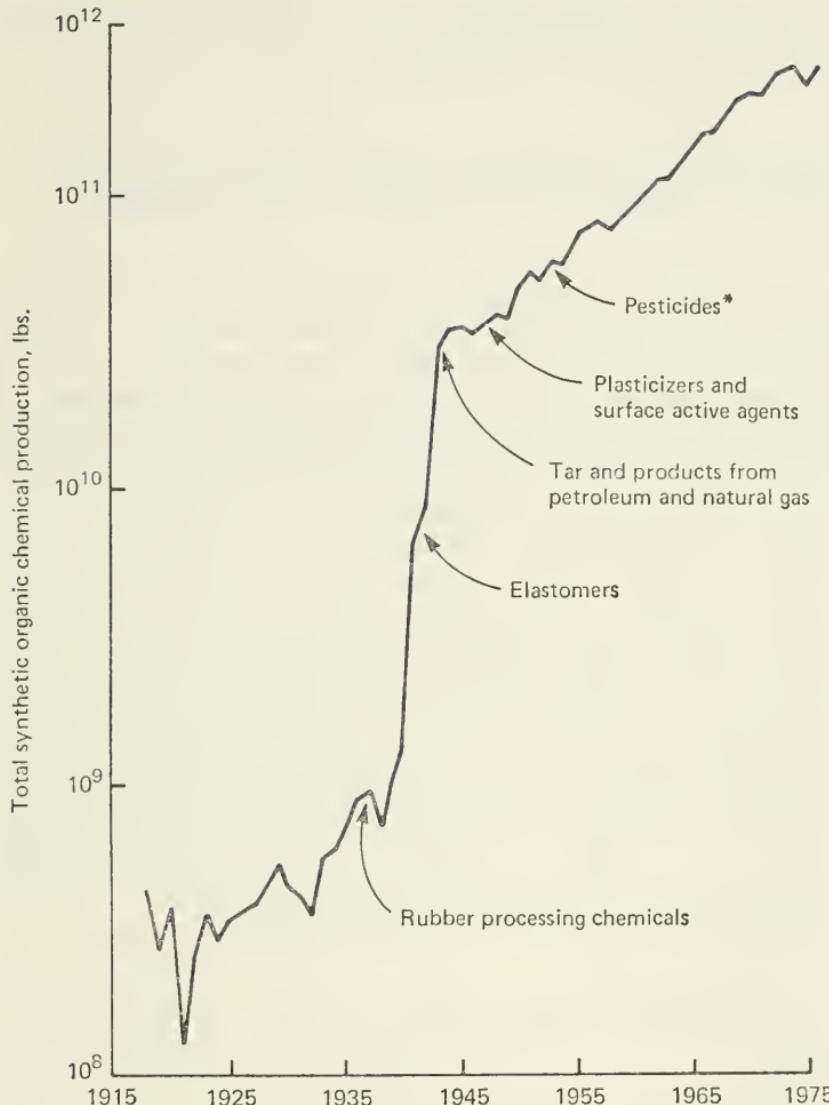


Figure 1.2 Production of Synthetic Organic Chemicals in the U.S. from 1918 to 1976

Source: U. S. International Trade Commission, 1978.

* Arrows indicate year when usage became sufficiently "significant" to be included as specific categories in Commission reports.

in 1976. Chemicals could be manufactured in limitless quantities and introduced into commerce and the environment with no effort to discover whether they were carcinogenic or otherwise toxic

to humans and other forms of life. (It remains to be seen whether the new legislation will be effective.)

The Cancer Prevention Scoreboard

The public is now undeniably aware of the cancer problem. There has been an unending barrage of media coverage of environmental and occupational cancer disasters involving the air we breathe, the water we drink, the food we eat, and the industries in which we work. Now there is fear that supersonic planes will deplete the ozone layer of the stratosphere and increase the incidence of skin cancer. Chloroform, known to cause cancer in rodents, has been found in drinking water in many major cities. Drinking water in New Orleans, derived from the Mississippi River, contains over 200 synthetic organic pollutants, including a wide range of known chemical carcinogens and many yet unidentified and untested chemicals. Automobile emissions and urban air pollutants contain a great variety of known carcinogens. Saccharin has been shown to cause cancer in animals. Some common food additives and animal feed additives are proven carcinogens. In addition to these, a still wider range of chemicals used in the workplace are known to be carcinogenic, potentially exposing millions of workers to cancer hazards.

- Asbestos workers have a high lung cancer rate relative to the general population.
- Some plastics workers develop a rare form of liver cancer, besides other more common cancers, from exposure to vinyl chloride.
- Workers with nickel and chromium have high lung cancer rates.
- Dye workers have high rates of bladder cancer.
- Workers exposed to benzene have increased rates of leukaemia.

The public has responded to this assault of information on cancer risks with generally fatalistic reactions: "Everything causes cancer, so why bother?" or "You've got to go somehow, so it

might just as well be cancer." Industry on the other hand, has been quick to minimize the scope and extent of cancer risks, to attribute them to personal habits such as smoking and diet, and to exaggerate the difficulties and costs of their control. In this denial of responsibility, industry has been supported by academic consultants who usually speak under the guise of independent scientific authority. And industry has not failed to exploit the awakening anti-cancer consciousness of consumers with appropriate responsive campaigns, such as for low-tar cigarettes.

The cancer prevention scoreboard has low entries in all categories, except confusion. While there is clearly need for improved understanding of the scientifically complex problems behind cancer, there is an even greater need for corrective political action. The decisions that are made today will have long-lasting effects on our own and on future generations.

PART I
THE SCIENCE
OF CANCER

The human animals that provide the raw material are available in immense numbers; the wild ones are an independent lot and some of them behave in peculiar enough ways to satisfy the demands of the most imaginative investigator.

Richard Doll, British epidemiologist.

Chapter Two

Cancer: The Human Experiment

Historical Background

From earliest times, it has seemed logical to search for the cause of a disease by examining the characteristics common to those contracting it. The logic of this approach includes studying groups of people who have differing chances or risks developing the disease, not just those already afflicted with it. The science that encompasses such studies is called epidemiology. Epidemiological studies, by exploiting the “natural experiments” that people perform on themselves or that society or the environment inflict on them, are as close as we can reasonably get to performing actual experiments on humans.

Epidemiology has been much more successful in the study of acute infectious diseases, such as typhoid and cholera, than in the study of chronic diseases like cancer. Most infectious diseases

spread rapidly and can be reproduced in the laboratory. Various hypotheses as to cause, effect, and prevention can thus be tested quickly, and once an infectious agent is isolated, it can be comparatively easily shown to cause the disease.

The epidemiology of cancer is more complex. In its broadest sense, cancer epidemiology is the study of the environment of the types of people who do and who do not get a particular type of cancer. Unfortunately, cancer epidemiology is a search for clues to the causes of cancer in a world where clues are both scarce and difficult to interpret.¹ It is a search for factors that differentiate cancer patients from other individuals, pursued in the hope that discovering such factors will lead to the development of preventive methods for those who have not contracted the disease. Epidemiological evidence is often the first clue that a problem exists. Occasionally, it is the only clue as to cause and prevention. The peculiar nature of cancer, especially the long natural history of the disease, in which clinical evidence of illness often occurs several decades after initial exposure to a carcinogen, makes cancer epidemiology frustrating, often controversial, and sometimes a useless exercise.

Some Perspectives and Pitfalls of Cancer Epidemiology

The fundamental problem of epidemiological research is that it is quite difficult to assemble a large enough number of cancer cases of a particular type upon which to draw conclusions about its causes. In numbers of people affected cancer is a major killer, but from a statistical point of view a particular type of cancer is a relatively rare event. For example, the overall incidence of lung cancer in the general population in 1970 was about forty cases for each 100,000 people, although its incidence is much higher in the middle-aged and elderly.² As the probability of an individual contracting lung cancer in that year was thus about one in 2,500, an extremely large number of people would have to be observed to ensure that there would be enough cases of the disease to study.

The very task of assembling a sufficient number of persons to satisfy the statistical requirements of such an investigation is often the principal obstacle to the study, demanding as it does access to large population groups and substantial financing for salaries of interviewers, statisticians, and other investigators.

Identifying a sufficient number of cancer cases, together with their medical and exposure histories, is central in the use of epidemiology as a tool for investigating the cause of the cancer. To assist in this undertaking, a number of localities and states have set up cancer registries for the purpose of identifying all new cases of cancer. The nation's oldest such registry is that of the state of Connecticut, which maintains computerized files for use by epidemiologists and statisticians.³

Even in the best of circumstances, however, registries cannot predict what types of exposure to ask patients about, so that the "right" type of questions may simply not be asked. Cancer cells are not, after all, labeled for "carcinogen of origin." The clinician discovering cancer at a specific site may not have any useful idea what its cause could have been and what past exposures of the patient should be investigated.

Even when a particular chemical product or process has been shown to be carcinogenic in animals, hence suspect in humans, recognized human cancer cases due to the chemical may, for a long time, be too few to show up above background levels in the general population induced by other carcinogens.* Additional difficulties may be posed by latency, which for some carcinogens is decades (twenty to forty years for smoking and up to fifty years for asbestos).

Quite apart from these intrinsic difficulties in performing adequate epidemiological studies, there are also methodological problems which plague even the best designed ones. The most serious is the inability to obtain adequate data on exposure to carcinogens at times which preceded the finding of cancer by many years. It is nearly impossible to reconstruct industrial exposures to chemicals twenty years or more in the past if specific measurements were not recorded, because in that period the original processes often have

* For this and other reasons, epidemiology is weak at identifying relatively low levels of cancer risk. The lowest clearly identified excess cancer risk, after some twenty years of intensive study, is the 30 percent excess risk for childhood leukaemia following irradiation in later pregnancy.

changed radically or disappeared altogether. Even for chemicals voluntarily taken by people, such as saccharin, reliable information on how much was ingested or even whether it was taken at all, is difficult to obtain from interviews. This is the case because persons who have a disease which they suspect to be related to a particular chemical may selectively "recall" its use even sometimes when it never took place, and ignore other relevant chemical exposures.

Another major difficulty in most epidemiological studies is sorting out the relevant from the irrelevant and controlling for unknown and unsuspected risk factors. Claims of relationships between certain influences or exposures and disease may be due, not to those particular influences, but to other factors such as diet, location of residence, or lifestyle which the investigator may have overlooked or discounted.

Basic Epidemiological Techniques

The basic epidemiological techniques used in investigating environmental and occupational causes of cancer can be illustrated by describing their use in the tobacco-cancer problem.

The Informed "Hunch"

The informed hunch is often an important first step in developing a hypothesis about which type of exposure might be linked with a given cancer. It was responsible for early suspicions linking tobacco and lung cancer.

Lung cancer has not always been a major killer. In 1912 a British doctor published a book on the then obscure disease, wondering: "Is it worthwhile to write a monograph on primary malignant tumors of the lung?"⁴

In 1939, however, a German researcher observed that many lung cancer patients he was treating were heavy cigarette

smokers.⁵ About the same time, a similar observation was made in the United States by the now renowned heart surgeon, Michael DeBakey. These observations stimulated speculation, but without some way of comparing the lung cancer patients to healthy people, there was no way to exclude a host of other factors besides smoking as causes for the cancer. The main problem was that the number of lung cancer cases then seen by any one doctor was relatively small. The epidemic of what is now the most common cause of cancer deaths had only just begun. Only when the number of cases began climbing in the decades after World War II, could scientists begin to check out this hunch further.

Many, if not most, leads for epidemiological studies were developed in just this way, through astute observations by clinicians. The association, for example, between maternal medication with diethylstilbestrol and vaginal cancer in their daughters was developed after a doctor noted a number of similar cases of cancer and began a thorough investigation of use of the drug by obstetricians. This testifies to the importance of close links and communications between clinicians and epidemiologists in the cancer research effort.

Follow-up Studies

By the late 1950s a number of classical epidemiological studies on lung cancer and other disease complexes thought to be due to cigarette smoking were in progress in different countries. Some of these were follow-up or prospective cohort studies, which is to say a large number of healthy people are followed for several years in order to determine which of them contract and die from a specific disease.⁶ A follow-up study begun in 1959 by E. Cuyler Hammond of the American Cancer Society is a good example.⁷ In a massive effort by volunteers in twenty-five states involving about \$1 million of public funds, about one million men and women were questioned about their age and disease and smoking histories. The American Cancer Society managed to keep track of over 90 percent of the initial subjects for a dozen years. Updated questionnaires were supplied every four years or so, or, if a subject

died, a death certificate showing the cause of death. The number of deaths observed among people in a specific category was divided by the number expected for people in the category, yielding a value known as the Standard Mortality Ratio (SMR).†

The American Cancer Society found that the SMR from lung cancer increased dramatically with the number of cigarettes smoked and with the inhalation of smoke. It also found that the SMR for ex-smokers decreased as the time since quitting lengthened. More recent analysis also shows some lessening of the lung cancer death rate among smokers who switched from high to low-tar cigarettes.⁸

A single epidemiological study cannot alone validate or invalidate an assumed link between exposure and disease. However, over the past twenty-five years a parade of other follow-up studies conducted in the United States, England, Japan, and elsewhere, has extended and confirmed the causal association between smoking and lung cancer.‡

Case-Control Studies

The logistic problems of follow-up studies, which require enrollment of great numbers of healthy subjects in order to observe a statistically meaningful number of cases of disease, prompted epidemiologists to develop the case-control approach. A case-con-

† The society regards the tapes containing the raw data of this study as proprietary, and has declined to make them available to outside scientists.

‡ However, these studies have generally failed to inquire into occupational histories and have thus neglected a probable role of exposure to occupational carcinogens. Of further interest in this connection is the fact that deaths from pleural mesotheliomas due to asbestos are listed as lung cancers in the International List of Causes of Disease (which is used as the basis for reporting cancer mortality data). Thus, malignant lung disease due to occupational exposure or by such exposure interacting with the effects of tobacco smoke are misrepresented as being exclusively lung cancer deaths exclusively due to tobacco. It is thus likely that the role of occupational exposure to industrial chemicals as a cause of lung cancer has not been adequately recognized. (For a more extreme expression of this position, see T. D. Sterling, "Does Smoking Kill Workers or Working Kill Smokers, or The Medical Relationship Between Smoking, Occupation, and Respiratory Disease," *International Journal of Health Services*, 8 (1978), pp. 437-52.)

trol (or retrospective) study depends on locating patients with a particular disease (the cases) and another group of people, either healthy or with some unrelated disease (the controls) and asking them the same set of questions. This approach is particularly appropriate for use in hospitals, where most people with serious disease eventually come. (In studies of lung cancer, the questions asked obviously include detailed smoking histories.) A figure called the relative risk is estimated from the replies. Relative risk is to a case-control study what an SMR is to a follow-up study, namely, a measure of the strength of association between exposure and disease. Both of these are measures of risk relative to the control group. But follow-up studies have an advantage over case-control studies in that they can be used to calculate absolute disease rates as well as relative ones.* Thus, one can determine whether the incidence of the disease being studied is unusually large or small in the population being studied. However, this advantage is far outweighed by the enormous logistical difficulties and scale of follow-up studies.

The case-control studies of lung cancer and smoking performed during the last twenty-five years have confirmed the conclusions of the follow-up studies. However, case-control studies have also shown that not all types of lung cancer are affected by smoking to the same extent. A type of lung cancer called adenocarcinoma is much less closely related to smoking than the more usual types, squamous, or oat cell, cancers.⁹ Some of the studies also showed that the risk of lung cancer is greater among urban than rural dwellers, thereby supporting the case for an additional role of air pollution in lung cancer. A final important finding was that the risk of lung cancer is lower in smokers of filtered than non-filtered cigarettes.¹⁰

By 1964, based on the remarkable agreement of seven follow-up and twenty-nine case-control studies, U. S. Surgeon General Luther Terry, in his famous report on smoking and health, could bluntly state: "Cigarette smoking is causally related to lung cancer in men."¹¹

* Additionally, risk estimates in case-control studies are strictly valid only when the disease under study is statistically a rare one. Most cancers satisfy this mathematical restriction. J. Cornfield and W. Haenszel, "Some Aspects of Retrospective Studies," *J. Chronic Diseases*, 11 (1960), pp. 523-34.

Historical Follow-up Studies†

Many of the currently accepted occupational causes of cancer have been verified in human populations through a technique which exploits the follow-up approach, but in which the initial population of exposed workers, known as the cohort, is identified many years after the initial exposure. This is called a historical-follow-up or a retrospective-cohort study. This method has been successfully used by NIOSH and other investigators to identify such carcinogens as asbestos, vinyl chloride, and benzene.¹²

In brief, the cohort of workers is defined to be all those engaged in a particular process at some time in the past. In the follow-up, a variety of documents are searched, such as employment, social security, or motor vehicle records, to ascertain the vital status of each cohort member at some later time. Causes of all deaths are obtained from death certificates. Then, based upon actuarial tables the SMR is calculated. The greater the SMR, the stronger is the inference of carcinogenicity.

Epidemiology: Conduct and Misconduct

Epidemiological investigation of a chronic disease, such as cancer, is difficult under the best of circumstances. But because of the major economic impact of a finding that an industrial product or process can cause cancer, industries have often compounded these difficulties by failing to undertake necessary studies or encouraging interpretation or even manipulation of the data to bias the studies in their favor.

Until recently, most industries have been opposed to any epidemiological study of their work force. They have either refused to cooperate in proposed studies, and in many cases have failed to accumulate meaningful records, or even destroyed these

† Also known as "cohort studies."

records. One reason for this has been their realization that such records could possibly damage the company in prospective Workman's Compensation claims or negligence suits.

Since passage of the 1970 Occupational Safety and Health Act, some companies have agreed to cooperate with government studies or else have hired their own staff or outside consultants to do the job. This apparent willingness to investigate the cancer risk to workers often masks a biased operation in which the preordained outcome is a clean bill of health. Indeed, a collection of statistical devices with built-in biases for handling data have become standard strategy to avoid regulation of carcinogens and other toxic chemicals. The tobacco industry alone has remained stalwart in its assertion that epidemiology, inasmuch as it is entirely statistical, is inappropriate for the study of cancer. This self-serving argument has been abandoned by virtually every other industry in favor of more sophisticated methods of manipulating numbers.

Many studies begin and end with the observation that workers in a given plant have a lower cancer or disease rate than the general population. This may in fact be correct, but it does not prove that workers in that industry are free from cancer or other illness due to occupational exposure, for it is well known that workers in any industry will have a death rate significantly lower than that of people of similar age drawn from the general population.¹³ The general population includes disabled and chronically ill individuals, while the industrial population is at least healthy enough to perform work.‡ Thus, even when a working population develops cancer from an industrial carcinogen, the overall increase in worker death rate may not be great enough to exceed the death rate of a similar age group in the community. The only meaningful comparison group for any given work force under investigation is a control group of workers from other industries where there is no exposure to the suspected carcinogens.*

The most common error in conducting prospective studies is failure to obtain an adequate follow-up. If a large number of persons have been lost to follow-up, serious errors in computing cancer death rates can arise. For example, industry studies on retirees

‡ This is sometimes known as the "healthy worker effect."

* This is the major reason why so few industries have yet received any epidemiological evaluation.

often find living retirees in a far greater percentage than they find the death certificates of retirees who have died. Whether by mischance or by inadequate effort to identify deaths, this means seriously underestimating the death rate for employees of the industry. A related problem is simply attempting to do a study on too few people, known as the "too few" technique. If the cohort size is too small, then even a greatly increased risk of cancer or any other disease cannot be detected statistically.¹⁴

Another common error of cohort studies is to follow workers for too short a period of time. Since most cancers have a latent period of at least ten years (and many have twenty-year or greater latencies), it is essential to follow workers for at least this much time after their first exposure before a meaningful cancer death rate can be expected. An example of the "short follow-up" technique is the current industry claim of the rarity of leukaemia following occupational exposure to benzene. This claim is, in part, based on an average follow-up of only three years.¹⁵ Another example is the claim for the rarity of cancer in workers exposed to vinyl chloride. In this case the effects of vinyl chloride on workers with long-term exposures have been masked by including in the study many workers only recently exposed and by having a follow-up of only a few years, thereby resulting in a deceptively reduced cancer mortality rate.

Any particular epidemiological study can demonstrate various permutations and combinations of these different statistical devices, as will be illustrated in the various case studies in chapters 5, 6, and 7. For instance, using the "too few" and the "short follow-up" techniques, Shell Chemical Company has claimed that the pesticides aldrin and dieldrin are not carcinogenic, since workers engaged in their manufacture apparently did not have an increased cancer risk. Shell also used this argument as the basis for its claim that the overwhelming data on the carcinogenicity of these pesticides in rodents should be discounted in favor of the allegedly conclusive human evidence of safety.†

† In an attempt to improve the quality and reduce the bias of epidemiologic studies on the basis of which regulatory decisions are made, the Interagency Regulatory Liaison Group has developed guidelines for cohort studies, released in draft form on May 31, 1978, which recommend minimal criteria for the acceptability of such studies, including availability of supporting documentation, definition of follow-up procedures, discussion of potential bias, and disclosure of source of sponsorship and funding.

Cancer, Geography and the Environment

What do we know of other factors, besides smoking, that are causes of cancer? Are these factors environmental or genetic? Differences all over the world in the incidence of cancers of particular organs help answer these questions.

We now know that the incidence of various types of cancer exhibits great geographical variation. For example, in Scotland, the rate of lung cancer among men is the highest in the world, 78 cases per 100,000. In the United States, for white males, the rate is half that of Scotland and in Portugal only one-seventh. The death rate for stomach cancer in Japan is eight times that of U.S. whites, which is now the lowest in the world and still decreasing. The death rate from prostate cancer for U.S. blacks is the world's highest, ten times that of the Japanese.¹⁶

An almost unbelievable geographical variation exists in a broad belt of central Asia. The Ghurjev district of Khazak in the USSR has an extremely high incidence of esophageal cancer, over 500 cases per 100,000 males. In a small section of Iran near the Caspian Sea, the rate of this disease among women varies by a factor of as much as thirty over a distance of only 100 miles. This high-cancer region has been mapped and inexplicably has a very sharp edge.¹⁷ Similarly inexplicable is the fact that breast cancer also varies geographically by a factor of six, from its lowest national incidence in Japan to its highest in the Netherlands.¹⁸

Cancer of the mouth is relatively rare in the United States, representing about 3 percent of all cancers. In parts of Asia, however, it accounts for up to thirty-three percent of all cancers. In this instance, the reason for such a striking difference is known. It results from the habit among many Asians of chewing betel nuts and leaves, wads of which are wrapped around shredded tobacco and lime and held in the mouth for long periods.¹⁹

The fact that there are such geographical differences in cancer rates does not tell us whether environmental or genetic factors are

involved. However, epidemiological studies have shown that when people migrate from one area to another, their disease patterns tend to adjust to that of the country to which they migrate. A 1968 study on the offspring of Japanese migrants to the United States showed that their stomach cancer rate was reduced by two-thirds, their colon cancer rates tripled, and their rates of cancer of the pancreas and lung, and of leukaemia increased (Table 2.1). These changes in cancer patterns were all in the direction of matching the comparable cancer rates for the U.S. white population. Since this second-generation group tended only to intermarry among themselves or with new migrants from Japan their genetic characteristics as a group remained basically the same. Such studies give strong evidence for the environmental rather than genetic causation of cancer.

The National Cancer Institute has recently published an "Atlas of Cancer Mortality for U.S. Counties: 1950–1969."²⁰ This is a set of colored maps ranking U.S. counties by cancer mortality rates of white males and females, adjusted for age. A similar study for non-whites was subsequently published.²¹

Table 2.1 *Mortality Rates of Offspring of Japanese Migrants to the U.S.*

Cancer Site	Relative Cancer Mortality Rates		
	Japanese	Offspring of Migrants	U. S. Whites
Stomach	100	38	17
Colon	100	288	489
Pancreas	100	167	274
Lung	100	166	316
Leukaemia	100	146	265

Source: W. Haenszel and M. Kurihara, "Studies of Japanese Migrants. I. Mortality from Cancer and Other Diseases Among Japanese in the United States," *J. Natl. Cancer Inst.* 40 (1968), pp. 43–68.

The "Cancer Atlas" has proved a valuable resource for epidemiologists. Its value lies in its use of 3,056 U.S. counties in forty-eight states as the basic units for the study. These units are

sufficiently small to be homogeneous in factors which might influence cancer risk, yet large enough to provide statistically useful estimates of cancer rates at specific body sites. Since the U. S. Census provides basic social and economic information also broken down by counties, it is possible to correlate these with the cancer death rates, and thus to test hypotheses about the association between cancer mortality and suspected socioeconomic variables.

For example, males show a striking variation in distribution of cancer mortality rates, with highest rates of certain cancers in counties with heavy concentrations of petrochemical industries. Salem County, New Jersey, where 25 percent of the men are employed by the chemical industry, has the highest mortality from bladder cancer for white males in the United States.[‡] High bladder cancer rates are also found in industrial cities like Buffalo, Toledo, and Chicago. Liver and lung cancer rates are high in the petroleum refinery and shipbuilding areas of the Texas Gulf Coast and Louisiana. Excess lung cancer rates are also correlated with locations of chemical and paper industries. Lung cancer is also high in counties where copper, lead, and zinc smelters are located. Lung cancer rates are consistently higher for both men and women in all U.S. counties in which non-ferrous metal smelters that emit arsenic are located than in non-smelter counties. Deer Lodge County, Montana, has the tenth highest lung cancer mortality rate among all U.S. counties from 1950 to 1969. It also had the world's largest smokestack located at an Anaconda copper smelter plant that emits up to 22 tons of particulates daily, much of it the known carcinogen inorganic arsenic. The fact that the corresponding cancer rates among women in some cases show less striking variations suggests the cancers in the men are substantially occupational in origin.* However, since excess cancer rates are

[‡] Interest in the high cancer rates in New Jersey has been recently highlighted by the discovery of a cluster of six cases of acute childhood leukaemia in the 21,000 population of Rutherford over the last five years. On the basis of chance alone, not more than one case should have occurred in this time.

* The present-day cancer incidence reflects exposure perhaps ten or twenty years ago, when the percentage of women in the industrial work force was much lower than at present. Thus, male-female differences in cancer incidence, except of course for sex organs, can give evidence of occupation-related cancer.

also seen in women living in heavily industrialized states and counties, it is clear that environmental factors are also critically involved (Tables 1.9 and 1.10). Further confirmation of the risks of living near chemical plants has come from a recent NCI study showing higher rates of cancer of the lung in men and women, as well as cancer of the nasal cavity, skin, testis, and other sites in men living in counties with major petroleum refineries.²²

The nature of these environmental factors involved in geographical clustering of excess cancers in heavily industrialized locations is gradually becoming clearer. Evidence is accumulating of the discharge or escape of a wide range of occupational carcinogens from inside petrochemical and smelting plants into the air and water of the surrounding community, or the dumping of carcinogen-containing wastes in hazardous waste or other undesignated disposal sites. Although only relatively few investigations of this kind have so far been made, carcinogens such as nitrosamines, vinyl chloride, kepone, tetrachloroethane, benzene, benzidine, arsenic, and asbestos, have all been found and measured in nearby communities outside particular industries or hazardous waste disposal sites. Another source of family exposure is the carcinogenic chemicals and dust brought home on workers' skin and clothes.

In tracking down specific industrial and environmental correlations with cancer, the cancer maps are valuable only up to a certain point. At best, the data can be used to obtain clues or leads as to identification of possible high risk groups, which must be further investigated by additional epidemiological methods and chemical monitoring of the industries. For example, the bladder cancer map reveals a clustering of high risk counties for both white males and females in easily delineated industrial locales. Since many different types of industry tend to be located near each other, however, identifying the specific industries responsible can be difficult. Also, other variables known or suspected to cause cancer are more prevalent in urban industrial areas. Explanations for higher cancer rates in these areas should also take other possible urban-rural differences into account.

Epidemiology versus Animal Testing

In conclusion, epidemiology is used to study the incidence of cancer in populations who have already been exposed to carcinogens. While of obvious value in helping to establish causal relationships, particularly for high-risk populations, these studies must invariably rely for their data on people who have already contracted cancer, or who do so during the course of the study. In preventive terms, it is a case of "locking the barn door after the horse has run out," at least for the population being studied.

In contrast, animal testing of new chemicals not yet introduced into commerce allows relatively simple and rapid determination of carcinogenicity, allowing the possibility of subsequent control prior to human exposure.

The major categories of twenty-five known human carcinogens, the majority of which are occupational carcinogens or industrial processes (the remainder being drugs), are listed in Appendix I. In the case of the five industrial processes, the precise chemical identity of the causative agents is unknown. As can be seen, there is very good general correspondence between the human and the experimental animal data.

The bottom line on carcinogenesis testing is this. You can drown an animal in a pool of some substance, suffocate an animal under a heap of it, or beat an animal to death with a sock full of it, but if it isn't carcinogenic, you can't give an animal cancer with it.

William Hines and Judith Randal,
Washington, D.C. Journalists.

Chapter Three

Cancer: The Animal Experiment

Whenever it is announced that a chemical has been shown to be carcinogenic in animals, there is usually an accompanying disclaimer that "the chemical has not been found harmful to humans." Every time you read this kind of statement in the press, or hear it announced on the radio or television, you should mentally insert the word "yet." You should ask yourself the question, "If the chemical *is* carcinogenic to humans, how would we know?" As we have seen, we can only know if the appropriate epidemiological study has been done and its results are conclusive beyond doubt—which is rare—or if the chemical induced an extremely rare tumor.

This chapter explains the rationale for animal experiments, the standard test methods used on animals, and how animal test results should be interpreted. It also deals with some current controversies in interpretation, particularly when major economic interests are threatened.

Some Historical Perspectives

Experiments studying causes of cancer in laboratory animals are not new, but the systematic use of animals to test whole classes of chemicals (e.g., food additives) for the purpose of deciding whether they can be safely used or not is a relatively recent development. This lies at the heart of much of the modern cancer controversy. However, there is now overwhelming agreement by most qualified scientists that if a chemical causes cancer in well-designed animal tests, then there is a strong likelihood that it will also cause cancer in exposed humans.¹ Experience continues to prove that this is, indeed, the case.

Distasteful as it may seem to some to use animals in experimental research, even in accord with standard humane guidelines for the prevention of unnecessary pain and suffering, there is no practical and reasonable alternative to their use. Modern medicine, including vaccines, antibiotics, drugs, and transplants, would not have been possible had it not been for animal studies. The same is also true for cancer research.

During the early 1900s, scientists, familiar with the classic writings more than 100 years earlier of Percival Pott on the role of soot in scrotal cancer among chimney sweeps, tried unsuccessfully to reproduce this in animals using coal tars prepared from soot.² Then, in 1916, two Japanese scientists succeeded in inducing skin tumors on rabbit ears by daily application of coal tar for a period of more than six months.³ This single experiment suddenly opened up the use of animals in cancer research.

It is important to appreciate the difficulty that early investigators experienced in inducing cancers in laboratory animals. First, the time required to produce cancer in an animal was found to be much longer than the time to produce an infection such as rabies or typhus. Such unforeseen delays alone caused many researchers to abandon their experiments. Second, the Japanese scientists were fortunate in their choice of the rabbit as a test animal, for rabbits appear to be particularly sensitive to the effects

on skin of this kind of carcinogen. It took three more years before the results of the coal tar experiments were confirmed.⁴

Another reason why work proceeded so slowly was that, in addition to the experimental difficulties in inducing cancer, scientists in the early 1920s didn't believe that cancer could even be caused by a particular chemical. The conventional wisdom of the day was rather that the tumors resulted from a generalized irritation of cells and tissues, irrespective of the identity of the agents causing the irritation.

During the 1930s, the experimental foundation of chemical carcinogenesis was firmly established by a research team led by Sir Ernest Kennaway at the Royal Cancer Hospital in London.⁵ In a short period, his team demonstrated the carcinogenicity in mice of tars extracted from pitch and oils. They showed that the cancer-causing activity was greatest in the chemical fractions with the higher boiling points.⁶ These chemicals, called polycyclic aromatic hydrocarbons, are found in cigarette smoke and air pollutants, and are the products of incomplete combustion of organic matter.

In their most dramatic experiment, the London researchers produced tumors by applying a pure synthetic chemical, dibenz[a,h]anthracene, which was also known to be one of the many components of tar.⁷ This was the first time it had ever been shown that an individual pure chemical, rather than a mixture such as coal tars, could cause cancer. Finally, one of the group, J. H. Cook, proceeded to test various chemical fractions extracted from a pitch sample originally weighing two tons, and thereby identified benzo[a]pyrene, another powerful skin carcinogen and also a major component of tobacco smoke.⁸

About the same time, epidemiological studies in the United States and elsewhere were finding a clear relationship between the high incidence of bladder cancer among workers in the dye industry and their exposure to particular chemicals, such as benzidine and 2-naphthylamine.⁹ In order to study the basic mechanisms involved here, it was logical to try to reproduce this disease in animals by exposing them to these dye chemicals. Not until 1938 was this successfully performed by the late Wilhelm C. Hueper, one of the great early pioneers of environmental and occupational carcinogenesis.¹⁰ His good fortune was to have chosen the dog as the

test subject, rather than the usual experimental animals, rodents. Dogs and humans have similar sensitivity to 2-naphthylamine, which induces bladder cancer in both, whereas rodents are relatively resistant to this carcinogen, and when cancers are induced they are found in organs other than the bladder.

From Mouse to Man

Unless we can relate the occurrence of cancer among other species of animals, however induced, to human cancers, the most elegant animal experiment will have been at best academic.

The legitimate inference that what is found to cause cancer in one species must also be assumed to cause cancer in others (known as the species-to-species extrapolation) is fundamental to cancer research. This inference rests on over half a century of intensive scientific investigation into the biology and chemistry of carcinogenesis and carcinogens in many organisms, including humans. Acceptance of the extrapolation principle is grounded in the fact that fundamental life processes in mammalian and other animals are basically the same as those in humans. Thus information on the origin of cancer drawn from observations of animal experiments can be applied, with appropriate reservations, to man. While the substance of these reservations has often been the source of intense controversy in specific instances, the basic fact that extrapolation is a reasonable undertaking is nearly universally accepted by biomedical researchers and is indeed fundamental to all experimental biology and modern medicine.

By the time a cancer has developed in a test animal, a great many events have taken place at the molecular, cellular, and organ levels. Also, a relatively long period of time, the latency period, has passed since the initiation of the cancer process. Cancer probably begins with a single identifiable event within a cell, such as the breakage of some critical genetic component of the cell by the carcinogen. While such events are probably frequent, and normally handled by cellular repair and detoxification mechanisms, in certain cases they may go unrepaired, and the cancer

process begins. The cancer cells grow in an uncontrolled fashion, invade local tissues, and often spread (*metastasize*) to distant parts of the body.¹¹

There are very striking similarities between cancer in humans and other living organisms with regard to the widest possible range of biological characteristics. Cancer is found in multicellular organisms, including insects, fish, and even plants. The probable reason for this is the essential similarity of their cellular ultrastructures, in particular their genetic structure and coding. Carcinogenic chemicals thus tend to be similarly active in many different test animals. However, there are often differences in the susceptibility of various animal species, in differing strains of any species, and in different individuals in any particular strain or sub-strain. Additionally, the target organ affected by the carcinogen may vary from species to species. Nevertheless, if a carcinogen is active in any one species, it is likely to also be active in others, including man.

The use of small mammalian animals, particularly mice and rats, has been and continues to be standard practice in routine carcinogenicity testing. Considerations of convenience apart, the key role of these rodents in carcinogenicity testing has been repeatedly endorsed by numerous expert committees and authorities, as illustrated by the following statement from the National Academy of Sciences in 1960:

The rat and mouse have been shown to be susceptible to the carcinogenic action of a large variety of compounds and, indeed, most of our knowledge of chemical carcinogenesis is based on the use of these species. The hamster and guinea pig are relatively resistant to the carcinogenic action of several compounds which produce tumors readily in the rat and mouse. On the other hand, no known carcinogens for the hamster and guinea pig are inactive in the rat and mouse.¹²

It must be realized that the activity of many known human carcinogens was first recognized in rodent tests. These include 4-aminobiphenyl, bischloromethylether, aflatoxins, vinyl chloride, mustard gas, melphalan, and diethylstilbestrol. Conversely, all chemicals known to induce cancer in man, with the possible exception of arsenic, also do so in experimental animals, generally

rodents.¹³ In any one instance where a chemical is found to be carcinogenic in a proper animal test, there is no possible way in which absolute assurances can be given that the chemical will also be carcinogenic in humans. However, the general similarity in response to carcinogens of a very wide range of species, including humans, and also the good track record of animals as predictors of human response, afford strong reasons for accepting the results of well-conducted animal experiments as surrogates for human experience.

The predictive value to humans of carcinogenicity tests in mice has been repeatedly challenged by industry.* It has been claimed by Shell Chemical Company and other segments of the chemical industry that the mouse is an unsuitable animal for carcinogenicity testing of products such as pesticides because it is unusually sensitive and because it has a high incidence of spontaneous tumors. These criticisms have been particularly focused on the supposed unreliability of mouse liver tumors as an indication of response to carcinogenic chemicals.† There are just no scientific grounds for these allegations. On the basis of an extensive review of the literature on chemical carcinogenesis, Lorenzo Tomatis of the International Agency for Research on Cancer in Lyon, France, published recent studies which demonstrate that the results of carcinogenicity tests in mice are closely similar to and predictive of those in rats or other rodents.¹⁴ Tomatis found that of fifty chemicals producing liver tumors in mice, all induced

* Few epidemiological studies have been undertaken for carcinogens found active in rodent tests, and industry sometimes equates this absence of epidemiological data with evidence of noncarcinogenicity in humans. Accordingly, industry argues that regulation should primarily, if not exclusively, be directed at those few carcinogens identified by human epidemiologic studies. A *reductio ad absurdum* of this position has been put forward by Vaun Newill, Medical Director of Exxon Corporation, in *Cancer Bulletin* 29 (1977): 177-78: "A regulatory program based on experimental screening models to evaluate new chemicals prior to their introduction into the environment, however, will hinder the better documentation of this correlation [between human and animal carcinogenicity data] than we have presently. When a carcinogen is prevented from entering the environment on the basis of screening results, there can be no data regarding that exposure in man."

† Those industries such as Shell which challenge the significance of the induction of cancers in test mice by their products continue to use the failure of other products to induce cancers in mice as proof of their safety.

tumors of the liver or other organs when adequately tested in rats and hamsters.

A major deficiency in current carcinogenicity tests is their simplistic nature, dictated in part by practical considerations, such as testing the effects of one chemical at a time. Carcinogenicity tests thus do not adequately reflect the realities of multiple concurrent and sequential exposures to a wide range of carcinogens in the general environment and the workplace. Because of the relatively small numbers of animals that can be tested and the impossibility of predicting human sensitivity from animal tests, there is also substantive evidence of interactions between individual carcinogens making the carcinogens together much more potent than either separately. Also interactions between carcinogens and a wide range of non-carcinogenic chemicals may increase the potency of the carcinogens. For example, the incidence of liver cancers induced in trout by feeding as little as 0.4 parts per billion (ppb) of aflatoxin[‡] is sharply increased by addition of various non-carcinogenic oils to the diet.¹⁵ Similarly, the carcinogenic effects of low concentrations of benzo[a]pyrene on mouse skin are increased 1,000-fold by the use of the non-carcinogenic n-dodecane as a solvent.¹⁶ Benzo[a]pyrene and ferric oxide injected in the trachea of adult rodents induce a high incidence of lung tumors, only if the animals are pretreated at birth with a single low dose of another carcinogen, diethylnitrosamine. The quantitative response to a particular carcinogen can be substantially influenced by a wide range of factors, including interaction with other carcinogenic and non-carcinogenic chemicals. Thus, these so-called *synergistic* effects further confound attempts to find safe levels of carcinogens. Such interaction studies clearly confirm that threshold levels of carcinogens cannot possibly be predicted by calculations based on setting a dose arbitrarily lower than the lowest apparently carcinogenic animal dose in a particular experimental situation. Epidemiology has given important clues on interactive effects between carcinogens, such as smoking and asbestos or uranium, and between carcinogens and non-carcinogenic chemicals, such as arsenic and sulfur dioxide. There are now critical

[‡] Allowable limits for aflatoxin contamination of milk and other foods are 0.5 and 20 parts per billion, respectively.

needs for large-scale interactive tests designed to elucidate such additive and synergistic interactions as they occur in daily life, particularly when suggested by epidemiological observations.

Principles of Animal Testing

Test Guidelines

The National Cancer Institute has recently published a set of specific recommended procedures for carcinogenicity testing in rodents.¹⁷ Useful guidelines have existed since the early 1960s, but they are too general for current regulatory needs. As the results of more and more animal tests are now subject to public scrutiny, the proposed NCI guidelines will probably have an increasing influence on carcinogenicity testing.

There is now general acceptance of the need to conduct tests in accordance with accepted humanitarian principles.

Test Animals

Just as the chemist pulls a bottle of chemicals off the shelf and is assured of reasonably standard quality, so does the cancer biologist like to use particular species and strains of animals in which a reasonably standard response can be expected.¹⁸ As noted above, the two species used more than any others are rats and mice. There are various strains of each species available, each with its own characteristic biological properties and sensitivities. There are some important advantages to using highly inbred rodent strains. Their incidence of spontaneous cancers and of cancers following treatment with various chemical carcinogens is more predictable than is the case with random-bred animals. Additionally, strains can be selected that are either highly sensitive or highly resistant to certain classes of carcinogens.

On the other hand, as human populations represent a genetic

smorgasbord, it is more likely that random-bred animals will give results more in line with expected human responses. A compromise, which is now currently favored, is to use a hybrid of two inbred strains which combines the advantages of predictable responses with genetic heterogeneity.

Routes of Tests

Among the many possible methods and routes by which a carcinogen can be administered to an animal are feeding, inhalation, and skin painting. The same carcinogen administered through different routes can produce cancer in either different or in the same organs; there is no way of predicting the type and site of response. The most common test route for tests of food additives and other dietary compounds is by incorporating the test substance in animal feed or administering it directly into the stomach by a tube (this process is called *gavage*). Feeding is also a standard test method for administering many other types of possible carcinogen. Feeding of test animals can be and is also used when the route of human exposure is by the skin or lungs, especially when there is a likelihood that cancers will result in internal organs, such as the liver or kidney.

When exposure on the human skin results in skin cancer (or is suspected to cause skin cancer), as in workers exposed to petroleum and shale oils, then skin painting in animals is the proper method to use. Skin painting, however, is not sufficiently sensitive for investigating carcinogenic effects of chemicals such as amine hair dyes and textile fire retardants, which are absorbed through the skin and induce cancers at distant sites.* A technical background statement in the NCI "Guidelines for Carcinogen Bioassay in Small Rodents" makes this clear:

Although this type of test (skin painting) might provide useful information on some chemicals, it might be unreliable for measuring the effects of such chemicals on internal organs.¹⁹

* The insensitivity of skin painting is due to the fact that it is difficult to apply sufficiently high concentrations of test material by this route. For this reason, a positive result is all the more significant.

If a chemical is suspected of causing lung cancer when inhaled by humans, the logical way of testing is by inhalation. However, inhalation studies are technically difficult and relatively expensive. They are also complicated by the fact that a rodent, unlike humans, can breathe only through its nose, filtering the chemical being tested through a highly developed defense system and possibly reducing its effects. Despite the obvious importance of inhalation as a major route of human exposure, particularly for air pollutants, industrial chemicals, pesticides, and cosmetics, relatively few chemicals have so far been adequately tested for carcinogenicity by long-term inhalation.²⁰

Dosage

In well-designed tests, a range of doses is used. If the dose of a carcinogen is too low, few or no animals in the typically small test groups may get cancer. If it is too high, animals will die quickly from toxic effects of the chemical, well before cancer has had a chance to develop. To determine the proper dosage range for a carcinogenicity study, it is standard practice to perform preliminary toxicity tests to estimate the maximally tolerated dose (MTD). This is defined as the highest quantity or dose of a chemical that can be administered over the lifetime of an animal, during the course of a carcinogenicity test, without producing toxic effects, such as reduction in the life span or weight loss in excess of 10 percent of control animals, other than those directly resulting from the induction of cancers.† In well-designed studies, additional doses, based on one or more fractions of the MTD are also tested. The various dosages used in an experiment are usually expressed as so many milligrams (mg) of chemical per kilogram (kg) of animal body weight, mg/kg. This allows a comparison of the effects of equivalent doses in different animal species with different typical body weights.

† Administration of a carcinogen at doses in excess of the MTD, resulting in toxicity and premature death, will generally result in a decreased tumor response (competing toxicity), and such tests cannot be accepted as valid evidence of non-carcinogenicity. Subject to qualified scientific consideration, however, carcinogenic effects induced by doses in excess of the MTD are acceptable.

The duration and periodicity of the dose are also important. Some carcinogens will induce only a relatively low incidence of cancers when given in one large dose, but will produce a higher incidence when broken up into a series of intermittent and lower doses over the course of months.

Use of Relatively Large Dosages Perhaps the aspect of cancer research most distorted by industry and misunderstood by the public is the necessity to use much larger doses of a substance being tested than humans could possibly be exposed to. The superficial absurdity of a rat consuming the human equivalent of about a thousand cans of diet soda per day from fetus to adulthood has been exploited by industry, misinterpreted by the press, and misunderstood by the lay public, which has come to believe that anything given in large enough doses will cause cancer in animals.[‡] This simply is not true. The need for large dosages of chemicals (as the highest of a range of doses) in some experiments is a reflection of the facts (1) that some carcinogens are much less potent than others and (2) that animal experiments, no matter how well planned, must make use of finite animal resources. To illustrate this point, let us suppose that humans and rats are equally sensitive to some chemical carcinogen which causes one case of cancer in every 10,000 persons (or rats) to which it is given. If 220,000,000 Americans were exposed to this chemical, 22,000 cases of cancer would occur. On the other hand, if fed to the typical fifty rats used in an experiment, the chances that even one rat would get cancer is one-half of one percent; 10,000 rats would have to be fed the chemical (at human dosages) to observe even one cancer.²¹

Given that a human-level dosage might not produce a detectable result in a small rat population, even for a carcinogen which may be the cause of many thousands of cases in humans, the only alternative is to increase the dose, and thereby increase the probability of inducing a cancer in a particular animal. Once the dosage is increased above real-life levels, scientists must begin to make assumptions about their findings in the following vein. If the

[‡] In addition to being carcinogenic at relatively high dose levels, saccharin is also carcinogenic in rats at doses in the diet extending down to 0.01 percent, equivalent to the amount of saccharin in one and one-half cans of diet soda.

equivalent of, let us say, 1,000 cans of saccharin-containing soda per day produces one tumor in 50 rats, then it is plausible to assume that 100 cans will produce one-tenth as many tumors, or one tumor in 500 rats. Continuing the argument, the equivalent of 10 cans per day would produce one-tenth as many as before, that is, one tumor in 5,000 rats. Finally, one can per day would produce one tumor in 50,000 rats. If, as we assume, humans and rats are equally sensitive to this carcinogen, one can of soda per day would produce one tumor in 50,000 people, or about 4,000 cases of cancer in the nation's population.*

Two basic assumptions are involved in the above argument. First, as stated, we assumed humans to be as sensitive as rats. Of course, in any particular situation, humans may either be less sensitive or more sensitive than rodents to the toxic or carcinogenic effects of the chemicals in question. For example, the lowest dose of thalidomide inducing birth defects in pregnant women is 0.5 mg/kg/day; the corresponding values for the mouse, rat, and dog are 30, 50, and 100 mg/kg/day, respectively. Thus, humans are 60 times more sensitive than are mice to thalidomide, 100 times more sensitive than rats and 200 times more sensitive than dogs.²² Moreover, certain aromatic amines, such as 2-naphthylamine, are potent bladder carcinogens for man, monkeys and dogs, but not for rats, mice and other rodents, in which tumors at other sites are produced.²³ Hence there is no known method for predicting a safe human level or threshold for carcinogens on the basis of experimental animal data, if indeed such safe levels for humans exist at all.²⁴ Second, we assumed that equal proportions of tumors would occur at all dosages, known technically as a linear dose-response extrapolation. This assumption is the least strong, because it is simply not practically verifiable by direct experimentation. As a conservative method for extrapolating animal data from high to low doses, however, it has become standard practice. By conservatism, we mean use of a mathematical method which errs, if at all, on the side of safety to humans. As former NCI Director Frank Rauscher, Jr., admitted to an American Enterprise Institute roundtable on saccharin on April 21, 1977, "In protecting the public's health, there is no choice but to assume that the extrapolation is linear."

* This argument has been simply explained in R. W. Rhein and L. Marion, *The Saccharin Controversy* (New York: Monarch Press, 1977), p. 58.

The justification for the conservative approach to the absence of a threshold for carcinogens or the inability to determine its existence rests largely on our ignorance of the nature of the lower ends of dose-response curves. There is, in fact, no evidence at all of the existence of thresholds for the irreversible processes involved in carcinogenesis. There is also no evidence of complete repair of DNA damaged by any carcinogen; any residual unpaired DNA would perpetuate the carcinogenic hazard.†

Finding the Evidence

One of the most poorly conducted areas of animal cancer research is the identification of the cancer in the animals' bodies. The process of finding a cancer in the fresh carcass of a mouse or rat is different from the discovery of cancer in a human by a doctor. The rodent cannot complain of painful symptoms before death. Also, since carcinogens may cause cancer in any of a wide range of organs, the entire body of the animal must be meticulously searched. This is not possible if, through neglect or poor husbandry, the animal has been allowed to die and decompose before an adequate autopsy, as is often the case.

The Statistical Significance of the Evidence

The ideal experiment is one in which either the chemical being tested induces no tumors in the test group with none in controls, in which case the chemical is determined to be non-carcinogenic, or the chemical induces a high incidence of tumors in the test

† Jerome Cornfield, in "Carcinogenic Risk Assessment," *Science* 198 (1977): 693-99, proposed a hypothetical model for carcinogenesis which in effect gives a threshold. Cornfield, however, stressed that his model is based on the assumption that all of a carcinogen below a given dose level, administered on a single occasion, could be inactivated instantaneously, by some unknown defense mechanism. The unverifiable and unrealistic nature of Cornfield's assumption invalidates his model. (C. C. Brown et al., "Models for Carcinogenic Risk Assessment," *Science* 202 [1978]: 1105.) Cornfield has, however, protested that only a "misreading" of his article could have led to the conclusion that he was proposing a threshold model (*Science* 202 [1978]: 1107-8).

group with none in controls, in which case the chemical is determined to be carcinogenic. Unfortunately, the results are rarely this clear. Typically, the test animals have a certain percentage of tumors, which are considered to be induced, and the controls have a smaller percentage, which are considered to be spontaneous. It is then the job of the statistician to sort out the data and decide whether the difference in tumor yield between the test and control groups is statistically significant or simply due to chance. The statistician is also concerned with the time from the initial dose which elapses before the tumors appear, as not only do carcinogens increase the number of cancers in test animals in contrast with those occurring spontaneously in controls, but they also induce these cancers earlier in the life of the test animals. The statistician thus deals with four factors in a standard carcinogenicity test: the number of animals tested; the number of given types of cancers induced in each animal and in each test and control group; the time required to induce these cancers; and the number of tumors in both the test and control groups. Apart from the individual importance of each of these factors, their effects interact with each other statistically.

A critical factor in these tests is the number of animals tested. The greater the number of animals tested in each of the various dosage groups and in the control group, the more meaningful is any observed difference. A 20 percent tumor rate among the test group, compared to a 5 percent spontaneous rate among controls, unambiguously indicates a carcinogenic response in a group of 200 animals. But in a group of only 20 animals with the same exposure the difference between 20 percent and 5 percent is not statistically significant and the carcinogenic effects of the exposure cannot be established.

Short-Term Tests

Over the last two decades, some dozen or so short-term tests have been developed for predicting the carcinogenicity of chemicals by methods that, in contrast to conventional animal tests, are

inexpensive and rapid, taking a few days or sometimes only a few hours.²⁵ Short-term tests are based on underlying chemical, physical, or biological properties that are shared, or rather are believed to be shared by carcinogens but not by non-carcinogens. The successive appearance of each short-term test has characteristically been initially greeted with uncritical enthusiasm. This becomes progressively damped when subsequent studies on more extensive series of chemicals reveal poor correlations with carcinogenicity, at which stage the test gradually falls into more limited use or disuse. For this reason, there is now recognition that the utility of short-term tests must depend on their validation with large numbers of carcinogens and non-carcinogens from a wide range of different chemical classes.

The most recent short-term test was developed in 1975 by Bruce Ames.²⁶ In the initial validation of this test, about 90 percent of 174 carcinogens from selected chemical classes were shown to induce mutations in bacteria, while only 13 percent of a group of 108 non-carcinogenic chemicals were found to be mutagenic. Besides the rapidity and economy of the Ames test, an additional attraction is that it is based on the detection of types of genetic damage which are thought to be critically involved in the induction of cancer (somatic mutation theory). The test system utilizes bacteria, as indicators of mutagenic damage, combined with rodent liver homogenates to allow activation of the chemicals tested and thus approximate to the major types of metabolic transformations in the human body.

Since its introduction, the Ames test appeared promising and is now being widely used, particularly in conjunction with a battery of other short-term tests. Since it allows large numbers of chemicals to be screened rapidly, the pharmaceutical, pesticide, and other chemical industries are using it routinely in early development phases for screening chemicals for possible carcinogenic activity. Additional applications of the test include looking for carcinogens in complex, ill-defined organic mixtures such as extracts of air and water pollutants of hair dyes, and for carcinogenic metabolites in the urine or blood of workers with suspected exposure to occupational carcinogens. Presumptive evidence of carcinogenicity of several important industrial chemicals has been recently obtained with the Ames test, often in conjunction with a

battery of short-term tests. These include the flame retardant Tris (manufactured by Velsicol Chemical Co.), hair dyes, and the Japanese food additive AF2 (furylfuramide).

Apart from responsible uses of the test, it has also been used by some segments of industry to argue that animal tests are too expensive, impractical, and unreliable and, in the absence of conclusive human epidemiological evidence of carcinogenicity, should be replaced by the Ames test. This would create a "no-lose" situation. A negative Ames test would be taken to exculpate any chemical from questions of carcinogenicity and to allow its marketing. Depending on economic considerations, a positive test could either be accepted or rejected in the full knowledge that regulatory agencies would be reluctant (and rightly so) to base regulatory actions exclusively on the results of tests in bacterial systems.

An example of misuse of the Ames test is afforded by the recent controversy surrounding the fire retardant, Fyrol FR-2, which is now used in some polyester children's sleepwear. During attempts to ban the carcinogenic Tris, Stauffer Chemical Company advertised and sold a substitute, Fyrol FR-2, claiming that it was inactive in the Ames test and therefore safe. Suspecting the claim to be in error, since Fyrol is similar to Tris in chemical structure, Fyrol was then independently tested and found to be Ames positive. This then led to the withdrawal of Fyrol which by then had found its way into approximately three million pairs of children's sleepwear (mainly those sold by J. C. Penney Co.).

Although short-term tests are now being widely and successfully used, they do have their limitations. First, several non-carcinogenic chemicals have been found to be mutagenic in one or more short-term tests (false positives). Second, they miss several important classes of carcinogens (false-negatives).‡ In fact, about half of the carcinogens discussed in the case studies in this book are inactive in the Ames test. Additional false negatives include most heavy metals; many polycyclic aromatic hydrocarbons; steroids; azonaphthols; antimetabolites; some carcinogens activated

‡ In classic quality-control terminology, a false negative result represents a "consumer risk" (in that it underestimates risk to the consumer), and a false positive a "producer risk" (in that it overstates risk to the producer). Units of producer and consumer risk are not fixed and can be expressed in terms of duration of disease-free life or dollars, and the proper balance between these can be expected to vary according to particular circumstances.

by intestinal rather than liver enzymes, such as cycasin; carcinogens of the chloroform class, and major classes of carcinogenic organochlorine pesticides, such as DDT. Third, the correlation between mutagenic effects and carcinogenicity are not as good as 90 percent for every chemical class (particularly for carcinogens with complex metabolic routes). In a recent survey of 273 carcinogens of a wide range of different structures, an overall correlation with mutagenicity of 77 percent was found.²⁷ While for some classes of carcinogens, the correlation was shown to be excellent, it was poor in others. In fact, correlation was shown to be a function of the structural type of carcinogen selected for test. Fourth, the test has become more complicated as more types of liver activation systems have been introduced in attempts to decrease false negatives. Fifth, the test only picks up a genetic damage at the gene level, and cannot detect chromosomal mutations that are considered to be involved in cancer and other human diseases.* However, it is not clear whether there are many chemicals (other than possibly the drug Griseofulvin) that induce chromosomal but not gene mutations. Finally, recent studies with the carcinogen dimethylbenzanthracene have indicated that different types of molecular interactions with DNA are involved in its effects in the Ames test (using rat liver) and in its carcinogenic effects on the skin of mice.²⁸ (However, the ability of short-term tests to use activation systems from tissues of different species, including humans, may well be advantageous.)

It is now widely agreed that the Ames test, especially when compared with a battery of other such short-term tests based on mutagenicity, such as neoplastic transformation and DNA damage and repair, and on structure-activity relations have a range of useful applications.²⁹ A positive result in these tests with a chemical for which no carcinogenicity data are available is clearly a cause for concern, especially if potential human exposure is involved. However, a negative result cannot be taken as presumptive exculpation of carcinogenicity, unless the chemical belongs to a particular class for which strong correlations with carcinogenicity have already been established. For this reason, particularly, exclusive reliance on data from these tests seems unwise, especially for

* Furthermore, the Ames test detects only certain types of reverse mutations.

regulatory purposes. There is just no reliable substitute for animal carcinogenicity tests.

The Practicality of Animal Testing

The practicality of animal testing is often challenged by industry on the grounds that too many new chemicals are being introduced into commerce each year to be handled by conventional animal testing and that the cost of such testing would be prohibitive. In fact, this has been used as one of the main arguments for the need for short-term tests.³⁰ However, based on various recent estimates including those by the Council on Environmental Quality, it seems that the number of these new chemicals which actually reach commerce is under 700 annually. There is every reason to believe that current facilities could be expanded to cope without excessive strain with this number of chemicals. In addition, there are large potential facilities at the National Laboratories, such as Oak Ridge, Tennessee, and Argonne, Illinois, besides an underutilized facility at the National Center for Toxicological Research, in Arkansas. There seems every reason to believe that the NCI Bioassay Program, given high priority (particularly under its new direction by the National Toxicology Program), could increase its present efforts to handle 700 or so chemicals annually, rather than the 120 which the NCI projected for 1979.

With regard to expense, the annual costs of testing one chemical for carcinogenicity in groups of fifty mice and rats of each sex at two dose levels is under \$300,000. Properly conducted carcinogenicity tests also provide information on a wide range of chronic toxic effects, including testicular damage leading to sterility, central nervous system damage leading to paralysis or behavioral changes, and damage to the liver leading to cirrhosis. The maximum \$210 million costs for testing 700 chemicals would be unlikely to result in substantial increases in production and retail product costs.† These testing costs should be contrasted with

† Much of these costs could be redistributed through tax write-offs and price pass-throughs.

chemical industry 1975 gross sales of \$72 billion (of which they represent about 0.2 percent) and after tax profits in excess of \$5.5 billion.

The costs of testing should be further contrasted with the far greater costs of failure to test and regulate, including the majority of the \$30 billion recognized annual costs of cancer due to preventable causes and the even greater costs of surveillance of workers exposed to occupational carcinogens. It is clear that the costs of failure to test and regulate are inflationary.

PART II

**THE SCIENCE AND
POLITICS OF CANCER**

Industrial concerns are in general not particularly anxious to have the occurrence of occupational cancer among their employees or of environmental cancer among the consumers of their products made a matter of public records. Such publicity might reflect unfavorably upon their business activities and oblige them to undertake extensive and expensive technical and sanitary changes in their production methods and in the types of products manufactured. There is moreover, the distinct possibility of becoming involved in compensation suits. . . . It is therefore not an uncommon practice that some pressure is exerted by the parties financially interested in such matters to keep information on the occurrence of industrial cancer well under cover.

Wilhelm C. Hueper, the modern pioneer of environmental and occupational carcinogenesis, 1943.

Chapter Four

Introduction to the

Case Studies

In the next three chapters case studies on some twelve individual carcinogens or classes of carcinogen are examined.* These are grouped according to their site of greatest social impact: in the workplace (chapter 5), in consumer products (chapter 6), and in the general environment (chapter 7). While convenient, this grouping is somewhat artificial. Carcinogens such as asbestos, vinyl chloride, and benzene pose major hazards to the exposed

*The case studies are generally based on information available up to April, 1979.

work force. However, these same carcinogens also escape or are discharged into the air outside the plants where they are being processed or manufactured and can produce cancer and other disease in people living in the local community. While carcinogenic pesticides are widely recognized as environmental contaminants, they represent still greater hazards to workers engaged in their manufacture, formulation, and application. Concerns about carcinogens in consumer products, such as sex hormones used as drugs and animal feed additives, have stimulated subsequent concerns about their role as occupational carcinogens.

While discussions of each substance are particular, all the case studies deal essentially with two basic sets of questions:

(1) *What do we know?* What are the patterns of manufacture and use of the product or process? What are the patterns of human exposure? What is the evidence of carcinogenicity from animal tests or epidemiological studies? What will be the economic and social impacts of regulation and of failure to regulate?

(2) *To what use has this information been put?* How has the affected industry reacted? What was the response of the regulating agency? What roles have public interest groups and organized labor taken? Also of concern are the roles of the Administration, Congress, courts, press, professional and scientific communities, and the nature of public perceptions.

A few common themes will emerge throughout the case studies. Most of the information we have on the products and processes involved has come from industry itself, either through in-house technical staff or indirectly through commercial consultants and laboratories. Apart from their general poor quality, built into most industry-sponsored studies is a tendency to minimize risks and maximize benefits, and to emphasize the difficulties and costs of regulation. They may fail to ask the relevant questions to assess risks and benefits, and in doing so fail to undertake the necessary studies to answer them. Worse yet, the results are occasionally manipulated or even destroyed.

The most serious effect of this information bias is the inappropriate shift in the burden of proof from the private to the public sector. The consumer or worker who bears the risk from exposure to an untested or poorly tested product then must also bear the

burden of raising questions about its safety or proving its dangers or of ensuring that the federal government proves its dangers.

The regulatory role of federal agencies is often complicated by inherent ambiguities and inconsistencies in the statutes under which they operate. Be that as it may, the major problem here is not one of inadequate laws but of unwillingness to enforce the law. The track record of federal agencies in regulating industry and in protecting workers and consumers from carcinogenic hazards reflects extreme laxness often compounded by undue responsiveness to special interests.

Over the last decade, many regulatory actions against carcinogens in the workplace, in consumer products, and in the environment have been developed only at the initiative of public interest groups or organized labor. The scientific community has been largely indifferent. The exceptions are the few independent professionals who have worked with public interest groups and labor, and a small but influential segment of the scientific community working closely with industry in efforts to impede or block attempts to regulate environmental and occupational carcinogens. Over two decades ago, President Eisenhower warned against the growing national threat of the military-industrial complex. The medical-industrial complex now appears to be as serious a threat.

'Tis a sordid profit that's accompanied by the destruction of health. . . . Many an artisan has looked at his craft as a means to support life and raise a family, but all he has got from it is some deadly disease, with the result that he has departed this life cursing the craft to which he has applied himself.

Bernardino Ramazzini, an Italian physician, considered the founder of occupational medicine, 1705.

Chapter Five *The Workplace:* *Case Studies*

The total U.S. work force numbers approximately 100 million.* Various categories of workers are at high risk of exposure to carcinogens. These include approximately 670,000 workers in the petrochemical industry, 365,000 in metallic and non-metallic mining, and 1.1 million in the metal processing and smelting industries.¹ These figures do not reflect the extent of exposure to occupational carcinogens. Estimates by HEW in 1978 indicate that from 8–11 million workers have been exposed to asbestos since World War II. On the basis of a recent National Occupational Hazards Survey, the National Institute for Occupational Safety and Health (NIOSH) estimates that 880,000 workers are currently exposed to just those carcinogens or other toxic substances that are currently regulated by the Department of Labor's Occupational Safety and Health Administration (OSHA).² The range of

* Of these, 41 million are women. The numbers of women in the work force are growing. In 1977, 48 percent of all U.S. women were in the work force, as opposed to 38 percent in 1960.

industries involving exposure to occupational carcinogens is shown in Table 5.1.

In general, workers are denied knowledge of what chemicals they are exposed to, and in what concentrations.³ They are also not informed whether these have been adequately tested, whether they are toxic under conditions of exposure in the plant, or whether they are carcinogenic. This is in striking contrast to chemicals in consumer products, which must be tested in animals before they can be used, and for which there are labeling requirements, however imperfect.

The toxic and carcinogenic chemicals to which workers may be exposed at relatively high concentrations in the workplace also are discharged or escape into the air and water of the surrounding community. The worker may be exposed to the same chemical carcinogens through consumer products and the general environment as in his or her workplace.

What are the conditions of exposure to toxic and carcinogenic chemicals in the workplace and what precautions are taken to protect workers from such exposures? What is the role of government, industry, and the medical community in preventing and regulating such exposures? The British medical journal *Lancet* gives some answers to these questions in a recent editorial, "The Medical Industrial Complex":

Involved in this sinister complex are numerous big industrial manufacturing firms who are reluctant to believe that any product they use or manufacture, from asbestos insulation to benzidine or beta-naphthylamine, can be harmful. The medical men and scientists directly employed by these firms are chiefly concerned with their employers' and their own profits, and are indifferent to the health of the exposed employees. Some of the firm's employers have, it is alleged, ignored even legal regulations and got away with it. Another alleged tack is for the firm singly or in combination with like firms, to set up supposedly independent research institutes whose scientists seem always to find evidence to support the stance taken by the firm, despite massive contrary evidence. Thus, when some high-sounding institute states that a compound is harmless or a process free of risk, it is wise to know whence the institute or the scientists who work there obtain their financial support. But there are Government agents, Federal and State, to enforce safety measures and draw

Table 5.1 *Occupations Associated with an Excess Risk of Cancer*

Site of Cancer	Carcinogen	Occupations
Liver	Arsenic, vinyl chloride	Tanners, smelters; vineyard workers; plastic workers
Nasal cavity and sinuses	Chromium, isopropyl oil, nickel, wood and leather dusts	Glass, pottery and linoleum workers; nickel smelters, mixers and roasters; electrolysis workers; wood, leather, and shoe workers
Lung	Arsenic, asbestos, chromium, coal products, iron oxide, mustard gas, nickel, petroleum, ionizing radiation, bischloromethyl-ether	Vintners; miners; asbestos users; textile users; insulation workers; tanners; smelters; glass and pottery workers; coal tar and pitch workers; iron foundry workers; electrolysis workers, retort workers; radiologists; radium dial painters; chemical workers
Bladder	Coal products, aromatic amines	Asphalt, coal tar, and pitch workers; gas stokers; still cleaners; dyestuffs users; rubber workers; textile dyers; paint manufacturers; leather and shoe workers
Bone marrow	Benzene, ionizing radiation	Benzene, explosives, and rubber cement workers; distillers; dye users; painters; radiologists

Source: P. Cole and M. B. Goldman, "Occupation," chapter 11 in J. F. Fraumeni, Jr., ed., *Persons at High Risk of Cancer* (New York: Academic Press, 1975), pp. 167-84.

up others, to see that regulations are in force, and to monitor dangerous processes. Alas, it seems that these people, too, are often involved in the medical/industrial complex, and are reluctant to enforce regulations, to emphasize risks to employees, or to see that measures are taken to warn or protect them against industrial hazards. They also seem, as individual contractors or as members of

research organizations, to attract an undue proportion of Federal research grants.

The indictment is a strong one, and is coupled with accounts of factories where employees work in fogs of asbestos dust and beryllium dust, or with beta-naphthylamine and benzidine slopped about. Ever greater numbers of employees are being recognized as suffering from pulmonary asbestosis, berylliosis, bladder and lung cancer, and mesotheliomas. The greatest danger, as far as the numbers exposed go, seems to be asbestos, and the carcinogenic properties of this material are creating general alarm. Large numbers of the general public are exposed to it through the drinking water in one city. The number of industrial hazards and of workers killed or injured by them seems to be increasing, and the public has reason to be worried. The industrial/medical complex is now required to answer the case, and as its credibility has been seriously impugned it had better be a clear answer.⁴

This chapter presents case studies on four substances: asbestos, vinyl chloride, bischloromethylether, and benzene. These are chosen to illustrate some fundamental problems of exposure to carcinogens in the workplace.⁵

Asbestos

Asbestos, known as the "magic mineral,"¹ has been used in one form or another for centuries, dating back to its first recorded use for pottery making in Finland some 4,500 years ago.† Virtually indestructible, it is highly resistant to fire, has high tensile strength, and its fibers can be spun into yarn and woven into cloth. The asbestos industry has grown phenomenally since the first North American asbestos mine opened in 1879 in Thetford,

† Asbestos is a generic name for a group of naturally occurring fibrous mineral silicates, which consist of two major classes: serpientes, largely represented by chrysotile, a relatively pure magnesium silicate that comprises 90–95 percent of the world's asbestos production; and amphiboles, including five main types (actinolite, amosite, crocidolite, anthophyllite, and tremolite) in which the magnesium component is partially or wholly replaced by other cations. Chrysotile is often known as white asbestos, amosite as brown asbestos, and crocidolite as blue asbestos.

Quebec, with a first-year output of 300 tons. Johns-Manville was founded in the United States in 1901 and is still the world's largest asbestos company, and Turner Brothers, still the largest British company, in 1916. World production of asbestos in 1920 was only 20,000 tons, about 0.5 percent of present levels (about 4.3 million tons). Of the present world output, 1.7 million tons are mined in Canada (and fabricated largely in the United States) and 2.5 million tons in the Soviet Union. At the heart of this booming industry is a research effort which has led to use of asbestos in cement, asphalt, wallboard, pipes, textiles, insulation, food and beverage processing, brake linings, and countless other everyday products.² It has also led to approximately 50,000 deaths per year in the United States from cancer and other diseases.³

Occupational Exposure

Occupational exposure to asbestos dust occurs in a wide range of operations from the mining and processing of the ore to its fabrication and use in many industries, particularly construction, shipbuilding, insulation, and textiles.

By 1918 enough was known about the dangers of asbestos to lead to the decision of U.S. and Canadian insurance companies to stop selling life policies to asbestos workers.⁴ It was not until the early 1920s that descriptions of a new respiratory disease resulting from exposure to asbestos (*asbestosis*) first appeared in the medical literature. An often fatal disease, involving progressive scarring of the lungs and leading to respiratory disability and heart failure, asbestosis is akin to black lung and other chronic chest diseases (*pneumoconioses*) which afflict miners and processors of various kinds of minerals and fibers. In England, where it was first studied and reported in the medical literature, asbestosis was covered under Compensation laws in 1931, after which some efforts were made to improve working conditions and reduce exposure to asbestos dust.⁵

By the 1930s, based on numerous case reports of asbestosis and lung cancer occurring together in asbestos workers, scientists began to suspect that asbestos is carcinogenic. But no full-scale studies were made on asbestos plant workers until the 1950s,

when the British epidemiologist Richard Doll investigated employees with at least twenty years exposure in an asbestos textile plant. Doll found that this group experiences ten times the lung cancer deaths of non-asbestos workers of the same age.⁶

Also during the 1950s, Irving Selikoff, now a leading occupational epidemiologist at Mt. Sinai Hospital in New York City, noted that fifteen of seventeen of his patients employed at Union Asbestos and Rubber Company in Paterson, New Jersey, had developed asbestos-related lung disease. By the early 1960s, the disease incidence was climbing at an alarming rate, prompting Selikoff to inquire into the employment records of workers in this and other asbestos plants. After being refused this information by industry, he contacted the New York and New Jersey locals of the International Association of Heat and Frost Insulators and Asbestos Workers, the union representing many of the men. Selikoff then conducted a cohort study based on all men belonging to those locals who had been employed in the asbestos industry over a particular length of time. Starting with 632 workers listed on the union rolls in 1943, he inquired into their fates, checking how many had died and the cause on each death certificate. This type of study is ordinarily difficult because it involves tracing the whereabouts of a worker twenty years after employment in a particular job. In this case the union had kept fairly detailed records of work histories. The union also administered the death benefits for its members, who as retirees had good reason to keep in touch right up to the time of their deaths.

By 1973, 444 of the original 632 workers were dead.⁷ Table 5.2 is an epidemiological analysis which shows the number who had died of various causes, compared with the number who would have been expected to die of each cause.‡

Table 5.2 shows that by 1973 this cohort of workers had experienced a death rate 50 percent greater than the average white male. Among these "excess" deaths, lung cancer by far exceeded the expected experience of such a group of men by a factor of seven. The rate of all cancers combined was four times as great for these men, and there were thirty-five cases of mesothelioma,

‡ The ratio of observed to expected numbers of deaths is the *standard mortality ratio*. The larger this ratio is than 1, the more likely it is that a particular occupational exposure was the cause of death.

which for non-asbestos workers should not have occurred at all.* Finally, even the rates of cancer of stomach, colon, and rectum were more than three times that expected.

Conditions at the Johns-Manville plant in Scarborough, Ontario, give further insight on conditions of occupational exposure to asbestos. This plant opened in 1946 for the manufacture of asbestos and silica cement pipes and fiberglass insulation. Within a few months, men were working without respirators in dust that

Table 5.2 Causes of Death in 444 Asbestos Workers

Cause of All Deaths	Number of Deaths, 1943-1973		
	Expected	Observed	Ratio (observed/expected)
Total deaths, all causes	300.65	444	1.48
Cancer—all sites	51.26	198	3.86
Lung cancer	11.68	89	7.62
Pleural mesothelioma	0	10	...
Peritoneal mesothelioma	0	25	...
Cancer of stomach	5.10	18	3.53
Cancer of colon-rectum	7.50	22	2.93
Asbestosis	0	37	...
All other causes	249.39	209	0.84

Source: I. J. Selikoff and E. C. Hammond, "Multiple Risk Factors in Environmental Cancer," chapter 28 in J. F. Fraumeni, Jr., ed., *Persons at High Risk of Cancer* (New York: Academic Press, 1975), pp. 467-83.

was so thick that they could not see more than a few yards ahead of them.† Even after a new ventilation system was installed in 1952, counts of 50 million fibers per cubic meter (m^3) of air persisted in some areas. Selikoff visited Scarborough in the mid-1960s and predicted a high incidence of cancer deaths in the coming decade. Management dismissed these concerns as alarmist, and made little attempt to improve working conditions. Since

* Mesothelioma is a form of cancer of the lungs (pleural mesothelioma) or abdomen (peritoneal mesothelioma). It should be noted that deaths from pleural mesothelioma are reported as lung cancer deaths in cancer mortality records (based on the International List of Causes of Disease) and can thus be falsely attributed to smoking rather than asbestos.

† Dust counts were probably about 80 million fibers per cubic meter (m^3) of air.

then, over fifty workers of a total work force of approximately 500 have been disabled by chronic respiratory diseases and there have been twenty-seven deaths from lung cancer.

Regulation of Occupational Exposure

The ultimate acceptance of the carcinogenicity of asbestos has not been easily achieved. Even today, the controversy persists, but now the questions are not "whether" but "how much" and "what type." The importance of this issue is directly related to the vast economic stake which industry has in winning its battle with the government over the standard regulating levels of exposure to asbestos in the workplace.

When OSHA began hearings in 1972, the industry fought strenuously against any reduction in permissible exposure levels on the alleged grounds that the dangers of asbestos were minimal.⁸ The basis for the industry case was strongly argued by academic consultants, some from medical schools or schools of public health, some of whose research and publications were supported directly or indirectly by grants or funds from the industry or industry-financed foundations.⁹

Regulatory standards for asbestos are based on the number of fibers in a unit volume of air.¹⁰ The current OSHA standard is 2 fibers per cubic centimeter or 2 million fibers per cubic meter, over an eight-hour working day.¹¹ In the course of an average day, a worker inhales about 8 cubic meters of air, equivalent to an allowed inhalation of 16 million asbestos fibers. Even where the standard is met total exposure levels are much higher. Current optical microscopic techniques for counting fibers in the workplace only detect those which are relatively long, more than 5 microns in length. Smaller fibers, or fibrils, which can only be counted by electron microscopy and not by optical microscopy, may outnumber the longer ones by as much as 100 to 1.‡ Thus, occupational exposure to asbestos at currently regulated levels of 2 mil-

‡ Asbestos counts in the workplace are invariably counted by optical microscopy and hence reported as fibers per cubic meter of air. In contrast, electron microscopy is the only practical technique for measuring public exposure in the general environment, and these counts of fibrils and fibers are translated into mass and reported in nanograms rather than counts per cubic meter.

lion fibers, may result in the daily inhalation of as many as 1.6 billion short fibers. It should be recognized that these are believed to be more carcinogenic than the long fibers. It should finally be recognized that there are critical needs for the development of practical and sensitive methods for monitoring of total asbestos fibers, both long and short, in the air breathed by exposed workers.

The key issue in the 1972 OSHA hearings was the proposal by NIOSH to lower the then temporary exposure standard of 5 million asbestos fibers per cubic meter of air to 2 million fibers, the 1969 British standard. This lower standard, however, was primarily designed to protect just against asbestosis, without any consideration of the cancer problem.* The asbestos industry argued at the hearings that the 5 million standard exposure level did not cause much disease, and that to lower it further would create severe economic dislocation and unemployment. In spite of the threat of job losses, organized labor fought strongly for the improved standard, pointing out that asbestos is a major health hazard not only for asbestos workers, but also for workers in many other chemical and manufacturing industries which use asbestos in many forms.

The involvement of the asbestos industry in health research, and its propagandizing of the public is longstanding. While the asbestos industry takes some pro forma precautions in the open scientific forum, these are not apparent in its public relations literature. Some good examples of this can be found in a recent publication by the Quebec Asbestos Mining Association (QAMA) of a bilingual pamphlet, "Asbestos and Your Health."

Can a little bit of asbestos kill you? No—long-term medical studies of workers who are exposed to asbestos show that low to moderate levels of exposure do not lead to an increased rate of disease. In these studies, a higher-than-normal incidence of disease was found only among employees exposed to extremely high asbestos concentrations for long periods of time.

* Later, the British standard was subsequently shown by U.S. investigators to be inadequate for protection against asbestosis, let alone against lung cancer.

Note the deliberate omission of the word "cancer." Also, the statement is simply false. Short term and low-level exposures are known to cause disease.

The lung's normal cleaning mechanisms quickly remove the majority of inhaled particles, including respirable-sized asbestos fibers.

On the contrary, the majority of fibers either remain in the lung or move to the gut, where it is suspected they contribute to the development of cancer of the gastrointestinal tract.

Some cases still occur among long-service employees whose exposure began at a time when little was known of the amount of asbestos a human could tolerate . . . With expanding medical knowledge and today's improved dust control measures, however, there is every reason to believe that these cases will decrease in the future and asbestos-related disease will cease to be an occupational problem.

The controls which industry fought for at the OSHA hearings were sufficient to cause levels of disease among New York insulation workers at which 20 percent died of lung cancer, 10 percent of gastrointestinal cancer, 10 percent of mesotheliomas, 10 percent of other cancer, and 10 percent of asbestosis.

Over the past decade, industry has also supported major scientific studies at McGill University in Montreal, by the Industrial Health Foundation in Pittsburgh and by Tabershaw-Cooper Associates on the West Coast, all of which have minimized the danger of working with asbestos. One of the most controversial of these studies, involving more than 11,000 employees and ex-employees of Quebec asbestos mines, was carried out by J. Corbett McDonald, then in the Department of Epidemiology and Public Health at McGill. In presenting his results to the OSHA hearing officers, McDonald introduced himself as a full-time employee at McGill University, and an independent research worker.

I do not work, nor am I associated with any asbestos producer or manufacturer. The research I shall be describing is supported by grants, not to me but to McGill University, from a number of sources—the Institute of Occupational and Environmental Health,

the Canadian government, the British Medical Research Council, and the USPHS [U. S. Public Health Service].¹²

However, anyone glancing at his paper, published in 1971 in the Archives of Environmental Health, would have noticed, in the customary small typeface at the end of the text, the acknowledgment:

This work was undertaken with the assistance of a grant from the Institute of Occupational and Environmental Health of the Quebec Asbestos Mining Association.¹³

McDonald made several claims on the basis of his study. First, he maintained that "the findings suggest that our cohort of workers in the chrysotile [a kind of asbestos] mining industry had a lower mortality than the population of Quebec of the same age." Second, he claimed that while indeed some workers did seem to get more lung cancer than others the "excess" cancer deaths were confined to those workers who had been much more heavily exposed than the rest. Lastly, he concluded that "these findings strongly suggest . . . that chrysotile is less likely to cause malignant disease of the lung and pleura than other forms of asbestos, such as crocidolite."

Criticism came swiftly from independent scientists in the United States. Major objections were directed not only at the overall design of the study, but at the statistical analysis of the data as well. McDonald had selected a method for computing death rates which seemed to ignore the long latency period of lung cancer. This resulted in an underestimate of the excess deaths which occurred among men with a long duration of employment.¹⁴ Faced with mounting criticism and complaining that his "life had been made hell," McDonald resigned his position at McGill.¹⁵ Taking his asbestos-cancer research funds, including continuing support from the National Cancer Institute (NCI),¹⁶ he returned to England, where the London School of Hygiene and Tropical Medicine appointed him to the Trade Union Congress Chair of Occupational Medicine.

Another illustration of the industry position was afforded when a recent NIOSH study demonstrated an increased risk for lung

cancer and other lung diseases among South Dakota gold miners exposed to asbestos dust levels even lower than the 2 million fiber standard proposed by NIOSH in 1972.¹⁷ A sharp response from Paul Kotin, the medical director and senior vice president of Johns-Manville, the world's largest asbestos manufacturer, was subsequently circulated in attempts to minimize the impact of these findings and to persuade the safety of exposure to levels of 2 million fibers.^{18†} The NIOSH group prepared a rebuttal which defended their original analysis and demanded:

Why should it surprise Drs. Kotin and Chase that asbestos at concentrations less than 2 million fibers per cubic meter is associated with excessive risk of respiratory cancer? Indeed, it is known that asbestos fibers have been previously demonstrated to be carcinogenic to man at all fiber concentrations studied under adequate epidemiologic method.¹⁹

On December 15, 1976, John F. Finklea, as Director of NIOSH, communicated with Morton Corn, then Assistant Secretary of Labor for OSHA, pointing out that the 1969 British 2 million fiber standard, which had been the basis of the 1972 proposed NIOSH standard, had since been shown to be excessively high and should be reduced. Finklea referred to studies on exposures as low as 250,000 fibers per cubic meter, at which workers had twice the likelihood of the general population of dying from lung cancer or asbestosis. Finklea further proposed that the standard should be lowered to a maximum of 100,000 fibers. NIOSH clearly recognized that even this proposed lower standard did not represent a safe exposure level. Finklea finally stated:

Because it is not possible to specify a safe exposure level for a carcinogen, only a ban on the use of asbestos can ensure complete protection against this mineral's carcinogenic effect. Therefore, emphasis should be placed on prohibiting the occupational use of asbestos in other than completely closed operations and on substituting other

† These and other current positions on chemical carcinogenesis are in striking contrast to views expressed by Kotin when in government employ in 1970 (see Appendix II), and in even more striking contrast to his testimony at the Mirex cancellation proceedings (FIFRA Docket 293, EPA, November, 1973).

products whenever possible. Asbestos should be replaced where technically feasible, by substitutes with the lowest possible chronic toxicities.²⁰

NIOSH also pointed out that all forms of asbestos, including chrysotile, amosite, crocidolite, and tremolite, can induce asbestosis and also cancer.

The OSHA standard still rests at 2 million fibers, twenty times in excess of the level that NIOSH now recommends. The stance of industry in fighting even the unsatisfactory OSHA standard is further illustrated by the record of R. T. Vanderbilt Company, Norwalk, Connecticut, which owns a number of talc mines in up-state New York and Vermont.²¹ Shortly after OSHA promulgated its 1972 standard, R. T. Vanderbilt belatedly realized that the high asbestos content of its talc threatened its market, as several purchasers of its products had been advised by NIOSH to switch to other, safer materials. Vanderbilt, realizing it had missed its legal chance to comment on the regulations before they became law, put pressure on Congressmen Robert McEwen (R-N.Y.) and Jerry Pettis (R-Cal.) to help out. On June 20, 1973, McEwen wrote OSHA Secretary John Stender, "Should these mines be forced to close, you can readily understand that it would have a serious and adverse economic effect in that area."²²

Over the objection of his own Health Standards Chief, Standards Director Gerald Scannell encouraged Vanderbilt in December, 1973, to do its own sampling to determine whether or not their talc contained asbestos, and to advise their customers of the results of the tests. Vanderbilt took the hint and immediately redefined tremolite so as to exclude its classification as asbestos, even though it is clearly defined as such in the legal standard. Vanderbilt then notified its customers "that our talc products used in their manufacturing processes are not subject to the asbestos standard."

The illegality of this procedure came to a head after an OSHA inspector cited a Vanderbilt customer, Borg-Warner, for a violation of the asbestos standard on July 9, 1974. This involved a material purchased from Vanderbilt, Nytal, which was accompanied by "self-certification" that it contained no asbestos. The case went to the Occupational Safety and Health Review Commission, the

highest arbiter of OSHA cases. On June 28, 1976, Judge Jerry W. Mitchell, ruled against the company.²³ In the lengthy interim, OSHA issued a field directive supporting Vanderbilt's claim that its talc was asbestos-free, but failed to order its field operatives to enforce the directive.

The seriousness of this evasion is emphasized by the results of a NIOSH epidemiological investigation on workers at Vanderbilt's mines. This identified "both respiratory diseases and lung cancers which appear to be significantly above those expected."

Smoking and Occupational Exposure

Many epidemiological studies have indicated that asbestos workers who smoke have a much greater lung cancer risk than asbestos workers who don't smoke. Industry has argued that these studies prove that smoking and not asbestos is the real problem for asbestos workers, and that the development of lung cancer in these workers was their own fault for smoking. However, recent studies, including one by NIOSH in 1977, indicate that the smoking effect is less clear-cut than earlier reports suggested, and that non-smoking asbestos workers also have excess risks of lung cancer.²⁴ Additionally, smoking is unrelated to the risks of developing mesotheliomas which occur with equal and increased frequency among smoking and non-smoking asbestos workers.

The Asbestos "Pentagon Papers"

A new era in the history of asbestos has dawned with the discovery of a voluminous set of industry documents dating back from 1933 to 1945, dubbed the Asbestos Pentagon Papers.²⁵ These were obtained during pre-trial discovery proceedings in recently-proliferating product liability suits against the asbestos industry. The documents (which were publicly released in San Francisco at the October, 1978, hearings of the Subcommittee on Compensation, Health and Safety of the House Committee on Education

and Welfare) include correspondence among senior executives, lawyers, physicians, consultants, and insurance companies of Johns-Manville, Raybestos-Manhattan Inc., and other asbestos industries. According to South Carolina Circuit Court Judge James Price, the only judge to have reviewed the correspondence so far, "it shows a pattern of denial and disease and attempts at suppression of information" that is so persuasive that he ordered a new trial for the family of a dead insulation worker whose earlier claim had been dismissed. Judge Price noted that the correspondence "further reflects a conscious effort by the industry in the 1930s to downplay, or arguably suppress, the dissemination of information to employees and the public for fear of promotion of lawsuits." Judge Price also recognized compensation disease claims filed by asbestos insulation workers against several companies, which quietly settled them, including eleven asbestosis cases settled by Johns-Manville in 1933 to keep them out of a New Jersey court, "all pre-dating the time (1964) when these companies alleged they first recognized the hazard to insulators." Judge Price concluded that settlement of these claims "constitute compelling proof of actual notice to certain manufacturers that asbestos-containing thermal insulation products indeed caused disease in insulation workers."

The Asbestos Pentagon Papers afford unusual and detailed insight as to the mechanics of suppression and distortion by industry of information on the hazards of asbestos, as illustrated in the following series of incidents. By 1932, the British had fully documented the occupational hazard of asbestos dust inhalation.²⁶ On September 25, 1935, the editor of the trade journal *Asbestos* wrote Sumner Simpson, President of Raybestos-Manhattan, requesting permission to publish an article on the hazards of asbestos, and referred to the magazine's past acquiescence to the American industry's desires that this dirty linen not be publicly aired.

Always you have requested that for certain obvious reasons we publish nothing and naturally your wishes have been respected. . . . [However] discussion of it [the alleged asbestos hazard] in *Asbestos* along the right lines would serve to combat the rather undesirable publicity given to it in current newspapers.

While Simpson was unpersuaded, in a letter (October 1, 1935) to Vandivar Brown, Secretary of Johns-Manville, he praised the magazine for "not reprinting the English articles," and observed that "the less said about asbestos the better off we are . . ." Brown agreed and suggested that if an article on asbestosis had to be published, it should reflect "American data rather than English."²⁷

The American data referred to was a study by Anthony Lanza on behalf of Raybestos-Manhattan, Johns-Manville, and the Metropolitan Life Insurance Company, the insurance carrier for both manufacturers. The Lanza study, based on X-rays of 126 workers with three or more years asbestos exposure, was begun in 1929 and completed in late 1931, but the results remained unpublished until 1935.²⁷

Brown's confidence in the American (Lanza) data was well founded, as he and other industry officials and lawyers were to serve in an editorial capacity prior to its publication. Lanza submitted his galley proofs to Brown on December 7, 1934. Brown returned the galleys on December 10, 1934, commenting that Lanza had omitted from his final draft a sentence that had appeared in an earlier draft: "Clinically from this study, it [asbestosis] appeared to be of a type milder than silicosis." Hobart, Johns-Manville's New Jersey attorney, further explained in a letter to Brown (December 5, 1934) why Johns-Manville needed to portray asbestosis as a disease milder than silicosis. Referring to pending Workmen's Compensation legislation in New Jersey, Hobart stated that Johns-Manville opposed the inclusion of asbestosis as a compensable disease.

It would be very helpful to have an official report to show that there is a substantial difference between asbestosis and silicosis: and by the same token, it would be troublesome if an official report should appear from which the conclusion might be drawn that there is very little, if any difference, between the two diseases.

On December 21, 1934, Brown forwarded Hobart's suggestions to Lanza and asked that "all of the favorable aspects of the survey be included and that none of the unfavorable be unintentionally pictured in darker tones than the comments justify." Lanza

agreed, and in his eventual publication concluded that asbestosis was milder than silicosis. Presumably in the further spirit of cooperation, Lanza omitted reference in his paper to the findings that 67 of the 126 workers (53 percent) he had examined were suffering from asbestosis.

Seeking ammunition for courtroom use "against ambulance chasing attorneys and unscrupulous doctors" (memorandum Brown, January, 1933), Simpson wrote F. H. Schulter, President of Thermoid Rubber Co., on November 10, 1936, suggesting that several manufacturers jointly fund asbestos experiments at Saranac Laboratories (Trudeau Institute). Simpson allowed that the benefactors "could determine from time to time after the findings are made whether we wish any publication or not." The decision to publish, of course, being a function of the nature of the results of the study. "It would be a good idea to distribute the information to the medical fraternity, providing it is of the right type and would not injure our companies."

Conferences between industry and Saranac representatives culminated in a deal being struck whereby certain experiments would be conducted, with the decision whether or not to publish the scientific results resting entirely with the sponsors. In a letter of November 20, 1936, Brown emphasized to Leroy Gardner of the Saranac Laboratories:

It is our further understanding that the results obtained will be considered the property of those who are advancing the required funds, who will determine whether, to what extent and in what manner they shall be made public. In the event it is deemed desirable that the results be made public, the manuscript of your study will be submitted to us for approval prior to publication.

In a reply to Brown on November 23, 1936, Gardner agreed to accept the industry sponsors as the sole arbiters of publication of the results of the experiments. "The Saranac Laboratories agree that the results of these studies shall become the property of the contributors and that the manuscripts of any reports shall be submitted for approval of the contributors before publication." Even this arrangement was not watertight. On learning that Gardner was presenting papers which referred to his preliminary asbestos findings, Simpson complained to Brown (letter May 4, 1939):

"The reports may be so favorable to us that they would cause us no trouble, but they might be just the opposite which could be very embarrassing."

In a survey of a Johns-Manville Canadian plant in which seven workers were found to have asbestosis, the medical director, Kenneth W. Smith, deemed it inadvisable that the workers should be warned of their peril.²⁸

It must be remembered that although these men have the X-ray evidence of asbestosis, they are working today and definitely are not disabled from asbestosis. They have not been told of this diagnosis, for it is felt that as long as the man feels well, is happy at home and at work, and his physical condition remains good, nothing should be said. When he becomes disabled and sick, then the diagnosis should be made and the claim submitted by the *Company*. The fibrosis of this disease is irreversible and permanent so that eventually compensation will be paid to each of these men. But as long as the man is not disabled, it is felt that he should not be told of his condition so that he can live and work in peace and the *Company* can benefit by his many years of experience. Should the man be told of his condition today there is a very definite possibility that he would become mentally and physically ill, simply through the knowledge that he has asbestosis.

The Johns-Manville policy of refusing to advise workers of early evidence of asbestosis was characterized in a sworn statement on January 11, 1978, by Wilbur Ruff, a former plant manager, as a "hush hush policy" and one that persisted until the late 1960s.

The mid-1950s found the asbestos industry embroiled in Workmen's Compensation litigation with asbestos workers who were lung cancer victims. The escalating cancer claims moved Smith in March, 1956, to request the Asbestos Textile Institute retain the Industrial Health Foundation to conduct a cancer study which would enable industry to "procure information which would combat current derogatory literature." Smith suggested an alliance with the Quebec Asbestos Mining Association (QAMA) which was conducting a similar study. After agonizing over this proposal for over four years, the Asbestos Textile Institute finally rejected it in March, 1957, for the following reasons:

- (1) QAMA has a similar program;
- (2) There is a feeling among certain members that such an investigation would stir up a hornets' nest and put the whole industry under suspicion.
- (3) We do not believe there is enough evidence of cancer or asbestos in this industry to warrant this survey.

Perhaps the most graphic illustration of the corporate mores of Johns-Manville comes from the testimony of Smith before he died in 1977. In response as to whether he had ever advised Johns-Manville officials to place warning labels on asbestos containing insulation products, Smith replied:²⁹

The reasons why the caution labels were not implemented immediately, it was a business decision as far as I could understand. Here was a recommendation, the corporation is in business to make, to provide jobs for people and make money for stockholders and they had to take into consideration the effects of everything they did, and if the application of a caution label identifying a product as hazardous would cut out sales, there would be serious financial implications. And the powers that be had to make some effort to judge the necessity of the label vs. the consequences of placing the label on the product.

In June, 1963, Institute members obtained copies of Selikoff's cancer study of insulation workers,³⁰ (as described in Institute minutes of June 6, 1963, and October 8, 1964) and braced itself for the 1964 New York Academy of Sciences Symposia on Asbestos by discussing the retention of a "public relations man to get accurate publicity to the public."³¹ In minutes of a February 4, 1971, General Meeting of the Institute, an industry medical consultant labelled Selikoff a "dangerous man." To the question as to whether the American Medical Association might be able to control Selikoff, the consultant replied that "pressure" on Selikoff's hospital, Mt. Sinai, might be "effective."³²

In a report of September 23, 1963, by Thomas Mancuso to Phillip Carey Manufacturing Co., he emphasized that the asbestos-cancer relationship was beyond dispute, and that the company should warn all concerned.

Internally within the company the question has been raised as to why medical problems, particularly relating to cancer and asbestos were not recognized before. Actually, they were recognized, but the asbestos industry chose to ignore and deny their existence.

Phillip Carey responded by declining to renew Mancuso's contract, and failing to warn its workers and customers.

Legal Impact. These documents are likely to affect more than 1,000 asbestos-related lawsuits, totalling more than \$1 billion and involving more than one hundred different law firms all over the nation. Ronald Motley, a South Carolina attorney, who is informally directing these actions, has established an "Asbestos Litigation Group" for the purpose of disseminating information and coordinating this extensive litigation. While most plaintiffs have worked with asbestos for over thirty years, others include spouses who have contracted mesotheliomas from washing asbestos-laden clothes of workers, and a case involving Franklin Brooks, a former Georgia Tech All-American football player, who developed asbestosis although only exposed for three consecutive summers. The largest lawsuit to date was filed in Los Angeles in October, 1978, on behalf of five hundred present and former workers who contracted various asbestos-induced diseases at Todd Pacific Shipyards in San Pedro and the Long Beach Naval Shipyard. The suit asks for general and punitive damages, besides medical expenses and loss of earnings.

In the typical product liability or third-party insulator case (of which *Borel v. Fibreboard Paper Products Co.*, 493 F.2d 1076 [5th Circ. 1973] is precedential), there are often as many as ten defendants because the average worker has used products from that many different companies, such as Johns-Manville, Raybestos-Manhattan, Owens-Corning Fiberglas Co., Celotex, Pittsburgh-Corning Co., and Standard Asbestos Manufacturing and Insulating. Of pivotal importance is the question of whether the companies concerned knew about the hazards of asbestos products prior to the 1964 report by Selikoff on the high incidence of lung cancer, mesothelioma, and asbestosis in insulation workers,³³ when they claimed they were first made aware of this, and what use if any they then made of this information. The

primary defense in such cases is that there was no medical or scientific information on risks from asbestos-containing products prior to 1964. Additional lines of defense include statute of limitation exemptions, "contributory negligence" of workers, and their smoking. Johns-Manville's Kotin has been able to persuade the courts in four of five cases in which he has so far testified, that the pre-1964 studies were not definitive, thus absolving the industry from the need to have labelled their products and to have issued warnings. The asbestos "Pentagon Papers" are likely to diminish both the vigor of such arguments and the likelihood of their future success.‡

In September, 1978, at hearings before the Senate Human Resources subcommittee on labor on S.3060 (a bill designed to provide comprehensive reform of workers compensation programs including extended use of product liability suits to compensate workers or their heirs), Johns-Manville expressed the view that product liability suits were inadequate and inefficient methods of compensation. As an alternative, Johns-Manville proposed that government and labor join with industry to defray the costs of workers compensation through the creation at a state level of a "second injury fund" an alternative that industry, in general, is now vigorously supporting.

Public Exposure

In 1960 an alarming report came from J. C. Wagner in South Africa of sixteen new cases of the rare mesothelioma.³⁴ While six of these were in asbestos mine workers, none of the other ten had ever worked in the mines. All had lived in the vicinity of the mines, though, many as children. Public or non-occupational mesotheliomas have since been reported from nine other coun-

‡ In spite of these revelations, Johns-Manville devoted six of the fifty-two pages in its April, 1979, annual report to castigating the news media for its "sensationalized coverage" of asbestos-related health problems, which reflected "a very apparent antibusiness bias." In the following month Johns-Manville threatened Congressman George Miller (D-Calif.) with a libel suit if he repeated outside Congress statements he had made charging the industry with decades of "cover-up and lies" and failing to disclose the other workers' information on compensation settlements.

tries, including the United States. These cases are generally thought to be due to exposure of family members to asbestos brought home on the clothes of asbestos workers. Additional sources of exposure include contamination of the air with asbestos from nearby plants or factories. High concentrations of asbestos fibers have recently been demonstrated in communities adjacent to asbestos industries.

The indestructibility of asbestos, its indiscriminate use, and the careless disposal of its waste products make it difficult to predict the extent and level of exposure of the general public. For instance, Certain-Teed Products Corporation, an asbestos-cement pipe manufacturer, has in the past dumped about 2,700 tons each year of crushed asbestos pipe in an open-air landfill site in Ambler, Pennsylvania.

The dump not only snakes diagonally through the very center of the town, which has a population of 8,000, but it is fifty feet high, anywhere from one to two city blocks wide, and about ten city blocks long. In fact, it is estimated to contain some million and a half cubic yards of waste material . . . Kids play on an asphalt basketball court that has been built smack on top of material from the dump, and is literally covered with loose asbestos fiber and wads of waste material containing (chrysotile) asbestos.³⁵

Drinking water is an additional possible source of non-occupational exposure to asbestos. Reserve Mining Company, a subsidiary of Armco and Republic Steel, for years has been dumping taconite mine wastes, rich in asbestos fibers, into Lake Superior at levels of about 67,000 tons a day. Not unreasonably, this gave rise to fears that polluting the drinking water of Great Lakes communities with asbestos would lead to excess cancer rates, especially of the stomach and colon.³⁶

In April, 1974, Federal District Judge Miles Lord issued an injunction in Duluth, Minnesota, restraining the Reserve Mining Company from further dumping its taconite mine wastes into Lake Superior. Reserve Mining witnesses attempted to prevent this ruling by testifying that there were no alternatives to this lake dumping, although it appears that the company had developed plans for land disposal sites as early as 1970.

It is not yet known whether the resulting asbestos contami-

nation of drinking water of Lake Superior towns, including Duluth, will lead to cancer. Preliminary studies with laboratory animals have so far yielded ambiguous results. Certainly, it has been established that persons occupationally exposed to asbestos have an increased risk of alimentary tract cancer* as well as lung cancer. Without waiting for answers to these questions, a Federal Appeals Court reversed Judge Lord's decision, on grounds that it was not based on adequate proof of risks to health, and permitted Reserve Mining to resume dumping its tailings into the lake, pending the development of alternate land disposal sites.

In May, 1975, Congress approved \$4 million to build a water treatment plant in Duluth to filter out the asbestos fibers from drinking water. The State of Minnesota appropriated \$2.5 million in local funds for the project, which became operative in November, 1976. Reserve Mining is now phasing out lake dumping, and is building a land disposal site, in accordance with a court order that dumping is to be terminated by 1980.³⁷

In addition to environmental exposure to asbestos in air and water, the general public receives a wide range of further exposures.³⁸ Particularly important sources are construction operations involving the spraying of asbestos, the use of crushed stone containing unbound asbestos in roads and driveways, and demolition. Exposure to asbestos also results from its use in fireproofing and insulation, air ducts, automobile brake linings, cement water pipes, filter pads for beers, wine, and drugs, cosmetic talcs, and hand-held hair dryers. Resulting levels of public exposure can be high. For example, counts of 10 million fibers per cubic meter of air have been found in the vicinity of construction sites during asbestos spraying, and counts of 3 million fibers have been found in public buildings, and schools treated with asbestos as a fire retardant.^{†39}

* These include pharynx, esophagus, stomach, colon and rectum cancers.

† In May, 1979, the House Education and Labor Committee voted to establish a three-year, \$330 million program to detect and remove asbestos material from schools, where it had been widely used for soundproof ceilings and insulation from about 1960 to 1973, when its use was banned. Under heavy lobbying, the Committee voted against levying the industry for a \$30 million detection fund, but directed the Justice Department to investigate whether the government "should or could" sue the industry to recover all or part of the costs. Johns-Manville, which supplied the asbestos to the manufacturers and construction industries, contends that levels in

Regulation of Public Exposures

In an ineffective attempt to protect the general public from asbestos air pollution, EPA developed an emission standard for asbestos as a hazardous air pollutant in April, 1973. The standard, however, is only based on visible emissions and on poorly enforced work practices, and not on asbestos fibril counts.‡

Acting on a petition from a public interest group, the Natural Resources Defense Council, the Consumer Product Safety Commission announced in December, 1977, that patching and spackling compounds containing asbestos would be banned from the \$400 million market by June, 1978. Under the commission's order, fifty manufacturers ceased production in January, 1978, leaving retailers the next six months to clear their shelves. While these patching compounds are used primarily by professional builders, about 10 percent of the market is for home hobbyists and craftsmen.

The Future

Realization is gradually dawning that except under the most restrictive conditions all forms of asbestos have become too expensive in terms of human disease for commercial use. Further illustration of this are the individual and class action suits for asbestos cancer and disease, in the multimillion-dollar range now being filed by some of the four and one-half million workers employed in Naval shipbuilding yards during World War II.

The Navy has since abandoned the use of asbestos in shipbuilding in favor of alternative materials, including fiberglass. How-

schools are too low to cause cancer. Also in May, 1979, Gloria Zwerdling, a former school teacher, filed a \$2.5 million suit in Manhattan Supreme Court against fourteen corporations including Johns-Manville, claiming that she had contracted lung cancer from asbestos insulation used in schools.

‡ The only effective method of measuring community exposure to asbestos is by counting fibrils using electron microscopy, which in fact is rarely done. Results are expressed as a mass in nanograms per cubic meter.

ever, there are also reasons for concern on the use of fiberglass as an asbestos replacement. Experimental studies indicate that fiberglass, particularly the more modern short-fiber products which were introduced into large-scale use in the early 1960s, may produce a type of disease and cancer similar to that produced by asbestos.⁴⁰ Epidemiological studies are now only suggestive of an increased cancer risk, probably because exposed workers have not been followed up for the three or so decades it generally takes for asbestos fibers to induce cancer. Industry is attempting to quiet these concerns in moves which reflect the growing shift from asbestos to fiberglass for insulation and a wide range of consumer products, including draperies. An interesting insight into such tactics was afforded by a recent letter to *New Times* by Johns-Manville's Kotin, bearing no reference at all to his industry employment, protesting that "epidemiological studies show that there is no chronic health effect in humans as a result of exposure to fibrous glass."⁴¹

Apart from fiberglass, other possible replacements for certain asbestos applications include long inorganic fibers made from aluminum or zirconium, such as those manufactured by Imperial Chemical Industries of England.

Another area of growing concern relates to the emerging trend in the asbestos industry to relocate in lesser developed countries, such as Mexico and Taiwan, where their capital investment is welcomed and not restricted by governmental health and safety regulations.⁴²

On April 26, 1978, HEW Secretary Joseph Califano issued the most explicit warning ever made by government on the dangers of asbestos. Califano estimated that as many as half of all workers exposed to asbestos could develop serious diseases such as cancer of the lung and gastrointestinal tract, mesotheliomas, and asbestosis. Califano also estimated that from 8 to 11 million workers may have been exposed to asbestos since the start of World War II. Besides urging exposed workers to have a chest X-ray, HEW has sent a "physician advisory" letter regarding the dangers of asbestos to the nation's 400,000 doctors.* While Califano properly

* The gravity of the Califano statement has been underlined by preliminary findings in May, 1978, of lung abnormalities in 59 percent of 360 workers in northern California shipyards, and by the subsequent report that of 6,640

stressed the added danger of smoking to asbestos workers, an impression of "blaming the victim" appears to have been created by the absence of any balancing reference to the more urgent needs for control of exposures in the workplace.

Califano's statement appears to have been prompted by the growing number of lawsuits filed against federal agencies for having failed to notify workers in the past of the known hazards of asbestos exposure.[†] As such, Califano's statement is also important for what it failed to say. Workers were not informed of their rights to sue the government. Nor were any plans announced for organization of a surveillance program, including contacting and examining former government workers. Nor was any mention made of the long overdue need to implement the recommendation of NIOSH for a 100,000 fiber standard as the only meaningful way to protect against asbestos-induced cancers and disease. Finally, no mention was made of the growing evidence of the hazards to the public-at-large, particularly those living in the vicinity of asbestos plants, quite apart from exposures due to asbestos-containing consumer products.[‡]

In spite of all the problems of omission and emphasis in the Califano statement, its significance is epochal and unique. It opens the door of national health care policies to preventive medicine. Specifically, the statement recognizes in principle that prospective surveillance is needed for groups at high risk of cancer, although how this will be achieved for asbestos workers is still unclear. It is likely that the high costs of surveillance may well act as future incentives to reduce risks of occupational exposure to carcinogenic and other highly toxic agents, forcing the ultimate realization that prevention is cheaper than "cure."

workers who handled asbestos products for over seventeen years at the Long Beach Naval Shipyard, 31 percent are now suffering from asbestosis. In spite of Califano's warnings, as of January, 1979, neither NCI, NIOSH, nor any other agency has yet developed plans for the surveillance and examination of the millions of asbestos workers at risk.

[†] So far, about 1,000 asbestos law suits have been filed and some 500 asbestos workers have collected \$20 million in damages, including \$5 million from the federal government.

[‡] Effective regulation of the countless asbestos-containing consumer and industrial products must necessitate complete inventorying and material balance audits of all asbestos imported, mined, processed, and fabricated in the U.S.

Summary

While the dangers of asbestos have been well recognized for over five decades, the industry was able to largely ignore or suppress these until studies in the 1950s by Doll in England and by Selikoff in the U.S. (sponsored by the asbestos insulators union) established the relationship between asbestos and asbestosis and cancers at various sites. Since then the industry has employed scientific expertise to advocate its position in professional journals and to successfully resist and prevent effective government regulations. With an estimated 8 to 11 million workers having been exposed since World War II, the toll of asbestos occupational disease and cancer is now reaching epidemic proportions. Workers have begun to exercise legal initiatives, including third-party and medical malpractice suits, resulting in multimillion dollar awards.

Concerns are also mounting on the dangers to the public from "low-level" asbestos contamination of air and water and from asbestos-containing consumer products such as hair dryers.

As the realization is dawning that asbestos is too expensive in terms of disease and death to continue using, the industry is beginning to develop the strategies of relocating in lesser developed countries and promoting the use of fiberglass as an asbestos substitute in the United States. There are serious unresolved questions as to the dangers of fiberglass and there are possibilities that it may be no less hazardous than asbestos.

The massive human toll taken by asbestos is probably the single most important incentive to the development of coherent national policies recognizing preventive medicine as a major future component in the delivery of health care.

Vinyl Chloride

One of the most common pejoratives applied to modern times is "the plastic age." And just as age-old natural materials like wood,

glass, and metal have been replaced by cheaper synthetic plastics, this seems to imply, so has the value of our lifestyle been degraded. Many things we now touch or use daily are made of plastic. Yet the plastic transformation of our society has only taken place over the last forty years. The consequences to society of its plasticization, in terms both of high energy and health costs, have only recently been appreciated. One of the major costs is from cancer.¹

Manufacture

Plastics are the leading product of the modern petrochemical industry. This era of plastics dawned in the 1930s with the realization that petroleum was the cheapest and simplest starting material for the synthesis of the vast array of organic chemicals now used by modern industry. Petroleum then gradually replaced coal, which had been previously used for this purpose, and is now almost the exclusive basis of the organic chemical industry.

Vinyl chloride (VC) lies at the heart of the plastics industry. VC was first discovered in 1837. Large-scale production, however, did not start until the 1930s, when it was synthesized from chlorine and ethylene, largely for the manufacture of synthetic rubber.² Production levels increased rapidly after World War II at a rate of 15 percent per year, reaching a total of about 7 billion pounds this year.

VC is a simple chemical consisting of a small single molecular unit (a *monomer*) which is normally a gas but can be shipped and stored as a liquid under pressure. VC reacts under conditions of heat and pressure and in the presence of plasticizing chemicals to form large molecular chains (*polymers*) of polyvinyl chloride (PVC) resins. The polymerization of the VC monomer never proceeds to completion, but always leaves some unreacted VC entrapped in the PVC resin. Depending on the production process, this unreacted VC has concentrations ranging as high as 8,000 parts per million (ppm).³ This residual VC can be dissolved out of the polymer or released by heating it.⁴

PVC resins are molded, injected, and extruded in the fabrication of a wide array of plastic products. These include phono-

graph records, wire and cable insulation, floor coverings, garden hose, furniture, upholstery fabrics, car bodies, coating of fabrics and wallpaper, containers, bottles, and food wrappings. It is difficult to get an accurate count of the number of U.S. workers involved in all the various stages of PVC production. There are about seventeen VC manufacturing plants, employing about a thousand workers, and forty PVC plants, employing about six thousand workers.⁵ There are no figures available, however, on the number of fabricating plants or on the number of their employees. These must run into the hundreds of thousands.

Suppression by the Industry of Data on the Carcinogenicity of Vinyl Chloride

In May, 1970, an Italian toxicologist, Pier Luigi Viola (employed by Solvar Manufacturing Corporation), reported at an international cancer congress in Houston, Texas, that long-term intermittent exposure of a small group of rats to 3 percent of VC in air (30,000 ppm) resulted in the production of cancers in a wide range of organs.⁶

This first report on the carcinogenicity of VC created little impact because Viola had claimed that the type of tumors induced were peculiar to rats and without human significance, and also because of the very high levels of VC to which the rats were exposed. In fact, Viola had induced tumors at much lower concentrations, extending down to less than 5,000 ppm. These facts were discussed in detail at a Manufacturing Chemists Association meeting in November, 1971, where it was concluded that they should not be published, as this would otherwise "lead to serious problems with regard to the vinyl chloride monomer and resin industry . . . and force an industrial upheaval via new laws or strict interpretation of pollution and occupational health laws."⁷ Union Carbide further expressed its concerns that in view of the large stake it had in "areas most likely to be affected, such as food, food packaging, fiber and aerosols [it] would be seriously hurt by arbitrary or panic-induced government restrictions."

Prior to this, there had apparently been no studies in the plastics industry on the possible carcinogenicity of VC, although tens of thousands of workers the world over had been exposed to it for

over three decades and at least seven fatal cases of liver cancer had occurred in VC/PVC workers prior to 1970.⁸ Disturbed by Viola's public report, a consortium of giant European chemical industries, led by Italy's semi-governmental Montedison, and with contributions from British, Belgian, and French firms, financed a major study initiated in July, 1971, by Cesare Maltoni of the Bologna Cancer Institute.*⁹ An extensive series of tests were conducted in which adult, infant, and pregnant mice, rats, and hamsters were exposed to VC in inhalation chambers at concentrations ranging from the relatively low 50 ppm level to the toxic 100,000 ppm (10 percent) level. By late 1972, Maltoni had confirmed and extended Viola's results. VC was shown to be a potent carcinogen, inducing a rare type of liver cancer (called angiiosarcoma), as well as more common liver cancers (hepatomas) and cancers of other organs, including kidney, brain, and lung. The cancers were subsequently found even at the lowest level then tested, 50 ppm. The overall tumor incidence was concentration-dependent, with higher doses increasing the incidence and rate of development of the cancers.¹⁰

In October, 1972, the Manufacturing Chemists Association, the major trade association of the U.S. chemical industry, entered into an agreement with the European consortium to share their information, but not to disclose it without prior consent.¹¹ In January, 1973, the U.S. industry representatives visited Maltoni and were given full details of his experimental studies. The Manufacturing Chemists Association (and Maltoni) subsequently failed to disclose this information, in spite of the fact that NIOSH, in the same month, had publicly requested all available data on the toxic effects of VC. In March, 1973, the Manufacturing Chemists Association recommended to NIOSH a precautionary label for VC that made no reference to toxic or carcinogenic effects on animals or humans.

Four months later, however, representatives of the Manufacturing Chemists Association met in secret with Marcus Key, then Director of NIOSH and now Professor of Occupational Medicine at the University of Texas, Houston, and a small group of his sen-

* An additional reason for initiating these tests, revealed by Maltoni in 1975, was his hitherto undisclosed finding in 1969 of malignant cells (of a large cell adenocarcinomatous type not seen in smokers) in the sputum of VC/PVC workers, suggestive of early lung cancer or pre-cancerous changes.

ior staff. They were informed that Maltoni had induced tumors in rats exposed to VC levels of 250 ppm. At one stage of the meeting, an industry representative, V. K. Rowe of Dow Chemical Company, adjourned to a separate office for a private meeting with Key.¹² Rowe subsequently commented that "this private discussion of the carcinogen problem was worth the whole effort." Finally, industry concluded that as a result of a meeting "the chances of precipitous action by NIOSH on VC was materially lessened. NIOSH did not appear to want to alienate a cooperative industry or they did not want to know too much unpublished data."

In March, 1973, following complaints of an unpleasant taste, Schenley Distillers found 10-20 ppm levels of VC in their liquors sold in PVC bottles. On the basis of these findings, and still knowing nothing about the carcinogenicity data, FDA then banned the use of these liquor bottles. In December, 1973, the Society of Plastics Industry, the plastics industry trade association, provided the FDA with data on migration of VC from PVC containers to food, but made no reference to problems of carcinogenicity.

On January 22, 1974, B. F. Goodrich announced that since 1971 three PVC workers in their Louisville, Kentucky, plant had died of angiosarcoma of the liver. On that same day, the Manufacturing Chemists Association revealed the by now fifteen-month-old Maltoni data to NIOSH.

According to a recent special committee report of the American Association for Advancement of Science, the Manufacturing Chemists Association "appears to have deliberately deceived NIOSH regarding the true facts. . . . Because of the suppression of these data, tens of thousands of workers were exposed without warning, for perhaps some two years, to toxic concentrations of vinyl chloride."¹³

Distortion by the Industry of Data on the Carcinogenicity of Vinyl Chloride

The first published case reports of angiosarcoma of the liver in VC/PVC workers generated an intensive epidemiological investi-

gation of cancer mortality in the industry in several countries. A British Petroleum Corporation study, published in *Lancet* in 1975, claimed that the longer one worked in a VC plant, the less was the risk of getting cancer.¹⁴ Closer examination by NIOSH, however, questioned the interpretation of the English data. Expected death rates in workers exposed to VC for fifteen or more years were artificially reduced, and rates in workers with lesser exposures were artificially inflated. Re-analysis of the data by NIOSH, using standard methods, showed a clear excess of mortality from all causes and all cancers, including digestive system and lung cancers, besides angiosarcoma of the liver (Table 5.3).

Exaggeration by the Industry of the Costs of Regulating Occupational Exposure to VC

As information on the carcinogenicity of VC began to surface, OSHA was prodded into action. On April 5, 1974, OSHA reduced permissible exposure levels from 500 ppm to a new emergency standard of 50 ppm. Under pressure from labor and independent scientists, who insisted that the new standard was too high for safety, on May 10, 1974, OSHA proposed a VC standard "at no detectable level" (in the range of 0 to 1 ppm) to be achieved by the use of engineering controls, rather than worker use of respirators. Faced with strenuous industry opposition and alarming economic impact analyses, OSHA did not proceed to adopt this standard, but on October 4, 1978, instead issued the more lenient final 1 ppm standard.¹⁵ Even at that time, however, it had been shown that exposure of small numbers of rats to 5 ppm VC induced an increased incidence of cancer, and there was no evidence then (or now) of any safe exposure level for VC, or indeed to any other carcinogen.†

Nevertheless, industry objected strongly to the "no detectable level" proposal on the grounds that it was unnecessary, too expensive, and beyond their compliance capability. To bolster these claims, contracts were given out by the Society of the Plastics In-

† Later studies by Maltoni and others demonstrated carcinogenic effects, including breast cancer, in rodents following inhalation of VC at levels as low as 1 ppm.

Table 5.3 Comparison of Causes of Death in VC Workers Reported by British Petroleum (BP) and Recalculated by NIOSH

Cause of Death, Reported by BP and Recalculated by NIOSH	Standard Mortality Ratios* for Workers Exposed to VC for Varying Times		
	Years of Exposure		
	9 or less	10-14	15 or more
All causes			
BP	112	107	61
NIOSH	79	137	353
All cancers			
BP	123	58	73
NIOSH	86	76	428
Digestive system cancer			
BP	106	47	121
NIOSH	75	62	702
Lung cancer			
BP	129	101	62
NIOSH	90	133	366

Source: J. K. Wagoner, P. F. Infante, and R. Saracci, "Vinyl Chloride and Mortality," *Lancet* 2 (1975): 194-95.

* Values greater than 100 indicate excessive deaths relative to expected population values.

dustry, Inc. to Arthur D. Little, Inc., of Cambridge, Massachusetts. Also, OSHA gave out a contract to Foster D. Snell, a division of Booz, Allen and Hamilton, for the purpose of estimating the economic impact of the new standard. The consulting firms predicted costs as high as \$90 billion and losses up to 2.2 million jobs, persuasive arguments in the depressed economic climate of 1974. However, these estimates were shown by the subsequent experience of the plastics industry to be gross exaggerations.¹⁶ In spite of massive industry lobbying and pressures, OSHA stood firm on the new 1 ppm standard, which was passed on April 1, 1975.

The Society of the Plastics Industry then petitioned the 2nd Circuit Court of Appeals to review the 1 ppm final OSHA standard stating:

The evidence clearly demonstrates that the Standard is simply beyond the compliance of the industry. . . . The general increase in raw materials costs (an unavoidable result of this Standard), and the costs of monitoring, respiratory protection, medical surveillance and record keeping all militate against the likelihood that the bulk of this segment of the industry would be able to survive economically. The evidence is clear (that these various industries) would at the very least suffer economic disaster if not close down completely.

Within one year, the VC/PVC manufacturing industry had successfully met the new standard, and without any major economic dislocation or plant shutdowns. B. F. Goodrich, one of the industry giants, redesigned its manufacturing technology to enclose VC manufacturing and handling processes and plug possible sources of leaks. Additionally, a "stripping" process was developed to reduce levels of the unreacted VC monomer in the PVC resin and to decrease VC loss in the process. The initial capital costs of the compliance technology were only \$34 million. Contrary to the estimates of the industry consulting firms, B. F. Goodrich found that the new clean-up technology actually cut labor costs and could be profitably leased. (In spite of this, B. F. Goodrich increased the price of its PVC products in 1976, claiming higher production costs and blaming these on regulatory standards.) The experience of Union Carbide is similar. In late 1975, R. N. Wheeler, a senior technical official expressed surprise as to how unexpectedly easy it had been for his company to comply with the 1 ppm standard. However, earlier intercompany reports had documented the economic advantages of compliance through recovering and recycling VC which would have otherwise been discharged into the environment. Estimates of the economic impact of compliance had ignored the major costs to industry from losses of VC gas, with resulting air pollution of the plant and adjacent community. They had also ignored or discounted the major costs to society, both direct and indirect, from failure to regulate, with resulting VC-induced disease. Finally, these estimates did not reflect the emergence of a small and booming industry manufacturing the monitoring equipment now required to meet OSHA regulations.

It is clear that, despite uniform and overwhelming protestations and prophecies to the contrary, the industry had no major difficulty in meeting the 1 ppm standard. It is also clear that the industry is flourishing with high production, strong demand, growing capacity, and steady prices. The slump in the PVC market in 1974 and 1975, reflecting the 1973 oil embargo and a general pattern of recession, has been replaced by a boom, well recognized in chemical trade publications since 1976. (See for instance, *Chemical and Engineering News*, July 24, 1978, p. 12, and September 4, 1978, p. 13.)

Cancer and Other Diseases Due to VC

Long before the 1974 reports of angiosarcoma in VC/PVC workers, VC was known to be toxic to experimental animals and to humans at relatively high concentrations. Studies on experimental animals in the early 1960s, by Dow Chemical Company and others, established that VC induced toxic effects in the liver and kidney at concentrations as low as 500 ppm, then the U.S. occupational standard.¹⁷ At higher levels skin and bone abnormalities were also noted.

Acute toxic effects, such as headaches, disorientation, dizziness, drowsiness, and loss of consciousness had been noted in VC/PVC workers as long ago as 1949.¹⁸ In the same year, the Russian scientific literature reported the occurrence of chronic gastritis, hepatitis, and skin lesions from VC exposure. In 1957 there appeared the first report of a new occupational disease among vinyl plastic workers called acroosteolysis, characterized by a thickening or clubbing of the fingers and toes, spasmodic contraction of the blood vessels, painful bone changes, and arthritis of the knuckles. Additional cases of acroosteolysis have since been noted from plastic plants all over the world. By 1966, it was recognized that liver damage, hepatitis and cirrhosis, was common among VC/PVC workers and in some cases occurred after only one or two years of employment.

Since 1974, seven independent retrospective epidemiological studies have identified over seventy deaths from angiosarcoma of

the liver in VC/PVC plants in the United States and elsewhere.[‡] While most have involved polymerization workers, others have occurred in workers exposed to lower concentrations of VC, including four cases in PVC fabricating plants, where PVC levels were probably below 10 ppm. Cancers at various other sites including the lung, brain, kidney, and digestive tract, besides lymphomas and leukaemias, have also been found in VC/PVC workers.* The lung cancers were mainly of a type (adenocarcinoma and undifferentiated large-cell) not generally associated with smoking, and were found in workers engaged in a wide range of VC/PVC operations, including PVC milling and packaging. While the occupational exposures preceding these various cancers have generally ranged from thirteen to twenty years, there have been four reports of liver angiosarcoma following less than six years of exposure. The true incidence of VC/PVC cancers in exposed workers is still unknown, because of considerations of latency, and also because of the ever-increasing number of cancers reported in organs other than the liver, which can no longer be considered the exclusive or even predominant site of VC/PVC-induced cancers.¹⁹ It should be noted that the wide range of VC cancers found in workers is, in general, similar to the types and distribution of cancers induced in animal tests.

Despite the growing evidence of chronic human disease and the many thousands of workers at risk worldwide, the industry failed for more than thirty years to undertake any carcinogenicity tests in animals. Such tests could as easily have detected the carcinogenic effects of VC in the 1940s as they eventually did in the 1970s.

There are still elements of the academic community who minimize the risks of VC exposure. A recent brochure from the University of Louisville's Vinyl Chloride Project, a multimillion dol-

[‡] At least seven fatal cases of primary carcinoma of the liver, subsequently diagnosed as angiosarcoma, had been recognized in VC/PVC workers before 1970. Six of these cases occurred in the United States between 1961 and 1968, and the other in Sweden.

* An excessive incidence of brain tumors (glioblastoma multiforme) has been noted among VC workers in Union Carbide and Monsanto plants in Texas City, Texas, and is now being investigated by OSHA and NIOSH. There have been ten deaths from the brain tumor among workers at the Carbide plant since 1962.

lar NCI-funded program for the prevention and detection of VC-induced occupational cancer and other diseases, states:

The low incidence of cancer development among people with prolonged exposure to vinyl chloride is a reflection of the body's ability to remove the chemical agent safely without developing cancer. Some individuals do not have this capability and develop cancer after years of exposure.²⁰

The brochure makes no reference to the fact that the present apparent "low incidence of [VC] cancer" may simply reflect its long latency period. Additionally, the independence of this University project has been questioned following recent disclosure of its receipt of undisclosed support from the Manufacturing Chemists Association.†

Cancer and Other Diseases Due to PVC

While in the past concerns have focused on VC itself as the major toxic and carcinogenic agent to VC/PVC workers, there is growing realization of other serious hazards posed by PVC dust to far greater numbers of workers in operations involving the packaging and milling of PVC, and its fabrication into innumerable plastic products. These hazards most probably reflect the presence of unreacted VC entrapped at concentrations up to about 1 percent (10,000 ppm) in the PVC resin or products, and which can be released by their heating or processing, or can be dissolved from inhaled PVC dust by tissue fluids. Additionally, VC gas can be absorbed on PVC or on other dusts which may act as inert carriers.

Experimental studies have shown that inhalation of PVC dust or its instillation into the lungs of rodents can induce acute inflammation followed by chronic granulomatous changes. Similarly, a wide range of abnormalities has been recognized in the lungs of workers exposed to PVC dust in a variety of operations involving bagging and packaging of PVC resins and their fabrication of PVC

† This was admitted at an NCI site visit meeting at the University of Louisville on September 26 and 27, 1977.

products, where dust levels have been found to range as high as 20 mg/m³, and where the dust may be so fine that most is inhaled deep into the lungs. The lung abnormalities reported include reduction of lung function, radiological changes, and chronic lung disease (pneumoconiosis). "Meat-wrapper's asthma" is a possibly related problem well recognized among supermarket and wholesale meat workers who, in packaging cuts of meat, use a "hot wire" or "cool rod" to cut and seal the sheet of Saran Wrap‡ or other PVC plastic film used for wrapping.²¹ In the cutting process, particularly when high temperatures are used, irritant fumes, including hydrochloric acid, are given off. While the industry has readily ascribed the asthma to such irritants, it is not yet known whether there are any carcinogenic hazards posed by unreacted VC, or other related carcinogenic agents, such as vinylidene chloride, which may be liberated from the plastic film by the heat cutting.

More ominous than the inflammatory lung changes, an excess frequency of cancer deaths has been reported in four retrospective epidemiological studies of workers predominantly exposed to PVC dust.²² These include lung cancer (of the same type as described in VC workers), and cancers of the urinary tract, digestive system, and lymphatic system.

Public Exposure to VC

The public and the regulatory agencies are now beginning to realize that what goes on in a plant often affects the health of those living nearby in the community. The closer you live to a plant manufacturing VC or PVC or fabricating PVC products, the more VC you are likely to breathe. EPA has estimated that 4.6 million people live within five miles of VC/PVC plants.²³ No estimates are available for the presumably greater number of people living near the uncounted PVC fabricating plants scattered over the country. Measurements by EPA in 1974 and 1975 indicated that in 90 percent of cases, VC levels in the vicinity of VC/PVC

‡ Saran Wrap, a product of Dow Chemical, is a co-polymer of VC and the related vinylidene chloride, which has recently also been shown to be carcinogenic in rodents, inducing angiosarcoma of the liver in addition to other cancers.

plants were below 1 ppm; EPA estimated that average exposure within a five-mile radius would be about 17 parts per billion (ppb). Higher levels, however, were found in 10 percent of communities sampled—33 ppm at a distance of one-third of a mile from the center of one plant.

EPA also estimated that VC/PVC plants were losing 220 million pounds of VC into the air annually, mainly from PVC plants. These considerations, together with reports of excess birth defects in Ohio women living near VC/PVC plants, prompted EPA in October, 1976, to propose regulating VC as a "hazardous air pollutant" and to limit plant emissions to 10 ppm. These regulations would be expected to reduce VC emissions by about 95 percent of previous levels and to reduce community exposure by a similar amount. However, no regulations have yet been developed for plants fabricating PVC products nor for municipal incinerators, which discharge VC into the air from thermal processing and combustion of plastic products, respectively.

The results of a June, 1977, EPA investigation of an elementary school in Saugus, California, located across the road from Keysor-Century Corporation, which manufactures PVC and phonograph records, are disturbing.²⁴ Levels as high as 2.8 ppm VC have been measured in the air in classrooms. This heavy contamination largely results from VC losses during tank car unloading at the plant in the night.

The occurrence of VC disease in the general population has been suggested by preliminary findings of an incidence of 18 congenital malformations per 1,000 live births in women living in three Ohio communities near PVC plants, in comparison with an incidence of 10.5 per 1,000 in those living at a distance.²⁵ Most of these malformations were of the brain. In addition, an excessive number of brain tumors in adult males were found in those communities near the PVC plants. A similar excess of birth defects over a period from 1966 to 1974, has been recently noted in Shawinigan, Quebec, where a large VC/PVC plant is located.*²⁶

* More recently, five cases of angiosarcoma of the liver have been reported in women who have lived for prolonged periods close to VC polymerizing or PVC fabricating plants, and who have never worked in these plants or been exposed to other carcinogens known to induce angiosarcoma (such as arsenic or thorium dioxide).

These various effects have been associated with the detection of VC in the air of communities adjacent to VC/PVC plants.

Another way in which the public has been exposed to VC is from aerosol propellants in consumer products such as insecticides, hair sprays, disinfectants, and furniture polishes.²⁷ EPA studies show that during use of hair or insect sprays, users breathed VC in the 100 to 400 ppm range. After much prodding, the FDA banned the use of VC as a propellant in cosmetic products, including hair sprays. However, the FDA did not consider the matter serious enough to order a recall of VC-containing products so that the public could avoid further exposure. The Health Research Group eventually pried out from the FDA the brand names of hair sprays that used VC as a propellant, identifying Clairol as a top selling product. According to a recent survey by Consumer Product Safety Commission staff, no new consumer products containing VC have been manufactured since 1974, and no VC-containing products remain on the market in 1978.

The FDA also showed reluctance in moving against the use of PVC containers for food products, although it was aware that unreacted VC was leached out of the container walls by the foods or fluids inside. By 1974 the FDA knew that VC levels as high as 9 ppm had been found in vegetable oils sold in rigid PVC containers.²⁸ High levels were also found in other PVC-packaged products, including beverages and cosmetics. While the FDA proposed a ban on the use of rigid PVC containers for food products and beverages, the use of PVC film for wrapping foods is still sanctioned.

Extensive research is now being done by industry with the object of reducing VC levels in PVC products, especially those intended for food packaging and medical applications.²⁹ However, as indicated in a recent trade journal article, the prospects of success seem slim:

At present conventional devolatilizing techniques cannot be successfully offered to PVC. . . . It cannot be expected, however, that a completely monomer-free PVC resin will be a commercial reality in the near future.³⁰

Summary

Vinyl chloride (VC) is a simple gaseous chemical which can be polymerized to form a wealth of plastic materials. Despite recognition for several decades of a wide range of chronic toxic effects in animals and exposed workers, it was not until 1970 that the carcinogenicity of VC was first established experimentally. A consortium of European plastics manufacturers then funded further carcinogenicity testing of VC which confirmed and extended the earlier findings. These results, which were shared with the Manufacturing Chemists Association, remained unpublished for over eighteen months until the announcement by B. F. Goodrich in January, 1974, of the occurrence of three fatal cases of an extremely rare cancer, angiosarcoma of the liver, among its VC/PVC workers. On the same day, the Manufacturing Chemists Association revealed the results of tests showing VC to be a potent carcinogen in rodents, inducing angiosarcoma of the liver and a wide range of cancers at other sites at exposures of 50 ppm and below.

In the absence of available information on the carcinogenicity of VC in animals, its effects in exposed workers were only finally recognized because of the occurrence of the three rare angiosarcomas of the liver. Had VC only induced lung cancer, its carcinogenicity would in all probability have remained unrecognized or ascribed to smoking.

The present occupational standard of 1 ppm was promulgated by OSHA in spite of estimates by industry of grossly exaggerated costs and unemployment. While the standard affords some degree of protection to workers in VC/PVC plants, it is clearly excessive. Furthermore, it does not protect the greater number of workers in PVC packaging and fabricating plants, nor does it prevent exposures to VC of the public-at-large, particularly those living in the vicinity of VC/PVC plants, with attendant risks of cancer and also possibly birth defects.

Quite apart from VC itself, there has been recent recognition of

the carcinogenic hazards of exposure to PVC dusts in a wide range of operations involving bagging and packaging of PVC resins, and their formulation into innumerable plastic products.

My own company is very conscientious and careful about the chemicals we use in the manufacturing process.

Ellington M. Beavers, Medical Director and Vice President, Rohm & Haas Company, 1974.

Bischloromethylether

It is surprising how quickly the scandals of yesterday become today's respectable textbook classics. A standard 1975 medical text, *Occupational Medicine*, contains the following matter-of-fact account of the discovery of bischloromethylether (BCME) as a potent human carcinogen:

[Dr. William Figueroa] reported on lung cancer found in chloromethylmethylether workers and suggested another occupational hazard that increases the risk of lung cancer. They surveyed and studied a chemical manufacturing plant with approximately 2,000 employees where periodic chest X-ray surveys had been carried out for many years. In 1962, management became aware that an excessive number of workers suspected of having lung cancer were reported in one area of the plant, and promptly engaged consulting services to identify and resolve what appeared to be a serious problem.¹

Claims of "prompt" action by this company, Rohm and Haas (R&H), one of the world's dozen largest chemical manufacturing companies, have often been reiterated in the medical literature. The facts prove the contrary. As shown, among others, by Phila-

adelphia *Inquirer* reporters William Randall and Stephen Solomon in the award-winning investigative book, *Building Six*, the response by R&H was not prompt.² As documented in the book, the company did its best not only to obstruct studies of the lung-cancer outbreak, but also to discredit those studies.³ Finally, R&H tried to block protection of other workers by fighting against adequate exposure standards for BCME and other occupational carcinogens.⁴

Discovery of BCME

BCME was developed in 1948 by R&H chemist Robert Kunin at the company's Bridesburg laboratories in Pennsylvania. Attempts to scale up the laboratory process to a 100-gallon batch, however, revealed that BCME was intensely caustic, so much so that it virtually destroyed the plant machinery. By 1950, BCME was replaced by the closely related chloromethylmethylether (CMME), which in its industrial form contains from 1 to 7 percent BCME as a contaminant. Based on BCME and CMME, R&H chemists developed manufacturing processes for ion-exchange resins and promoted their application in various technologies, including water purification, and fabrication of nuclear weapons and fuel for power plants.

The scale-up of the BCME manufacturing process is typical of the way in which industries move newly developed technology from the laboratory to the production line. BCME is not an end-product chemical, but an intermediate which is produced and used at the production site during synthesis of ion-exchange resins. In 1948, after R&H chemists were convinced they had developed a valuable material, the first stage of large-scale production commenced in the "semi-works," so-called because it was a sort of half-way house for testing chemical processes on a larger scale than the laboratory.

As long as BCME synthesis had been confined to the laboratory, work proceeded under ventilated hoods, which drew toxic fumes up and away from the chemist. At the semi-works, however, there was no such ventilation. And the chemical was

prepared not in test-tube quantities but in 100-gallon batches in open kettles that continued to be used after BCME was replaced by CMME in 1950.

In 1954, the process was moved from the semi-works to building 6, a windowless five-story building also used for the manufacture of insecticides such as Rothane, a mainstay of R&H's operations. Randall and Solomon quote an R&H spokesman's description of the CMME process in building 6:

The operation started at the top floor, where the CMME was actually manufactured by shovelling paraformaldehyde flakes and aluminum chloride into kettles of hydrochloric acid. There were a good bit of fumes from the aluminum chloride, a fine powder, as soon as the air hit it. The kettle had to be charged quickly or it would become gummy. The men would cough, then turn away. . . . Then the CMME would go down a chute to the level below, where agitators would mix it in kettles that men would have to open from time to time so they could check on its progress. When they did lift the lids, vapors came rolling up at them. Then the mixture was dropped to the level below, where water was poured in on top to quench the reaction. This time, when the men hit the switch on the agitator, the fumes billowed out and they would have to run from the building gasping for air, then wait to go back in again.⁵

One of the insecticide workers who shared the building with the CMME process, was quoted:

When the CMME fumes hit the floor, it was like a London fog. Everybody had to run outside to breathe. It was so goddamn hot in there you couldn't wear a mask. They were old rubber masks and you couldn't get your breath through them and so whenever there was a spill, and it happened a couple of times a day when the foreman pushed the men a little and they added the flakes a little too fast, everyone in the whole building got a shot. And if you tried to smoke after getting a shot of that stuff, it made you puke.⁶

Medical Problems

By 1962 it had become obvious that there was something wrong at R&H. Fourteen BCME workers had died of lung cancer in the

preceding seven years. Their average age at death was 50, ten years younger than the average age of death of lung cancer victims. Among these was a woman of 28 and men aged 33, 38, 41, 43, and 49. The national death rate for lung cancer in white males in that age group was then about 15 per 100,000. To have seen even one or two lung cancers in workers under 50 in a 2,000-person plant should have immediately alarmed the company.

R&H claims that it "warned" its employees about the possibility of the cancer risk as soon as it knew. None of the employees has ever recalled any such warning. A memorandum, which the company maintains was read to small groups of its employees in 1962, contains a cryptic reference to "our concern over the cases of cancer that have appeared among building 6 personnel." It is clear however, that the main thrust of the memorandum was different:

The personnel department is currently in the process of making arrangements for the next chest X-ray survey of the Bridesburg employees . . . During several of these surveys, cases of TB (tuberculosis) have been uncovered, and as a result, people who worked around these individuals have been and are now being checked to be sure they have not contracted the disease.⁷

"Making arrangements" refers to the company's consultation with Katherine Boucot Sturgis, a well-known Philadelphia chest specialist, who for several years had been X-raying some Bridesburg employees as part of the Philadelphia Pulmonary Neoplasm Research Project. Sturgis' advice came in two parts. First, she agreed to add the entire building 6 and semi-works personnel to her yearly project X-rays, although this was never in fact done. Second, she recommended R&H to contract with Norton Nelson of New York University, to do carcinogenicity tests on BCME. Sturgis agreed to turn over all her findings directly to the company, but none of her patients, the workers, seems to have received any warning from her or the company.†

† Recently juries have awarded damages in lawsuits against company-retained doctors who concealed medical findings from employees. They rejected company arguments that, since the company bought the medical service, only they were entitled to know the results of the examinations.

Animal Experiments

The negotiations between R&H and Nelson over company sponsored carcinogenicity tests on BCME collapsed after two years, apparently over Nelson's insistence on permission to publish any findings. After another year's delay R&H instead contracted with Hazleton Laboratories, a commercial testing company, to do carcinogenicity tests on BCME, CMME, and other chemicals in use at the Bridesburg Plant. By 1966, Hazleton reported that BCME and CMME, as well as some of the other chemicals, were carcinogenic.

Meanwhile, the New York University team had also begun a study of the carcinogenicity of BCME and CMME using government funds. By 1971 they found that BCME was one of the most potent carcinogens ever tested.⁸ At 0.1 ppm in the air they breathed, rats developed a high incidence of lung cancers.

Human Experimentation

Between 1962 and 1968, when the screening phase of the Philadelphia project ended and the X-rays stopped, workers continued to die. Although their impending deaths were often picked up on X-rays, too late to save them, no meaningful effort was made to prevent further exposure. The X-ray reports were sent to the R&H medical office and were simply filed away. Even in 1968, one of the Philadelphia project physicians noted an excess of R&H lung cancer deaths, but failed to draw any conclusions, not having been told of worker's exposure to the carcinogenic BCME in the semi-works and building 6.

Then, in 1971, one of the workers with lung cancer was referred to William Figueroa, an internist at the Germantown Dispensary and Hospital near Philadelphia for treatment. Figueroa was surprised to find that this worker had never smoked, since the type of lung cancer he had (oat cell) is rare in non-smokers. The worker recalled several other men who had pre-

viously died of cancer after working at similar jobs in the plant. Figueroa consulted one of his former professors at Hahneman Medical College, Philadelphia, William Weiss, who had conducted much of the Philadelphia Pulmonary Neoplasm Research Project, to see what information was available for the other men. He also attempted to obtain occupational exposure histories for the group of 125 R&H workers for whom he had X-rays and medical and smoking histories. As he later found out, of the fifty-four lung cancer deaths at R&H, four occurred in the project group during the screening period from 1963 to 1968.⁹ R&H, however, insisted, that they had no work histories and exposure records on any of these 125 workers, and that they did not know why these workers had been selected for screening. Subsequently, R&H did manage to produce some of these records at a workman's compensation hearing to show that a particular worker had not been exposed to BCME and was therefore ineligible for benefits.

The importance of knowing which of the 125 workers had been exposed to BCME and which had not was critical to a prospective-type epidemiological investigation of the lung cancer epidemic at R&H. Figueroa had to calculate a death rate among exposed workers and compare it with that of the general population. He knew that 4 of the 125 workers had lung cancer, but without the exposure data, he could not calculate a cancer rate and thus, assess the significance of these findings. In the absence of company cooperation, Figueroa turned to his only available source of information, the lung cancer patient who, in his years of working at R&H, had come to know many of the plant employees. From memory, the man reconstructed the work histories of many of the plant employees on the Pulmonary Neoplasm Project list. The results were astonishing. Of the 125 men screened, only 44 had definite exposure to BCME. (Thus, the death rate was 4 out of 44, or 9 percent.)‡ This excessive rate, coupled with the young age of many of the victims, was remarkable. Figueroa immediately published his findings in the *New England Journal of Medicine*.¹⁰ His paper stands as an indictment of BCME as a potent carcinogen and, more telling, an indictment of R&H.

‡ More recent follow-up of the Pulmonary Neoplasm Project screenees resulted in the identification of seven more lung cancer deaths at R&H.

Simultaneous with the appearance of Figueroa's publication, NIOSH released the results of an investigation at a Diamond Shamrock CMME plant, Redwood City, California, initiated in 1971.¹¹ This study also showed a high incidence of lung cancers in relatively young workers. A number of other epidemiological studies in the United States and Germany have since confirmed the extreme carcinogenicity of BCME.¹²

Industry Fights Back

In 1972 R&H launched a campaign to discredit the experimental and epidemiological findings on the carcinogenicity of BCME. They informed NIOSH of their position that none of the cases of lung cancer in their plant could possibly have been due to BCME exposure; that instead they were caused by smoking and air pollution.

In the spring of 1973, R&H Senior Vice-President for Health Ellington M. Beavers, who in 1971 had refused to provide Figueroa with exposure data on BCME, was appointed to OSHA's Standards Advisory Committee on Occupational Carcinogens. Beavers urged the committee to reject proposals for minimal regulation of occupational exposure to carcinogens, and argued against the identification of occupational carcinogens by animal tests, recommending instead the need for more convincing human studies.

R&H and the Manufacturing Chemists Association also lobbied strongly against enactment of a workplace exposure standard for BCME, which was finally promulgated in an emasculated form in a package of standards for fourteen occupational carcinogens in January, 1974.

It has recently been discovered that BCME can be formed spontaneously in reaction mixtures containing the common chemicals hydrochloric acid and formaldehyde.¹³ This places many thousands of workers in danger of potential exposure to BCME. For example, many textile workers use formaldehyde in making permanent press fabrics, which are then treated with an acid wash.

A Needless Tragedy

Fifty-four workers at R&H have so far died of lung cancer. Yet the deaths due to BCME were unnecessary, as shown by the experience of Dow Chemical Company, R&H's closest competitor in the manufacture of CMME and BCME.

On the basis of findings in the late 1940s that BCME was an intense lung irritant to animals, Dow enclosed the manufacturing process at its Midland, Michigan, facility since its inception in 1949. Dow's Research Laboratory director commented on the cost of providing this type of protection:

At first thought, it seemed to me that such methods would be so expensive that they could not be used in normal chemical manufacture. Actually, this may not be true. The enclosure for the manufacture of chloromethylether need not be a six-foot wall of concrete, but only a normal airtight building . . . If such operation proves impractical, I believe we should abandon large-scale work with chloromethylether.¹⁴

A 1972 NIOSH field inspection of the Dow facility reported that

the industrial hygiene philosophy employed is to completely contain the product inside the process equipment and to have local exhaust ventilation at points of potential leakage, such as around seals with rotating shafts. This allows the worker to be in the production area without having to rely upon respiratory protection.¹⁵

In fact, the health record of Dow BCME employees is difficult to evaluate. In its twenty-five years of operation, only about 120 workers were known to have been potentially exposed. Dow claims that only one of the workers, a heavy cigarette smoker, developed lung cancer. R&H had allowed eighteen years to elapse before, in 1967, it finally followed Dow's example of enclosing the CMME manufacturing process.

Summary

Bischloromethylether (BCME) is used to manufacture ion-exchange resins and appears virtually indispensable as an intermediate product in nuclear fuel processing. BCME has been manufactured on a large scale at only two industrial sites during the past 25 years, and by only two chemical companies, Dow Chemical and Rohm & Haas. While Dow engineered its process from the start to reduce human exposure to BCME, Rohm & Haas scaled up production with little regard for its obvious toxicity or emerging information on its carcinogenicity.

Workers in Rohm & Haas started dying of lung cancer in the early 1960s. The company attempted to conceal this information, and subsequently to ascribe the cancer to smoking. When the need for animal testing became inescapable, Rohm & Haas aborted negotiations with New York University over the issue of open publication of results, contracting instead with a commercial testing laboratory. Even after BCME was shown to be one of the most powerful carcinogens ever tested in animals, and in the face of the increasing lung cancer death toll in its employees, Rohm & Haas resisted paying compensation to its employees' families and vigorously fought attempts by OSHA in 1973 to regulate BCME and other occupational carcinogens.

Benzene

Benzene is one of twelve chemicals used in largest volume by U.S. industries. Both production and manufacturing capacity have increased steadily by about 5 percent per year over the last decade. U.S. benzene production in 1977 was approximately 11 billion pounds, some 90 percent of which was produced in petroleum refining and petrochemical industries, and the remainder in the coke ovens of the steel industry.¹ The manufacture of tires ac-

counts for approximately half of all benzene used. Commercially, benzene is also used as an intermediate in the production of a wide range of chemicals, such as nitrobenzene, phenol, cyclohexane, cumene, maleic anhydride, and detergent alkylate. Another major usage is as an octane booster in gasoline. Further end-products of the use of benzene include nylons, pesticides, adhesives, laminates, coatings, inks, paints, varnishes, and moldings.

Occupational Exposure

The occupational hazards of benzene have long been recognized, although their seriousness has, until recently, been underestimated. While in the past exposures in the range from 100 to 500 ppm were commonplace, current levels in some workplaces are generally lower, reflecting the 1971 occupational standard of 10 ppm. Workers in petroleum and petrochemical refineries, in chemical plants (especially those manufacturing rubber products and solvents), and in the steel industry are at particularly high risk from benzene exposure. Additional categories of workers exposed include printing pressmen and lithographers, shoemakers, gasoline pump attendants, and professional artists and craftsmen.

A National Occupational Hazards Survey published by NIOSH in 1977, found that nearly 50,000 full-time workers are exposed to benzene, of whom 55 percent work at facilities that have no engineering controls or protective equipment.² More than 75 percent of the workers do not receive periodic blood tests to check for benzene toxicity. NIOSH estimates that about 2 million workers are now exposed to benzene.

Public Exposure

While benzene has been well known as an occupational problem for more than eighty years, recognition of the hazards posed to the general public is only recent. Public exposure to benzene falls into three major categories: communities near industries producing, processing, or using the chemical; the general public (from

gasoline); and the homeowner (from benzene-containing consumer products).

Based on recent estimates by Stanford Research Institute, it is clear that while these exposures are at much lower levels than occupational exposures, they are virtually unregulated at present and affect much of the U.S. population (Table 5.4).³ These rough estimates of general population exposure in the vicinity of petroleum refineries and gasoline service stations have, in general, been subsequently confirmed by limited industry monitoring, including that by the American Petroleum Institute.

Over half the benzene supply in the United States comes from a small number of petroleum refineries in Texas, California, Louisiana, and Illinois.⁴ These four states, together with Pennsylvania and New Jersey, account for about 70 percent of the total national refining capacity. It is estimated that more than 6 million people who live in the vicinity of these refineries are being constantly exposed to benzene emissions in the 0.1 to 1 ppb range. An additional 64,000 people living still closer to the plants received exposures up to 2 ppb.⁵

A wide range of chemical manufacturing plants throughout the United States, but particularly concentrated along the Gulf Coast, leak substantial quantities of benzene into the atmosphere.⁶ A 1971 study by Mitre Corporation indicated that annual losses are in the region of 260 million pounds, about 2.5 percent of total production. The worst offenders seem to be facilities manufacturing aniline and maleic anhydride. The actual concentrations to which local populations are exposed are highly variable, depending on factors such as height of gas stack, temperature of exhaust gas and wind patterns, but more critically on proximity to the plant. Average benzene levels are estimated to be in the 100 to 3,000 ppb range directly outside some plants, with progressive reduction at increasing distances.

Relatively little is known about the amounts of benzene used in solvent industries, for purposes such as manufacture of tires, natural and synthetic rubber products, adhesives, printing inks, paints, paint removers, leather and leather products, and floor coverings.⁷ Limited monitoring data have found benzene levels as high as 700 ppb within a quarter of a mile of a B. F. Goodrich Company solvent operation.⁸ There is a gradual trend, particularly in the

Table 5.4 Industries Causing Exposure of the General Public to Benzene

Source	Number of People Exposed to Various Concentrations of Benzene, ppb*				Total Number of Exposed People
	0.1-1	1-2	2-4	4-10	
Petroleum refineries	6,529,000	64,000	4,000	319,000	6,597,000
Chemical manufacturing	7,497,000	970,000	453,000	319,000	9,883,000
Solvent operations	208,000	5,000	2,000	215,000
Coke ovens	15,726,000	521,000	50,000	2,000	16,299,000
Gasoline stations					
People using self-service					
People living nearby	87,000,000	31,000,000	37,000,000
Urban exposures from autos	68,337,000	45,353,000	118,000,000
					113,690,000

Source: S. J. Mara and S. S. Lee, "Human Exposures to Atmospheric Benzene," Center for Resources and Environmental Systems Studies, Report No. 30, Stanford Research Institute, 1977.

* Based on estimates of annual averages.

rubber industry, to substitute toluene as a much safer and effective alternative for benzene.

Sixty million tons of blast furnace coke are produced from coal each year in sixty-five U.S. steel plants, most of which are concentrated in four states: Pennsylvania, Indiana, Ohio, and Alabama.* For each ton of coke, about four gallons of "light oil," most of which is benzene, are produced as a by-product. Most coke ovens are old and "leaky," allowing the escape of benzene and other volatile toxic materials such as carbon monoxide, hydrogen sulfide, and sulfur oxides. Benzene levels are estimated to range as high as 50 ppm inside the plants and 300 ppb immediately adjacent to them, decreasing to a few ppb at twelve miles distance. It is further estimated that about 16 million people are exposed to annual average concentrations in the 0.1 to 1 ppb range and 50,000 in the 2 to 4 ppb range.⁹

By far the most extensive operations resulting in benzene exposure to the general population are gasoline stations, of which there are about 200,000 in the United States. With the gradual phasing out of gasoline lead additives, the use of benzene as an octane booster has doubled over the last four years to current levels from 1 percent to 2.5 percent in most gasoline brands. Most of the vapor liberated during a typical fill-up operation results from the displacement of benzene trapped within the gas tank, and not from the gasoline being pumped. Recent measurements in U.S. self-service stations found benzene levels averaging 250 ppb immediately adjacent to the gas pumps. It is estimated that about 37 million people are intermittently exposed to such benzene levels through the use of self-service facilities. Gasoline attendants, of course, are continuously exposed to them. So are also the 118 million people, more than half the U.S. population, who are exposed to levels between 0.1 to 2.0 ppb by virtue of living near a gas station.¹⁰ And automobiles themselves are mini-dispensers of benzene, both from tailpipe emissions and evaporation from the gas tank. Estimates of average benzene levels from these sources range from 1 to 4 ppb in downtown Dallas, Los Angeles, St. Louis, and Chicago, where the highest levels were found. Concentrations in the suburbs of these cities were from two to ten times lower.¹¹

* These plants consist of an estimated 13,000 ovens contained in about 230 coke oven batteries.

Many commonly used consumer products contain benzene. These include solvents, adhesives (including the cement in bicycle tire patch kits), carburetor cleaners, and paint and wood strippers. A popular paint stripper, Red Devil Paint and Varnish Remover, contains over 50 percent benzene. Recent NIOSH measurements in a closed garage after a half-hour of furniture stripping found benzene levels ranging from 75 to 225 ppm.¹² Professional artists, craftsmen, and hobbyists are often exposed under poorly ventilated conditions to benzene in their homes, studios, and workshops from the uses of common materials, such as resin and fluorescent dye solvents, paint and varnish removers, and silk-screen washes. Another NIOSH survey at the Cooper Union School of Art and Architecture in New York, measured benzene levels of 37 ppm in a breathing zone sample on a photoetcher. A 1977 investigation by a New York public interest group, the Center for Occupational Hazards, found the following benzene consumer products readily available.¹³ Seventeen of twenty randomly selected hardware stores sold products listing benzene on their label, but with little or no indication of the dangers involved. Paint removers are particularly hazardous since they may be from 15 to 100 percent benzene.

<i>Brand Name</i>	<i>Products</i>
Red Devil's Paint Products	Red Devil's Paint and Varnish Remover Liquid #99 Liquid #66 No-Wash #88 Paste #77
Wilson Imperial Products Products	Imperial Wonder-paste Paint Remover Imperial Rapid Brush Cleaner Imperial Cleanwood Wil-Bond Sanding Liquid
KWIK Products	KWIK Liquid No-Wash Paint and Varnish Remover KWIK Semi-Paste Paint and Varnish Remover
Classic	Classic Rubber Repair Cement
Kleen Kutter	Klean Kutter Paint Remover

Source: Art Hazards Project, Center for Occupational Hazards, Inc., 1976.

A most dramatic example of community exposure to benzene and other carcinogenic solvents is afforded by the case of the Galaxy Chemical Company, Elkton, Maryland.¹⁴ This company started operations in 1961 for the purpose of recovering solvents from the wastes of major chemical industries, such as Du Pont. The company first stored these wastes in tanks vented directly to the atmosphere. Following processing at Galaxy, the "bottoms" or residues were discharged into open drying beds. After evaporation, the final wastes were dumped in nearby landfills. Additionally the company periodically had large spills of carcinogenic and other chemicals.[†] Complaints of foul odors commenced as soon as the plant opened and became almost constant by 1964. Monitors outside the plant in 1970 found levels of benzene as high as 23 ppm and other solvents such as carbon tetrachloride, at levels of 140 ppm.

By 1974, a local pathologist, Pietro Capurro, who had himself been involved in the monitoring, noted an excess of lymphoma cases in Elkton. Capurro, after trying in vain to get help from the Maryland State Department of Health, prepared in March, 1974, a preliminary manuscript reporting his findings, but not specifying Galaxy as the source of the pollution. *Medical World News* subsequently interviewed Capurro and printed an article naming Galaxy as the pollution source. The director and owner of Galaxy, Paul Mraz, claimed that Capurro's article was defamatory and resulted in the loss of business, and sued Capurro for over \$2 million. The case came to jury trial in December, 1977. Edward Radford, Professor of Epidemiology at the School of Public Health, University of Pittsburgh and consultant to Galaxy, claimed that Capurro was "reckless and irresponsible" in writing the draft of his article, and that Galaxy could not possibly have been responsible for the admitted excess of lymphoma cases in Elkton. On the basis of the scientific and other evidence, the jury found for Capurro.¹⁵ Mraz appealed this verdict to the Maryland Special Court of Appeal.

Galaxy Chemical Company was dissolved in 1975, and has

[†] According to a deposition of the director and owner of Galaxy, Paul Mraz, the company "spilled" about 1,000 gallons of trichloroethylene in 1965, and several hundred gallons of acrylonitrile in 1971 or 1972. Mraz estimated that the company "spilled" on the average of 1,250 gallons of chemicals each year.

since reopened as Solvent Distillers, again under the ownership of Mraz.[‡] In spite of some improvements in the operations of the new company, complaints of odor persisted, as indicated at the trial. Continuous monitoring in 1976 revealed periodic benzene levels in the 200 to 900 ppb range.

Occupational Diseases¹⁶

Virtually all knowledge of the effects of benzene on humans comes from studies on exposed workers. Benzene is highly toxic, inducing a wide range of acute and chronic adverse effects. Unless contaminated with other more readily absorbed solvents, benzene is poorly absorbed through the intact skin. The primary route of entry into the body is inhalation, with rapid absorption from the lungs into the blood. Benzene accumulates in various organs and sites of the body in proportion to their fat content. Most is rapidly metabolized, primarily by liver enzymes, to water soluble derivatives which are excreted in the urine. One of the early metabolic products of benzene is benzene epoxide, which is highly reactive and may ultimately be responsible for the toxic bone marrow effects noted below.

Aplastic Anaemia Benzene is a potent marrow poison, inducing a wide range of toxic effects, the best recognized of which is aplastic anaemia, which is characterized by pallor and fatigue and can exist alone or together with a condition known as *pancytopenia*. In this condition, bleeding can occur in the skin and elsewhere in the body, and there also is increased susceptibility to infection.

It is difficult to assess the long-term outcome of aplastic anaemia. While the immediate prognosis of early and mild cases may be good if benzene exposure is discontinued, apparently complete recovery is sometimes followed by the development of acute leukaemia up to twenty or so years later.

[‡] Solvent Distillers has been renamed Spectron, Inc. On May 8, 1978, an explosion at the plant involving release of white fumes from barrels containing polyurethane and ink resins resulted in the evacuation of more than fifty residents from Elkton. Mraz characterized the vapors as "nonlethal."

Case histories of aplastic anaemia/pancytopenia in benzene-exposed workers have gradually been accumulating in the U.S. and European literature over the last five decades. Cases have been reported in a wide range of occupations, including printers in rotogravure plants, rubber workers, aircraft construction workers, and leather and shoe workers. One of the most important series of studies has been based on Turkish shoe workers, who between 1955 and 1960 started using adhesives containing high levels of benzene, and were exposed to levels in the 150 to 650 ppm range.¹⁷ Individual cases of aplastic anaemia were noted in 1961. By 1977, 46 workers had developed aplastic anaemia, of whom 14 died from the disease. Five of these workers later developed leukaemia, from which they subsequently died.

Chromosomal Effects Since the early 1960s, several European studies have shown that there is a relatively high incidence of chromosome abnormalities in the lymphocytes (white blood cells) of workers, with varying degrees of marrow damage following benzene exposure.¹⁸ These abnormalities were generally found in workers intermittently exposed to benzene levels from 25 to 150 ppm. The literature then was conflicting with regard to chromosome damage at lesser exposure levels.

By the summer of 1977, Dow Chemical Company had completed extensive chromosome tests on some forty workers in its Freeport, Texas, plant exposed to "low" benzene levels, believed to be under 10 ppm. The Dow scientists reportedly found clear-cut evidence of chromosome damage, particularly in men over forty. The Michigan corporate offices of Dow initially decided not to disclose these results.* The news, however, leaked out. NIOSH sent two letters to Dow in late 1977 and another in January, 1978, requesting details of this study, which Dow finally released in March, 1978. This study confirmed the occurrence of chromosome damage in workers with average exposure levels of 2 to 3 ppm.

Unpublished studies from Sweden also seem consistent with the results of the Dow studies, with the findings of chromosome dam-

* This would have jeopardized the industry position of fighting against the 1977 proposed OSHA reduction of the benzene standard to 1 ppm.

age in industrial workers and crews of petrol tanker ships, following exposure to benzene in the 5 to 10 ppm. range.¹⁹

The occurrence of chromosome damage in the absence of any other evidence of benzene toxicity is important for several reasons, particularly when found at relatively low exposure levels. First, there are theoretical grounds for associating induced chromosome damage with the subsequent development of leukaemia. Second, similar abnormalities are induced by X-rays, which can also produce leukaemia. Third, these changes can persist long after there has been apparent recovery from benzene poisoning, and well before leukaemia develops. Finally, these changes are commonly found in leukaemic blood cells.

Leukaemia in Humans Four major types of this fatal form of cancer of white blood cells are recognized: acute myelogenous, chronic myelogenous, acute lymphocytic, and chronic lymphocytic. The association between acute myelogenous leukaemia in humans and benzene exposure is unequivocal. There are three major lines of supporting evidence for this: First, benzene is known to be toxic to bone marrow, producing aplastic anaemia/pancytopenia and also chromosomal abnormalities, both of which are probable precursors of leukaemia. Second, there have been over 100 case reports of acute myelogenous leukaemia following occupational exposure to benzene, many of which first developed as aplastic anaemia. Finally, and most important, various epidemiologic studies have concluded that benzene induces leukaemia and is thus a carcinogen.

For example, an impressive series of studies has been done by Muzaffer Aksoy based on 28,500 shoe workers in Istanbul, Turkey, exposed to benzene levels from 210 to 650 ppm over a period ranging from one to fifteen years.²⁰ Of these cases, 26 developed acute myelogenous leukaemia from 1967 to 1973; this is an annual incidence of 13/100,000 and about four times that seen in the general population. Additionally, the average age of these leukaemia cases was 34 years, which is much lower than the 60-year average age of leukaemia deaths in adults.

Similar results have been reported in Italian shoe and rotogravure workers in Milan and Pavia, where the risk of acute myelogenous leukaemia was calculated in 1964 to be approxi-

mately twenty times greater than that of the general population. It is of particular interest that no new cases of aplastic anaemia or leukaemia were observed in the rotogravure industry during the ten-year period following the substitution of toluene for benzene in 1964.²¹

In 1974, J. Thorpe, Associate Medical Director, Exxon Corporation, published a large-scale epidemiological study of leukaemia mortality, based on 36,000 employees and retirees of eight European affiliates exposed to "low levels" of benzene from 1962 to 1972.²² Thorpe found no excess risks of leukaemia. However, there was a wide range of problems in this study, some of which were admitted by the author. These included inadequate follow-up of older employees (who were most likely to develop leukaemia), incomplete exposure histories, inadequate measurement of exposure levels, and suspect diagnosis reporting. As one critic expressed it, "With case finding techniques as apparently relaxed as those in the Exxon study by Dr. Thorpe, one cannot help but doubt the accuracy of the data presented."²³

A recent epidemiological study by Peter Infante of NIOSH† involved a cohort of 748 men who had been exposed to benzene from 1940 through 1949 at the Akron and St. Mary's, Ohio, plants of the Goodyear Tire and Rubber Company, while engaged in the manufacture of "pliofilm," a natural rubber cast film.²⁴ A virtue of this study was the "purity" of the exposure; that is, the workers were exposed only to benzene, rather than to the mixture of other organic solvents usually encountered in the rubber industry. Although a 1946 report by the Ohio Industrial Commission indicates that benzene levels in the pliofilm operation were relatively low, ranging from zero to 10 ppm, the value of this study is probably more qualitative than quantitative. Of 140 deaths observed by 1975, 7 were leukaemias, mainly acute myelogenous, while only 1 or 2 would have been expected from U.S. death rates. The risk of workers in this plant dying from leukaemia was calculated to be about ten times that of the general population. Unpublished reports from Lund, Sweden, in 1977 also indicated a high incidence of acute myelogenous leukaemia in gasoline pump attendants.

There is a clear relationship between benzene and acute myelo-

† Now in OSHA.

genous leukaemia, and there is growing information incriminating benzene in other forms of leukaemia and other malignancies. Much of this evidence, however, comes from studies in which there are mixed exposures to other solvents besides benzene, such as in the rubber industry. For instance, a 1963 HEW study reported 54 percent increase in death rates for "cancer of the lymphatic and haematopoietic system," besides excess cancers of other sites in the rubber industry compared with other manufacturing industries.²⁵ A comprehensive study of rubber workers by scientists of the University of North Carolina showed an excess death rate from all forms of leukaemia, including lymphatic leukaemia, and also lymphosarcoma and Hodgkin's disease. Other studies of the rubber industry have also confirmed the findings of excess lymphatic leukaemia. There have also been scattered case reports on the association between benzene exposure and lymphosarcoma, Hodgkin's disease, multiple myeloma, and reticulum cell sarcoma.²⁶ For instance, six cases of Hodgkin's disease have been recently reported in Turkish shoe workers following one to twenty years of occupational exposure to benzene.

Leukaemia in Animals

In 1897, a German physician, G. Santesson, investigating an outbreak of skin haemorrhages in a group of women working with benzene, was able to reproduce these effects in rabbits by injection and skin application of the chemical. Since then, there have been numerous investigations on the effects of benzene in animals. In general, these have shown that benzene is a marrow toxin, depressing marrow function, and producing an aplastic anaemia/pancytopenia-like condition. In more recent studies, chromosome damage, of a type similar to that found in occupationally-exposed workers, has been found in circulating lymphocytes.²⁷

Attempts to induce leukaemia and other cancers in experimental animals by chronic administration of benzene have on the whole been unsuccessful until very recently. It has been customary to regard benzene as one of two major exceptions to the rule that all chemicals found to be carcinogenic in humans will also induce cancer in animals (arsenic is the other). However, there are

grounds for questioning whether benzene is really an exception. First, many claimed negative animal experiments are inadequate in that they used too few animals or observed them for too short a period. Second, there are several animal studies which, while individually flawed, together are highly suggestive of the induction of leukaemias or lymphomas. Examples are a 1932 German study, in which eight out of forty-four surviving mice developed leukaemia or lymphosarcoma, and a 1963 Japanese study, in which fibrosarcomas were induced in five of eight mice surviving chronic benzene administration.²⁸ Finally, two recent unpublished studies seem to confirm the carcinogenicity of benzene. The preliminary results of one study were presented by Cesare Maltoni at a meeting sponsored by Chemical Week in New Orleans, October 21, 1977. Groups of sixty to seventy rats of both sexes were fed benzene at doses of 50 and 250 mg/kg. Five rare ear gland tumors, five skin tumors and three other tumors were found in the high dose group. No such tumors occurred in 300 controls. The second, still incomplete, study from New York University has established that benzene induces leukaemia in rodents. This study is based on exposure of groups of forty to sixty rats and mice to benzene by inhalation at 100 or 300 ppm for up to two years. So far, one rat and one mouse have died from chronic myeloid leukaemia, another mouse from acute leukaemia, and a third mouse from a leukaemic-like disease. Additionally, most mice at the higher dose level developed severe anaemia.

Regulatory Developments

The year 1977 was a year of regulatory confrontation for benzene, as moves were finally made by federal agencies to limit and control exposures in the workplace, in the general environment, and in the home.

Regulation in the Workplace The 1977 occupational standard of 10 ppm was originally based on a standard developed by the American Conference of Governmental Industrial Hygienists in 1969.²⁹ This is one of several industry-oriented organizations in whose hands occupational standards were set prior to passage of

the 1970 Occupational Safety and Health Act. The American National Standards Institute is another such organization. Standards set by these organizations are often referred to as "consensus standards," although the consensus did not generally reflect the views of consumers or organized labor. While Section 6(a) of the Occupational Safety and Health Act allows conferring of federal authority on such standards, these have recently come under increasing scrutiny and revision. The consensus standard, adopted as an OSHA standard in 1971, allowed average benzene exposures of 10 ppm, with an acceptable ceiling of 25 ppm, and periodic excursions up to 50 ppm. Both the consensus and resulting OSHA standard were based on the general toxic effects of benzene, without any consideration of risks of leukaemia, in spite of the substantial evidence of this effect which then existed.

The risks of leukaemia could no longer be ignored when the results of the Turkish shoe worker study by Aksoy were published in 1974.³⁰ Accordingly, NIOSH submitted a criteria document to OSHA on benzene admitting that "the possibility that benzene can induce leukaemia cannot be dismissed."³¹ Nevertheless NIOSH recommended retention of the 10 ppm standard. Resentment against this standard surfaced on April 23, 1976, when the United Rubber, Cork, Linoleum and Plastic Workers of America wrote to Secretary of Labor William J. Usery urging that an Emergency Temporary Standard regulating occupational exposure to benzene be issued in order to protect workers from leukaemia. According to the Act, an Emergency Temporary Standard may only be issued if there is a condition of grave danger, and if action by OSHA can mitigate this. Under the Nixon and Ford administrations, OSHA showed extreme reluctance to engage in such emergency rule-making. Usery denied labor's request on May 18, 1976.

In June, 1976, the National Academy of Sciences released an EPA-contracted review on the "Health Effects of Benzene," prepared by its industry-dominated Committee on Toxicology.³² This emphasized the need for further research and study but admitted that "benzene must be considered as a suspect leukemogen," a conclusion which was, however, sharply qualified:

It is probable that all cases reported as "leukaemia associated with benzene exposure" have resulted from exposure to rather high concentrations of benzene and other chemicals.

This statement has been exploited by the American Petroleum Institute and other industry as the basis for their view that further study rather than further regulation of benzene is needed, and in support of their objections to the 1977 proposed OSHA standard of 1 ppm.

These views of the National Academy of Sciences Committee are also in sharp contrast to the unequivocal statement that benzene was a leukemogen, contained in an updated criteria document submitted to OSHA in August, 1976, by then director of NIOSH, John Finklea, clearly reversing the agency's 1974 assessment.³³ The updated document stated, "It is apparent from the literature that benzene leukaemia continues to be reported, . . . [thus] no worker [should] be exposed to benzene in excess of 1 ppm in air." The document also recognized that the risks of leukaemia were such that no safe level of exposure to benzene can be established. NIOSH followed this move by a letter to OSHA on October 27, 1976, recommending that the standard be revised downwards from 10 to 1 ppm.

The next development was the completion, in January, 1977, of the NIOSH pliofilm industry study by Infante, which clearly confirmed excess leukaemia risks from benzene at apparently relatively low exposure levels.³⁴ OSHA, already sensitized by the 1976 update of the NIOSH criteria document, reacted promptly to these new studies. In February, 1977, OSHA alerted industry to the imminent and urgent need for reducing exposure levels, by issuing a "guideline" recommending a new standard of 1 ppm and outlining probable requirements for engineering controls, monitoring, and employee medical surveillance. Reaction from the industry was prompt. Without waiting for the formalization of the guidelines into proposed standards, the National Petroleum Refiners Association, in a March press release, attacked the proposal as unnecessary and unjustified, claiming that it would entail a \$267 million capital outlay and subsequent annual costs of \$75 million.³⁵

On April 29, 1977, Secretary of Labor F. Ray Marshall and Assistant Secretary for OSHA Eula Bingham announced an Emergency Temporary Standard of 1 ppm, reducing the 25 ppm ceiling level to 5 ppm and eliminating permissible peaks of 50 ppm.³⁶ This was scheduled to go into effect on May 21, 1977, and to become a permanent standard six months from then. In announcing the measure, Marshall recognized the historic and critical importance of the proposal by declaring that

[this] signals a new day for an agency which in the past has been criticized for acting too slowly when lives were at stake. . . . We are going to focus our primary attention in OSHA on major, rather than minor problems. . . . We are going to catch whales rather than minnows.³⁷

OSHA made it clear that it did not regard the 1 ppm standard as safe, but rather as the lowest feasible level for the current detection and control of benzene exposure. In fact, practical instrumentation is available which is sensitive down to 0.05 or 0.1 ppm. OSHA pointed out that if this new level was not found to be adequately protective, it would then urge for the large-scale substitution of less harmful solvents for benzene. Of the 2 million workers whom NIOSH estimates are exposed to benzene, only approximately 153,000 workers and 1,200 work sites will be covered by the emergency standard. For the time being, however, gasoline pump attendants and industries using less than 1 percent benzene in any liquids or formulations are exempted. OSHA indicated that the costs of meeting the emergency standard would be of the order of \$40 million, and that for the permanent standard a maximum of \$500 million. These are fractions of the costs claimed by the American Petroleum Institute and the National Petroleum Refineries Association.

The practicality of the emergency standard and also of a zero exposure standard were further emphasized in May, 1977, by an Economic Impact Statement submitted to OSHA. This stressed that benzene has already been or soon will be replaced by other chemicals in a wide range of processes; that most benzene is already used by large industry in closed systems; and that the price of benzene had quadrupled from 1973 to 1976, providing eco-

nomic incentives for the further use and perfection of closed systems. The impact statement also quoted the American Petroleum Institute to the effect that since 1970, 90 percent of benzene exposures in the petrochemical industry are under 1 ppm.

The proposed emergency standard came under immediate attack from several quarters, from industry as being too stringent, and from labor and the Health Research Group as being too weak. The Industrial Union Department of AFL-CIO, filed a petition in the U. S. Court of Appeals for the District of Columbia Circuit, on the basis that there is no known safe exposure level for a carcinogen. Labor and the Health Research Group made no secret of their strong support for the OSHA action as a first step in the right direction.

The Manufacturing Chemists Association on behalf of the chemical industry, and the American Petroleum Institute, on behalf of ten major oil companies, strongly protested the proposed standard. On May 29, 1977, the American Petroleum Institute petitioned the Federal Court of the New Orleans Fifth Circuit for a stay of execution of the emergency standard, which was granted. The petition was transferred in June to the District of Columbia Circuit, which denied an appeal by OSHA and continued the stay. The industry's position in the appeals brief was inconsistent and questionable. Shell Oil claimed that the emergency standard would make it necessary for them to monitor about 150 workplaces. A survey by the Oil, Chemical and Atomic Workers Union however, showed that Shell owns only seventeen chemical plants and eight refineries. Standard Oil of Ohio claimed that it had only about ten respirators that it could use for the new regulations, whereas the workers in its Toledo refinery found over 100 cartridge and 32 self-contained respirators in that one plant alone. Union Oil Company of California made similar statements.³⁸

Some industry groups, however, were more cooperative. Good-year Tire and Rubber Company said that it expected to be able to meet the new emergency standard and reported that it was well along in replacing benzene in its operations. Other chemical industries, and also some universities, announced that they were switching from benzene to safer solvents, such as toluene and petroleum ether. A memorandum from Atlantic Richfield to its employees said, "We believe some aspects of OSHA's new stand-

ard may be overly restrictive, but intend to comply as quickly as possible with all of its provisions."

Public hearings on the proposed OSHA standard began on July 19, 1977. OSHA's main exhibit, apart from the 1976 NIOSH criteria document, was the Infante study. Also testifying was Louis Beliczky, of the Rubber Workers Union, who called for a stricter standard and for economic protection through "rate retention" of workers found to have toxic effects from benzene exposure. Sidney Wolfe, of the Health Research Group also testified in favor of stricter standards, pointing out that the only safe exposure level for benzene, as for other carcinogens, is zero and that this could be achieved by product substitution and engineering controls. It should be noted that support for the zero exposure standard has been clearly stated by Donald Hunter in 1969 in his internationally recognized standard text on occupational diseases:³⁹ "The safe concentration of benzene vapour in a factory or workshop is zero parts per million." The Health Research Group also demanded that all employers proposing to use benzene should first be required to obtain a "use permit," which would allow OSHA to regulate more effectively, to physically inspect the workplace before issuing a permit, and to institute uniform work practices and labeling.

The industry attacks against the standard focused on three major points: They claimed that the Infante study was invalid, that the current 10 ppm standard was a safe threshold against leukaemia risks, and that any possible remaining risks were far outweighed by the benefits to society of the continued use of benzene under currently regulated conditions.

The major criticisms against the Infante study, by then published in *Lancet* (July 9, 1977), were presented by the chief industry witness, Irving Tabershaw, long-time industrial consultant and editor of the industry-oriented *Journal of Occupational Medicine*.⁴⁰ Tabershaw attempted to recalculate the Infante data so as to minimize the excess leukaemia incidence in the exposed work force. He did this by the device of computing mortality rates on groups of workers as a whole, in a way similar to that used by McDonald to minimize the cancer risk of asbestos miners, rather than by computing rates on workers at risk for specified periods of exposure time. The latter approach is essential to the analysis

of mortality rates for diseases with a long latency period, such as cancer. The Tabershaw argument was published in a letter to *Lancet* on October 22, 1977, together with a counter-rebuttal by Infante.⁴¹

One of the industry witnesses was Robert E. Olson, Chairman of the Department of Medicine, St. Louis University, whose seventeen-page testimony, a quarter of which was devoted to listing his own academic achievements, attacked the Infante study on the grounds, among others, that none of its authors had an M.D. Olson made it clear that he was under the impression that the literature had established thresholds for carcinogenic effects:

The carcinogen, vinyl chloride, shows clear-cut threshold behavior in both animals and man. The threshold for tumor induction by vinyl chloride in animals is 10 ppm, a concentration at which hepatic glutathione levels were not depressed and no tumors occurred. After 25 years of observation, doses of vinyl chloride in the air of approximately 2,000 ppm in industrial plants have been shown to cause tumors in man, whereas levels below 200 ppm have not.⁴²

Stranger still was Olson's belief that benzene could not be regarded as a human carcinogen, because human experience had not been validated in animal experiments. "In my opinion benzene cannot be called a primary carcinogen, because no cancer has been demonstrated in animals after benzene exposure and no mutagenic activity has been demonstrated in mutant microorganisms (Ames test)." Robert Synder, Professor of Pharmacology, Thomas Jefferson University, another industry witness, agreed with Olson on this point: "The major stumbling block to general acceptance of the theory that benzene induces leukaemia has been the inability to produce any form of this disease in mice or rats exposed to benzene." (These statements are reversals of the usual industry position of demanding human validation of carcinogens established in animal tests.)

A leading industry witness was James J. Jandl, Professor of Medicine at Harvard University Medical School and a prominent hematologist, testifying on behalf of Organization Resources Counselors, Inc., a New York-based consulting firm that represents about fifty top national corporations, including Du Pont and Union Carbide. Jandl maintained that leukaemia had been caused

only by long-discontinued exposures in the 50 to 100 ppm range. He further reported that of 4,448 case reports of workers exposed to 100 to 1,000 ppm of benzene since 1939, which he had reviewed, "only" 169 (4 percent) had developed aplastic anaemia, and of these 148 (88 percent) had recovered completely. Jandl provided no documentation for these case reports. Apart from the fact that he found eleven deaths from aplastic anaemia or leukaemia, his follow-up period for the aplastic anaemia cases averaged only three years. The literature, however, makes it clear that the latency period for leukaemia can extend for fifteen years or more.

Jandl also supported the industry position of "blaming the victim," claiming that only hypersusceptible workers developed leukaemia following benzene exposure, and that these could be detected by periodic surveillance and screening programs. One of the flaws in this argument, apart from the fact that there was no evidence presented for it, became apparent in a report subsequently submitted by Dow Chemical Company, which found a four-fold excess of leukaemias in employees exposed to benzene in its Michigan plant, in spite of the fact that the company has elaborate pre-employment and blood screening programs for exposed workers.

The Jandl testimony included a critical but poorly substantiated analysis of the Infante study, unfavorable references to the "explosive interest" of Aksoy on "an alleged but undocumented 28,500 Turkish workers in the shoe making industry," and sarcasm directed against OSHA, which he charged with engaging in "self-serving . . . dramatization."

The final argument presented by the Manufacturing Chemists Association at the OSHA hearings summarized the views of its consultants and alleged that "the best available evidence" indicates that there are two thresholds for toxic effects of benzene, 100 ppm for leukaemia and 40 ppm for aplastic anaemia. Anyway, argued the Manufacturing Chemists Association, why worry about aplastic anaemia, especially in view of Jandl's reassurances that the mortality rate for this disease is so low? For these reasons, they protested, why revise the standard downwards, especially as this would involve considerable expense?

Following the public hearings in February, 1978, OSHA promulgated its permanent benzene standard, which prohibited

worker exposure to an average concentration above 1 ppm, and which also prohibited skin contact with solutions containing more than 0.5 percent benzene. The new, tougher standard was, however, never enforced, as the American Petroleum Institute, the National Petroleum Refiners Association, and other trade groups immediately petitioned the Fifth Circuit Federal Court of Appeals in New Orleans for a stay, on the grounds that no health hazard had been demonstrated below 10 ppm, and that the health benefits of the standard (to the workers) did not justify the costs (to the companies) of implementation.[‡] A temporary stay of the standard was granted in March, 1978, by the Fifth Circuit. In October, 1978, the Court permanently overturned the standard, leaving workers subject to the previous 10 ppm standard.

The specific ground for setting aside the 1 ppm standard was OSHA's alleged failure to provide an estimate, supported by "substantial evidence," of expected benefits from the lower limit. The Fifth Circuit Court specifically rejected OSHA's arguments that the benefits of regulating a known carcinogen would be "appreciable," and that regulations should be based on whether industry compliance is feasible. The language of the decision exemplified the Court's belief that economic feasibility and costs of compliance are the prime determinants in standard setting, and that the burden of proving that these costs would be outweighed by the health benefits should be borne exclusively by OSHA. Even as the Court was drafting its final decision, Foster D. Snell released a study for the Manufacturing Chemists Association showing that control of process vents and benzene storage tanks could achieve 95 percent reduction of all emissions for considerably less cost than previous estimates.

The government, clearly unable to allow the Fifth Court's position on economic constraints to determine future policies of the Labor Department, in December, 1978, filed an appeal to the Supreme Court, with the Industrial Union Department of AFL-CIO as an intervenor.

[‡] The Fifth Circuit Court is known not to be unsympathetic to the interests of the petrochemical industry. OSHA standards on chemical exposures are now being developed with growing expectations that they may well be litigated in this Court.

Regulation of Public Exposure By early 1977, evidence of OSHA's growing concerns on occupational hazards of benzene encouraged the extension of these concerns to similar hazards in the general environment and home.

On April 14, 1977, the Environmental Defense Fund petitioned EPA to list benzene as a "hazardous air pollutant" under section 112 of the Clean Air Act. EPA did so on June 7, 1977, and recommended that industrial emissions of benzene be reduced to the "lowest possible level." This action required the agency to develop appropriate standards and abatement programs within a subsequent ninety-day period.

EPA, meanwhile, was preparing the scientific basis for its proposed action. This consisted of three key documents: "Benzene Health Effects Assessment, an External Review Draft," dated October, 1977, the chief author of which is Bernard D. Goldstein, a hematologist at New York University Medical Center;⁴³ "Human Exposure to Atmospheric Benzene," a preliminary draft by Stanford Research Institute, dated October, 1977;⁴⁴ and "Preliminary Report on Population Risks to Ambient Benzene Exposures," prepared by the Carcinogen Assessment Group of EPA.⁴⁵ The first document is a comprehensive literature review up to the summer of 1977, confirming the leukemogenicity of benzene at levels under 100 ppm, confirming the occurrence of chromosome damage in levels down to 25 ppm, and dismissing any suggestion that only the "susceptible" worker develops aplastic anaemia or leukaemia from exposure to benzene. The Stanford Research Institute document identified all major industrial sources of benzene emissions into the air, estimated the average and worst-case levels of exposure for various population groups, and concluded that exposure levels of the general population were in the 1 ppb range, although much higher levels could be found in the vicinity of various industries. On the basis of these two documents, the third EPA document estimated that thirty to eighty cases of leukaemia could be anticipated each year in the general population from exposure to estimated average 1 ppb levels. These are minimal estimates, as they ignore the likelihood of synergistic interactions between benzene and other environmental carcinogens, which could result in much greater numbers of leukaemias and cancers.

Flanked by its lawyers and consultants, the American Petro-

leum Institute, Organization Resources Counselors, the Manufacturing Chemists Association, the American Iron and Steel Institute, and other concerned industries launched into an attack on the EPA position at a meeting of the Environmental Health Advisory Committee, December 12, 1977. The Stanford Research Institute document was attacked as speculative and based merely on estimates, rather than hard monitoring data, which the industry claimed could have easily been obtained from them by the government.

Direct questioning of the industry by members of the advisory committee, however, made it clear that in the summer of 1977, EPA had requested industry to supply it with monitoring data in the general environment, but received virtually no response. Just before the advisory committee meeting the American Petroleum Institute released some limited monitoring data which agreed well with the Stanford estimates. Additionally, EPA had submitted a draft of the Stanford Report to the industry and had included all their limited comments in the final draft, which the industry subsequently attacked at the advisory committee meeting.

The industry was questioned as to the availability of the Dow study on chromosome abnormalities in workers exposed to levels of benzene believed to be under 10 ppm which NIOSH had repeatedly requested since late 1977. Dow finally made these data available on March 1, 1978. The results of the Dow studies clearly demonstrated the occurrence of a statistically significant incidence of chromosome abnormalities in a group of fifty-two workers exposed to benzene for an average period of fifty-six months, ranging from one month to twenty-six years, at estimated time-weighted average levels of 2-3 ppm.⁴⁶

Shell Oil submitted a written statement which chided EPA for failing to differentiate between a carcinogen and a leukemogen. The statement reflected puzzlement that thresholds for benzene could not be found for the general public, since "they can be determined for workers." Finally, Shell dismissed the Stanford document as based largely on estimates rather than on hard monitoring data when, like the rest of the industry, Shell had failed to supply such information requested by EPA.

Jandl attacked the EPA position which he claimed was unscientific. However, he was unable to explain why he based his

claims for the high recovery rate from benzene-induced aplastic anaemia and the rarity of leukaemia on an average of only three years follow-up.

In February, 1978, the Advisory Committee concluded that available scientific evidence strongly supported the proposed EPA action to regulate benzene as a "hazardous air pollutant." The scientific basis underlying the proposed regulation was confirmed by a subsequent report prepared for EPA by Pedco Environmental of Cincinnati. In addition to stressing the occurrence of chromosome damage at benzene exposure levels of 2 to 3 ppm, the report describes two other significant toxic effects at exposure levels of 3 to 15 ppm—reduction in serum complement levels, and interference in the synthesis of heme, the oxygen-carrying blood pigment of hemoglobin, manifested by the accumulation of a precursor (delta-aminolevulinic acid).

Consideration of the health risks both to the general population and the work force from exposure to benzene is clearly going to be influenced by the costs of achieving reduction in emissions. It is likely that there will be increasing emphasis on the important fact that steps taken to reduce benzene emissions will also result in concomitant reduction of emissions of a wide range of other toxic and carcinogenic chemicals. This is certainly the case for coke oven emissions, as well as for emissions from petrochemical plants.

The NCI maps on cancer mortality have already focused attention on excess cancer rates in counties with heavy concentrations of petrochemical industries. In October, 1977, William J. Blot of the NCI published a further study based on thirty-nine counties where at least 100 persons and at least 1 percent of the population work in petroleum refining plants.⁴⁷ Blot found a 6 percent higher overall cancer death rate in petroleum counties than in matched non-petroleum counties. Much higher excesses were found for cancers of various sites: nasal cavity, 48 percent higher; lung, 15 percent higher; skin, 10 percent higher; testes, 10 percent higher; stomach, 9 percent higher; and rectum, 7 percent higher. Excess lung cancer rates were also found in female residents of the petroleum counties, clearly suggesting the role of carcinogenic emissions from industry into the surrounding community. The NCI study suggested that some of the excess cancers could also be

due to other classes of carcinogens emitted by refineries or other chemical industries located nearby.

While OSHA, NIOSH, and labor were moving to reduce occupational exposure to benzene, and EPA, prodded by the Environmental Defense Fund was moving to control industrial emissions to the general environment, concerns were growing that the home and arts and crafts schools are major sources of exposure, particularly for artists, craftsmen, and hobbyists. The only current regulatory restriction for such products is a requirement under the Federal Hazardous Substances Act for special labeling if they contain 5 percent or more benzene. In May, 1977, two public interest groups, the Health Research Group and the New York Center for Occupational Hazards, petitioned the Consumer Product Safety Commission to ban benzene-containing household products, including paint strippers and adhesives.⁴⁸ The petition noted the poor or nonexistent labeling practices of the manufacturers of these products and concluded that "there is no safe way for artists, craftspeople, hobbyists or children to work with benzene in their home or studio." The Commission has not yet taken action on this petition.

Summary

Literally millions of Americans are exposed to benzene, in many instances almost continuously, from sources including coke ovens, petroleum refineries, petrochemical plants, gasoline stations, auto exhaust, and a variety of consumer products including rubber cement and paint remover. While exposure to benzene has been known for nearly 100 years to cause blood diseases, growing epidemiological evidence over the last two decades has shown that it also causes aplastic anaemia and leukaemia, as well as chromosomal damage.

Following initiatives by organized labor and public interest groups, steps were taken in 1977 by OSHA, EPA, and the Consumer Product Safety Commission to regulate benzene exposure in the workplace, general environment, and the home. Industry, led by the Manufacturing Chemists Association and the American Petroleum Institute and with the support of their academic con-

sultants, attacked EPA estimates on environmental levels of benzene, while having failed to previously supply such information on request and in spite of the fact that the government estimates agreed well with industry findings. Industry also attempted to discredit the epidemiological evidence on the leukaemogenicity of benzene and to assert that there was a "threshold" below which it was safe to expose workers to benzene, in spite of the overwhelming rejection of the threshold concept by the informed and independent scientific community. Industry also argued against accepting human evidence on the carcinogenicity of benzene because earlier studies had failed to produce these effects in animals, while at the same time rejecting more recent animal studies which appear to confirm the carcinogenicity of benzene.

Out of the industry experience in mobilizing support to attack proposed federal regulations of benzene, a new organization, the American Industrial Health Council, was spawned from the Manufacturing Chemists Association to fight current attempts by OSHA to develop "generic" standards for carcinogens in the workplace.

Chapter Six

Consumer Products:

Case Studies

Consumer products represent the most direct way in which the consumer is exposed to industrial chemicals. Regulatory responsibility for different classes of consumer products is shared by various agencies, including the Food and Drug Administration (FDA), for food and animal feed additives, cosmetics, and drugs; the Consumer Product Safety Commission, for household products, including cleaning agents, flame retardants, refrigerants, and paints; the Environmental Protection Agency (EPA), for pesticides; the United States Department of Agriculture (USDA), for grading and labeling of meat, poultry, fruits, and vegetables; and the Federal Trade Commission, for advertising of all classes of consumer products, including tobacco which is otherwise virtually unregulated. Requirements for testing and labeling of the various classes of consumer products, and for evidence of their efficacy, are inconsistent. The ways the consumer is exposed to chemicals in these products are highly varied.

Smoking is generally regarded as a voluntary action, although it is usually initiated in adolescence and in response to massive advertising campaigns and peer pressures. However, smoking also

exposes non-smoking bystanders involuntarily. Similarly, the use of certain food additives, such as saccharin, is also generally considered voluntary, especially in the case of adults deliberately taking it in various beverages such as diet sodas and foods or as drugs. However, exposure of the embryo to the carcinogenic effects of saccharin, and other carcinogenic food additives, is clearly involuntary. Many classes of additives, such as the food dye Red #40, are so ubiquitous and poorly labeled in the food supply that the consumer, wishing to avoid them, has only limited options to do so. Consumer options are similarly limited for a wide array of chemicals, including: flame retardants in fabrics and textiles; chemical additives to cattle or poultry feed, residues of which are found in meat products; pesticide residues in food; and residues of chemicals that migrate from plastic food packaging. Drug taking, especially prescription drugs, is essentially involuntary and often without informed consent of the consumer-patient. The pharmaceutical industry and prescribing physicians usually do not make available to the patient full information on risks.

This chapter presents a series of five case studies: tobacco, Red dyes #2 and #40, saccharin, acrylonitrile, and female sex hormones.

*A custom lothsome to the eye, hateful to the nose,
harmful to the braine, dangerous to the lungs, and in
the blacke stinking fume thereof, neerest resembling
the horrible Stigian smoke of the pit that is
bottomellesse.*

James I, 1604.

Tobacco

Within 24 hours of setting foot on the soil of the New World, Christopher Columbus picked up the tobacco smoking habit from

American Indians and later introduced it to Europe. The habit spread like wildfire, being particularly popularized in England by Sir Walter Raleigh, whose smoking, like his politics, was offensive enough to James I to eventually have him beheaded.

A century later, the Italian physician, Bernardino Ramazzini, one of the great pioneers of industrial medicine, noted that Italian tobacco workers, who prized their jobs, did so in spite of headaches and stomach disorders from tobacco dust.¹ "The sweet smell of gain," Ramazzini commented, "makes the smell of tobacco less perceptible and less offensive to those workers. . . . This vice will always be condemned and always clung to." Emotional and other considerations apart, this clinging is now seen to be the result of physiological habituation or addiction to nicotine.

Many people feel that the book on tobacco has been closed, that we know as much as we need to about its cancer-causing properties, and that whatever lessons need to be learned about the prevention of tobacco-related diseases have already been learned. But the continued study of the relation between tobacco smoking and disease is still necessary for several reasons: first, to provide further understanding on how tobacco smoke causes cancer, respiratory, cardiovascular, and other diseases; second, to provide information on the interaction of tobacco smoke with other environmental and occupational carcinogens and toxic chemicals; third, to further educate the public on the hazards of smoking in order to better pressure the government and voluntary health agencies, such as the American Cancer Society, to develop more aggressive approaches to regulating tobacco sales and advertising; and finally, to provide surveillance of the tobacco industry, including monitoring the effects of constantly changing tobacco products and markets.*

The pattern of cigarette smoking in the United States is changing.² The total number of adult smokers, particularly in the upper socioeconomic groups, has been declining since 1970. However, the number of smokers among teenagers and pre-adolescents, particularly young girls, is on an alarming rise. In 1977, 27 percent of all teenage girls smoked cigarettes, compared to 22 percent in

* Further research would be largely unnecessary if the government were to ban tobacco advertisement and mount a massive campaign to persuade people to give up smoking. An even more effective curtailment of the industry would result if it were forced to accept financial responsibility for each tobacco-related death.

1964. This is happening despite a growing awareness among all age groups that smoking is a serious health hazard.³ Because of the long time from the first cigarette puff to the appearance of cancer, current trends will not affect disease rates for many years to come. Even so, the male lung cancer rate is increasing at a lesser rate than previously. The rate for women, however, continues to climb as sharply as before and may eventually reach that of men.⁴

The Chemistry of Tobacco Smoke⁵

The chemical composition of tobacco smoke is quite complex, which probably comes as a surprise to most smokers, who tend to think of smoke only in terms of nicotine and "tar." Tobacco is a cured, dried plant leaf. When burned in a paper wrapper, it produces a variety of products from incomplete combustion of the leaf, the wrapper, and the many curing agents, additives, fillers, and a wide range of pesticide contaminants also present in cigarettes. These combustion products are either completely vaporized or are released as a suspension of microscopic particles in the smoke. The gas phase of the smoke contains a great variety of toxic and carcinogenic gases, some of which are listed in Table 6.1. These include several nitrosamines, such as dimethylnitrosamine (DMN), nitrosopyrrolidine, nitrosopiperidine, and N-nitrosonornicotine (found exclusively in tobacco smoke), which are all potent carcinogens.

The gas phase of cigarette smoke also contains a number of other chemicals which are either tumor promoters, such as formaldehyde, or impair the lung's natural defenses by disabling the cilia, as nitrogen oxides do, thereby permitting carcinogens from tobacco smoke and polluted air to penetrate and remain in the lungs.

When the gas phase is separated from tobacco smoke by filtration, a moist substance called total particulate matter is left behind. When the moisture and nicotine are then removed, a dry condensate known as tar remains. The tar contains literally innumerable chemicals, at least 1,200 of which have been identified. Many of them are known carcinogens and tumor promoters.

Table 6.1 Quantities and Concentrations of Some Gaseous Components of Cigarette Smoke

Substance	Quantity ($\mu\text{g}/$ cigarette)	Concentration (ppm)	TLV† (ppm)	Activity‡
Acetaldehyde	770	3,200	100	CI
Acetone	578	1,100	1,000	...
Acrolein	84	150	0.1	CI
Ammonia	80	300	25	...
Benzene	67	CA
Carbon dioxide	50,600	92,000	5,000	...
Carbon monoxide	13,400	42,000	50	...
Dimethylnitrosamine	0.08	CA
Formaldehyde	90	30	2	P
Hydrazine	0.03	CA
Hydrogen cyanide	240	1,600	10	CI
Hydrogen sulfide	...	40	10	...
Nitric oxide	...	250	5	...
Nitrosopiperidine	0.01	CA
Nitrosopyrrolidine	0.1	CA
Toluene	108
Vinyl chloride	0.01	...	1	CA

Source: E. L. Wynder and D. Hoffmann, *Seminars in Oncology*, 3 (1976): pp. 5-15; and I. Schmeltz, D. Hoffmann, and E. L. Wynder, in *Trace Substances in Environmental Health*, D. D. Hemphill, ed., 7 (1974): pp. 281-95.

† Threshold limit value, maximum concentration permitted for workers exposed to the same substance in the air of their workplace.

‡ CA=carcinogen, CI=ciliotoxic agent, P=promoter.

The Epidemiology of Lung Cancer⁶

Many factors are involved in the association between tobacco smoking and lung cancer.

Type of Tobacco Product Smoked Cigarette smokers have a higher lung cancer rate than cigar or pipe smokers.⁷ This is probably due to the fact that the smoke of cigars and pipes is more alkaline than that of cigarettes and is not likely to be inhaled so deeply. Alkaline nicotine is more toxic than its neutral form and

is more readily absorbed through the mouth and nose. Because of the rapid absorption of nicotine, cigar and pipe smokers need to smoke less to maintain a given nicotine level. Additionally, cigar and pipe smokers usually inhale less than cigarette smokers.⁸ Among those few cigar and pipe smokers who inhale, lung cancer and coronary heart disease rates are as high as for cigarette smokers. Additionally, cancers of the lips, tongue, mouth, and esophagus are as high if not higher among pipe and cigar smokers, irrespective of the degree of inhalation.

Quantity Smoked Nearly every epidemiological study has found a dose-response relation. The more cigarettes, cigars, or pipes smoked per day, the greater is the cancer risk.⁹

Duration of the Habit The longer a smoker continues to smoke, the greater is the risk of cancer.¹⁰

Inhalation Most recent studies confirm the obvious notion that inhalation increases the risk of cancer.¹¹ An interesting sidelight comes from studies of smoking in France, where the lung cancer rate is the lowest in the Western world, yet cigarette consumption is among the highest. This is probably due to the fact that French smokers inhale less than Americans. One reason for this is that French smokers favor the government-distributed brand, Gauloises, made with a black variety of tobacco rather than the blond Burley blends of American and English cigarettes; black tobacco smoke is highly alkaline, while blond smoke is acidic.*

Smoking Cessation There is ample evidence that stopping smoking decreases the cancer risk, and also the risk of heart disease, even for long-term smokers.¹² However, the extent of relief is still unclear (see Table 6.2).

Tar Yield It has long been assumed that the major carcinogens in tobacco smoke are found in the particulate rather than the gas phase. Tar condensates have been measured annually by the Fed-

* The nicotine from alkaline smoke is more easily absorbed through the mouth and tongue, allowing the smoker of French cigarettes to satisfy the craving for nicotine without inhaling the carcinogenic smoke.

eral Trade Commission for over a decade and the results must now be displayed in advertisements.

When filter cigarettes first became popular in the mid-1950s, their major role was the reduction of tar. This single step has led to lower death rates from lung and larynx cancers among smokers of filtered cigarettes, compared with smokers of high-tar cigarettes.¹³ However, death rates among filter cigarette smokers are in excess of those in non-smokers.

Only half the cigarettes smoked in the United States in 1960 were filtered. Today over 90 percent are filtered and have tar levels less than 20 mg per cigarette. Federal Trade Commission ratings have also shown a very marked increase of cigarettes with tar levels under 10 mg, as many as 28 brands being available by June, 1977.

One problem with low-tar cigarettes is that they have a lower nicotine/tar ratio than unfiltered cigarettes. To compensate for this lower nicotine content, smokers of filtered cigarettes may inhale more and use more cigarettes than would be the case if they smoked unfiltered cigarettes. Thus filter cigarette smokers may end up inhaling more tar than they would from high-tar cigarettes. Low-tar cigarettes also produce relatively higher levels of carbon monoxide, due to relatively incomplete combustion, and increased carbon monoxide inhalation appears to promote heart disease. Additionally, there may well be unrecognized risks from the extensive use of hundreds of secret and untested flavor additives used to restore flavor lost in the high filtration process in low-tar cigarettes. From all points of view, there is absolutely no better way to deal with these problems than to stop smoking.

Histology of Lung Cancer There are several different types of lung cancer. The most common type, *squamous carcinoma*, comprises cancers of the epithelial cells lining the trachea and bronchi and is caused by smoking. A second type, called *oat cell carcinoma*, is also strikingly related to cigarette smoking. Smoking probably causes a third type, *adenocarcinoma*, but much less frequently than the other types.

Worldwide Data Many countries now either support limited epidemiological surveys on smoking or participate in programs

Table 6.2 Comparison of Relative Lung Cancer Death Rates for Men Aged 50-69 for Cigarette Smokers, Ex-Smokers, and Non-smokers

Smoking Habits	Death Rates Relative to Non-smokers
Non-smokers	1.0
Current smokers (cigarettes/day)	
1-9	3.5
10-19	8.8
20-39	13.8
40 or more	17.5
Current smokers with different inhalation practices	
None or slight	10.6
Moderate	11.7
Deep	13.9
Ex-smokers of 1-19 cigarettes/day who had quit for specified number of years	
1 or less	7.2
1-4	4.6
5-9	1.0
10 or more	0.4
Ex-smokers of 20 or more cigarettes/day who had quit for specified number of years	
1 or less	29.1
1-4	12.0
5-9	7.2
10 or more	1.1

Source: E. C. Hammond, "Smoking in relation to death rates of one million men and women," National Cancer Inst. Monogr. 19: pp. 129-204, 1966.

developed by international health agencies. The British Tobacco Research Council, an industry trade association, publishes reports on the use of tobacco products by Britons, as does the Verband der Cigarettenindustrie in Germany.

Recently, a high degree of correlation has been demonstrated between the present lung cancer mortality rate in nineteen different countries and their per capita cigarette consumption

thirty years ago.^{14†} Three countries that did not fit this correlation well were France, Ireland, and Japan. The French data can be explained by the fact that smokers in that country tend to inhale less than Americans. The Japanese anomaly was thought due to the Japanese custom of *kazami*, in which the cigarette is puffed, but not inhaled. The Irish data are largely unexplained, but may reflect lesser concomitant exposure to occupational carcinogens.

Differing Cancer Rates in Various Groups Until about 1950, few American women smoked. The rapidly rising cancer rate among women today reflects the smoking habit established about thirty years ago and continued since then. The cigarette-smoking habit is now increasingly common among adolescents of all classes and working people, while the white-collar classes, particularly professional men, are giving it up in increasing numbers. Also, a greater proportion of black men smoke than whites and they are more likely to use non-filters than whites. The lung cancer incidence rate among black males in this country is about one-third greater than that for white males.¹⁵

Smoking and Air Pollution Various surveys in England and the United States have indicated that smokers of a given age, sex, and level of tobacco consumption have a higher lung cancer rate if living in urban areas with high air pollution levels, than if living in the relatively unpolluted suburbs. It seems likely that there is a synergistic interaction between smoking and urban air pollution.‡

Lung Cancer among Non-smokers and in Workers About 20 percent of lung cancer deaths occur in non-smokers, and the incidence of lung cancer in non-smokers is on the increase. While there is a marked increase in the incidence of lung cancer in asbestos workers and uranium miners who smoke, there is also an

† The thirty-year lag reflects the long latency period for lung cancer.

‡ According to Schneiderman (*Preventive Medicine* 7 (1978) pp. 424-38), there has been a decline in cancer rates in England since their Clean Air Program was initiated in the mid-1950s. Schneiderman also points out that from 1947 to 1970 there has been an increase in U.S. lung cancer rates in the order of 10 to 20 percent which cannot be accounted for by smoking.

increase, though a lesser one, in non-smokers who work in these industries. An important role of exposure to occupational carcinogens in lung cancer deaths previously exclusively attributed to smoking is likely. It must be recognized that the role of work history and occupational exposures to carcinogens was ignored in the classical epidemiological studies relating smoking to lung cancer. This has led to a possible overestimate of the risks of smoking compared to the risks of exposure to occupational carcinogens or interaction between the two.* (This has been compounded by the fact that lung cancer mortality rates based on the International List of Causes of Disease fails to distinguish between lung cancer of different histological types, some of which, such as adenocarcinoma, are unlikely to be due to cigarette smoking and other forms of malignant disease of the lung, such as pleural mesothelioma, which is due to asbestos and not smoking.) As Schneiderman of the NCI has recently pointed out (see statement to OSHA, Docket 090, April 4, 1978), "We are unable to say how much of the risks attributed to cigarettes is a 'pure' cigarette risk and how much is cigarette times another, possibly on-the-job hazard."

It should be noted that these various epidemiological studies proving the tobacco-cancer relationships were all based on analysis of groups of individuals with varying smoking habits as compared to non-smokers. In the absence of population groups with such differences in exposure, epidemiology cannot readily establish causal links between disease and exposure. (This is why epidemiology is of limited value for the detection of such environmental carcinogens as food additives and pesticides to which the population-at-large is extensively exposed.) One possibility that has not been adequately recognized is that some cancer cases identified in these epidemiological studies derive from exposure to occupational carcinogens, such as asbestos, as well as or instead of tobacco smoke.

This epidemiological summary would be incomplete if it left the

* Echoing Wilhelm Hueper's earlier warnings, Joseph Wagoner of OSHA has recently stated that overemphasis on smoking has been a major barrier to research into occupational causes of lung cancer. (For a more detailed discussion and confirmation of this viewpoint, see J. G. French et al., NIOSH, "Interactions Between Smoking and Occupational Exposures," The Surgeon General's Report on Smoking and Health, January 11, 1979.)

impression that lung cancer is the only type of cancer caused by smoking. Tobacco smoking is also incriminated in cancers at other sites, including the lip, tongue, mouth, larynx, pharynx, esophagus, urinary bladder, pancreas, and possibly kidney and liver.[†] In addition to cancer, smoking is the major cause of chronic bronchitis and emphysema in the United States. Smoking also has a striking relationship to coronary heart disease, stroke, aortic aneurism, and other diseases, including peptic ulcers.

Astoundingly enough, industry claimed for some time that the association between tobacco and all of these diseases showed that their product could not possibly be at fault. In this they were supported by academic consultants, including the well-known statistician, Joseph Berkson,¹⁶ of the Mayo Clinic, who protested in 1958; "I find it quite incredible that smoking should cause all of these diseases. It appears to me that some other explanations must be formulated." In view of the fact that tobacco smoke contains hundreds of identifiable chemical components, it is now surprising that smoking causes so few diseases.

Involuntary Smoking

Passive or involuntary smoking is the inhalation by non-smokers of the secondhand products of cigarette smoking, usually in situations not of their own choosing. This type of exposure is potentially serious, because the toxic and carcinogenic chemicals released from the burning tip of a cigarette enter the atmosphere totally unfiltered. This so-called sidestream smoke contains high concentrations of tar, carbon monoxide, nicotine, and nitrosamines. (The smoker thus breathes the double load of mainstream and sidestream smoke.) Many non-smokers are highly sensitive to cigarette smoke, the most noticeable effects of which are eye and throat irritation. In poorly ventilated enclosed areas, such as bars, automobiles and conference rooms, allowing one pack of cigarettes to burn has produced levels of nitrosamine carcinogens ten times higher than in inhaled smoke itself, a tar concentration

[†] The attributable risk (the proportion of a disease to a given cause) of lung cancer due to smoking has been estimated as 0.8 to 0.85 (80–85 percent); for bladder cancer, 0.4–0.5; for pancreas cancer, 0.3–0.4.

of 17 mg/m³ and carbon monoxide levels of 70 ppm.¹⁷ In such an environment, the carboxyhemoglobin level of a non-smoker, a measure of carbon monoxide inhalation, has been found to double. Such studies have shown that this environment for the passive smoker, especially the elevated carbon monoxide, is particularly dangerous for people with cardiovascular disease, and can aggravate or bring on anginal symptoms.¹⁸ It is not yet known what effect such exposure has on lung cancer risks, although on theoretical grounds it is likely that they are increased.

A second category of involuntary smoker is the fetus. Many studies have found a marked decrease in birth weight of infants born to mothers who smoked during the second half of pregnancy, even as little as one cigarette per day.¹⁹ The immediate effect of maternal smoking on the health of the child can be seen in the poor survival rate for these infants with a lower birth weight. The 1974 surgeon general's report estimated that of 87,000 perinatal deaths in the United States, 4,600 were a direct result of the mother's smoking. The smoking mother is also 80 percent more likely than the non-smoker to have a spontaneous abortion. Other effects also occur, such as the increased carbon monoxide in the mother's blood causing a more rapid heartbeat in the fetus. In addition, both nicotine and the carcinogen benzo[a]pyrene cross the placental barrier and reach the fetus, which at that stage in development is particularly sensitive to carcinogens. Children of smoking parents also have a higher incidence of bronchitis and pneumonia than the children of non-smokers. Finally, the role parents play as models for their children should not be overlooked; children of smokers are probably more likely to smoke than children of non-smokers. In spite of such evidence, the Tobacco Institute,‡ supported by the NCI's Gori, says that there

‡ The Tobacco Institute was created in 1958 to handle the industry's lobbying and imagemaking. Its current budget of about \$5 million is largely derived from tobacco company dues, half of which can be deducted from taxes as the institute is chartered as a non-profit trade association. The institute's legal bill (for lawyers including former Kentucky Senator Marlow Cook and former North Carolina Representative Henderson) topped \$1 million in 1977. Over the last two decades, the institute has spent about \$74 million on "independent research" on tobacco and health. The institute encourages new legislators from tobacco states to seek seats on key committees. The president of the institute is Horace B. Kornegay, former North Carolina congressman, and its chief lobbyist is Jack Mills, former Republi-

is no hazard in involuntary smoking and that there is no need for regulatory controls to protect the non-smoker.

Financial Costs of Smoking

While it is difficult to properly calculate the financial costs of smoking, it seems clear that these are much greater than the \$6 billion annual tax revenues generated.²⁰ Annual costs in the United States include treatment and deprivation of earnings of the 80,000 or so tobacco-associated lung cancer victims and the approximately 200,000 victims of respiratory and cardiovascular diseases caused by smoking. The costs of passive smoking have not yet been adequately recognized, let alone estimated. Other direct costs include the millions of public research dollars spent on tobacco-induced diseases, income loss from tobacco-induced diseases, and excess fire protection costs. In the latter category for example, fire protection and fire damage costs from smoking in Massachusetts alone are estimated to be \$18 million and \$26 million, respectively. Recent estimates of total annual costs from smoking are in the \$20 billion range.

The Role of Government in "Prevention" of Tobacco-Related Cancer

What is the government doing to reduce the number of cases of tobacco-related cancers? The only major effort now federally funded is a coordinated set of projects administered by the NCI, known as the Smoking and Health Program. The program's fundamental premise is that since an outright ban on cigarettes is not possible now, the best compromise is to develop a "less harmful cigarette."²¹ However, it is inappropriate for the taxpayer to fund this research through the NCI, especially when it is clear that the

can party power-broker. The Tobacco Institute is probably one of the most powerful trade associations in its ability to mold the legislative and regulatory process to the advantage of the industry. The American Cancer Society provides virtually no effective opposition to these activities.

industry will profit from apparent successes in the research program. The most serious criticism of the Smoking and Health Program, apart from its token budget, is its lack of anti-smoking education activities. Instead of opposing smoking as its main goal, the government program merely seeks to reduce the risks entailed in smoking, thereby supporting the industry efforts to persuade smokers to persist in their habit but switch to "less harmful" cigarettes.

The avowed goal of the Smoking and Health Program is to attempt to reduce the risk for the smoker who refuses to or allegedly cannot quit. The project consists of a range of activities with this common theme. The major current tobacco blends are analyzed to identify their chemical constituents. These are then tested in animal models to determine their individual roles in tobacco cancer. On the basis of these results, an experimental cigarette is "built," which contains a minimum of toxic products. Flavor agents or additives are then added to this "less harmful cigarette" to make it more palatable to the average smoker. The possibility of toxic or carcinogenic effects from these tobacco additives does not seem to have been adequately investigated.

To oversee the smoking program, the NCI set up the Tobacco Working Group, consisting of health and industry experts, including vice presidents and research directors of Liggett & Myers, the Brown & Williamson Tobacco Company, R. J. Reynolds Industries, Lorillard Research Center, and Philip Morris, not to mention representatives of major consulting firms, such as Hazleton Laboratories and Arthur D. Little, Inc. Apart from the industrial domination built into the Tobacco Working Group, research and educational activities were trivial in relation to the importance of smoking as the number one cancer killer. The Tobacco Working Group, which was disbanded in 1977,* funded only a single large-scale epidemiological study on smoking and cancer and failed to fund studies on interactions between smoking and industrial chemicals in the workplace and in the general community. Additionally, the pattern of research support awarded by the Tobacco Working Group has demonstrated clear conflicts of interest in that much of the support was awarded to the members of the

* Since then, there do not appear to have been any major changes in NCI policies on tobacco.

Group or to the institutions to which members of the Group belonged.

An example of how similar were the perspectives of the Tobacco Working Group to those of industry is the allegation by its recent director, Gio Gori (deputy director of the NCI's Division of Cancer Cause and Prevention and now on leave of absence as a student at Johns Hopkins' School of Public Health), that a so-called "practical threshold" exists for each popular brand of cigarette, constituted by the number that can be smoked daily without leading to a detectable increase in risks of lung cancer.²² An immediate rebuttal was issued by Arthur Upton, NCI Director, and Robert Levy, Director of the National Heart, Lung and Blood Institute, in a joint statement of August 10, 1978.

We fear Dr. Gori's paper may mislead the public. We are even more concerned about his assertion that the risk involved with low-tar-and-nicotine cigarettes is "tolerable."

This was followed by a similar disclaimer from Assistant HEW Secretary Julius B. Richmond.²³

No one should be misled by Dr. Gori's study into the belief that there is some way that one can adjust one's smoking habits and the cigarettes one smokes and thus avoid all health risks.

NCI statisticians John Gart and Marvin Schneiderman (in an unpublished but widely circulated letter to *Science*) attacked Gori's methods as "so seriously in error that we find the conclusions based on the statistical analysis . . . to be invalid."²⁴ Correcting for errors, Gart and Schneiderman showed that recalculation of Gori's own data proved that smoking as few as one cigarette every five days, considered by Gori to be "tolerable," produced as much as a 10 percent increase in risks of lung cancer. Other critics pointed out that Gori had considered only six components of cigarette smoke (tar, nicotine, carbon monoxide, nitrogen oxides, hydrogen cyanide, and acrolein), quite apart from ignoring hundreds of other known toxic components; that he had not considered potential toxic or carcinogenic effects of newer untested cigarette additives; and that he had not dealt adequately

with the behavioral problem of "compensation," whereby persons who switch to lower tar cigarettes often smoke more cigarettes or inhale more deeply to adjust for the lower nicotine level of their adopted brand. The tobacco lobby, however, was jubilant. Senator Paul Huddleston of Kentucky remarked that the NCI study "indicated our efforts to produce a safer cigarette and reduce potential hazards are drawing some beneficial results."²⁵ *The Wall Street Journal* reported that at least 10 percent of the nation's 63 million smokers would try Carlton, the lowest-tar brand, as a result of the Gori report.²⁶

The NCI, with a current annual budget of over \$900 million, last year spent less than \$9 million on all its tobacco research projects, most of which went to the Smoking and Health Program. Much of this research support is channelled through a prime commercial contractor, Enviro Control, of Rockville, Maryland. Less than \$2 million a year is spent by the NCI on educational programs, in contrast with the \$400 million the industry now spends annually on cigarette advertising in magazines and newspapers.

The Role of the Government in the Increase of Tobacco-Related Cancer

The extent of federal support of the industry is not generally appreciated. This support is more than amply compensated by massive revenues from tobacco sales. Federal, state, and local governments collect about \$6 billion in tobacco taxes annually. In 1977, \$97 million was spent by the government in direct assistance programs and in indirect support of the industry. This includes a \$50 million USDA research program studying better ways to grow and process the crop, and contract-supported research at the universities of Kentucky and North Carolina. Other federal subsidies include inspection and grading of domestic crops, administration of tobacco price support programs, and loans for sales abroad under the 1954 Food for Peace program.† In December, 1977, Presi-

† Federal tobacco "subsidies," established by President Roosevelt in the 1930s as a means of stabilizing a market of thousands of small farmers and only a few large conglomerates who purchased their crops, are more accurately described as price support programs. Some justification for their re-

dent Carter pledged continued federal support for tobacco growers, expressing the view that the assistance programs and health dangers of tobacco should be considered as separate issues.

In a speech on January 12, 1978, HEW Secretary Joseph Califano announced, on the occasion of the 14th anniversary of the surgeon general's classic report on smoking and health, an anti-smoking campaign particularly aimed at the nation's youth.²⁷ Calling smoking "slow-motion suicide," he asked the major broadcasting networks to increase anti-smoking commercials; called for a ban on smoking in most public areas of HEW buildings; endorsed the Civil Aeronautics Board proposal to ban cigarettes on commercial airliners; urged an increased tax on cigarettes; asked insurance companies to give premium discounts to non-smokers; and asked the FDA to amend labeling on oral contraceptives to indicate the even greater risk of strokes and heart attacks for smokers.‡

Asked to comment on the apparently contradictory thrusts of the Carter and Califano statements, White House Press Secretary Jody Powell commented:

The Administration does not feel that there is any logic in asking thousands of families and communities to bear the burden of economic ruin which would result if we abolished the part of the farm program because of the habits of an entire nation.²⁸

The reaction of the tobacco industry to Califano's speech was summarized by Raymond J. Mulligan, President of the Liggett Group, Inc., who called the Secretary "a silly ass."²⁹ The Kentucky state legislature went further and demanded Califano's res-

tention, in the absence of effective regulation of tobacco, is provided by a 1978 Congressional Research Service Report (to Congressman Andrew Maguire) "Information on Tobacco Production, Marketing and Government Programs." This report contends that removal of "subsidies" would result in the decline of tobacco prices, increase domestic consumption, and increase the consolidation of small farms into large conglomerates.

‡ While these proposals are to be welcomed, they are merely proposals to other agencies, without any regulatory force and without any preventive economic measures, such as increased tobacco taxation or incentives to tobacco farmers to develop other crops (for a recent discussion of non-regulatory approaches to decrease tobacco consumption, see M. A. Schneiderman, "Legislative Possibilities to Reduce the Impact of Cancer," *Preventive Medicine* 7, 1978, pp. 424-38).

ignation. It is clear that an administration attack on tobacco price supports would be damaging to the base of Carter's political support in the South. It is not clear how the administration weighs political expediency against 300,000 American deaths each year.

The Role of Industry

The tobacco industry did not welcome the early reports of the adverse health effects of smoking. During the 1950s, when many of these studies were just getting under way, the industry did its best to discredit them by sponsoring their own studies in search of contrary results and by supporting highly publicized and unproductive forays into improbable areas of research. These strategies were relatively successful for many years, as the few independent scientists who devoted their careers to tobacco and health research were repeatedly forced to enter public forums to respond to industry challenges.

It is important to understand the claims of the tobacco industry, because many of them are being echoed in the present-day debates over other environmental carcinogens. The standard gambit then, as now, was that the health research implicating smoking was based only on statistics and not on medical observations. If a real cause and effect sequence from cigarette smoking inhalation to cancer could be shown, the industry cried, rather than all these statistics, that indeed would constitute proof.

Another favorite industry fallback was, and still is, the genetic, or constitutional issue. This claims that some people, predestined by their genes to get cancer, are also by nature predisposed to smoke cigarettes. In simpler terms, cancer causes smoking!¹³⁰ The logical conclusion of this argument is that "susceptible" people somehow should be identified and discouraged from smoking so that the rest of the population can continue to be exposed "safely." This line of reasoning is sometimes applied to the debate on exposure standards in the workplace, where other industries talk of finding and screening out "hypersusceptible" workers.

In terms of funding research, the tobacco industry remains at consultant's length from the NCI smoking program, as it would not do to have government money paid directly to tobacco com-

panies for health research. On April 12, 1977, the industry launched its own Tobacco and Health Research Institute on the University of Kentucky campus.* In a three-day conference held in Lexington to mark the dedication of this institute, the thrust of research to be undertaken there was revealed. Of nineteen talks given by well-known speakers invited from academia, ten were devoted to the genetic factors and immune response involved in "hypersusceptibility" to tobacco smoke. Indeed, the title of the program, "Pulmonary Disease: Defense Mechanisms and Populations at Risk," only hinted at the reality. The institute appears to have adopted the tobacco industry's tactic of shifting the burden of proof away from themselves and onto the victims.

Early efforts at regulating the sale of tobacco, based on health reports in the 1950s, inspired massive counter-lobbying by the industry and tied up the Federal Trade Commission for years in administrative logjams.³¹ Even when the writing at last appeared on the wall with the famous 1964 warning of Surgeon General Luther Terry that smoking presents "a health hazard of sufficient importance . . . to warrant remedial action," industry decided to dig its heels in still more firmly.³²

The biggest blow against cigarette smoking was initiated in 1970 by John Banzhaf II, Director of a public interest group known as Action on Smoking and Health. Banzhaf petitioned the Federal Communications Commission to use the Fairness Doctrine to require TV and radio stations that broadcast cigarette ads also to give equal time to anti-smoking ads. The commission and the courts agreed with Banzhaf. Tough anti-smoking spots began giving the public the other side of the smoking story. So strong were the spots that the cigarette industry decided to remove their ads from the airwaves, which had the effect of removing the anti-smoking spots also.

The tobacco industry's voluntary withdrawal from TV and radio advertising was one of the most successful gambles in the history of mass marketing. The industry thus saved hundreds of millions of advertising dollars, which were then used to strengthen its printed advertising, which would continue unthreatened by anti-smoking commercials. Advertising revenues to newspaper and

* The Institute is an operation of the Commonwealth of Kentucky, and is entirely supported by an allocation from the state cigarette tax.

magazine publishers have increased nearly seven-fold since 1970, reaching a current annual total of approximately \$400 million. Also, to get further media exposure, the industry sponsors athletic contests, such as the Virginia Slims Tennis competition.[†] A new organization of health professionals called "Doctors Ought to Care" has filed a request that the U.S. attorney general forbid televising the Virginia Slims Tournament under that name on the grounds that such advertising is against Federal Communication Commission regulations.

The latest marketing gimmickry is the introduction by R. J. Reynolds of a new brand of cigarettes called Reals. Reals were launched in 1977 with a \$50 million promotional campaign described in the press as "the most heavily advertised cigarette introduction of all time," and as "the biggest marketing campaign in the history of consumer packaged goods." The industry itself promised that "before long you won't be able to turn around out there without having Real hit you over the head."³³ The thrust of this advertising campaign, which bombed because it failed to stress low tar strongly enough, was that Reals are "natural" cigarettes containing no synthetic flavoring or other additives. The clear and misleading inference is that Reals are safer than other cigarettes and should be favored by health-conscious consumers.

Senator Edward Kennedy (D-Mass.) is currently exploring new initiatives designed to deter adolescents from smoking. These are based on the use of HEW funds to support private and public educational programs on TV and through other media. Additional approaches also being considered by Senator Kennedy include mandating the use of more effective and explicit labels on cigarette packs.

The Role of the American Cancer Society

Much of the early work on the causal association between smoking and cancer was supported by the American Cancer Society. In fact, the society was one of the few major health groups to request

[†] In 1975, the Florida Chapter of the American Cancer Society offered to cosponsor the tournament. The offer was abruptly withdrawn when the national office in New York found out what was happening.

President Kennedy in 1961 to take action against tobacco. Having made this important contribution, the society took the position that the matter was out of its hands. In its own words, the society "had used [its] resources to uncover the health risks of smoking. Now it was up to the government to take a stand and to respond accordingly."³⁴

This attitude has typified subsequent policies of the American Cancer Society. Following publication of the 1964 surgeon-general's report, the society expressed disappointment at the failure of government to act. However, when Banzhaf petitioned the Federal Communications Commission in 1971 for equal time against tobacco ads, the society refused to support him, let alone defend the subsequent FCC ruling in his favor.‡

Since the Banzhaf episode, the record of the society has remained mixed. It has supported ordinances to prohibit or restrict smoking in public places, to request more stringent warnings on cigarette packs, including use of the word "death," and to establish a graduated federal excise tax on cigarettes based on their tar and nicotine content.

In October, 1976, the society created a National Commission on Smoking and Public Policy, under the direction of Victor Weingarten (an experienced public relations consultant), with Philip R. Lee (University of California School of Medicine, San Francisco) as acting chairman. The Commission was asked to assess the effectiveness of current anti-smoking activities and make appropriate recommendations for new strategies. The Commission held extensive hearings, took testimony from over three hundred individuals, and examined voluminous published and unpublished data, including industry files. The Commission reported back to the society in January, 1978, recommending the development of strong legislative action, and endorsing earlier recommendations to this effect by Nutrition Action (a Washington-based public-interest group). The Commission further recommended that the Society set up a powerful anti-tobacco lobby in Washington, D.C., and spend the maximum amount of money permitted by law for

‡ According to Banzhaf, the society "has never participated in a judicial, regulatory, or legislative petition related to smoking . . . [their usual response being] We don't want to get involved in anything controversial." (Frank Greve, "Cancer Society's Efforts Found Wanting," *Philadelphia Inquirer*, April 30, 1978.)

legislative activities. The American Cancer Society rejected these recommendations, but, in an apparent compromise move, published a report critical of its own past performance, and pledged to support HEW Secretary Califano's new anti-smoking initiatives.

The "Target 5," five-year program of the society, designed to reduce the number of young people and adults who smoke and to reduce the toxicity and carcinogenicity of tobacco smoke, stands little chance of success without a well-organized lobbying activity. The society still has not announced plans to lobby Congress or to file petitions with the Federal Trade Commission and other concerned agencies. The society has a part-time lobbyist in Washington, D.C., Tanny Pollster, whose major activity seems to be protecting the NCI budget, and who views his role primarily as a "collector of information for the society," rather than as a lobbyist. It is widely rumored that Pollster's salary is defrayed by a direct pass-through to the society from Mary Lasker. In early 1978 the society hired the late Marvella Bayh, wife of Senator Birch Bayh and a breast cancer victim, as a full time lobbyist.* It would not seem unreasonable to expect that the society should develop strong lobbying activities in order to secure legislative and regulatory support for its anti-smoking programs and objectives.†

The Role of the Press

The press is now the almost exclusive medium of major advertising for the tobacco industry. The massive coverage given the Vietnam War, with some 40,000 U.S. deaths in all the war years combined, and the violent crime deaths of some 20,000 per year contrasts with the virtual silence of the press on a single agent in-

* The society appears to have placed Mrs. Bayh in a position of potential conflict of interest. Senator Bayh, as a member of the subcommittee on Labor and HEW of the Appropriations Committee, has considerable influence on the NCI budget. He has, however, failed to persuade Senator Kennedy that the "War on Cancer" be made an integral part of proposed National Health Insurance plans.

† Under the Tax Reform Act of 1976 (Sec. 4911, Tax Code Amended, 1976), tax exempt organizations such as the American Cancer Society are allowed to spend up to \$1 million annually on lobbying.

criminated in about 300,000 preventable deaths a year. The enormous revenues generated probably account for the apparent lack of interest of the press in devoting proportionate space to tobacco health hazards.

There are, however, some notable exceptions. The *Reader's Digest*, which does not accept cigarette advertisements, has published a series of authoritative articles on the dangers of smoking over the last two decades, and *The New Yorker* has published several outstanding articles by Thomas Whiteside on the political and advertising strategies of the tobacco industry.

The Role of the Courts

The courts have not been helpful in the past in gaining legal redress for victims of tobacco cancer. At least fifty such suits have been filed, but none has ever resulted in an award. During the 1950s and 1960s, the main argument of the plaintiffs was that the producers had failed to supply a product of marketable quality and that they had not fulfilled their responsibility to make sure that cigarettes were harmless, while implying such in their advertising. The successful defense of industry was that there had been no way to foresee the harm their product might do a consumer.

The farthest such a case has ever gone was *Green v. American Tobacco Co.* Edwin Green of Miami contracted lung cancer in 1956, after smoking Lucky Strikes for thirty years. A jury found in favor of the company at first, but the Court of Appeals, acting on an appeal by the heirs of the by then deceased Green, directed a new jury trial. The second jury found that Luckies were indeed "reasonably fit for general public consumption," since as one juror later told reporters, if it took twenty to thirty years to affect the plaintiff, they must be reasonably safe. This juror, however, gave up smoking after the trial.³⁵

A new appeal by the heirs against this adverse decision resulted in a temporary reversal, in which the Court stated:

We are now left in no substantial doubt that under Florida law the decedent was entitled to rely on the implied assurance that the Lucky Strike cigarettes were wholesome and fit for the purpose in-

tended and that under the facts found by the jury [his widow is] entitled to hold the manufacturers absolutely liable for the injuries already found by a prior jury to have been sustained by him.³⁶

But this consumer triumph was short-lived. In April, 1969, thirteen years after the case had been started and with Edwin Green long in his grave, the U. S. Fifth Circuit Court reversed the decision and found in favor of American Tobacco.³⁷ Shortly afterward, the universal labeling of cigarette packages with health warnings seemed to virtually close the door on this type of law suit. The smoker now stands warned with every pack he buys and with every advertisement he reads, that cigarette manufacturers do not claim their product to be entirely harmless. The main impact of this warning, advocated by many to help discourage smoking, may in the end be to release tobacco companies from liability and further shift the burden of smoking-induced disease to the victim.

On December 20, 1976, Donna Shimp, an employee of New Jersey Bell Telephone Company, obtained a court injunction ordering Bell to provide a workplace free of cigarette smoke for its non-smoking employees.³⁸ The court took into account expert testimony that carbon monoxide, nitrogen oxides, tar, and nicotine given off by cigarette sidestream smoke can aggravate lung and heart disorders, and that up to 10 percent of the population may be allergic to the smoke. The court ruled that smoking was not necessary to the operation of Bell's business, and that no employee should have to assume the risks of inhaling smoke as a condition of employment. The court also noted that, considering that smoking is prohibited near certain telephone equipment because "delicate parts" may be damaged, a human being should be entitled to at least as much protection.

Probably one of the most effective ways of decreasing the tobacco death toll would be to make the industry pay for tobacco-associated cancer and other diseases, as well as other national costs. Cigarette companies have in the past successfully defended themselves against lawsuits by claiming an "assumption of risk" by the victim or his or her family. This claim could be countered by the fact that the industry advertises widely to entice people, including minors, to start smoking. Such advertisements create "an attractive nuisance," often with fatal consequences. Perhaps what

is needed now is a series of large successful lawsuits against the industry, still a distant hope.

The Role of Consumer Groups

The rights of the non-smoker to breathe air unpolluted by tobacco smoke have been vigorously asserted recently by a number of public interest groups created especially for this purpose. Recent information on the dangers of passive smoking have lent further emphasis to these rights. Prominent among these is the Washington-based Action on Smoking and Health. This public interest group has appeared before the Federal Trade Commission in hearings to beef-up warnings on cigarette packages, and to impose stricter advertising rules; before the Federal Communications Commission to get "little cigar" commercials off the air and more anti-smoking ads on; and before the FDA to provide labels on birth control pills warning women about higher disease risks among pill takers who smoke. At the instigation of Action on Smoking and Health, the Civil Aeronautics Board voted on November 23, 1977, to authorize banning of all cigar and pipe smoking on commercial airlines and took steps that could eventually prohibit cigarette smoking as well. In January, 1979, the Board moved to further tighten anti-smoking restrictions including avoidance of "sandwiching" non-smokers between groups of smokers, special segregation of pipe and cigar smokers, and the prohibition of all smoking whenever the airplane's ventilation system is not fully operating.

Environmental Improvement Associates, the New Jersey-based group set up by Donna Shimp after her court victory against Bell, is demanding smoke-free working conditions for the non-smoker. The first "Nonsmoker's Guide to Washington," produced by Washingtonians for Nonsmokers Rights, a project of the Washington, D.C., Lung Association, lists restaurants and hotels which offer non-smoking areas, besides tips on handling smokers tactfully and effectively. The guide also gives a good rundown on the legal rights of non-smokers.

Future Trends

The facts speak for themselves. There is a steady and progressive overall increase in tobacco sales in the United States.³⁹ The smoking habit is extending to younger and younger ages. An HEW survey in April, 1979, found that about 12 percent of 3.3 million adolescents between the ages of twelve and eighteen are smokers. The administration has made it clear that it opposes effective regulation or further taxation of the industry and that it intends to continue subsidies. NCI expenditures on tobacco research are not only trivial but indirectly support the industry by focusing on "less harmful" cigarettes, rather than on an aggressive anti-smoking campaign. The American Cancer Society's efforts are weak where it really counts, at the legislative and regulatory levels.

It is true that cigarettes in the United States and other developed countries, have 50 percent less tar and nicotine and that the carcinogenic activity of the remaining tar has been decreased.‡ It is also true that filters are becoming more effective at removing selected gases, such as volatile phenols. However, the possible benefits, in terms of reduced cancer risks, are likely to be counterbalanced by increased tobacco consumption and inhalation in some smokers due to the lowered nicotine content of low-tar cigarettes and due to consumers being misled by the illusion of safety of the low-tar cigarettes. Additionally, smokers of low-tar cigarettes are likely to have increased risk of heart disease from the proportionately higher carbon monoxide content of these cigarettes.

More hopeful trends, however, are that the middle class are giving up smoking, and that vigorous public interest groups are carrying the battle into the legal and political arenas.

An important recent development has been the adoption of tough public smoking regulations, effective July 1978, by the New

‡ The industry's continued insistence on their product's safety contrasts with their aggressive marketing strategies on low-tar cigarettes, reflecting sensitivity to the public's cancer concerns.⁴⁰ Low-tar cigarettes are the only growth segment of the industry, inspiring the biggest and most competitive advertising and marketing campaigns since filters were introduced in the mid-1950s.

Jersey Public Health Council under the state sanitary code. The council acted following refusal of the New Jersey legislature to address this problem. According to the new regulation, smoking is restricted in restaurants seating more than 50, and prohibited except in areas designated as "smoking permitted," which may not exceed 75 percent of the total area. The non-smoking area must be equally attractive and convenient and have ventilation adequate to prevent build-up of levels of carbon monoxide above those outside the restaurant. The New Jersey legislature, under pressure from the hotel and restaurant lobby, is threatening to override these new regulations.

A similar move to restrict smoking in restaurants and other public areas in New York was recently proposed by Assemblyman Alexander B. Grannis (D-Manhattan). In May, 1978, Grannis charged that the Retail Tobacco Dealers of America, Inc., which had failed to register under the state's lobbying law, had illegally generated over 30,000 postcards—the largest outpouring of public opinion in this year's legislative session—protesting the proposed bill. Regardless of the success or failure of the New Jersey and New York initiatives, they clearly presage the likelihood of increasing controls and restrictions on smoking by local government.*

As the anti-smoking campaign is beginning to gain ground among professionals and upper socioeconomic classes in developed countries, the tobacco industry is intensifying its promotional campaign in the Third World. British American Tobacco, Inc., is moving aggressively to exploit these newer markets unrestricted by government regulation or social pressures.† Efforts by international organizations, such as the World Health Organization and the International Union Against Cancer to counter this dangerous trend in the Third World are effectively neutralized by actions of the U. N. Development Program and the Food and Ag-

* A proposed ordinance to ban or severely restrict cigarette smoking in a wide range of indoor public places was defeated by only 835 votes of 190,000 ballots cast in a referendum in Dade County, Florida, in May, 1979. The narrowness of the defeat, in spite of a massive lobbying effort by the tobacco industry, signals the possible early success of future anti-smoking ordinances.

† Philippine Kent cigarettes have about three times as much tar as British Kents.

riculture Organization to encourage investment in tobacco as a cash crop.

Summary

Tobacco plays a central role in the modern subculture, fulfilling emotional and physical "needs" which are assiduously and skillfully promoted and nurtured by the industry, with increasing emphasis on the enticing of adolescents. Smoking is the single most important cause of lung cancer, as well as cancers at other sites, chronic bronchitis and emphysema, and cardiovascular diseases. There is growing evidence that switching to filter cigarettes may not necessarily reduce cancer risks and may actually increase the risks of cardiovascular disease. There is also growing evidence on potential hazards to non-smokers from "secondhand smoke." Finally, there is now firm evidence on the interaction of smoking and other carcinogens, particularly occupational, in the induction of lung cancer. All these adverse effects were emphasized as key findings of the Surgeon General's January 11, 1979, report on "Smoking and Health"‡ (released on the fifteenth anniversary of the first Surgeon General's report on the same subject). Conservative estimates indicate that the costs of smoking approximate 300,000 deaths and \$20 billion annually.

The response of government to this national disaster is fragmented and contradictory, reflecting the \$6 billion annual tax revenues and the political influence of the Southern congressional network. The USDA openly subsidizes the tobacco industry and, with the blessing of President Carter, sponsors research to improve crop yields. Educational and research activities of the NCI are weak. They include programs to develop "less harmful cigarettes" which are made palatable by chemical additives. Congress has banned cigarette advertising from broadcasting, but not from print.* Sensitive to \$400 million advertising revenues, the press has engaged in a "conspiracy of silence" to ignore or minimize the

‡ The report, which is an encyclopedic compilation of the published literature, avoids taking stands on the dangers of passive smoking and on the needs for more vigorous federal anti-smoking policies and regulation.

* A similar ban on print advertising would appear to present grave first amendment problems.

human death toll from tobacco. While the American Cancer Society played an important role in the early 1960s in proving and drawing attention to the dangers of smoking, its more recent activities, particularly at the legislative and regulatory levels, have been weak and diffuse. Although the courts are beginning to uphold the rights of non-smokers to unpolluted air, they have failed to take the only single effective step of controlling smoking, that is finding the industry liable for the costs of disease due to tobacco.

Recent trends that may have powerful impact on the tobacco market include regulatory initiatives being developed at the state and local levels, and industry attempts to counter the possible slowing of tobacco consumption in the United States by opening up massive new markets in lesser developed countries, where the population is poorly informed on the dangers of smoking.

Artificial colors are highly objectionable on ethical grounds because they deceive, and on hygienic grounds because they injure.

Harvey Wiley,
Chief, Bureau of Chemistry,
USDA, 1907.

Red Dyes #2 and #40

Food is the single most important route of exposure for humans to synthetic chemicals. In a year the average American eats about 1,500 pounds of food containing about 9 pounds of chemical additives (other than sugar and salt). Several thousand chemicals are added to food for a wide range of purposes.¹ These include preservatives, flavoring agents, stabilizers, and colors and are

known as *intentional food additives*. An additional class of chemicals, which become incorporated in food during some phase of processing, packaging or storing (such as pesticide residues or chemicals migrating from packaging materials) are known as *indirect food additives*.

Chemicals added to foods and beverages solely for the sake of improving their appearance are popularly known as *cosmetic food additives*. Since antiquity, foods and beverages have, to some extent, been artificially tinted to make them look more appealing and appetizing. Until the relatively recent development of synthetic colors, "natural" pigments such as lead, chromium, and arsenic compounds, were popular additives, although somewhat unpredictable in their coloring—as well as their toxicity. More sensibly, natural plant dyes have also been used for the same purpose.

The use of cosmetic additives often entails consumer deception, in that they make a food look better and more appealing than it really is, or than its condition really warrants.² Current labeling laws do not require that the consumer be given explicit information on the presence or concentration of these artificial colors in foods, which are instead labeled "artificial colors," FD&C (Food, Drug and Cosmetic) or U.S. certified colors. Additionally, many colored foods, such as cheese, butter, and ice cream, are exempt from even these minimal labeling requirements. This taken with absence of alternative, uncolored foods and beverages hardly allows the consumer to exercise free choice in the marketplace. To make matters worse, there is mounting evidence of the toxicity and carcinogenicity of synthetic colors, and this is in no way indicated on the labels of beverages or foods containing them.

Natural plant dyes were the cornerstone of the industry until the latter part of the last century, when they were ousted by synthetic dyes based on coal tars.³ The coal-tar dye industry had its origin in 1856, when an English college student, William Henry Perkin, attempting to synthesize quinine, succeeded only in obtaining a dirty reddish-brown precipitate. Intrigued, he repeated the reaction using a simpler starting material, aniline sulfate, and from the resulting black residue extracted a purple compound which was light-fast and stuck to textile fibers. Within the year, this new compound, which he dubbed mauve, appeared so useful

that the Perkin family began manufacturing it on a large scale. Similarly, in 1897, a German company, BASF, discovered a highly profitable technique for the synthesis of indigo from a derivative of coal tar, naphthalene. Indigo, long one of the most important dyes, had for centuries been manufactured from plant extracts.

The burgeoning synthetic dye industry was initially a closed German enterprise, stimulated by their expertise in organic chemistry and favorable tariff and financing laws. This lucrative industry got a sudden boost in the United States during World War I, when, deprived of German products, the American chemical industry developed its own synthetic methods and new dye products.

The largest single class of dyes are chemical derivatives of coal tars. These compounds are used for coloring beverages, food, cosmetics, and textiles, as well as paints and inks. The largest single user of FD&C colors is the beverage industry. At least two of the colors, tartrazine and amaranth, you probably ate or drank recently. Their common names are Yellow #5 and Red #2, respectively. According to FDA estimates, some children eat as much as one quarter of a pound of coal-tar dyes each year.

Many coal-tar derivatives and dyes are also known carcinogens, among them 2-naphthylamine and benzidine, which induce bladder cancer in occupationally exposed workers.⁴ As knowledge of the carcinogenicity of so many coal-tar dyes is well established, why should it come as any surprise that some dyes used by the food industry have also been shown to be carcinogenic? According to a recent analysis of FDA data by the Health Research Group, most of the seven coal-tar dyes (currently used as food additives) have not been adequately tested for carcinogenicity, although requirements for updating these data have been imposed by the FDA.^{5†}

† As an example, the Center for Science in the Public Interest petitioned the FDA on February 15, 1976, to ban Orange B, an azo dye similar to Red #2 and used mainly in hot dogs sold in the southeastern United States, on the grounds that its safety had not been demonstrated. In May, 1970, in the absence of any FDA action, the manufacturer of Orange B, the Stange Company of Chicago, announced it would "voluntarily" withdraw the product from the market, as it had been shown to be contaminated with the potent bladder carcinogen 2-naphthylamine, thereby pre-empting an anticipi-

However, there are pressures from industry to continue using "coal-tar" food dyes. In this, they have been abetted by the past regulatory laxness of the FDA. The Food Protection Committee of the National Academy of Sciences, with close ties with the food industry, from which it received about 40 percent of its funding, has taken the position that use of these dyes is "legitimate."⁶

A ban on the use of all cosmetic food additives would not cause undue marketing problems. As established in a Gallup poll commissioned by *Redbook* in March, 1976, 59 percent of all women surveyed favored banning all additives used only to improve the appearance of food. Banning cosmetic additives might also discourage the fad for non-nutritious "junk foods" such as soda pop, candies, and cookies, in which food colors are extensively used. Instead this might encourage use of more expensive natural dyes, such as beet juice. It should be noted that support for such a ban has not come from the FDA or from scientific and nutrition communities, but largely from public interest groups, such as the Health Research Group, the Center for Science in the Public Interest, and the Consumer Federation of America.

Red #2

The Congress probably did not consider cancer when it passed the Pure Food and Drug Act of 1906, which approved an initial seven "coal-tar" food colors, including Red #2, or amaranth. This was done over the strenuous objections of Harvey Wiley, chief of the Bureau of Chemistry, USDA, the agency then responsible for enforcing the Act. In the wake of Upton Sinclair's 1906 exposé of the meat industry in his classic book, *The Jungle*, food law reformers were more concerned with preventing people from dropping dead from bacterial contamination and poisonous adul-

pated FDA ban. In November, 1978, the FDA rejected the Health Research Group's petition to ban various coal-tar food colorings, including Citrus Red #2, Blue #1, and Yellow #5, on grounds of their carcinogenicity. In their notice of rejection, the FDA imposed unscientific and onerous criteria for carcinogenicity, including insistence on monotonic dose response relationships and denial of analyzing responses by individual sex. This general position appears consistent with that adopted by the FDA in allowing continued use of Red #40, pending conclusive resolution of substantial questions as to its carcinogenicity.

terants than from long-term risks such as cancer. Not surprisingly, therefore, the government permitted color manufacturers to have their products registered as safe, a procedure made mandatory by the 1939 Federal Food, Drug, and Cosmetic Act. This registration was supposed to be the public's guarantee that food additives were harmless. The burden of proof, however, was then on the government to demonstrate that a given additive was harmful. Nevertheless, sixteen previously "approved" coal-tar colors were tested and banned by the government before 1960, when a new set of Color Additive Amendments to the 1938 Act shifted the burden of proof, now requiring industry to prove new products to be safe. Far from being onerous, however, the new laws were actually beneficial to industry, as they allowed continued use of unsafe and inadequately tested additives by registering them provisionally.

The recent history of Red #2 is a saga of past regulatory incompetence coupled with preoccupation with industry interests.⁷ Between 1960 and 1975, the FDA extended the provisional registration of the dye fifteen times. Meanwhile, Red #2 was becoming one of the most widely used cosmetic food additives, accounting for over \$14 million in direct annual sales, and being incorporated in \$10 billion worth of food.

In 1970 the FDA learned of some new Russian studies in which the dye was shown to induce birth defects and cancer in laboratory animals. One of these studies concluded that "chemically pure amaranth possesses carcinogenic activity of medium strength and should not be used in the food industry."⁸ FDA scientists meanwhile had become convinced, on the basis of their own and the Russian studies, that Red #2 should be banned. On November 18, 1971, an internal FDA memorandum from scientists of the Bureau of Foods recommended:

It would be prudent to limit FD&C Red #2 only to indirect or incidental applications involving food; that is, limit use of the color to such applications as food packaging where migration to food is nil, color marking of animal food additives, and to external uses in drugs and cosmetics.

The FDA, however, still refused to take any regulatory action, claiming that it could not examine the Russian data or check the

purity of the dye used in their tests. In the wake of publicity about its procrastination, the FDA decided to pass the problem to the National Academy of Sciences, which initially rejected the request as too routine. However, under pressure from its Industry Liaison Panel, the academy subsequently conceded and set up an ad hoc subcommittee of its Food Protection committee. The subcommittee produced a report in June, 1972, favorable to the industry, finding "insufficient reason" to ban Red #2 or reduce its use.⁹

About the same time, the FDA decided to undertake on its own an extensive series of tests designed to finally resolve all the safety problems of Red #2. The first set of FDA tests showed that the dye is metabolized in all major organs in the body. A second group of studies explored the question of whether Red #2 causes adverse inheritable genetic mutations. Initial results were inconclusive, but the results of another set of experiments, begun in 1972, remained unanalyzed for over three years through "administrative oversight." A third set of studies showed that the dye would kill rat embryos at daily doses in excess of 15 mg/kg. Applying the standard 100-fold margin of safety used by the FDA for such toxic effects, this would result in setting a "safe level" of 0.15 mg/kg in humans, equivalent to less than one can of cherry soda daily. The FDA attempted to "resolve" this problem by proposing an unprecedented 10-fold reduction in the safety factor for Red #2, thus setting "safe levels" of 1.5 mg/kg.¹⁰

The big news, however, was the fourth set of FDA tests, those on carcinogenicity. These were initiated in March, 1972, using five groups of fifty male and fifty female rats each, four of them to be given different dosage levels and one to act as a control group. In January, 1973, only nine months into the two-year study, a technician noticed that one rat's identification tag did not match its cage number. Subsequent investigation revealed a fiasco.¹¹ There was widespread mixing of animals among assigned dosage groups, and a general neglect of husbandry that had left many rats dead and decomposed in their cages. Of the original 500 animals, 231 were unusable and 71 more had only a few of the necessary organs available for examination, leaving only 198 intact animals. Enough data were salvaged, however, to demonstrate that at the highest dose, at least, the dye induced a large number of malig-

nant tumors in female rats surviving to two years. That was enough to finally force FDA Commissioner Schmidt to ban the food color in January, 1976, though not enough to motivate recall of colored foods from grocers' shelves.

In spite of the fact that industry could conceivably have continued its fight for years to come, particularly in view of the obvious inadequacies of the FDA carcinogenicity tests, Red #2 seems to have been allowed to die a natural death, largely because of forceful protests by consumer and public interest groups, especially the Health Research Group. Allied Chemical, one of the six major U.S. manufacturers of Red #2, also holds the patent on what is claimed to be the best—in fact, the only—available substitute, Allura red, or Red #40.

Red #40

In 1965, Allied began to introduce Red #40 into the profitable food coloring market, and contracted with Hazleton Laboratories to do the required testing. The mainstay of the Hazleton studies was a planned two-year carcinogenicity test, using a total of 300 rats fed various concentrations of the dye. However, after only six weeks of testing, an epidemic of respiratory disease killed many young animals. To halt the infection, survivors were treated with antibiotics. The total mortality was so high that the test had to be terminated prematurely at twenty-one months, leaving only 59 of the original 300 rats available for examination. Clearly, this study has very limited value as a chronic toxicity or carcinogenicity test.¹² The only finding of note admitted by a Hazleton pathologist was kidney damage in some of the higher-dosed animals that died at six months. This diagnosis was subsequently discounted by senior Hazleton staff in a "retrospective histo-pathological analysis," and all references to toxic kidney effects were omitted from the final FDA report.^{13‡} On the basis of their Red #40 study, Hazle-

‡ On April 8, 1976, then Commissioner Schmidt testified before congressional hearings that the FDA had found major deficiencies in Hazleton testing, which it intended to investigate, stating that the firm did not examine many animals with gross lesions histologically, reported on non-existent slides, and rewrote their own pathologists' reports.

ton scientists nevertheless concluded that Red #40 was non-carcinogenic. Other Hazleton tests, including studies on birth defects in rats and rabbits, gave suspicious or marginal results. These findings were transmitted by Allied to the FDA in 1970, which accepted the Hazleton data and approved the dye for use in foods and drugs in 1971 and for cosmetics in 1974.

The FDA approval allowed Allied to go ahead with aggressive marketing and claims of safety. In early 1971, Allied claimed:

Allura red has undergone one of the most extensive batteries of testing ever used for a food colorant. The screening included two series of feeding tests—one lasting two years, another lasting five years.¹⁴

In fact, no five-year study was ever reported to the FDA.

The permanent approval given Red #40 by the FDA in 1971 contradicted its own guidelines, endorsed by several worldwide health organizations, that food additives should be tested for carcinogenicity in at least two animal species. In 1974, an expert committee of the World Health Organization refused to grant even temporary approval for the dye, "as only very limited information is available."¹⁵ Not surprisingly, the dye has not been approved for use in Canada, Sweden, Norway, Japan, Italy, Israel, France, Austria, United Kingdom, or Australia. The FDA has since claimed that they gave approval for the dye in 1971 because they were under the impression that it would be used only for maraschino cherries.¹⁶

Meanwhile, use of Red #40 was growing in the United States. It has become the standard coloring agent in a great many common beverages, processed foods including meats, "junk" foods, such as imitation fruit drinks, soda pop, hot dogs, jellies, candy and ice cream, and even cosmetics and pet food. With more than a million pounds certified by the FDA in 1976, Red #40 has grown in six years from zero sales to the second most prevalent food coloring agent in the U.S., behind only Yellow #5.* It is now virtually impossible to eat most normal meals uncontaminated by the dye. At the current rate of consumption, a child

* Red #40 is used in almost all artificially colored red, orange, and brown foods.

of today will consume one-third of a pound of this "coal-tar" dye in his or her lifetime.¹⁷

Faced with an urgent need for new test data to unblock foreign markets, Allied again contracted with Hazleton in late 1974 for further studies on rats and mice. About a year into this study, the results to date were presented to FDA. Nothing of particular interest had been observed in the rat experiment. However, early in the mouse test animals started developing cancers of the lymphatic system (*lymphomas*). Furthermore, the incidence of these cancers seemed related to dosage. An FDA advisor recommended that a large number of apparently healthy mice be sacrificed ahead of schedule—at 42 weeks—in order to see whether there were any undetected lymphomas in either controls or test animals.¹⁸ This action nearly wrecked the study, because it markedly reduced the number of mice in each group remaining at risk, that is, who could survive to develop cancer later in their lives.

On February 25, 1976, the Center for Science in the Public Interest petitioned FDA to prohibit the use of Red #40 on the grounds that it had been originally allowed into the food supply on the basis of crude studies that did not establish the dye's safety. On the same day, Allied Chemical was meeting with FDA to inform them of "ambiguous findings" in the 1974 mouse feeding study: six of a small group of dye-fed mice had died of cancer, whereas all controls had survived. However, as the experiment proceeded the controls eventually began developing tumors.¹⁹ The FDA responded by asking Allied to undertake a further study, but did not ban the dye. Allied agreed and contracted again with Hazleton in spring of 1976. The refusal of FDA to take any regulatory action at this stage seems contrary to its own guidelines, as spelled out by its own 1969 panel of experts. The guidelines define carcinogens not only in terms of an increased production of tumors in test animals, but also in terms of "an earlier occurrence of tumors in the treated animals than in the controls, the incidence being the same in both."

Apparently sympathetic to the position that Red #40 was industry's last good, cheap synthetic food color, the FDA convened in December, 1976, a special working group of senior researchers and statisticians, together with the NCI and the National Center

for Toxicological Research. This group receives monthly reports on the mouse studies, and undertakes independent analysis of the results. In the group's own words:

Consideration of the results of these studies by the working group will ensure that any decision subsequently reached by FDA regarding the safety and use of FD&C Red No. 40 are legally sound and scientifically supportable . . . The completion dates for the two mouse studies cannot be precisely ascertained.²⁰

In April, 1978, on the basis of one completed mouse test and another then in its seventy-sixth week, an interim report by the working group concluded that "experiments provide no evidence at this time" that Red #40 is carcinogenic. This conclusion was made in spite of the fact that mice on the lowest dose of color in the incomplete study have a higher incidence of tumors than in controls, and in spite of the fact that Adrian Gross, a senior scientist in FDA's Division of Scientific Investigations (now senior toxicologist in the EPA), on the basis of a statistical analysis of the latest carcinogenicity data, had warned the agency on February 8, 1978, that Red #40 was carcinogenic. In a forty-eight-page memo to FDA Commissioner Donald Kennedy, Gross responded to the report of the working group by criticizing their statistical techniques and conclusions. To resolve this dispute, Kennedy requested three outside consultants reevaluate the data. The consultants agreed with Gross, stating that the working group's statistical procedures "weren't well suited" for a determination of carcinogenicity. Kennedy then sent a warm note of appreciation to Gross, and reconvened the working group with Gross as a full member.

The comment of Sidney Wolfe, of the Health Research Group, that the working group is "playing a very deadly statistical game," seems apt.²¹ It is now over five years since questions of carcinogenicity of Red #40 were first raised. The FDA's refusal to have taken and to now take regulatory action, with continuing involuntary exposure of almost the entire U.S. population to the probably carcinogenic food color, constitutes an inappropriate shift in the burden of proof from industry to the public.

Summary

Red #2 and #40 are "coal-tar" dyes without any nutritional benefits which are added to foods, particularly junk foods, for cosmetic purposes, and in the general absence of explicit labeling which would allow the consumer the exercise of free choice. A recent Gallup poll established that about 60 percent of women surveyed favored the banning of all such cosmetic food additives.

Many coal-tar derivatives, including some previously used as food additives and since banned, are human carcinogens. There are serious questions as to the carcinogenicity, besides other chronic toxic effects, including birth defects, of those dyes in current food use. It is estimated that some children eat as much as one quarter of a pound of "coal-tar" dye additives each year.

The history of Red #2 and Red #40 reflects regulatory sluggishness of the FDA and the continued sacrifice of the interests of the consumer to the special interests of the food and chemical industries. Between 1960 and 1975, the FDA extended the provisional registration of Red #2 annually for a total of fifteen times, pending the submission by industry of the required toxicological data, meanwhile, allowing the dye to insinuate itself into an \$11 billion food market.

In face of mounting evidence of carcinogenicity, including that derived from one of its own bungled tests, the FDA refused to take regulatory action against the dye until it finally acceded to pressure from consumer and public interest groups and in 1976 reluctantly banned the dye.

Red #40 was approved for food use by the FDA in 1971 on the basis of tests by Hazleton Laboratories, under contract to Allied Chemical Company, the manufacturer, which were so inadequate that they were rejected by the World Health Organization and most countries. With the banning of Red #2, the use of Red #40 has expanded and it is now the second most commonly used food dye in the United States. Subsequent tests have raised further and still unresolved questions on the carcinogenicity of Red #40.

The FDA, in permitting the burden of proof to be shifted from industry to the public, is allowing continued use of the dye pending final resolution of these questions.

Anyone who says saccharin is injurious to health is an idiot.

Theodore Roosevelt, 1907.

Saccharin

Saccharin was discovered in 1879 by Ira Remsen, then professor of chemistry and later president of Johns Hopkins University, and also a good friend of President Theodore Roosevelt.¹ Remsen, though a good chemist, was a poor businessman. Constantin Fahlberg, the student who had helped him develop saccharin, took out a patent on its synthesis in his own name and made a fortune. Remsen did not make a nickel.

Manufacture and Current Usage

The method by which Remsen originally synthesized saccharin, known as the Remsen-Fahlberg method, was its major source for many years.² A superior method, known as the Maumee synthesis, was later introduced to get rid of the bitter after-taste caused by an impurity in the process, *o*-toluenesulfonamide.

Saccharin is a non-nutritive and non-caloric artificial sweetener, about 350 times sweeter than sugar. The current saccharin market is large and profitable. The foods and beverages in which it is

used have a net annual value of about \$2 billion.³ Sherwin-Williams is the only domestic producer of saccharin, although some is imported from Japan and Korea. In 1976, about 7 million pounds of saccharin were used in foods, 75 percent in diet sodas (a can of pop contains about 150 mg of saccharin), 15 percent in dietetic foods, and 10 percent in "table top" sweeteners. The relatively minor non-food uses of saccharin include flavoring of mouthwashes, toothpaste, cosmetics, cigarette paper, and animal feeds. Saccharin is also used as a non-prescription drug and as a flavoring agent in prescription drugs, especially antibiotics for pediatric use.

Saccharin is consumed by about 14 percent of the general population, largely by teenagers. In comparison, and contrary to popular belief, saccharin is used regularly by only about one-third of all diabetics.

Efficacy or Benefits

Saccharin is currently approved by the FDA as an intentional food additive. The current food additive law requires proof of safety and "function," but not of "efficacy" or benefit. This means that an additive must perform its registered function. For instance, a sweetener must sweeten food or a color must color food, but this function does not necessarily have to serve any useful purpose.

Claims have been made by the Calorie Control Council,⁴ an industry trade lobby, and a variety of other groups such as the American Diabetic Association, the American Weight Watchers Association, and the Grocery Manufacturers Association of the value of saccharin in the treatment of diabetes, obesity, dental caries, and other disorders. None of these claims, however, has been backed up by any published studies. In fact, the relatively scant available literature seems to indicate the contrary. The first clue to this came in 1947, when it was shown that as little as 50 mg of saccharin, equivalent to about one-third of a can of diet soda, decreases blood sugar in humans by about 16 percent.⁵ Since appetite and hunger can be triggered by a drop in blood

sugar, ingestion of saccharin may induce a person to eat more, hardly a good prescription for a low-calorie sweetener. These effects were subsequently confirmed in animal studies, in which it was also shown that rats fed low doses of saccharin actually ate more and gained more weight than saccharin-free controls.⁶

In 1956, a cooperative study by the nutrition department of the Harvard School of Public Health and the dietary department at the Peter Bent Brigham Hospital, Boston, on the use of saccharin and cyclamates in the management of diabetics and the obese concluded:

No significant difference was apparent when the weight loss of users and non-users of these products was compared. No correlation was found between the length of time these products were used and weight loss, nor was the degree of overweight associated with the use of these products.⁷

In 1974 a report by an expert subcommittee of the National Institute of Medicine of the National Academy of Sciences chaired by Kenneth Melmon, concluded:

The data on the efficacy of saccharin or its salts for the treatment of patients with obesity, dental caries, coronary artery disease, or even diabetes has not so far produced a clear picture to us of the usefulness of the drug.⁸

More recently, eminent diabetes and dietetic experts, including Jesse Roth, Director of Endocrinology and Diabetes at the National Institutes of Health, the late Max Miller, Chief of the Diabetic Clinic at Case Western Reserve Medical School, and Ann Galbraith, Chief Dietician at the Massachusetts General Hospital and past-president of the American Dietetic Association, have all endorsed this particular conclusion of the Melmon subcommittee. Further confirmation on the lack of any substantive evidence on the medical efficacy of saccharin was presented at hearings before Congressman Paul Rogers (D-Fla.) on March 22, 1977, by Sidney Wolfe, of the Health Research Group,⁹ and before Senator Gaylord Nelson (D-Wisc.) on June 7, 1977, by Donald Fredrick-

son, Director of the National Institutes of Health and Donald Kennedy, FDA Commissioner.¹⁰

Carcinogenicity Tests

Saccharin has been extensively tested for carcinogenicity in rodents over the last three decades. The majority of these studies are still unpublished, having been sponsored by industry or government, and until recently never subject to independent scrutiny. The quality of these studies is variable in regard to design, execution, and interpretation.

Approximately a dozen conventional feeding tests, one dating back to 1948, have shown that saccharin is carcinogenic in both rats and mice.¹¹ While each of these individual studies may be criticized on some grounds or other, taken together the weight of evidence proving the carcinogenicity of saccharin is overwhelming. The dietary concentrations of saccharin tested and found to be carcinogenic have ranged from as low as 0.01 percent, equivalent to a daily consumption of about one and a half bottles of diet pop, to 7.5 percent, equivalent to daily consumption of about 800 bottles.

In addition to cancer of the urinary bladder in rats, the predominant tumor induced in these tests (Table 6.3), saccharin also induced cancers in female reproductive organs, and lymphomas or leukaemias (Table 6.4) in both mice and rats.

Three of the most important studies were those by WARF (the Wisconsin Alumni Research Foundation) in 1973, the FDA in 1973, and Arnold, *et al.*, in Canada's equivalent of the FDA, the Health Protection Branch, in 1977. The WARF study confirmed that saccharin over a dose range from 0.05 to 5 percent, induced cancer of the bladder, the uterus, and the ovary. The 1973 FDA study involved groups of forty-eight male and female rats fed saccharin over a dose range from 0.01 percent to 7.5 percent. This study confirmed the induction of bladder cancer and also found breast cancer. The 1977 Canadian study was a crucial one because it was based on feeding pure saccharin, produced by the newer Maumee synthesis, to large numbers of rats over the course of two generations. A higher incidence of bladder cancer was pro-

Table 6.3 Tumors of the Bladder in Rats Fed Saccharin

Study	% Saccharin in Diet	Sex of Rat	Number Animals with Bladder Tumors (%)	
			Control	Treated
Lessel, 1959	5	F	0/20	2/20 (10%)
Litton, 1972	5	F	0/20	1/26 (4%)
FDA, 1973	5	F	0/24	0/28
	5	M	1/25 (4%)	1/21 (5%)
	7.5	F	0/24	4/31 (13%)
	7.5	M	1/25 (4%)	7/23 (30%)
WARP, 1973	0.05	F	0/17	1/17 (6%)
	5	M	0/16	7/16 (44%)
Munroe et al. (Canada), 1973	0.2	F	0/56	1/56 (2%)
	0.2	M	0/57	1/51 (2%)
	2	M	0/57	2/52 (4%)
Arnold et al. (Canada), 1977	5	M	1/78 (1%)	19/83 (23%)
	5	F	0/85	2/89 (2%)

Source: Based on a table prepared by Melvin Reuber, included in testimony of Public Citizen's Health Research Group, before the Subcommittee on Health, House Commerce Committee Hearings on Saccharin, March 21, 1977.

Table 6.4 Tumors Other Than of the Bladder in Rodents Fed Saccharin

Study	% Saccharin in Diet	Equivalent Pop "Bottles/Day"	Animal (Sex)	Number Animals With Tumors (%)		Type of Tumor
				Controls	Treated	
FDA, 1948	0.01 5	1.6 800	Rats (M) Rats (F)	9/30 9/20	8/14 (57%) 9/17 (53%)	Lymphosarcoma
Schmähl (Germany), undated	0.2 0.5	32 80	Rats (M) Rats (F)	4/104 4/104	4% (4%) 4% (4%)	Lymphoma
WARF, 1973	0.05 0.5 5	8 80 800	Rats (F) Rats (F) Rats (F)	8/104 9/17 9/17	8/104 (8%) 1/17 (6%) 2/15 (13%)	Lymphoma Malignant tumors of the uterus & ovary
FDA, 1973	0.01 0.01	1.6 1.6	Rats (F) Rats (M)	6/20 6/29	(23%) (21%)	Breast
NIHS (Japan), undated	0.2 1	32 160	Mice (F) Mice (F)	0/14 0/14	1/30 (47%) 1/25 (56%)	Breast
Bio-Research, 1973	1	160	Mice (M)	9/19	(11%)	Ovary
				14/29	(48%)	Lung

Source: Based on a table prepared by Melvin Reuber, included in testimony of Public Citizen's Health Research Group, before the Subcommittee on Health, House Commerce Committee Hearings on Saccharin, March 21, 1977.

duced in the second generation, warning of the increased sensitivity of the embryo to the carcinogenic effects of saccharin. Ortho-toluenesulfonamide (OTS), a common contaminant in most commercial saccharin,¹² was also tested and shown to be non-carcinogenic. The details of this study have been reviewed and confirmed by a panel of ten independent pathologists.

An extensive FDA analysis of the Canadian study concluded:

The upshot of the Canadian study is that the feeding of a "pure" sodium saccharin to rats for their lifetime, when either exposed from weaning or from time of conception, resulted in a significant incidence of urinary bladder tumors. The results confirm the findings of the earlier FDA and WARF studies. Further, the Canadian study showed that OTS was not the responsible agent, that urinary pH was not a factor, and that urinary calculi are likely not a factor. Therefore, the conclusion must be drawn that there are now at least three studies that show saccharin to be a urinary bladder carcinogen in the rat.¹³

David Rall, Director of the National Institute of Environmental Health Sciences, commented, "It's absolutely a superb scientific study—it was very well done. I think the data are pretty convincing that saccharin is carcinogenic."¹⁴

The Calorie Control Council has repeatedly attacked the Canadian carcinogenicity test, which precipitated the FDA ban, as being unscientific.¹⁵ However, prior to initiating the saccharin test in 1973, the Canadian government sent the council a full plan of its intended study with a request for suggestions and comments. The council returned the plan without criticism. In October, 1976, the council invited Harold Grice, of the Canadian Health Protection Branch, to report on the progress of the study at its annual meeting in Ottawa. At that stage, Grice was able to report that *o*-toluenesulfonamide was not carcinogenic, although the results of the saccharin test were not yet complete. The council seemed delighted by this news, and expressed no critical comment on the design of the study. Only after the subsequent findings of the carcinogenicity of saccharin did the council attack its scientific credibility.¹⁶

In addition to the findings of carcinogenicity in the Canadian and other conventional feeding tests, saccharin has also been

shown to induce bladder cancer in various other types of studies, including one in which pellets were implanted in rodent bladders, and another for "promoting activity," in which rats were fed saccharin after their bladders had first been primed by local instillation of very low doses of a nitrosamine-type carcinogen.¹⁷

Quite apart from problems of carcinogenicity, a metabolite of saccharin isolated from the urine of saccharin-fed rats, has recently been shown to induce bacterial mutations.¹⁸

Human Studies

A series of studies have been made on human populations consuming saccharin, with a view to determining whether this is associated with an excess risk of bladder cancer. The majority of these studies have either compared national bladder cancer rates with the patterns of saccharin usage¹⁹ or studied patients with bladder cancer to determine if they had been heavy saccharin users.²⁰ Other studies have examined the incidence of bladder cancer in diabetics,²¹ on the reasonable assumption that diabetics are more likely to be saccharin users than the general population. In general, these studies have not identified an excess bladder cancer risk in saccharin users, or presumed saccharin users. These apparently negative findings have been widely hailed by the industry as conclusive evidence that saccharin is non-carcinogenic, and that the extensive findings of carcinogenicity in animal tests should hence be disregarded.

Closer examination, however, reveals that the quality of these data does not support the claims of safety. The inherent limitations of epidemiology are particularly applicable in the case of saccharin. First, there may be a latency period of decades between exposure and disease, as with bladder cancer induced by occupational exposure to aromatic amine carcinogens. Second, the success of epidemiology depends on the availability, for comparative studies, of large populations of exposed and unexposed individuals. None of the studies done so far have identified and contrasted a large number of patients with bladder cancer who used and who did not use saccharin. Third, epidemiology, even under ideal conditions, is unlikely to be able to detect relatively small

increases in cancer incidence. Yet, increases of this order could still result in a large number of excess cancer cases in the U.S. population. Viewed against these general limitations, it is clear that none of the apparently negative human saccharin studies can be used to give it a clean bill of health with regard to bladder cancer. Large-scale usage of saccharin commenced in the 1960s, so that judging from what is known of other known bladder carcinogens, not enough time may have elapsed for any significant excess of saccharin-induced cancers to have appeared in the general population.[†] With regard to the diabetic studies, the number of cases involved are inadequate to detect any but the grossest increase in cancer incidence. Additionally, diabetics are more likely to die at a relatively young age from complications of their disease, rather than from cancer. Finally, there is no reason at all for the epidemiological studies on saccharin to have focused exclusively on bladder cancer, to the exclusion of cancer at other sites. Not only is there no necessary correspondence between the sites of action of carcinogens in different species, such as rodents and humans, but also the rodent studies clearly show that saccharin induces cancer in many sites other than the bladder.

In the fall of 1977, *Lancet* published a paper entitled "Artificial Sweeteners and Human Bladder Cancer," by a team of government and university scientists written under the auspices of the Canadian National Cancer Institute, a voluntary fund-raising agency.²² This study was based on recent interviews of all patients with newly diagnosed bladder cancer in three Canadian provinces. Each case was then matched to other individuals of similar characteristics living nearby, so-called neighborhood controls, who were also asked the same questions. It was found that men who used saccharin had a 65 percent greater risk of developing bladder cancer than those who didn't. It was also found that this risk increased with both duration and amount of use.[‡]

[†] The Connecticut Tumor Registry has found a large increase in bladder cancer over the past four decades (150 percent for men and 50 percent for women) which cannot be entirely accounted for by smoking and in which a causal and/or synergistic role for artificial sweeteners seems likely.

[‡] These results were confirmed in a preliminary U.S. study by E. Wynder, reported to the NCI in November, 1977, and presented to the Senate Subcommittee on Health and Scientific Research by Commissioner Kenney in May, 1979, which found that the risks of bladder cancer were doubled in men using saccharin.

Regulation and Politics

Questions on the safety of saccharin are longstanding. In 1911 saccharin was declared "a poisonous and deleterious substance" and banned from general food use on the basis of digestive disturbances and other evidence of toxicity in human studies. Until 1959 the use of saccharin was restricted to those with special medical needs who took it as a prescription drug or used it as a "table top" sweetener or in diet foods in preparations labeled:

Warning: to be used only by those who must restrict intake of ordinary sweets.

Saccharin was first suspected of being carcinogenic in 1948 on the basis of an FDA chronic toxicity test. The questions of carcinogenicity were raised again in 1959 when, with the explosion of the soda pop market, saccharin first came into widespread general use, initially as a one-tenth mixture with cyclamates, another artificial sweetener. These questions became more pressing in 1969, when cyclamates were banned on grounds of carcinogenicity, leaving saccharin the entire diet pop market.

In 1972 saccharin was removed from the GRAS (Generally Recognized as Safe) food additive list on the grounds of the WARF study. This action had the legal force of allowing a future ban on saccharin if there was any question of safety, irrespective of the provisions of the Delaney Amendment to the 1938 Federal Food, Drug, and Cosmetic Act which requires an automatic ban on food additives causing cancer in animals or man.

A recent report to Congress by the General Accounting Office, identified twenty-three studies since 1970 which indicate potential carcinogenic hazards of saccharin.²³

On March 9, 1977, Acting FDA Commissioner Sherwin Gardner announced a proposal to ban the use of saccharin in foods and beverages. The FDA press release stated that this action was based on the results of a recently completed Canadian carcinogenicity test in which rats developed bladder cancer after being fed daily the equivalent of 800 cans of diet soda. The press

release, however, hastened to reassure that "saccharin has been in use for more than eighty years and has never been found to harm people." The press release also stated that this action was unequivocally required by the terms of the Delaney Amendment.

This FDA press release was misleading. It implied that the Canadian carcinogenicity test was an isolated experiment. It questioned the value of the Canadian study by emphasizing the high doses of saccharin inducing carcinogenic effects, while ignoring the fact that this is standard practice in carcinogenicity tests. It cast doubt on the value of the study by ignoring the dozen or so other carcinogenicity studies known to the FDA, including its own 1948 and 1973 studies. In contrasting the Canadian study with the alleged human experience of safe use, the FDA press release in no way indicated the limitations of the human studies, which are so serious as to invalidate any inferences of safety. Finally, in invoking the Delaney Amendment as the legal basis for the proposed ban, the FDA showed an apparent ignorance of its own laws, which anyway require a ban on the basis of safety requirements of general food law.

The way the FDA handled this matter has been regarded by some as inept, and by others as a deliberate attempt to provoke a consumer and congressional backlash against the Delaney Amendment, which was implied to be both inflexible and unscientific. It was well known that many upper-level agency officials, including previous commissioners, notably Charles Edwards,* were openly sympathetic to the industry position that the Delaney Amendment was an unnecessary and unfair restriction to their freedom to add known carcinogens, at supposedly safe levels, to the American food supply.

Not unexpectedly, the FDA press release provoked a sharp reaction from the industry. The Calorie Control Council barraged Congress with cables and letters in protest, and took out full-page advertisements in leading national newspapers complaining about the unreasonable and unscientific proposal of the FDA.²⁴ These

* Edwards' career is a classic case of the "revolving door" between industry and Government. Prior to becoming FDA Commissioner he was a Senior Executive at Booz, Allen & Hamilton, a major management consulting firm. After a stint in the FDA, he returned to industry as Senior Vice-President for Research at Becton-Dickinson Medical Supply House. Edwards is now president of the Scripps Clinic and Research Foundation, San Diego, California.

advertisements went so far as to equate the proposed ban with an attack on democracy and freedom of choice of the consumer. The American Diabetic Association claimed that saccharin was necessary for the treatment of diabetes. The American Cancer Society attacked the ban on the grounds that the animal carcinogenicity data should be disregarded because saccharin was of great medical benefit and safe on the basis of human experience. The past president of the society, R. Lee Clark, protested that "banning saccharin may cause great harm to many citizens while protecting a theoretical few."²⁵ While the American Cancer Society cannot be necessarily faulted for this ill-considered statement, it has yet to retract or modify this position.†

Even the apparently informed scientific community joined in the attack. At hearings before Congressman Rogers on March 2, 1977, Guy Newell, Acting Director of NCI, Kurt Isselbacher, Professor of Medicine at Harvard and chairman of the Harvard University Cancer Committee, and Arnold Brown, Professor of Pathology at the Mayo Clinic (now dean of the University of Wisconsin Medical School at Madison) and then candidate for the NCI directorship, vigorously attacked the proposed FDA ban. Isselbacher, a well-known physician (although not a recognized authority on carcinogenesis or epidemiology), asserted:

I would submit to you that in the case of saccharin, the available data indicates, in my view, that the risk to humans for developing cancer from saccharin in the amounts ingested by the average individual is remote, while the harm, I believe, which may occur to millions in the absence of a non-nutrient sugar substitute, is great.²⁶

Brown recommended that the admittedly unequivocal animal carcinogenicity data be ignored, because of the alleged evidence of safe human use, and also that the *Delaney Amendment* be relaxed.‡ A lone voice on the side of the FDA at the Rogers

† Ignorance aside, questions have been raised as to the propriety of this position in view of the fact that the society had previously accepted a substantial grant from Coca-Cola, the manufacturers of diet soda, to defray the costs of travel expenses for a delegation of society staff and volunteers to attend a conference in Russia in June, 1976.

‡ Brown's highly qualified position on the predictive value of animal carcinogenicity tests also raised serious questions as to his fitness for the NCI directorship, as subsequently expressed in a letter of May 17, 1977, from

hearings was that of Sidney Wolfe, of the Health Research Group, who ably marshalled the scientific evidence supporting the ban.²⁷

This was then the background of events confronting the incoming FDA commissioner, Donald Kennedy, who within a few days of assuming his new post in April, 1977, issued a press release in which he made a determined effort to set the record straight. Commissioner Kennedy confirmed the proposed ban of saccharin in foods, beverages, and cosmetics, but also proposed in the Federal Register of April 15, 1977, that saccharin should be made available as an over-the-counter, non-prescription drug to diabetics and others requiring it for medical reasons. The hooker in this was the legal requirement that the industry would have to show evidence of efficacy, in accordance with the Kefauver-Harris amendments to the Federal Food, Drug, and Cosmetic Act. Kennedy also explained that the basis for the proposed saccharin ban was the general safety requirements of food law, quite apart from the Delaney Amendment. He endorsed the scientific merits of the Canadian cancer tests as confirming earlier carcinogenicity studies and explained that the relatively high test doses used were in accordance with standard test practices. He also explained that there was no valid basis for concluding that human experience had demonstrated the safety of saccharin, and quoted FDA estimates that lifetime ingestion of saccharin by the general population could lead to 1,200 excess cases of bladder cancers annually.

Finally, Kennedy dismissed claims for the medical benefits of saccharin:

I know of no other drug whose only use is to change the taste of food. I know of no other drug which is to be taken not for what it can accomplish in itself, but because the only alternative—in this case sugar—must be avoided.

Kennedy's actions could not, however, diminish the growing anti-ban and anti-Delaney sentiment, which was supported by the

Congressmen Andrew Maguire (D-N.J.) and Henry Waxman (D-Cal.) to HEW Secretary Califano. These questions are thought to have been instrumental in Brown's failure to gain the NCI post. Brown is still chairman of the Clearinghouse on Environmental Carcinogens, an advisory committee to the NCI bioassay program dealing with carcinogenicity testing in animals.

Calorie Control Council, the food chemical industry, and its extensive cadre of consultants. The council launched a massive lobbying campaign in the general press and in Congress protesting that the FDA ban was undemocratic and an outrage depriving millions of Americans of an important and useful additive, besides being unscientific: "We find it incredible that the new Commissioner would move to propose an action of this significance on less than scientifically supportable data."^{*} However, in spite of all the strident rhetoric on the importance of saccharin to the American consumer and on its alleged medical efficacy, the industry has not, so far, produced any scientific evidence to support these claims.

More than 100 senators and representatives have backed over a dozen bills to amend the Delaney Amendment or exempt saccharin from the ban. Congressman James Martin (R-N.C.) gathered vocal support for a bill allowing industry to continue using a carcinogen in food for economic reasons. Congressman Andrew Jacobs (D-Ind.) in the words of a recent article in *Consumer Reports*, "hit a comedic high and a know-nothing low" with a bill† calling for saccharin to be labeled "Warning: the Canadians have determined that saccharin is dangerous to your rat's health."²⁸

The voices of sanity and restraint in Congress were few and far between, notable Senator Gaylord Nelson and Congressman Paul Rogers, Richard Ottinger (D-N.Y.), and Andrew Maguire (D-N.J.). Senator Kennedy attempted to dampen the hysteria by referring the saccharin problem to the Office of Technology Assessment (OTA), which issued a well-balanced report on June 7, 1977, concluding:

1. The doses of saccharin used in the rat cancer tests were admittedly high, but were valid.
2. The most convincing animal cancer tests indicate that saccharin is a weak carcinogen in rats.

* Congress received more mail opposing the saccharin ban than it did on any day in opposition to the Vietnam War.

† Uncrazing of Federal Regulations Act of 1977, H.R. 6685, March 28, 1977.

3. Saccharin is also likely to be a relatively weak carcinogen in people.

4. Though weak, for several important reasons saccharin should be regarded as having the potential of posing a significant health hazard to humans.²⁹

Accepting the position of the OTA that neither the risks nor the alleged benefits could be adequately expressed in terms of the expected number of human cancer cases, Senator Kennedy stated in a June 10 conference:

I believe that, because of the division in the scientific community, because of the division in the OTA Panel, because of the genuine uncertainty on each side of the risk/benefit equation, the individual ought to be fully informed and then allowed to make a personal decision.

While this statement seems reasonable, it does not reflect the fact that the informational process is largely proceeding via full-page ads taken out by the Calorie Control Council and other partisan groups, and that the majority of saccharin users, adolescents, are hardly likely to be able to make reasoned decisions on the risks and benefits of saccharin. These considerations are still more cogent for the unborn generation exposed prenatally to saccharin.

Senator Kennedy also announced his intent to support legislation to suspend the FDA ban on saccharin for eighteen months to allow a detailed study of food additive law by the National Academy of Science. Kennedy proposed that saccharin-containing foods be labeled with a warning during this interim period. In his press release, Senator Kennedy appeared to rely on unsupported advice that the carcinogenic hazards from saccharin were remote and that its benefits were real.

The subsequent decision by Congress on October 17, 1977 (P.L. 95-203), to postpone the FDA ban for eighteen months (until May 13, 1979) was understandable in the circumstances. While heading off the concentrated industry attacks on the Delaney Amendment, quite apart from the proposed saccharin ban, the decision offered an opportunity for more deliberate examination by Congress of the underlying facts on risks and benefits. In

an attempt to limit further public exposure to saccharin during this interim period, Senator Nelson introduced legislation on September 14, 1977, to restrict usage of saccharin to those with a specific medical requirement and to require that saccharin products be labeled with a cancer warning. Senator Nelson, moreover, warned Congress of the unwise precedent it was setting by interfering with the specifics of the regulatory process and by legislating special treatment on a product-by-product basis:

By delaying a regulatory restriction on the use of saccharin in the food supply, Congress is risking the public health for the benefit of large economic interests. Saccharin is one of 2,100 food additives approved for use directly in food. Approximately 10,000 are approved for indirect uses, such as in packaging. Does Congress expect to react to every request for special consideration of food additives?³⁰

Nevertheless, Congress subsequently passed the eighteen-month moratorium, which was signed into law on November 21, 1977, by President Carter. Subsequent to this, the Canadian government, however, banned the use of saccharin in beverages and foods on the grounds of its carcinogenicity. Saccharin is still available in drugstores in Canada as a non-prescription drug.

The voices of reason have been belatedly raised in the scientific community. At a September 16–17, 1977, Washington conference on saccharin organized by the Society for Occupational and Environmental Health, leading protagonists discussed available data on carcinogenicity testing, epidemiology, and the efficacy of saccharin. There was a clear scientific consensus that the animal carcinogenicity data were sound and created a strong presumption of human cancer risk; that the earlier human studies provided no indication of safety; and that indeed the 1977 Canadian epidemiological study raised further serious questions as to the carcinogenicity of saccharin. In short, participants other than industry concluded that the use of saccharin entails significant risks and provides no matching benefits for the general population nor for those alleged to have special medical needs.

In accordance with the provisions of the Congressional moratorium, the National Academy of Sciences established two panels, one to study and report on risks and benefits of saccharin, and the

other to examine general food safety policy.‡ In November, 1978, the first panel issued its report confirming the validity of the animal tests on saccharin and concluding that saccharin had been demonstrated to be both a carcinogen and a promoter, and hence a potential carcinogenic hazard to humans.³¹ The panel further concluded that saccharin itself and not any potential impurities was the carcinogen. After thorough review of possible benefits, the panel agreed that "Essentially, there is no scientific support for the health benefits of saccharin." Finally, the report warned:

The observation that young children are becoming increasingly greater consumers of saccharin suggests that public health officials should take a prudent course of action since there has been insufficient time for the possible effects of this greater consumption to be manifest. This may be particularly important because of the anticipated long latent period between exposure to the potential carcinogen and the manifestation of cancer, and because of the recently recognized promoter effects that have been exhibited by saccharin in laboratory tests.*

Summary

Saccharin is a 100-year-old non-nutritive, non-caloric sweetening agent. Formerly popular mainly among diabetics, its use has exploded over the last twenty years as a staple of the diet food and

‡ The second panel report, issued on March 2, 1979, proposed revamping food safety laws to reflect benefit-risk considerations, including relaxation of the Delaney Amendment and the classification of additives into low, moderate, and high risk. A minority report strongly objected to these recommendations, particularly the concept that the adult or child consumer of all educational and cultural levels (quite apart from the fetus) is willing and able to make informed and appropriate benefit-risk calculations for every item of food purchased. This report makes it unlikely that saccharin will remain on the market until the Ninety-sixth Congress grapples with the broader issues of rewriting food safety laws (see R. J. Smith, "Institute of Medicine Report Recommends Complete Overhaul of Food Safety Laws," *Science* 203 [1979], pp. 1221-24).

* The first panel concluded that there was no meaningful way of developing quantitative assessments of the cancer risks of saccharin (see Table 9.11). This is at variance with the unsupported contention of the second panel that the risks can be defined, providing a rationale for benefit-risk approaches to continued usage of saccharin.

drink craze. Its major current consumption is in diet pop by teenagers, and not by diabetics and the obese. The public now firmly believes that foods containing saccharin are effective in weight control, and has been persuaded by the soft drink industry (through the Calorie Control Council) that these benefits outweigh any possible health risks.

The Calorie Control Council has also carefully cultivated the popular but mistaken belief that animal tests using large doses of a weak carcinogen are absurd, and has in this way undermined the public's trust in the use of standard animal tests for carcinogenesis, and their predictive value to humans. As a result, a powerful industry lobby backed up by popular sentiment has prompted Congress to take the extraordinary action of suspending the FDA's power to regulate saccharin until May, 1979, pending further scientific study.

In fact, there is no available evidence that saccharin is in any way effective in the treatment of diabetes and obesity. Some published studies indicate just the contrary. More than a dozen animal tests over the last thirty years have demonstrated the carcinogenic effects of saccharin in the bladder and other sites, particularly female reproductive organs, and in some instances at doses as low as the equivalent of one to two bottles of diet pop daily. Additionally, recent epidemiological studies have shown that saccharin usage is associated with an increased risk of bladder cancer.

The mishandling of the proposed saccharin ban dealt a serious setback to the whole field of environmental regulation. It brought to focus the failure of regulators to adequately inform the public about the underlying issues, the uncertainty that appears to exist in the informed scientific community, and the ability of concentrated industry interests to manipulate decision-making processes. In its unique pre-emption of the FDA's regulatory authority, by placing an eighteen-month moratorium on the saccharin ban, Congress forced an evaluation of the Federal Food and Delaney Law and the use of risk-benefit analysis in environmental regulation. In this, they were supported by the administration, which, through the Council on Wage and Price Stability, opposed the ban on economic grounds. Pending final resolution of the broader issues, the Congressional action has resulted in the continued expo-

sure of some 14 percent of the U.S. population to a carcinogen added to their diet more for its market than nutritional or medical value.

Acrylonitrile

The old talmudic saying, "Don't be concerned by the look of a bottle, but rather by what's inside it," doesn't seem to apply to modern experience with acrylonitrile. Monsanto, Inc., found this out at great expense, when the contents of its newly marketed plastic bottles were shown to contain the potent carcinogen, acrylonitrile.

Plastic Bottles

It all started about 1972, when Pepsi-Cola and Coca-Cola carried their rivalry into the search for a plastic bottle that would be lighter than glass, but tough enough to stand the pressure of carbonation. Each of the soft drink giants went to a chemical giant for help—Pepsi to Amoco Chemical Corporation, and Coke to Monsanto. Engineers at both Amoco and Monsanto then set about finding suitable plastic bottles for their respective clients. Amoco came up with a bottle for Pepsi made from a polyester, polyethylene terephthalate (PET).† Monsanto developed its bottle made from another widely used acrylonitrile (AN) plastic, a co-polymer of styrene and acrylonitrile.

Then came the test-marketing period. While both companies initially had a tough time interesting the public in their new products, the Pepsi PET bottle seems to have caught on well, and has since generated orders for about 50 million pounds, most being supplied by Goodyear Tire and Rubber Company.¹ Goodyear claims that its bottles have exceptional clarity, that they can be

† Coincidentally, this polyester was selected by Hoechst Chemical Co. as a replacement for the fire retardant Tris, which the Consumer Product Safety Commission banned because of its carcinogenicity and mutagenicity.

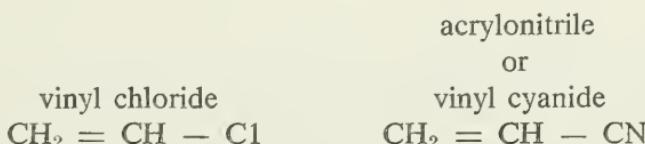
safely incinerated without giving off toxic fumes, and can be compacted for landfill and recycled. During this time, the rival AN, marketed by Monsanto under the name Cycle Safe, started running into problems of carcinogenicity, which the company had failed to anticipate in the earlier developmental stages.

Carcinogenicity and Other Problems

In a series of carcinogenicity tests sponsored by the Manufacturing Chemists Association in the laboratories of Dow Chemical Company, AN was administered to rats by feeding and inhalation.[‡] A high incidence of cancers of the breast, brain, and stomach were found in test animals.² Other studies showed that AN induced a wide range of birth defects in pregnant rats³ and mutations in bacterial (Ames) systems.⁴

Evidence on human effects was quick to follow. On May 23, 1977, the medical director of Du Pont reported, on the basis of preliminary epidemiological studies, that he had identified sixteen cases of cancer, with eight deaths occurring between 1969 and 1975 among 470 workers exposed to AN from 1950 to 1956 in the company's textile fibers plant in Camden, South Carolina.⁵ This was nearly three times the incidence of cancers that would have been expected in a similar group of unexposed workers. Six of these were lung cancers, three were colon cancers, and seven were in various other organs.

These findings should not have come as a complete surprise to anyone. There is an obvious similarity of chemical structure between VC, known by the industry since 1970 to be carcinogenic, and AN, which should at least have triggered earlier questions.



[‡] Requirement for these tests was imposed by the FDA, under interim food additive regulations, following the marketing of Cycle Safe bottles.

Relevance of Carcinogenicity Data to Safety of Coca-Cola Bottles

AN, like VC, is a small gaseous monomer, which under the influence of heat, pressure, and plasticizers can be reacted to form long-chain polymers, and then fabricated into solids or films. As with VC, the polymerization reaction never proceeds to completion, and there is always some unreacted AN monomer in the final polymeric product. The unreacted monomer will dissolve or leach out of bottles made from the polymer into the fluid it contains. The amounts leached out will vary widely, depending on the conditions in which the bottle was fabricated, its thickness and size, and the duration and temperature of storage of the product. This problem of leaching and migration of toxic or carcinogenic monomers or other chemicals from plastic bottles or food wrappings into their contents is a problem of major importance in the food, cooking oil, beverage, and cosmetic industries. It is not just unique to AN and VC.

Monsanto at first contended that there was no detectable migration of AN into the contents of the bottles, and that the bottles met the migration limits of 50 ppb (0.05 ppm) set by the FDA for food-contact or wrapping materials. Monsanto has since admitted, however, that it did not have test methods sufficiently sensitive to back these claims. In fact, FDA food-simulating extraction tests indicate that significant migration does occur, as confirmed by the finding of 13–20 ppb AN levels in Coke bought in retail stores.

Regulatory Developments on the Plastic Bottle

In January, 1977, on the basis of interim results of the still incomplete Dow carcinogenicity tests, the Natural Resources Defense Council petitioned the FDA to set a zero tolerance for AN migration, and to ban the plastic beverage bottles. In face of sharp protests from Coca-Cola, the FDA acted on this request on

March 11, 1977, and announced a ban on the sale of the bottles after they had been marketed for little over a year. The ban was made final in September, 1977. Monsanto was left with 20 million bottles worth \$2 million, and with lost 1977 sales exceeding \$30 million. The FDA ban also extended to the use of AN bottles manufactured by Borg-Warner for apple juice.*

Following the final September ban, J. Virgil Waggoner, Monsanto's executive vice president complained, "We do not agree with these findings. We believe that our Cycle Safe bottles are safe and that this action is unwarranted."⁶ In October, 1977, Coca-Cola decided not to wait out the predictably lengthy appeal by Monsanto, filed in November in the U. S. Court of Appeals, but switched instead to the rival Amoco's PET bottles. These bottles were described by their producer, Goodyear, as producing an extraction level 1,000 times lower than the FDA 50 ppb limit, requiring less energy to manufacture than any other soft drink package, and recyclable.[†]

Regulatory Developments in the Workplace

Current production of AN is approximately 1.6 billion pounds, and involves about 125,000 workers, 10,000 of whom are exposed to AN on a regular basis.⁷ Besides the planned use of AN in Coca-Cola bottles, it is widely used in the manufacture of acrylic and other synthetic fibers, such as Orlon, Acrilan, Creslan, synthetic rubber, and other plastics.

In the wake of unfavorable publicity, following disclosure of excess cancers among AN workers at Du Pont, the company voluntarily reduced its exposure limits from the then OSHA 20 ppm standard to 2 ppm in June, 1977.

* This prompt FDA action on the basis of incomplete test results contrasts sharply with its foot-dragging on Red #2 and more recently on Red #40.

† A recent editorial in the *Wall Street Journal* ("A Low Growth Microcosm," October 10, 1978) was critical of the FDA ban on grounds including the fact that the 13–20 ppb level found in Coke were equivalent to only one molecule per bottle of Coke. In a letter to the *Journal* of October 23, H. P. Pohlmann, Director of Amoco Chemicals Corporation, corrected the estimate to about 100 quadrillion molecules (10^{17}) of AN per bottle, or about 10^{14} molecules per cubic centimeter.

In January, 1978, on the basis of the experimental and epidemiological carcinogenicity data, OSHA concluded that AN constitutes "A potential carcinogenic risk to humans." Accordingly, OSHA issued an emergency temporary standard of 2 ppm for workplace exposure to AN. Countering industry's argument that the lengthy induction period of cancer makes such an emergency standard unnecessary, OSHA director Eula Bingham stated:

As a carcinogen, AN can pose its life-threatening danger in a very brief period of exposure. Without this emergency temporary standard, employees would continue to be exposed to this threat during the period of time necessary to complete normal rule-making procedures.⁸

Bingham also explained her reluctance to issue an absolute-zero exposure level. Noting that even though OSHA clearly recognizes that no safe level exists for carcinogens, she explained, "In this case a level was chosen to immediately minimize the hazard to the greatest extent possible within the confines of feasibility." The emergency standard was promptly challenged in the Cincinnati Circuit Court by the manufacturers of AN, including Monsanto, American Cyanamid, Borg-Warner, and Vistran Company, a subsidiary of Sohio, on the grounds that the danger was not grave enough to warrant emergency measures. In March, 1978, the appeals court denied the request for a stay. Meanwhile, President Carter's newly created Council on Wage Price and Stability, which had been examining case histories of specific standards as a means of exploring economic and other considerations involved in the standard setting process, selected acrylonitrile as a test case. Following a meeting on May 4 with Grover Wrenn, who heads health standards at OSHA, the Regulatory Analysis Review Group of the Council criticized the standard on the grounds that OSHA had failed to adequately weigh the anticipated benefits to workers health against the high costs of compliance. The new OSHA standard of 2 ppm, which became effective November 2, 1978, applies only to about 5,000 employees of nineteen major producers and users of AN, but not to the unknown but much

larger numbers of workers in fabricating plants. This standard gives industry two years to install engineering controls, while requiring submission of plans for compliance, including a schedule for implementation. It is clear from the reaction of industry that the new standard poses few if any problems. The Society of the Plastic Industry, which had vigorously opposed the emergency standard a few months previously, now commended OSHA for setting "a performance-based standard that will protect workers health." Monsanto called the standard "strict but realistic." While the new standard clearly provides an increased measure of protection to a limited number of workers, it is excessively high and should be revised downwards and extended to cover polymer fabricating operations and end users of AN fibers, who are currently unprotected.

Summary

The case of acrylonitrile (AN) is a clear-cut example of inadequate premarket testing of a major ingredient of a food and soft drink container. It is also a paradigm of the larger problem society faces as industries rush to market new products or, without regard for the deliberate process of testing needed to exclude possible public health hazards.‡

Following the original and unwise decision by Monsanto and Coca-Cola to market AN bottles, evidence of the substance's carcinogenicity was found in test animals by Dow Chemical and in exposed workers by Du Pont. The subsequent banning of AN bottles by the FDA and regulation of AN in the workplace by OSHA have been challenged in the courts by Monsanto, the same company that has recently launched a massive national advertising campaign to prove to the public that synthetic chemicals are essentially safe unless misused, and to assert that regulatory controls such as the Delaney Amendment are "unscientific." The 2 ppm

‡ This further typifies, at least with regard to health and pollution considerations, the conventional industry position of "shooting first, then drawing the bull's-eye around the hole."⁹

occupational standard is excessively high and should be revised sharply downward, and extended to fabricating, besides manufacturing plants.

Nobody has shown a cause-and-effect relationship between Premarin and cancer. It does not cause cancer. It just accelerates it.

A vice president,
Ayerst Laboratories, November 23, 1977.

Female Sex Hormones

Hormones are low-molecular weight chemicals secreted into the bloodstream by the endocrine glands which influence most biochemical and metabolic processes in the body.¹ The group that regulates all aspects of reproductive development and function are the steroid sex hormones, of which three major classes are recognized: estrogens and progestins, both female hormones, and androgens, male hormones. Natural estrogens are a mixture of three related hormones, estradiol, estrone, and estriol.* The balance between the levels and functions of the different sex hormones is exquisitely sensitive and imbalance, occurring spontaneously or following their administration for therapeutic or other purposes, seems to be associated with excess risks of cancer.

In addition to natural estrogens, diethylstilbestrol (DES) is a synthetic chemical which has high estrogenic potency, although it is chemically unrelated to steroids.

* While estradiol is the main secretory product of the ovary, the liver readily interconverts these hormones.

Uses

Second to tranquilizers, female sex hormones are the most commonly prescribed drugs in America today.² They are also extensively used as feed additives that stimulate growth in poultry, cattle, and hogs.

Oral Contraceptives During research on progestin fertility drugs in the mid-1950s, it was found that contamination with small amounts of estrogens reversed their effects, and instead effectively prevented pregnancy. Starting in 1956, large-scale trials of oral contraceptives in Puerto Rican and Haitian women, based on combinations of estrogens and progestins, demonstrated the nearly complete effectiveness of the "combination pill," which is now used commonly throughout the world.³ A second type of oral contraceptive is the "sequential pill," so-called because its three phase cycle consists of two weeks on estrogen, one week on estrogen and progesterone, and one week off.

In June, 1960, the FDA approved the first oral contraceptive pill, Enovid, marketed by G. D. Searle Company. This was rapidly followed by competitive products from other pharmaceutical companies, including Syntex, Ortho Pharmaceutical, and Eli Lilly. This enormous experiment, in which a non-medicinal drug was mass-marketed without adequate prior safety testing, took place with the approval of the FDA and an uncritical medical establishment. In this they were aided by a "diplomatic immunity" extended by the press to the pill for nearly a decade after its introduction.⁴

About eight million U.S. women now regularly use oral contraceptives, representing a pharmaceutical market in excess of \$100 million annually. The industry is highly protective of this market and, while enthusiastically promoting the unchallenged effectiveness of the pill, has shown extreme reluctance to admit or investigate any possible hazards involved. Searle, for example, set up a "Bad Press Committee" designed to counter any bad publicity in the medical and popular literature on Enovid.⁵ In fact, until

quite recently, national preoccupation with the effectiveness of the pill has been so great as to virtually repress the alarming information which has gradually accumulated on its dangers.

Estrogen Replacement Tantalized by promotional campaigns of "Feminine Forever," five million menopausal U.S. women regularly use estrogens for "estrogen replacement therapy," with an annual market over \$80 million, a market which has approximately quadrupled over the last decade.⁶ The object of estrogen replacement therapy is to "replace" the dwindling supply of estrogens secreted by the ovaries as the menopause approaches and menstruation ceases.

Since Victorian times, the medical profession has tended to view the menopause and some of its discomforting symptoms as an illness to be treated, rather than as a natural process.⁷ The symptoms for which estrogen replacement therapy is recommended in a standard medical text include

hot flashes alternating with chilly sensations, inappropriate sweating, paresthesias [tingling], formication [sensation of crawling ants], muscle cramps, and myalgias and arthralgias [muscle and joint soreness]. There is an unbearable uneasiness that gives rise to manifestations of anxiety, overbreathing, palpitation, dizziness, faintness, and syncope. Untreated, a few women become chronic invalids, some experience years of ill health, and most feel genuinely miserable and understandably lack vigor and initiative."⁸

In spite of this impressive plethora of symptoms, there is a growing body of informed opinion, particularly among younger, pro-feminist physicians, that what gynecologists label as estrogen-deficient illness in large measure reflects societal attitudes toward loss of fertility, as well as other social and family pressures to which middle-aged women are often subject.⁹ While it is true that a small proportion of women do experience severe post-menopausal problems, these are usually only temporary. Many women, however, are untroubled by their menopause, and continue to secrete reduced but significant quantities of estrogens from their ovaries and adrenals.

Why, then, do doctors prescribe estrogens to such an extent? For one thing, treatment is immediately satisfactory in those few

women with disabling problems, such as persistent hot flashes, drenching sweats, and vaginal atrophy:

Replacement-therapy is probably the most gratifying use of hormones both to patient and physician . . . The physician can achieve brilliant clinical results with small doses of hormones.¹⁰

A more important reason, however, is the reliance of the medical profession for guidance on the sales-representatives and promotional literature of the pharmaceutical industry. The most popular formulation for estrogen replacement therapy is Premarin,† a brand of natural estrogens which until very recently was prescribed for about 13 percent of all women in the 45 to 64-year age bracket.¹¹

The synthesis of DES in Britain in 1938 made available a cheap estrogenic drug which was widely used from 1940 to 1960 for replacement therapy in over three million women. Unlike natural estrogens, DES can be taken by mouth without loss of effectiveness. Based on the belief that habitual miscarriage and other complications of late pregnancy are due to estrogen deficiency, DES was widely used from 1945 to 1970 for the treatment of threatened miscarriages and for preventive purposes in women with a history of habitual miscarriage. The DES dosage varied widely from 2.5 to 150 mg per day, and the duration of treatment from 3 to 212 days, most women being treated with 50 mg daily for 150 days. Apart from being ineffective, this treatment has resulted in vaginal cancer in the daughters of the treated women and sterility and congenital genito-urinary defects in their sons, apart from excess breast and other cancers in the treated women themselves.

Other Medical Uses¹² Estrogens are prescribed for various gynecological problems, such as menstrual cramps and irregularity and genital itching, for some of which they appear effective. They are also extensively used for many other purposes for which the evidence of their usefulness seems slender. These include: acne and hirsutism, probably reflecting an assumption that feminine hormones can "soften" or neutralize these "masculine" conditions; "feminizing" ingredients in cosmetics; and, osteoporosis or thin-

† So named because it is manufactured from the urine of pregnant mares.

ning of bones, which normally occurs with aging and sometimes results in fractures and collapse of vertebrae, particularly in the upper back, producing the familiar "dowager's hump." An unquestionably effective but relatively minor use of estrogen is as a component in the treatment of advanced prostate cancer.

Another common use of estrogens is in the postcoital contraceptive, or "morning-after pill"¹³ for preventing the risk of pregnancy resulting from unprotected intercourse. DES is still prescribed for this purpose at many university health clinics, although not authorized for this purpose by the FDA. It is also made available to rape or incest victims by some agencies, at an approximately 250 mg dosage over a five-day period, equivalent to the estrogen content in about a two-year supply of oral contraceptives.[‡] There are, however, questions as to how effective DES really is as a postcoital pill. Quite apart from possible risks of cancer to any young woman from this massive dose of estrogen, there are also carcinogenic and other hazards to her infant if she is pregnant and the DES fails to terminate the pregnancy.

Feed Additives In late 1954, DES was approved by the USDA for use as a growth stimulant in poultry, hogs, and cattle. Its estrogenic effects make animals grow to marketable weight faster and on less feed. Poultry farmers found the increased growth and fat content of young roosters gave them the appearance of capons without the trouble and expense of castration, and, in advancing the feminine characteristics of young hens, yielded a product that according to one feed manufacturer was "juicier, more tender, and with better flavor." This effect, however, was largely achieved by increasing the conversion of feed to fat, rather than protein. Similar effects were achieved with DES fed to or implanted as pellets under the skin of cattle, two million head of which were put on DES-treated feed within three months of its availability. It has been estimated that a beef animal given DES reaches market weight of about 1,000 pounds approximately thirty-five days

[‡] The FDA will approve use of DES for such emergency situations if a manufacturer provides patient labeling and special packaging. The FDA has not given approval for any manufacturer to market DES as a postcoital contraceptive, and has withdrawn from the market the 25 mg DES tablets formerly used for this purpose.

sooner than an untreated animal, saving about 500 pounds of feed per animal. The direct savings to the cattle and feedlot industry were estimated in 1974 as over \$90 million a year. These advantages are, however, achieved at the expense of meat quality, which is reduced. A Department of Agriculture meat inspector, John S. White, made attempts in 1963 to draw attention to the inferior quality of DES-beef. Following threats of disciplinary action and dismissal if he attempted to pursue his concerns and findings, White resigned and subsequently published his conclusions in a farming journal in 1966.¹⁴

Interestingly enough, the original research on the basis of which DES was first introduced as a feed additive was conducted at Iowa State University, in Ames, which had a licensing agreement with the manufacturer, Eli Lilly, and received a royalty from its sales.¹⁵ This research was of questionable quality, being characterized in a 1972 report of the Agribusiness Accountability Project as "an example of land grant [college] research at its worst—it is at once a service to industry and a disservice to consumers—DES has produced a royalty of \$2.9 million for ISU, which means that the taxpayer has helped Eli Lilly . . . to sales of \$58 million."¹⁶

Carcinogenic Effects of "Estrogens"

There is overwhelming evidence of the carcinogenicity of sex hormones in both experimental animals and humans.¹⁷ The pharmaceutical and feed additive industries have attempted to minimize or explain away these findings on the grounds that natural hormones or chemicals based on them cannot possibly be carcinogenic, and that even if they are the risks involved are more than outweighed by the massive benefits. There is no question that the balance between the normal production and levels of sex hormones is delicate and sensitive, and that imbalance occurring naturally or following hormone administration to humans and experimental animals is associated with excess risk of cancer. This carcinogenic effect appears to involve some interaction between the steroid sex hormones and other hormones produced by the an-

terior pituitary gland, particularly prolactin. We will examine separately the animal and human studies:

In Experimental Animals Natural and synthetic estrogens and progestins have been found to induce cancer in animals in experiments dating back thirty years.¹⁸ Estradiol has been extensively tested in several rodent species, in which it produces a wide range of cancers both in reproductive and other organs. These include cancers of the breast, uterus, cervix, vagina, testes, pituitary, and lymph glands in mice; breast and pituitary in rats; uterus, stomach, and spleen in guinea pigs; and kidney in hamsters. Progesterone, the main progestin hormone, induces cancer of the ovary, uterus, and breast in mice, and pre-cancerous ovarian changes in dogs. It also increases the incidence of various tumors in mice, rats, and rabbits that have been pre-treated with other carcinogens.

When DES was first synthesized in 1938, it was also found to be carcinogenic, inducing breast cancer in male mice. Subsequent studies showed that DES was approximately ten times more potent as a carcinogen than natural estrogens. Experiments in 1964 showed that daily feeding of mice with 6.25 ppb of DES in their diet, equivalent to a daily dose of about 0.02 µg, produced breast cancers in female mice. Doubling this dose produced similar cancers in castrated male mice.*

In addition to breast cancer, experiments in 1959 and 1962 showed that feeding dogs with DES induced a high incidence of ovarian cancers. Injection of DES caused cancer of the cervix and leukaemia in mice, and kidney cancer in hamsters. Feeding hamsters with DES in late pregnancy resulted in tumors and other abnormalities in the reproductive tract of their female offspring and abnormalities in the testes of the males.¹⁹ Implantation of DES pellets under the skin of rodents, a standard route for administration to poultry and cattle, induces cancers of the testes in mice, breasts in rats, kidney in hamsters, and uterus in monkeys.

In Humans Administration of female sex hormones has been shown to induce cancer of the uterus, cervix, vagina, breast, and ovary in women, and of the breast in men.²⁰

* These doses are in the same order of magnitude as those prescribed for menopausal women, 10 µg/kg.

Many independent epidemiological studies have established that administration of Premarin increases the risks of cancer of the endometrial lining of the uterus from four to fourteen times.²¹ These and other studies also showed that the risk is proportionate to dose and duration of dosage, but was unaffected by the particular type and brand of estrogen prescribed, whether natural, such as Premarin (Ayerst Laboratories), or synthetic, such as Genesis (Organon, Inc.) and Estrace (Mead Johnson Laboratories).²² There seems little question that the recent dramatic increase in the incidence of uterine cancer is due to the large-scale use of estrogen replacement therapy, which started in the early 1960s and nearly tripled between 1965 and 1975. In some parts of the United States the incidence of uterine cancer has been increasing at a rate of 10 percent per year, an increase that has rarely if at all been paralleled in the whole history of cancer research.²³ The maximum incidence has occurred in women over fifty in high socioeconomic groups, those most likely to be given estrogen replacement therapy.

In November, 1978, two Yale physicians published a case control study alleging that the risk of uterine cancer from the use of estrogen replacement therapy was low.²⁴ The study maintained that previous contrary reports were biased by the fact that estrogen usage produces symptoms, particularly vaginal bleeding, in many women which bring them to medical attention earlier, and that this results in "finding" more cancers than would otherwise be detected. To counter this so-called "detection bias," they conducted a study on endometrial cancer patients as usual, but the controls were women hospitalized for a dilation and curettage (D&C) or hysterectomy. With this particular control group, the cancer risk appeared to be increased by only 70 percent (not quite double relative to the controls), as compared to a 1,000 percent increase in risk (ten-fold), when controls in previous studies were chosen in a standard way. The Yale study has been roundly criticized as utilizing "a method that was abandoned by others precisely because it introduced a large selection bias into a research design in which selection bias was not inherently an important feature."²⁵ While the alleged "detection bias" would scarcely affect the rate of diagnosis of endometrial cancer, it would probably increase the number of cases of various benign

conditions, such as uterine polyps, atrophy, and hyperplasia, which made up the majority of the Yale controls. If, as is generally accepted, these conditions are actually caused by exogenous estrogens and may, in fact, be pre-cancerous, then the Yale study used the worst possible set of controls, namely, a group of women also characterized by relatively high usage of Premarin or other estrogens. Compared to such a highly biased control group, the cancer cases then would not appear to have an unusually high estrogen intake. Furthermore, the Yale study failed to analyze their data by duration of estrogen administration; long term users would be expected to have the greatest risk, as other studies have shown. The Yale study was paid for by a grant from Ayerst Laboratories, the manufacturer of Premarin.

A more recent case-control study (*H. Jick, et al. New England Journal of Medicine*, February 1, 1979) suggests that the risk of uterine cancer declines rapidly after discontinuation of estrogen replacement therapy. The relatively brief duration of follow-up, however, suggests that conclusions on this study should be deferred for at least a further decade.

Premarin has also been recently incriminated as a cause of ovarian cancer, generally a rapidly developing and fatal disease which attacks about 10,000 women each year in the United States.²⁶ A 1977 NCI study has found that while there has been a gradual decrease in the incidence of ovarian cancer in younger women, this has been balanced by an increase in older women, the ones most likely to be given estrogen replacement therapy. The NCI study also found evidence of a strong relationship between Premarin dosage and the incidence of ovarian cancer. Besides uterine and ovarian cancer, risks of breast cancer seem to be approximately doubled by replacement therapy, this being particularly marked among those women receiving high and prolonged dosage and developing benign breast disease during treatment.²⁷

Worldwide use of birth control pills, in spite of conclusive evidence of carcinogenicity of estrogens in experimental animals, constitutes the largest uncontrolled experiment in human carcinogenesis ever undertaken. This reflects the failure of both industry and government to develop any large-scale system designed to detect and report long-term adverse effects, particularly cancer. While many scattered investigations of cancer and the pill

have been undertaken, their results have been somewhat ambiguous or negative. The number of women studied generally has been too few, not enough time has yet elapsed for an increased incidence of cancer to become apparent, and little or no attention has been directed to identifying subsets of susceptible women defined in terms of other risk factors (such as benign breast diseases). Nevertheless, suggestive evidence of a relationship between oral contraceptives and excess breast and cervix cancers has appeared periodically. A study involving a total of 34,000 women by New York researchers concluded that pill users had a higher cervical cancer rate than diaphragm users. While there are possible objections to the significance of these findings, including the fact that pill users tend to belong to lower socioeconomic groups, who are known to have a higher risk of cervix cancer, than diaphragm users, and that use of the diaphragm could block a possible sexually transmitted cancer virus, the study nevertheless merited publication. When an article based on the study was submitted to the *Journal of the American Medical Association*, which is heavily supported by advertisements from the pharmaceutical industry, the editors insisted that it could be published only if accompanied by a rebuttal statement in the same issue. Faced with these unusual demands, the authors instead published their findings in the *British Medical Journal*.²⁸

An extensive follow-up (or prospective) study has been under way for some time among nearly 18,000 female patients of the Kaiser Foundation Health Plan in the San Francisco Bay region. By 1977, thirty-five cases of cervix cancer and an additional thirty-one new cases of a possible pre-malignant condition, cervical dysplasia, were reported. A dose-response for cancer was found, with a cancer rate 5.4 times as great among long-term pill users (over four years) than among non-users.²⁹ In another recent investigation (known formally as the Kaiser-Permanente Contraceptive Study or informally as the Walnut Creek study after the location of its headquarters), elevated risks of malignant melanoma and skin cancer were found in long-term users of oral contraceptives.³⁰ This study is ongoing and, as its participants pass beyond the latent periods of other cancers, may well yield further information on cancer risk of the pill.

Another condition associated with pill usage over the last dec-

ade is *benign hepatic adenoma*, a proliferative liver tumor the incidence of which is now sharply increasing. These can prove fatal by eroding large blood vessels, with subsequent massive abdominal hemorrhages, and can also progress to frank liver cancers.[†]

In April, 1971, the Massachusetts General Hospital reported seven cases of a rare form of cancer of the cervix and vagina in young women aged fifteen to twenty-two. In most cases, these women had first consulted their doctors because of irregular or heavy periods, and were treated with hormone therapy on the assumption that this was due to irregular ovulation. Only after treatment had proved ineffective were thorough pelvic examinations performed, including direct microscopic inspection of the cervix, using an instrument known as a colposcope. Vaginal cancers were found, in addition to other possibly pre-malignant lesions of the cervix and vagina called adenosis. One of these seven women died eighteen months later, after unsuccessful surgery. A common thread was found linking the victims. Their mothers had been treated with DES during pregnancy for habitual or threatened miscarriage some two decades ago.³³

It is variously estimated that between 500,000 and 2 million young women have been exposed to DES *in utero* in the United States since its first clinical use in 1946, and that between 20,000 and 100,000 pregnancies were treated each year from 1960 to

[†] This association was first suggested in 1973 by a clinician who reported seven cases of the liver disease.³¹ Further cases were subsequently published, and a number of liver tumor registries were established. However, because liver cancer is so rare that studies in individual hospitals are difficult, the National Cancer Advisory Board requested that the American College of Surgeons' Commission on Cancer to estimate the scope of the problem nationwide. Results of the national survey of 477 hospitals revealed that while over 90 percent of all liver tumors found in men were malignant, over half of those in women were benign. Three fourths of the cases in women (with either of the two main types of benign liver tumors, hepatic cell adenoma and focal nodular hyperplasia) were found to be pill users, though fewer than 40 percent of U.S. women in the same age bracket are users. The investigators concluded:

[These findings] strongly support the association between use of oral contraceptives and some types of benign liver tumors, specifically hepatic cell adenomas and focal nodular hyperplasias. . . . the problem of the malignant potential of benign hepatic tumors should be addressed. There are case reports of an adenoma progressing to a malignant neoplasm and of hepatocellular carcinoma coexisting with focal nodular hyperplasia.³²

1970. While the incidence of vaginal cancer so far recorded is still relatively rare, estimated by HEW to range between 0.14 and 1.4 per 1,000 involved, vaginal adenosis occurs in 30 percent to 90 percent, the incidence depending more on how early DES was given in pregnancy rather than on dosage. There is, however, no way of telling how many adenosis cases will in time progress to cancer. All these women will require careful and regular follow-up for the rest of their lives.

Some women who took DES in the early 1950s did so apparently unwittingly as part of a large-scale clinical trial, the object of which was to investigate the value of DES in the prevention of complications of late pregnancy, including threatened miscarriage. These events took place at the Lying-In Hospital of the University of Chicago, where about 2,000 women were each given about 10 to 12 g DES, and an equal number received a control placebo.‡ The explanation given to these women was summarized in a 1953 publication by W. J. Dieckmann of the Department of Obstetrics and Gynecology of the University of Chicago and the Chicago Lying-In Hospital:

Each patient was told that previous reports indicated that the tablets were of value in preventing some of the complications of pregnancy and that they would cause no harm to her or to the fetus.³⁴

Not only were the women treated with a carcinogenic drug—evidence for which had been established over a decade prior to the test—but according to some they were told that the pills they received were vitamins.* The initial tests produced somewhat ambiguous results and were forgotten until the discovery in 1970 and 1971 of vaginal cancers in the daughters of DES-treated women.†

The vaginal cancer scare brought many of these DES-treated mothers into contact with each other. One of the original mothers

‡ The DES and placebos were supplied by Eli Lilly Company, a leading DES manufacturer.

* It should be recognized that medical ethics as then practiced did not require "informed consent" of a patient for experimental treatment.

† Subsequent studies have also shown that sons of the DES-treated women have not escaped and have been found to suffer from a wide range of congenital genito-urinary defects, and a high incidence of infertility and sterility.³⁵

was Assistant Secretary of State Patsy Mink, former Congresswoman from Hawaii. Ms. Mink filed a class action suit against the University of Chicago and Lilly on behalf of herself and about 1,000 other mothers in the experiment. In this she has been joined by the Health Research Group and the Citizen Litigation Group (both Nader affiliates). A motion by the University of Chicago to dismiss this case was rejected by the courts in March, 1978. Other such cases which are also pending include the \$100 million damage suit and a \$1 billion class action for punitive damages filed in March, 1976, by three Long Island mothers against a score of major pharmaceutical companies and five physicians.

Fuel has been recently added to the fire of the University of Chicago-Eli Lilly lawsuit by preliminary data indicating an approximate doubling of the incidence of breast, besides an increase in other hormone-related cancers in the women given DES in the 1950s.³⁶ These data, based on an August, 1977, progress report to the National Institutes of Health by the University of Chicago, were obtained by the Health Research Group under the Freedom of Information Act. Additionally, these breast cancers occurred in younger women than in untreated controls. While the University of Chicago has challenged the statistical significance of these conclusions, they seem consistent with the results of the 1977 NCI study which found a higher incidence of breast cancer in women treated with estrogen replacement therapy. In October, 1978, HEW Secretary Califano released a report of an NCI task force, set up in response to initiatives of the Health Research Group, which concluded that the risk of breast or gynecological cancer for DES mothers is "not established (although) sufficient cause for serious concern."

DES, used in the past for estrogen replacement therapy, has been incriminated, together with Premarin, as a cause of ovarian cancer. Cancer of the breast in elderly men has developed following treatment with DES and other estrogens for prostate cancer. Similar cancers have developed in young transvestites taking large doses of estrogen to promote female secondary sexual characteristics. While there is little in the way of substantive epidemiological evidence on the carcinogenicity of progestins, recent studies have incriminated progesterone as a cause of ovarian cysts.

Other Toxic Effects of Estrogens

Apart from cancer, various studies from all over the world over the last twenty years have focused suspicion on the pill as a cause of premature heart disease and stroke.³⁷ The FDA decision to market the first oral contraceptive in 1960 was based on tests with only 132 women for only 38 months. On this basis was begun the first mass prescription in medical history of a non-medical drug. Early studies suggesting blood clotting (*thrombo-embolic* disease) and other dangers of the pill were countered by authoritative FDA reassurances, such as those by Joseph Sawdusk, FDA's top physician and later vice-president of Parke Davis, that the pill is "safe when given under a doctor's supervision." The FDA was joined in these assurances by the medical journals, the medical establishment, leading physicians such as John Rock and Alan Guttmacher of Planned Parenthood, and the promotional literature of the industry.

In January, 1966, when the long-compliant FDA Commissioner George P. Larrick was replaced by James L. Goddard, an advisory committee warned of possible blood clotting problems due to oral contraceptives. The press, which had for years been silent on the dangers of the pill, belatedly and slowly started covering the growing information on this problem. In May 1968, a study published in the *British Medical Journal* clearly implicated the pill with excess thrombo-embolic disease, in which a blood clot forms within the vein and if dislodged can lead to a fatal stroke.³⁸ The FDA obtained agreement from the manufacturers to include a warning about blood clotting in the package labeling given to the pharmacists, but without any direct warning to the patient. In August, 1969, the FDA Advisory Committee on Obstetrics and Gynecology confirmed the thrombo-embolic risks of the pill and summarized the data on experimental carcinogenicity of estrogens, but nevertheless concluded that the pill was "safe."³⁹

In January, 1970, Senator Gaylord Nelson held widely publicized hearings on the safety of oral contraceptives before his Subcommittee on Monopoly. The hearings summarized the known

hazards of the pill and made it clear that users were not being adequately informed of these. It was also emphasized that the pill had not been adequately tested prior to its massive use. Industry, the FDA, and the medical establishment, including family planning and birth control organizations, on the other hand, insisted that the pill was perfectly safe and that users were being told all they needed to know. Nevertheless, after the hearings, about 19 percent of pill users quit.⁴⁰ Critics of Nelson claimed 100,000 unwanted pregnancies resulted and dubbed them "Nelson babies," an allegation which has never been substantiated.

These issues came to a climax in a 1977 publication of two British studies in *Lancet*, one conducted by the Royal College of General Practitioners on 46,000 women, and the other on 17,000 women by the Oxford Family Planning Association.⁴¹ Both studies concluded that death from coronary heart disease, hypertension, and stroke were five times more common among pill users than controls, and ten times as frequent among pill users who had been on the pill for over five years. The excess death rate among pill users was also further increased by cigarette smoking. Both studies recommended that all women over thirty-five years should stop taking the pill, that women between thirty and thirty-five should consider changing to different contraceptives, but that women under thirty need not worry. These findings supplemented previous knowledge that estrogen usage increases the risk of thrombo-embolic disease. Pill usage also affects fat metabolism, increasing serum triglycerides and thereby increasing the risk of coronary artery disease, especially in the presence of other risk factors such as smoking or hypertension. Both the pill and estrogen replacement therapy increases the risks of gall bladder disease by two to three times.

Several reports have also suggested a marked association between intrauterine exposure and congenital birth defects of the heart and limbs. The use of hormonal tests for pregnancy has also been incriminated as a cause of congenital defects of the central nervous system.‡

‡ As recently reported (*London Times*, June 7, 1978), responding to complaints of the newly formed "Association of Children Damaged by Hormonal Pregnancy Tests," an Ombudsman has been asked to investigate why the British Committee on Safety of Medicines had failed to warn doctors and the public of the dangers of birth defects of hormonal pregnancy test tablets until 1975, since their danger was first demonstrated in 1967.

Recent Occupational Problems

In 1966, the Oil, Chemical, and Atomic Workers Union organized the Dawes Laboratories in Chicago Heights, Illinois, an agricultural products and DES manufacturer.⁴² Ventilation was practically non-existent and the whole interior of the plant, including the cafeteria and toilets, was covered by dust containing as high as 10 percent DES by weight. From 1968 to 1971, many workers complained of sexual impotence and some men developed enlarged breasts, in one case requiring surgical removal.

In their subsequent contract negotiation, in 1971, the union demanded and obtained full medical examinations of all workers, provided by the company, as well as a commitment to improve working conditions. The union also requested an independent evaluation program of the effects of exposure to DES. On this program, eight male employees were admitted in 1973 to the National Institutes of Health Hospital in Bethesda, Maryland, where they were given testosterone therapy to relieve some of the symptoms. Following this evaluation, medical consultants of the union explained to the workers the effects of DES, and the workers renewed their demands for improved working conditions.

The years passed by without the plant being cleaned up. The recommendations for improved industrial hygiene made by Dawes' own insurance company were ignored. Then, in March, 1977, the Oil, Chemical, and Atomic Workers Union again inspected the plant and confirmed that conditions had not materially changed since 1971. This was followed by an OSHA inspection which resulted in a citation for willful negligence and a fine of \$46,000, one of the largest ever imposed for a health violation. Dawes will probably never pay the full amount, as the Act permits appeal of the dollar value of fines based upon subsequent cleanup or even a mere show of "good faith." The company has since appealed and the fine was lowered to \$21,000. An interesting legal sideline is that OSHA was obliged to cite the "General Duty Clause" of the Occupational Safety and Health Act as authority for these actions, since there is no occupational standard for DES.⁴³

A similar recent incident occurred at an oral contraceptive plant in Puerto Rico. Following complaints of enlarged breasts in male employees and menstrual disorders in females, NIOSH investigated the plant in May, 1976, and found evidence of excessive estrogen exposure. In this case, management instituted the necessary dust control measures and improved work practices, which appear to have resolved the problem.⁴⁴ In April, 1973, similar complaints were reported in male and female employees of a plant manufacturing birth control pills in Sao Paulo, Brazil. Following intervention by the Ministry of Labor, ventilation of the plant was improved, and the problem reportedly controlled.

Regulatory Developments

The large-scale use of female sex hormones as both feed additives and human drugs poses two sets of regulatory problems which, however different, are linked by the common theme of cancer risk.

Feed Additives It is currently the responsibility of the feed additive and animal drug manufacturers, when submitting an application for approval, to provide "a description of practicable methods" for the specific analysis and routine monitoring of animal drug residues in foods. The FDA has responsibility for approving the registration and use of human drugs and feed additives, besides other animal drugs, and for setting tolerances for permissible residues of animal feed additives and drugs in meat and other dairy products.*

Although the carcinogenicity of DES was established in tests as early as 1938,⁴⁵ the USDA in 1947 approved the fattening and caponizing of chickens by implanting 15 mg pellets under the skin

* From a regulatory standpoint, there are three kinds of residues: first, *permissible residues* of non-carcinogenic drugs below prescribed tolerance levels; second, illegal residues of non-carcinogenic drugs above tolerance levels, or *excessive residues*; third, illegal residues of any detectable level of carcinogenic drugs, *prohibited residues*. The USDA has authority to prevent the occurrence of illegal, prohibited, and excessive residues by monitoring meat and products from food-producing animals and birds, generally at the time of slaughter, using FDA-approved methods.

of the necks. Warning signals of trouble came quickly. Within three years the USDA was sued by mink ranchers whose animals had become sterile after eating the heads and necks of chickens containing DES residues. The USDA still allowed the use of DES in chickens. In 1954 permissible uses of DES were extended to cattle, which could be fed with 5 to 10 mg daily, providing treatment was stopped forty-eight hours prior to slaughter in order to prevent residues occurring in the meat. Highest residues levels are found in liver, and these are about ten times greater than in muscle meat.

Concerned by the mounting evidence on the carcinogenicity of DES, which the FDA seemed to be ignoring, Congressman James Delaney (D-N.Y.) introduced a statement to this effect in the Congressional Record in February, 1957.⁴⁶ The FDA immediately denied that DES was a carcinogen. Ensuing congressional concerns with DES were one of the main factors leading to the passage of the 1958 Delaney Amendment to the Federal Food, Drug, and Cosmetic Act which flatly prohibited the introduction to food of additives found to be carcinogenic in either animals or humans. At that time, the amendment made no distinction between chemicals added directly to food as food additives, and those which might enter human food indirectly through the diet of food-producing animals. This amendment, however, did not prevent the continued use of DES, as the FDA argued the technicality that it could not be applied retroactively to DES but could only be used for future applications on carcinogenic food additives.⁴⁷

Using improved analytic techniques, residues were found in poultry in 1959, each carcass containing about 25 µg DES, about a thousand times greater than daily doses found to induce breast cancer in mice. The situation was only resolved with the decision to ban the use of DES in chickens and the willingness of the USDA to buy and remove from the market an estimated \$10 million worth of treated poultry. The poultry ruling did not affect the use of DES for cattle and sheep, as residues had not apparently been found in their meat. Alarmed by the poultry ban, the industry lobby introduced the Kefauver-Harris 1962 Drug Amendment to the 1938 Federal Food, Drug, and Cosmetic Act. This is known as the Feed Additive Amendment or the DES Clause, and it specifically exempted DES and other carcinogenic feed addi-

tives, such as dinestrol diacetate, from the Delaney requirement. Their use was allowed, provided that the manufacturer made available a "prescribed and approved" monitoring method for the detection of prohibited residues, and that no residues were left when the additive was used according to "label directions that are reasonably certain to be followed in practice." The clear implication here was that any DES subsequently found in meat would be considered the result of bad feeding practices and not due to any inherent properties or danger of DES. In shifting the burden of responsibility from the legislative to the executive branch of government, Congress seemed willing to gamble on the regulatory discretion of the FDA and USDA.⁴⁸

The USDA and FDA rarely checked on compliance. They sampled only a relatively small number of carcasses with biological assay techniques which were impractical, non-specific, and sensitive only to 10 ppb, in spite of the fact that DES was known to produce breast cancer in mice at levels down to 6.5 ppb. The agencies took the additional precaution of keeping results of these samplings confidential. Meanwhile, use of DES was growing. By 1970, 75 percent of all beef produced in the United States, 30 million head per year, were fed with DES. Responsive to the growing DES market and to a request of Eli Lilly Company, the FDA in 1970 doubled permitted dosage levels to 20 mg per day per animal. The FDA, however, did not then take the opportunity to enforce the 1962 DES Clause requiring the manufacturer to provide a sensitive monitoring method for residues.

With the 1971 discovery of vaginal cancer in the daughters of DES-treated women, the USDA-FDA position on DES came under scrutiny and attack. Agency information was discovered proving that DES residues had been found in beef liver as far back as 1966, when 1.1 percent of 1,023 samples tested were positive, and again in 1967 when 2.6 percent of 495 samples were positive.† As typically found, DES residues of 2 ppb are equivalent to about 0.3 μg in a 150 gm serving of liver, an appreciable addition to natural hormonal levels.⁴⁹

In August, 1971, using a newly introduced chromatographic technique sensitive to 2 ppb, the USDA found high DES residues

† The number of cattle sampled continued to dwindle and by 1970 was down to 192.

in the livers of twelve cattle and sheep, in one case as high as 37 ppb.⁵⁰ These findings, while initially concealed, created a furor, especially since the USDA had previously denied finding any residues at all. Senator William Proxmire (D-Wisc.), introduced legislation to ban DES as a feed additive, and Representative L. Fountain (D-N.C.) held extensive hearings in November, 1971. DES critics pointed out that the additive had already been banned in over twenty foreign countries, that most Europeans would not buy U.S. meat because of its DES content, that any use of DES must obviously lead to residues in meat, and that there was an overwhelming scientific consensus that there was no known way for setting safe levels for carcinogens. The industry, supported by Agriculture Secretary Earl L. Butz and FDA Commissioner Charles C. Edwards, fought against a ban, claiming that this would cost from \$300 to \$400 million a year, and that DES residues in meat were so small as to be toxicologically insignificant.

In January, 1972, the USDA attempted to answer growing criticism by extending the 48-hour withdrawal period to 7 days, cattlemen being put on their honor to sign a "certificate of compliance" to this effect. The belief of the safety of a seven-day withdrawal seems to have been based on a single FDA experiment with one cow fed one dose of DES.⁵¹ Furthermore, such withdrawal periods are not only unenforceable, but unresponsive to the standard practice of slaughtering and selling just when the market prices are highest.

Following the finding of DES residues in nearly 2 percent of all cattle tested (in spite of the seven-day withdrawal period), the FDA announced its intent to hold further hearings in June, 1972. The meat lobby objected that the hearings were unnecessary, and public interest groups claimed that more than enough was known to ban without hearings. When asked, the American Cancer Society declined to take any position on the matter. By August, the FDA changed its mind and decided to cancel the hearings. The indecision continued until March, 1973, when the Senate Commerce Committee held hearings on the Federal Food Inspection Act of 1973, largely addressing problems of DES and other animal drugs, in which concerns on the deficiencies in Federal monitoring programs for carcinogenic residues in meat and dairy products were vigorously expressed. These concerns were heightened

by the discovery that the FDA was also in violation with regard to a wide range of other carcinogenic animal drugs, as it had no practicable test methods for detecting and measuring prohibited residues of seventeen of nineteen drugs then in widespread use.[‡] Such regulatory casualness was all the more serious in view of the burgeoning market in new animal drugs and feed additives, which by 1971 had increased to 1,372, including approximately twenty carcinogenic additives, a gain of nearly 25 percent over 1970 figures.⁵²

Still further concerns at the 1973 Commerce Committee hearings were provoked by a report of the National Academy of Sciences which found that there was only clear-cut evidence of efficacy for 18 percent of 706 animal drugs in current use. The highlight of the hearings, however, was the introduction of an internal FDA memorandum from K. R. Johnson, Director of the Division of Veterinary Medicine, in which, on September 27, 1972, he warned the FDA that "unless FDA resolves this drug residue problem, we will soon be in direct confrontation with Congress and the consumer, defending an untenable position. For the FDA to ignore this problem would be disastrous."⁵³

The FDA capitulated and following the hearings announced a partial ban on DES as a feed supplement from January, 1973, but still permitting its use in implants, which were later disallowed on April 25, 1973, when the ban became complete. A coalition of the meat and drug industries, including Dawes Laboratories of Chicago, appealed to the U. S. Court of Appeals in December, 1973, claiming that the ban would cost the country \$1.8 billion, a figure some 450 percent in excess of the 1971 estimates. The appeal was sustained on the grounds that the manufacturers had not been afforded adequate opportunity for a public hearing. Thus the ban was reversed, and DES was officially returned to the market on January, 1974. How did the industry cope during the nine

[‡] Dinestrol diacetate, for example, had been incriminated as a cause of vaginal cancer in young women whose mothers were given it in early pregnancy. In August, 1972, the FDA belatedly requested the manufacturer to provide an appropriate test method, as this drug had been illegally registered in the absence of such a method. Although the manufacturer failed to respond, the drug was still in extensive use in chicken and turkey feed at the time of the hearings seven months later.

months total ban on DES? They simply switched to substitute implants of other carcinogenic estrogens which had not been included in the DES ban, such as Synovex (Syntex Pharmaceutical Inc.) and Ralgro and Zeranol (Commercial Solvents Corporation), which were about six times as expensive as DES, although similarly effective.

Caught between the legislative mandate of the 1962 DES Clause and escalating consumer concerns, the FDA then decided to try to move against DES on two fronts, by attempting to ban its use and by attempting to regulate its residues. On January 12, 1976, the FDA proposed a total ban on all remaining feed additive uses of DES, this time allowing ample opportunity for public hearings. The chemical manufacturers, including Dawes and American Home Products, were the leading opponents of the FDA at the hearings which dragged on until January, 1978. On September 21, 1978, Administrative Law Judge Daniel Davidson ruled that feed additives were not safe, and upheld the FDA ban on their use. During the subsequent mandated fifty-day comment period, the DES manufacturers appealed the decision to Commissioner Donald Kennedy. Regardless of Kennedy's final decision, a further lengthy court battle is a certainty. In the meantime, public exposure continues.

In February, 1977, the FDA moved to tighten control of the uses of all carcinogenic feed additives within the framework of the 1962 DES Clause.⁵⁴ Their proposals emphasized the long-standing requirement for manufacturers to provide reliable, practical, and sensitive analytic methods for measuring residues, and also required the use of the most sensitive methods to become available at any time in the future. The required withdrawal period prior to slaughter would be that time, under normal conditions of livestock management, which would be necessary to reduce residues to below the lowest level of reliable measurements.

The proposed regulations were promptly challenged in the District of Columbia Federal District Court by the Animal Health Institute, not an animal producers' lobby but an organization with links to the pharmaceutical industry. In January, 1978, the Court ruled in favor of the drug companies, but the FDA appealed and the issue will probably not be resolved for several years.

Human Drugs In spite of repeated warnings from the scientific literature and from its own advisory committees, the FDA took no regulatory action against oral contraceptives for over a decade after they were first marketed in 1960.⁵⁵ On March 4, 1970 the last day of Senator Nelson's hearings on dangers of the pill, Commissioner Charles Edwards testified announcing an explicit proposed statement, "What You Should Know about Birth Control Pills," that the FDA was considering for package warnings. The American Medical Association and the pharmaceutical industry protested strongly and the FDA backed off, revising out most of the warnings and all mention of cancer. The modified statement provided the basis for package warnings ordered by the FDA in September, 1970.

By December, 1972, after the FDA had announced a ban on DES as a feed supplement, it had become public knowledge that DES was being dispensed by major university health clinics as post-coital contraceptives, in spite of the fact that it had never been approved for such use. The usual DES dosage of 250 mg was approximately a million times greater than a dose of 0.3 µg in a 100 gm serving of liver containing 2 ppb residues and equivalent to the estrogen content in about a two-year supply of oral contraceptives. The FDA has recently withdrawn from the market the 250 mg DES tablets formerly used for this purpose and has not given approval for any manufacturer to market DES as an oral contraceptive. The FDA, however, will approve use of DES in emergency situations, such as rape or incest, if a manufacturer provides patient labeling and special packaging. In view of the alarming outbreak of DES-related cancer, a special DES Task Force was set up in 1978 under the NCI's Division of Cancer Control. In the Task Force's summary report, women who had taken DES were advised to avoid any further estrogen usage. The report concluded that, while a further link with breast cancer had not yet been established, continuing studies were critically needed. In addition, Surgeon-General Julius Richmond issued a "Physicians Advisory/Health Alert" to all U.S. doctors discussing the known DES-related cancer risks, and recommending thorough follow-up for all women known to have taken DES, as well as their children of both sexes.

By 1976, evidence had accumulated that the sequential pill was

not only less effective than the combination pill, but also even more dangerous in terms of clotting disease, besides being incriminated in excess risks of uterine cancer. At the FDA's request, the manufacturer "voluntarily" withdrew sequentials from the market.

With mounting evidence on the carcinogenicity of Premarin and other forms of estrogen replacement therapy, and following the recommendations of its Advisory Committee on Obstetrics and Gynecology in December, 1975, the FDA finally took firm steps to control the burgeoning use of estrogens and replacement therapy. In October, 1976, the FDA ordered the pharmaceutical manufacturers to insert explicit patient package warnings in formulations of natural and synthetic estrogens in addition to DES. Patients had to be informed and warned against uterine cancer and a wide range of other risks, including other cancers, particularly of the breast and liver, and cardiovascular and thromboembolic diseases.

The ruling on labeling of estrogens used in replacement therapy was unusual for the FDA, which in the past has only required a mandatory "patient package insert" for oral contraceptives, intrauterine devices, and isoproterenol drugs used by asthmatics. The Pharmaceutical Manufacturers Association, joined by the American College of Obstetricians and Gynecologists and supported by the American Cancer Society, protested that information on drugs should be withheld from patients, and challenged the constitutional authority of the FDA to require such informative labeling. In September, 1977, the Pharmaceutical Manufacturers Association and the American College of Obstetricians and Gynecologists filed suit in the U. S. District Court in Delaware against the FDA proposal, claiming

that it interferes with the practice of medicine by physicians according to their best professional judgment and by dictating the way in which they may practice their profession. . . . The regulation will discourage patients from accepting estrogen therapy when prescribed by their doctors which will impair the reputation of estrogens and reduce the sale of the drug and others.⁵⁶

The Center for Law and Social Policy and Consumers Union have intervened against the suit on behalf of the FDA. The case is still pending. A successful outcome to the suit could well open up

the Pharmaceutical Manufacturers Association and the American College of Obstetricians and Gynecologists, quite apart from individual gynecologists, to malpractice liability actions by women developing uterine cancer, as well as cancer of other sites, from the continued use of estrogen replacement therapy.

The FDA followed up their move to label estrogens used in replacement therapy by a request to Congress in October, 1977, for authority to order patient package inserts when necessary.* Of particular interest is the recent announcement by FDA that manufacturers of oral contraceptives must supply physicians and patients with revised labeling, by April, 1978, warning of the dangers of heart attack and cardiovascular disease from the combined effects of smoking and contraceptives.† The labels also warn that estrogens can cause cancer in certain animals and may, therefore, also cause cancer in humans, although it is stated that studies to date of women taking currently-marketed oral contraceptives have not confirmed this.

Finally, in October, 1978, the FDA withdrew approval for the use of estrogens to relieve "postpartum engorgement" (to dry up the milk supply in newly delivered mothers), on the basis that the known risks of estrogens exceed the benefits.

Summary

Worldwide use of the contraceptive pill, dating back to 1960, constitutes the largest uncontrolled experiment in human carcinogenesis ever undertaken. This was only made possible by the importunity of the drug industry; in its massive marketing and heavy promotional campaigns for a poorly tested product and its unwillingness to face substantive questions on risk of cancer and

* The FDA estimates that such warnings on adverse drug effects will be required in 50 percent to 75 percent of all prescription drugs.

† One of the unique elements of these new warnings is the information provided on the relative effectiveness and risks of oral contraceptives compared with other forms of contraception. However, the statistical basis for the association between the combined effects of the pill and smoking with excess cardiovascular disease has been recently challenged by Tobacco Institute staff and consultants (Hearings of the House of Representatives Intergovernmental Relations and Human Resources Subcommittee of the Committee on Government Relations, October 3, 1978).

cardiovascular disease that subsequently developed; by the FDA's allowing the marketing of a poorly tested drug and refusing for years to take minimal regulatory action, and by the silence of the press on the growing evidence of dangers of the pill. Not surprisingly, the public accepted assurances of the pill's safety and abandoned other forms of contraception in its favor.

The carcinogenicity of estrogens and other female sex hormones has been repeatedly demonstrated in animal experiments begun as long ago as fifty years. Use of the contraceptive pill is associated with excessive risks of rare liver tumors, and there is also suggestive evidence of increased risk of cervix and breast cancers. Additional and major risks of the pill include heart disease and stroke, these being particularly marked in women who also smoke. The large-scale and common estrogen replacement therapy of menopausal women with Premarin, which is largely restricted to the upper socioeconomic brackets, is not only generally unnecessary but has also resulted in a virtual epidemic of uterine cancer. In spite of this, the Pharmaceutical Manufacturers Association and the American College of Obstetricians and Gynecologists, joined by the American Cancer Society, have challenged the legality of the FDA's recent label warning on the grounds that this will reduce the sale of the drug, and that it interferes with the doctor-patient relationship.

Evidence for the carcinogenicity in animals of DES, a synthetic chemical with estrogenic activity, dates back to 1938. Nevertheless, DES has been widely prescribed in attempts to prevent the complications of late pregnancy, although there is no substantive evidence to support such efficacy. This has resulted in an excess of breast cancer in the women themselves, vaginal cancers and the more common vaginal adenosis in the daughters of these women, and infertility and genito-urinary abnormalities in their sons. In spite of all the evidence on its dangers, DES is also still commonly prescribed as a post-coital contraceptive, in the absence of clear evidence as to its effectiveness, although the FDA is now attempting to regulate this.

DES was introduced as a feed additive in 1947. Extreme regulatory laxness by both the USDA and FDA, coupled with 1962 legislative exemption, at the urging of the industry, of DES from the Delaney Amendment, has resulted in the extensive and

increasing use of DES and other carcinogenic estrogens as feed additives. In spite of the requirement for withdrawal periods prior to slaughter, residues of these additives continue to be found in meat products. A powerful coalition of the meat and drug industries has now effectively blocked FDA attempts to regulate the use of these carcinogenic additives in animal feeds.

Chapter Seven

The General Environment: Case Studies

This chapter deals with two sets of case studies: the pesticides aldrin/dieldrin and chlordane/heptachlor, and nitrosamines, a large group of organic chemicals now found throughout the environment, many of which have been shown highly carcinogenic in animal tests. These are chosen to illustrate some basic problems of exposure to chemical carcinogens that are so widespread in the general environment as to be ubiquitous. While these particular pesticides are synthetic, nitrosamines, in contrast, can be produced by interactions between different classes of chemicals which may be common and naturally occurring.

Pesticides

Pesticides are chemicals that are intended to kill pests such as insects (insecticides); mites (miticides); weeds and unwanted vegetation (herbicides); fungi (fungicides); and rats and other “vermin” (rodenticides).*

Historical Background¹

We are now entering what is generally recognized as the “third generation” of pesticide use. The first generation of pesticides, which were developed and used until the 1940s, included naturally occurring organic chemicals such as pyrethrum and rotenone, and inorganic compounds, such as copper, zinc, mercury and lead salts, and arsenates. The inorganic pesticides created significant problems of toxicity, carcinogenicity, and environmental contamination (though these effects were generally confined to the area of application). Another problem with first-generation pesticides was that they were relatively expensive and variable in supply. The second generation was based on synthetic organics, the large-scale production of which commenced about 1940 with the advent of DDT and related organochlorine pesticides. The use of other major classes of synthetic organic pesticides which entered production about this time, including organophosphate insecticides and phenoxy herbicides, has substantially increased over the last decade. The third generation of pesticide use is based on an appreciation of fundamental ecological principles and on the maintenance of pests at economically acceptable levels rather than on futile and counter-productive attempts at eradication. Third generation strategies are based on integrated use of biological control, pest-resistant crop varieties,

* Fumigants are another class of pesticides used to kill a variety of pests by volatilization in confined spaces such as grain elevators and other food storage facilities.

crop rotation, insect predators, insect hormones, viruses, and sterilizing agents, either alone or in combination with minimal application of highly selective, "narrow spectrum" pesticides. Such programs of pest control, known as "integrated pest management," are still in their infancy, due largely to industrial indifference and scanty federal support, but they have shown great promise in agricultural and urban pest control, including home lawn and garden applications.²

In March, 1977, Secretary of Agriculture Bob Bergland announced that the USDA would work to move farmers away from their dependence on chemical pesticides and encourage greater emphasis on integrated pest management. There is, however, no material evidence yet of this intent.

The Toxic Effects of Pesticides

The second generation of pesticides was initially greeted with uncritical enthusiasm, as a triumph of modern synthetic chemistry, heralding a new era of agricultural efficiency. In nature, however, there are no "free lunches," and problems soon began to surface. First, it was noted that insects can acquire resistance to a particular insecticide or class of insecticides, necessitating progressively greater, more costly applications, and resulting in progressively smaller agricultural yields, until the infestation eventually becomes uncontrollable.³ This is known as the "pesticide treadmill." Second, many pesticides produce "broad spectrum" effects, damaging various forms of insect, animal, and plant life other than the intended target.⁴ Third, many classes of pesticides, particularly organochlorines, are highly stable, resist degradation, and accumulate in the food chain at levels often more than a millionfold in excess of those found in the environment. Fourth, many pesticides have been found to induce a wide range of toxic effects in experimental animals, including birth defects, sterility, and cancer, thus posing grave public health hazards, especially in view of their widespread environmental dissemination and persistence. Finally, some of the more stable pesticides become widely dispersed in the environment, air, food, water, and the human body, at locations far distant from their initial application. Pes-

ticides are thus now one of the most important classes of general environmental pollutants, and result in extensive involuntary exposure and contamination of human populations.

Many of these concerns were lucidly and cogently expressed by Rachel Carson in her 1962 classic *Silent Spring*, with particular and illustrative reference to DDT.⁵ Reaction from the agrichemical community—including the Manufacturing Chemists Association, chemical industry equipment manufacturers, farm organizations, land grant colleges, industrial organizations such as the Nutrition Foundation,[†] industry consultants or grant recipients in university departments of nutrition, and state and federal departments of agriculture—was immediate and strident.⁶ Carson was attacked as unscientific and hysterical. Typical of the misleading criticisms leveled against Carson were the self-interested statements by William Darby,[‡] then nutritionalist at Vanderbilt School of Medicine:

Her ignorance or bias on some of the considerations throws doubt on her competence to judge policy. For example, she indicates that it is neither wise nor responsible to use pesticides in the control of insect-born diseases.⁷

Darby, like most of Carson's critics, made a great show of reporting what she had never said. What in fact Carson had questioned were the overall methods of combatting insect-borne diseases which relied almost exclusively on massive pesticide use. Carson summarized her position as follows:

[†] The Nutrition Foundation was incorporated in 1941 to support "fundamental research and education in the science of nutrition." Its membership consisted of fifty-four companies in the food and chemical industries, the president of whose companies served on the Foundation's Board of Trustees. The foundation funnelled industry money, as research grants, to nutrition departments of many prestigious universities, whose recipients were among Carson's most vociferous critics. As part of its educational activities, in 1963 the foundation published a "fact kit" attacking *Silent Spring* and defending large-scale use of chemical pesticides.

[‡] Darby is a veteran member of the Food Protection Committee of the National Academy of Sciences, long dominated by industry, and now the director of the Nutrition Foundation. He is also member of the EPA Science Advisory Board and was recently appointed to a special subcommittee to review EPA policies on pesticide tolerances on food in response to continued grave Congressional charges of mismanagement.

It is not my contention that chemical insecticides must never be used. I do contend that we have put poisonous and biologically potent chemicals into the hands of persons largely or wholly ignorant of their potential for harm—. I contend, furthermore, that we have allowed these chemicals to be used with little or no advance investigation of their effect on soil, water, wildlife, and man himself. Future generations are unlikely to condone our lack of prudent concern for the integrity of the natural world that supports all life.⁸

The book, however, made a deep impact on the independent scientific community and on the nation.⁹ President Kennedy requested his Science Advisory Committee to create a special Panel on the Use of Pesticides to review the charges against pesticides. Both the Kennedy Committee and another Science Advisory Committee appointed by President Johnson in 1965 reported that the charges were indeed scientifically well founded. They concluded that organochlorine pesticides were dangerous, quite apart from often being ineffective, and that their production should be phased out as soon as possible. The importance of these recommendations has been more recently emphasized by growing information on the carcinogenicity of organochlorine pesticides as a class (Table 7.1).

Of the twenty-five organochlorine pesticides listed, nineteen have been shown to be carcinogenic in animal tests. There are no data available on four of the remaining six pesticides, while data on the other two (endosulfan and tetradifon), which are claimed to be non-carcinogenic, are still incomplete. Industry has repeatedly attempted to dismiss these findings by such tactics as selective interpretation of the data, challenging their human relevance, and asserting that alleged human experience of safe manufacture and use has vindicated their products. In fact, there are no published human epidemiological studies on carcinogenicity and other chronic toxic effects for the majority of organochlorine and other pesticides. Recent review of twelve organochlorine pesticides by an expert committee of the World Health Organization International Agency for Research on Cancer concluded that there are no valid human data which can possibly justify the conclusions of safety claimed by industry.¹⁰

Table 7.1 Organochlorine Pesticides: Production, Use, and Carcinogenicity

Class and Name of Pesticide	Manufacturer	1972 Production, Million Pounds	Major Use	Carcinogenicity
<i>Oxygenated compounds</i>				
Chlorobenzilate (Acaraben)	Geigy	1-4	Miticide	+
Dicofol (Keltthane)	Rohm & Haas	1-4	Miticide	No data
Dieldrin	Shell	Under 1	Insecticide	+
Endosulfan	FMC	1-4	Insecticide	-
Endrin	Shell; Velsicol	1-4	Insecticide	+
Kepone (Chlordcone)	Allied	No data	Insecticide	+
Methoxychlor	Multiple	5-14	Insecticide	+
Ovex (Chlorfenson)	Dow	No data	Miticide	+
Sulfenone	Stauffer	No data	Miticide	No data
Tetradifon (Tedium)	FMC	No data	Miticide	-
<i>Benzoid non-oxygenated compounds</i>				
Benzene hexachloride (BHC)	Diamond; Hooker	1-4	Insecticide	+
Dichlorobenzene (PDB)	Multiple	50-99	Fumigant	No data
Dichloropropene-propane (DD)	Dow; Shell	15-29	Fumigant	No data
DDT	Multiple	30-49	Insecticide	+
Lindane (Gamma BHC)	Diamond; Hooker	1-4	Insecticide	+

(continued on following page)

Table 7.1 (continued)

Class and Name of Pesticide	Manufacturer	1972 Production, Million Pounds	Major Use	Carcinogenicity
Pentachloronitrobenzene (Quintozone)	Olin Rohm & Haas Allied; Rohm & Haas	1-4 No data Under 1	Fungicide Insecticide Insecticide	+
Perthane				+
TDE (DDD)				+
<i>Non-oxygenated, non-benzoid compounds</i>				
Aldrin	Shell	5-14	Insecticide	+
Chlordane	Velsicol	15-29	Insecticide	+
Ethylene dichloride (Dichloroethane)	Multiple	5-14	Fumigant	+
Heptachlor	Velsicol	5-14	Insecticide	++
Mirex (Dechlorane)	Allied	Under 1	Insecticide	++
Strobane	Tenneco	No data	Insecticide	++
Toxaphene (Terpene polychlorinate)	Multiple	50-99	Insecticide	+

Source: Epstein, S. S. "The Carcinogenicity of Organochlorine Pesticides," pp. 243-65, in *Origins of Human Cancer*, Book A. ed. by H. H. Hiatt, J. D. Watson, and J. A. Winsten, Cold Spring Harbor Laboratory, 1977.

The Pesticide Market

There are approximately 1,400 active ingredients currently used in some 40,000 different pesticide products. A relatively small number of these products dominate the pesticide market, twenty basic ingredients accounting for 75 percent of total sales of agricultural formulations. Table 7.2 shows that about half of all pesticides are used in agriculture, while remaining uses are divided between industry (for purposes such as mothproofing carpets and fabrics and clearing rights-of-way), government (for brush and pest control on public grounds), and the general public (for home lawn and garden purposes).

Synthetic pesticides are one of the top classes of synthetic chemical products in the United States, with current annual sales in the region of \$4 billion, about 6 percent of the 1975 gross sales

Table 7.2 Estimated Average U.S. Use of Pesticides

Use	Percent of Sales
Agriculture	55
Industry	20
Home, lawn and garden	15
Federal, state, and local government	10

Source: Environmental Protection Agency, Office of Water Programs, "Patterns of Pesticide Use and Reduction in Use Related to Social and Economic Factors," Washington, D.C., 1972.

(\$72 billion) of the chemical industry.* From 1950 to 1975 overall pesticide production increased by about 15 percent per year, from an estimated 200,000 pounds to 1.4 billion pounds. The increase in production of herbicides and organophosphate insecticides was even greater during the same period. The only class of

* In 1975, approximately 588 million pounds of pesticides were exported, of which it is estimated (by the Natural Resources Defense Council) that approximately 15 percent were not registered for use in the U.S. Exporting unregistered pesticides is big business for U.S. manufacturers.

pesticides whose growth rate has declined are the organochlorines, particularly those belonging to a subclass known as cyclodienes, which include aldrin and dieldrin (A/D), chlordane and heptachlor (C/H), Endosulfan, and Endrin.

Support for the pesticide market comes from a politically and economically extremely powerful consortium of diverse interests.¹¹ In addition to the major agrichemical industries, this consortium includes pest control operators; aircraft applicators; agribusiness concerns such as banks, utility companies, and farm equipment manufacturers; food processors; key politicians, particularly from the corn and cotton belts; elements in federal agencies, particularly the USDA; elements in state agencies, particularly state departments of agriculture; segments of the media, such as the chemical and farm journals, rural newspapers, and chemical company house organs; professional societies such as those represented in the Council for Agricultural Science and Technology (CAST);† elements in land grant universities; and consultants in other universities.

At the bottom of this conglomerate of interests are the pesticide

† CAST is a consortium of agricultural science societies claimed to be an "educational" rather than a lobbying organization, and as such is tax exempt. The major spokesman for the organization is its Executive Vice President, Charles A. Black, Professor of Agronomy at Iowa State University, where CAST is presently located. In 1978, about 50 percent of the CAST's \$293,000 budget was directly contributed by Agribusiness (including fifty chemical, twelve seed, eleven manufacturing, twelve feed/processing, and other corporations totalling ninety-six). Ten of the world's twelve leading agribusiness firms, accounting for about 76 percent of total world sales, are supporting CAST members, as are six of the top twelve U.S. firms (Dow Chemical, Du Pont, Eli Lilly, Monsanto, Stauffer, and Union Carbide). CAST is a major resource for the industry, issuing a wide range of publications, including "consensus" Task Force reports on regulatory issues of critical interest to the industry, which it publishes by the thousands (about 8,000 copies of Report #77 on phenoxy herbicides were recently printed). CAST also employs a full-time Washington "liaison," who visits Congressmen, appears at regulatory hearings, and engages in a variety of related quasi-lobbying activities. CAST is also reputed to maintain a "hit list" of journalists, such as Jack Anderson, Lauren Soth, and Daniel Zwerdling who have published articles unfavorable to agribusiness (Unpublished Report, 1978, Charles Benbrook, University of Wisconsin, Madison; for further discussion of the pro-industry bias of CAST, see E. Marshall, "Scientists Quit Antibiotic Panel at CAST," *Science* 203 [1979], p. 723; and M. Burros, "The CAST Controversy: Impartial Scientific Research Group or Industry Advocate," *Washington Post*, March 8, 1979).

salesmen, who are generally ignorant of the efficacy as well as the hazards of their products.‡

Profits and Losses from Pesticide Use

What have been the agricultural returns for the recent massive uses of pesticides in agriculture? In spite of the fact that the total U.S. harvested acreage has remained steady over the past two decades, expenditures on pesticides for agriculture have increased about tenfold, an increase well above the inflationary rate and disproportionately greater than increases in crop value (Table 7.3).

According to estimates by David Pimentel of the Department of Entomology at Cornell University, the harmful recognized effects of pesticides represent a cost to the nation of at least \$3 billion annually, including

hospitalization costs for 6,000 human pesticide poisonings; costs of about 60,000 days of work lost from the pesticide poisoning hospitalizations; additional medical costs for 8,000 human pesticide poisonings treated as outpatients; and costs of about 30,000 days of work lost from humans not ill enough to be hospitalized.^{13*}

To these estimates can be added further losses from toxicity to domestic animals, livestock, fish, and wildlife; from losses of crop products; from seizure of food containing pesticide residues above

‡ Their role in the proliferation of pesticides has been questioned by many, including the late Robert Van den Bosch, the world's leading expert on integrated pest control: "The greatest absurdity in contemporary pest control is the dominant role of the pesticide salesman who simultaneously acts as diagnostician, therapist, nostrum prescriber, and pill peddler. It is difficult to imagine any situation where society entrusts so great a responsibility to such poorly qualified persons. (This characterization also seems generally apt for drug salesmen.) Pesticides rank with the most dangerous and ecologically disruptive materials known to science, yet under the prevailing system these biocides are scattered like dust in the environment by persons often utterly unqualified to prescribe and supervise their use."¹²

* Most cases of poisoning by accidental carelessness are due to the use of highly hazardous pesticides instead of less hazardous available alternatives. An important example is the widespread use of the highly toxic organophosphate Parathion. By replacing Parathion with Sumithion (a related but much safer insecticide not available for patent reasons in the United States), the Japanese have reduced their accident rate.

tolerance levels, from the approximately 200 people estimated by EPA to die annually from acute pesticide poisoning; and from an unknown number of deaths due to the carcinogenic and other chronic toxic effects of pesticides, alone or in combination with other carcinogenic and toxic chemicals. In sum, the total national losses from use of synthetic pesticides are probably in the same order of magnitude as the \$8.7 billion estimated by Pimentel as the cost of annual crop losses due to pest attacks.

Table 7.3 Increasing Costs of Pesticides, 1955 to 1975

	1955	1975
Number of harvested acres	335 million	340 million
Farmers' expenditure for pesticides	\$184 million	\$1.96 billion
Cost of pesticides per acre	\$0.55	\$5.76
Cost of pesticides in relation to farm production value	1 percent	4.4 percent

Source: Statistical Research Service, United States Department of Agriculture, 1978.

I mean there is no fooling around, the major issue is cancer.

Herbert L. Perlman, EPA Administrative Law Judge, 1974.

Aldrin/Dieldrin

Aldrin and dieldrin (A/D) are two closely related organochlorine pesticides. The former is naturally converted to the latter by an oxidation process both in the field and in the body.

Sales and Uses

Aldrin and dieldrin were first developed in 1947 and, from 1952 to 1977, were manufactured exclusively in the United States by Shell Chemical Company, a subsidiary of Shell Oil. At first they were chiefly used on cotton, but the increasing resistance of the boll weevil to A/D in the late 1950s caused these uses to decline. With growing concern about insect resistance and its toxicity, A/D sales declined from a peak of 22 million pounds in 1966 to about half that amount in 1972. Even then, A/D ranked sixth in sales among all U.S. insecticides, with registration for about 1,300 products handled by some 350 firms. Apart from termite control, which constituted about 15 percent of total sales, the major use of A/D was on corn. In the eight-state corn belt, where over 70 percent of the nation's five to six billion bushels of corn is grown, A/D were used prophylactically on approximately 8 percent of the crop as insurance against possible future infestation by the corn soil insect complex (rootworms, wireworms, and cutworms), rather than for treatment of actual infestations.

Environmental Contamination¹

Until about 1970, A/D were applied by aerial spray, even in the vicinity of lakes and streams, causing high levels of contamination of air and water. This contamination was found to persist, although at lower levels, even after use was restricted to direct soil application in accordance with recommended agricultural practice. The routes of this contamination by A/D were threefold: volatilization; transport on dust particles; and agricultural runoff of treated soils and dusts into waterways.

Dieldrin was found in 85 percent of air samples monitored by the EPA from 1970 to 1972, with average national values of 2 ng/m³ (nanograms per cubic meter), resulting in daily human intakes in the order of 0.1 µg (100 ng). Household dust levels in the corn belt averaged about 2 ppm. An additional and generally unrecognized source of household exposure comes from woolens

and rugs which have in the past been routinely mothproofed with dieldrin. Dieldrin was found more often in surface waters than any other insecticide, in average levels as high as 0.4 µg per litre.

Aldrin and dieldrin are highly persistent, and more than 50 percent of an original application of dieldrin can be recovered from soil after four years. Contamination of corn and forage grown on A/D-treated soil was the major source and route of residues in meat and dairy products, and ultimately also the major source of human contamination. Average residues of 10 ppb were found in soybeans rotated with corn in the corn belt. EPA monitoring programs from 1972 to 1974 found dieldrin residues in virtually all human body fat samples analyzed, with average levels of about 0.3 ppm and sometimes ranging as high as 15 ppm.² Levels in blacks were about twice those in whites. These residues are relatively stable and persistent: an average of 50 percent of initial residue levels are still present at about nine months.[†] Further, these residues are of the same order of magnitude, and in some cases greater, than levels in rodents which developed cancers after feeding with A/D.

Economic Losses

The profits Shell made by selling A/D have been at the expense of the national economy, which suffered major direct losses from the extensive environmental contamination caused by agricultural uses of A/D.³ In 1972, about half the catch of chub and trout from Lake Michigan had to be seized by the FDA, because they were found to contain residues over the permissible levels of 0.3 ppm. This came as a surprise to many, because dieldrin levels in Lake Michigan waters were "only" in the ppt range. However, the persistence and fat solubility of A/D allowed them to accumulate and concentrate in the food chain at levels nearly a billion times greater than those of the lake.

In the whole class of organochlorine pesticides, A/D are second only to Endrin in toxicity to lower species. A/D have been responsible for major kills, a single application resulting in the ex-

[†] The measure of this persistence is known as the biological half-life of a pesticide.

termination of one million fish of thirty different species in a Florida marsh. Some fish show toxic effects at 2 ppb levels, and oysters are damaged below 1 ppm, a level which killed 100 percent of quail chicks exposed. Egg shell thinning and breakage, induced by very small body burdens of dieldrin, has been particularly destructive for predators at the top of the food chain, and it has been estimated that A/D are responsible for about 10 percent of all bald eagle deaths.

Destruction of livestock and poultry due to excessive dieldrin levels has been commonplace since 1969, when the extent of this contamination was first appreciated. In February, 1974, a routine test by USDA inspectors discovered unusually high residues in a batch of chickens being processed by a Mississippi broiler farm. Within days, more lots of contaminated birds were identified from five poultry plants. As the residues in each chicken exceeded the allowable standard, they were ordered destroyed. By the end of March, more than eight million chickens had been gassed and buried, at a cost approaching \$10 million. The source of contamination was thought to be low-grade soybean oil containing dieldrin levels as high as 58 ppm and originally intended for industrial use but diverted instead into more profitable use in poultry feed.⁴

On March 26, 1974, a network of Southern senators headed by Senator James O. Eastland (D-Miss.), and supported behind the scenes by the Nixon administration, then anxious for sympathetic Southern votes against the pending impeachment charges, tried to rush through a bill indemnifying the poultry and egg producers and processors for the losses they had suffered. In fact, the major beneficiaries of this bill would have been five large conglomerates, and not the individual family farmers who serve as their sharecroppers. Senator William Proxmire (D-Wisc.) managed to put a last-minute hold on the bill, until the measure could be finally debated, when it was overwhelmingly rejected.

Are such economic losses, quite apart from questions of excess cancer risks, an inevitable and necessary penalty for maintaining the corn yield so vital to the national food supply? The answer seems to be no.⁵ There are, in fact, real questions as to whether A/D are of any actual agricultural value against the corn soil insect complex, the major use. A 1972 USDA survey of corn crops

found that of all acres treated with A/D, 60 percent were for rootworms, 16 percent for wireworms, and 24 percent for cutworms. However, rootworms and wireworms had by then become largely resistant to A/D. More important, rootworms and wireworms can be effectively controlled by other measures including crop rotation with soybeans. While Shell admitted this by labeling its products "Do not use in areas of suspected rootworm resistance," the pesticide salesmen countered this caution by aggressive sales pitches. As far as cutworms are concerned, infestation is relatively rare, occurs only in limited areas, and can then, if necessary, be treated by acceptable alternative pesticides, rather than by routine preventive application of A/D.

Most farmers are dependent on advice from salesmen for principles and details of pesticide use. Farmers also rely on university entomologists and economists, much of whose research is funded by the industry. There seems little doubt that A/D had been oversold by Shell and pesticide salesmen to farmers as an insurance against the entire corn soil insect complex, against most of which it was ineffective. Even for cutworms, recommended application levels seem to have been more than twice that actually needed for effective control.

A wide range of independent experts, including Robert Metcalf (University of Illinois), the late Robert Van den Bosch (University of California), and Donald Chant (University of Toronto), are agreed on the major ecological disruption caused by A/D and organochlorine pesticides.⁶ Many state entomologists are also agreed that A/D were unnecessary in the treatment of the corn soil insect complex. There is also a consensus that crop rotation is not only a more effective, but also a cheaper method of control.

Carcinogenicity of A/D

While information on the ineffectiveness of A/D and on its extensive environmental pollution was becoming increasingly appreciated, it was the question of carcinogenicity that finally influenced EPA to commence regulatory proceedings against these insecticides in 1971. The major issue in the subsequent agency hearings

was the validity of the experimental carcinogenicity data, and the relevance of such data to human risk.

Animal Tests By the time the proceedings started, A/D had been tested for carcinogenicity in several feeding studies in mice and rats by the FDA, Shell, and other laboratories under contract to Shell. In general, these studies had either reported negative findings or that A/D induced allegedly non-neoplastic liver nodules or "benign liver tumors" in mice (Table 7.4). In spite of these conclusions, however, the Mrak Commission in 1969 had concluded that A/D were carcinogenic on the basis of the 1962 FDA study.⁷

In an effort to explore these studies further, besides explaining fundamental principles of carcinogenesis to the court, EPA assembled a small team of independent experts that included Melvin Reuber, then of the University of Maryland, Umberto Saffiotti of the NCI, Arthur Upton, then from the State University of New York at Stony Brook and now Director of the NCI, and Adrian Gross of the FDA.[‡]

Apart from evaluating the specific findings of the various carcinogenicity studies, the EPA team made substantial contributions in broader areas of carcinogenesis. These were subsequently summarized and formulated by EPA as the following "nine cancer principles," and were of great importance in the final stages of the regulatory battle to ban A/D:^{*8}

1. A carcinogen is any agent which increases tumor induction in man or animals.
2. Well-established criteria exist for distinguishing between benign and malignant tumors; however, even the induction of benign tumors is sufficient to characterize a chemical as a carcinogen.
3. The majority of human cancers are caused by avoidable exposure to carcinogens.

[‡] The author was a member of this team.

^{*} These cancer principles have broad general applicability. They summarize the overall conclusions of many national and international committees on environmental carcinogenesis. (See, for example, Appendix II, the 1970 Surgeon General's Report on Environmental Carcinogens.) In the EPA brief the principles were followed by 29 pages of citations from reports and testimony.

Table 7.4 Summary of Carcinogenicity Tests on Aldrin/Dieldrin in Mice

Authors	Strain	Concentrations (ppm)		Carcinogenicity		Comments
		Aldrin	Dieldrin	Author's conclusion	Conclusion in subsequent independent re-evaluation	
Davis & Fitzhugh, 1962 (FDA)	C ₃ H	10	10	"Benign liver tumors"	Liver cancer	Liver cancer
Davis, 1965 (FDA)	C ₃ H	10	10	"Benign liver tumors"	Liver cancer	1. Liver cancer 2. Study still unpublished Unacceptable
Song & Harville, 1964	Swiss	15	15	Liver "neoplasia" in unspecified groups	None	
MacDonald et al., 1972	...	3-10		"Non-neoplastic" liver lesions	Liver cancer	1. Liver cancer 2. Study still unpublished
Walker et al., 1973 (Tunstall 1)	CF ₁	...	0.1-20	"Type A and B" liver tumors	Liver cancer	1. Liver cancer with no apparent threshold at 0.1 ppm, and following only 1-2 months treatment at 10 ppm. 2. Multiple site tumors at low doses. 3. Submitted to FDA
Thorpe & Walker, 1973 (Tunstall 2)	CF ₁	...	10	"Type A & B" liver tumors	None	1968, but unpublished till 1973. Liver cancer, with high incidence pulmonary metastases

Source: S. S. Epstein, "The Carcinogenicity of Dieldrin, 1," *Science of the Total Environment*, (4) 1975, pp. 1-52.

4. While chemicals can be carcinogenic agents, only a small percentage actually are.

5. Carcinogenesis is characterized by its irreversibility and long latency period following the initial exposure to the carcinogenic agent.

6. There is great variation in individual susceptibility to carcinogens.

7. The concept of a "threshold" exposure level for a carcinogenic agent has no practical significance because there is no valid method for establishing such a level.

8. A carcinogenic agent may be identified through analysis of tumor induction results with laboratory animals exposed to the agent, or on a post hoc basis by properly conducted epidemiological studies.

9. Any substance which produces tumors in animals must be considered a carcinogenic hazard to man if the results were achieved according to the established parameters of a valid carcinogenesis test.

In an effort to resolve some questions on the interpretation of the pathology findings of the various carcinogenicity tests, Reuber reexamined most of the original liver sections, and found that where "benign tumors" or "non-malignant" nodular liver lesions had been claimed, these, in fact, were often unequivocal cancers.⁹ In some instances, confirmation of the malignant nature of these tumors was obtained by other independent pathologists, and by the fact that some of the tumors spread or metastasized to the lungs and were also transplantable. Following Reuber's reevaluation, G. McDonald, a pathologist who had previously reported one of the industry-sponsored studies as negative, reexamined his original sections and was then obliged to admit that Reuber was substantially correct.

The available information, particularly as modified by the EPA reevaluation, clearly established that A/D were carcinogenic in five separate feeding tests involving three different strains of mice and at concentrations as low as 0.1 ppm and following only two months feeding. Simultaneous administration of the carcinogen DDT markedly enhanced the carcinogenicity of A/D in excess of

an additive effect. During the proceedings, evidence of carcinogenicity in two additional strains of mice was revealed. While the major cancer site was the liver, cancers were also found in various other organs, including the lung, particularly at relatively low dose levels.¹⁰

The rat data were less extensive, largely because the tests had generally been conducted at such high A/D concentrations that the animals died relatively early from toxic effects. Nevertheless, two studies, FDA 1964 and Tunstall 1, confirmed the carcinogenicity of A/D in rats, finding a wide range of multiple site tumors, particularly at lower doses. Reevaluation of the histology of one of these studies also confirmed the occurrence of liver cancers in treated rats.¹¹

How then could Shell contest the carcinogenicity of A/D, dragging out the proceedings over 1,700 days, the written record of which occupied nearly thirteen feet of shelf space? The answer is simple. The studies which were largely generated or contracted for by Shell were either handled in such a way as to discount, dismiss, or interpret away any findings of carcinogenicity, or alternatively were so inept as to invalidate the claimed conclusions of non-carcinogenicity. These tactics were facilitated by the practice of not publishing the reports but submitting them in confidence to a then uncritical FDA.

At the hearings, Shell further bolstered its claims that A/D were non-carcinogenic by developing, with the aid of an apparently impressive array of academic consultants, a novel approach to carcinogenesis based on an imaginative set of myths which were used in attempts to explain away the results of the animal tests. The Shell case largely rested on the claim that the liver tumors induced in mice were not real cancers, but only "hyperplastic" nodules or, using a newly invented terminology, benign "Type A" tumors. As a fallback position, Shell also argued that the mouse was an unsuitable animal for carcinogenicity tests, although for over a decade it had used negative data in mouse carcinogenicity tests as proof of safety of its products. The basis for this argument was that the mouse liver is "labile," and that all that A/D did was to somehow "augment" the induction of liver tumors, which were really due to an "unknown oncogenic stimulus."¹²

The tumors at sites other than the liver in A/D-treated mice were an obstacle to this set of propositions that had to be explained. What better way to do this than to produce some fresh information discounting them? This is just what Shell did. In the middle of the proceedings, when discussion on extra-hepatic tumors had become critical, Shell suddenly produced some "missing" data sheets going back to the 1967 studies at its Tunstall Laboratories in England purporting to prove that sixty additional test mice had no extra-hepatic tumors, and that statistical analysis of the new and old data combined proved that the incidence of these tumors was insignificant.¹³

The lengths to which Shell's consultants were willing to go is illustrated by the testimony of Paul M. Newberne, Professor of Nutritional Pathology, MIT, who said, "It is my feeling that mice as a species . . . should not be used for safety testing," and agreed with Shell scientists that all the extensive mouse data on carcinogenicity should be ignored.^{14†}

The rat carcinogenicity data were sharply contested by Shell, particularly Reuber's finding of an excess incidence of liver cancer in treated rats in his reevaluation of the 1964 FDA study. In an effort to discredit this, Shell created an Ad Hoc Committee of Pathologists headed by Stephen Sternberg, a pathologist at the Sloan Kettering Institute, New York, who had written the section on carcinogenesis in the report of a 1972 advisory committee appointed by the National Academy of Sciences claiming that A/D were non-carcinogenic. The ad hoc committee examined slides from twenty-two treated rats (among whom Reuber had found twenty carcinomas) and reported two carcinomas, one borderline carcinoma, and eleven animals with "hyperplastic nodules." This does not seem to constitute a substantive difference of opinion, particularly as it is generally agreed that nodules are premalignant, and are in fact now classified as neoplastic nodules, and particularly as liver carcinomas and nodules are exceptional in rats other than those treated with carcinogens.¹⁵

Shell and its witnesses adamantly insisted on a progressive escalation of the standards of proof for the carcinogenicity of A/D, which were so extensive and difficult to meet that their

† Newberne is also an advisor to the NCI bioassay program for carcinogenicity testing, which was and still is largely based on the use of mice.

compliance would exclude almost every known chemical carcinogen. These standards included:

1. Induction of carcinogenicity must be statistically significant at all dose levels.
2. A uniformly positive dose-response relationship must be found at all doses, even if there is competing toxicity and high mortality at high doses.
3. A causal association between A/D treatment and carcinogenic effects cannot be sustained unless the mechanism of action of the carcinogen can be demonstrated.
4. Conclusions on carcinogenic effects of A/D cannot be accepted until the possibility of unknown "augmenting factors" has been excluded.
5. A carcinogenic effect must be consistent and reproducible in a series of different tests before it can be accepted.
6. The induction of liver tumors in mice is no indication of carcinogenic effects, even if they are unequivocally malignant.
7. Tumor production in mice, even in various different organs and even when replicated, cannot be accepted as evidence of carcinogenicity.
8. Even the finding of carcinogenic effects in two or more animal species is unacceptable proof in the absence of evidence in humans.¹⁶‡

Human Evidence The final fallback position of Shell was that the animal tests should be discounted, whatever their findings, because epidemiological studies on workers exposed to "high levels" of A/D had conclusively established that there was no excess of cancers. This claim was based on a study, published by K. W. Jager in 1970, of a cohort of 826 full-time male workers, including maintenance crew and operators, employed between 1954 and 1967 at a Shell insecticide plant in Pernis, Holland.¹⁷ Some of

‡ This position was unequivocally reiterated more recently by M. J. Sloan, director of the Regulatory Division of Shell Chemical Company, at a discussion of a paper on "The Carcinogenicity of Organochlorine Pesticides," which the author gave at a conference on "The Origins of Human Cancer" at Cold Spring Harbor Laboratories in September, 1976.

them had additional exposures to unrelated pesticides. During the proceedings, the study was updated to 1973 by a Shell witness. There was a high turnover rate at the plant, as the largest number of workers at any one time, 1962, was only 230, and there was also "more or less frequent movement of workers between units" in the plant. Of the 826 workers, only 166 had more than four years exposure and fifteen years observation, and there were only 69 workers with more than ten years exposure and fifteen years observation. Finally, no worker had been exposed for more than nineteen years.¹⁸ Although a leading Shell witness admitted that this study "cannot be considered as statistical proof of non-carcinogenicity," other industry witnesses repeatedly cited it as proving that A/D were non-carcinogenic. Sternberg, for example, made the proposition that if A/D were really carcinogenic, then pre-cancerous symptoms should by now have developed in the exposed workers.¹⁹

The Pernis study was reviewed in detail by leading independent epidemiologists, including Marvin Schneiderman of the NCI, and Herbert Seidman of the American Cancer Society, who unanimously agreed that the study was so flawed and inadequate that it was not possible to draw any conclusion at all from it. The International Agency for Research on Cancer also agreed, stating that the study "does not allow any conclusions on the existence of an excess risk of developing cancer."²⁰ Not only was it based on too few workers, exposed and observed for too short a period for any significant excess of cancer other than a catastrophic one to be noted, but it was also clear from blood analyses that over 30 percent of the workers never had any substantial exposure to A/D in the workplace. Additionally the study had failed to follow up hundreds of other exposed employees.

Three studies in the general population have developed suggestive evidence of an association between excess human residues of dieldrin and cancer.²¹ A 1967 New Zealand study has shown that dieldrin levels in the lungs of patients with lung cancer are significantly higher than in non-cancerous controls. A 1968 study in Hawaii found that dieldrin levels were highest in patients with a variety of cancers. Another 1968 study reported higher dieldrin fat levels in patients dying in Florida with various malignant dis-

eases, including leukaemia and Hodgkin's, than in normal controls.

Other scattered cases of association between A/D exposure and malignant disease have been noted. In 1970 a federal court in Missouri (*Burke v. Stauffer Chemical Co.*) ruled that a case of Hodgkin's disease had been caused by prior exposure of a worker to dieldrin.²² Since then, there have been several other product-liability suits, most of them brought by pesticide operators involved in termite proofing with A/D formulations, which Shell has settled out of court, presumably to avoid the possibility of creating a legal precedent.

The Battle to Ban A/D

The battle to ban A/D has been long and bitter. In this, Shell was aided by powerful friends in Congress, headed by Senator Eastland and Congressman Jamie Whitten (D-Miss.), and in the USDA, which intervened in support of Shell's position. Useful behind-the-scenes support came from staff of the EPA Office of Pesticide Programs, particularly those who had transferred from the Pesticide Regulation Division of the USDA when EPA was created in 1970. Final and enthusiastic support came from Shell's university consultants and the land grant colleges.

The first round of the battle began in May, 1963, when a special panel of President Kennedy's Science Advisory Committee published a review on "Use of Pesticides," which called for reexamination of FDA tolerances for seven pesticides, including A/D. The review concluded that "elimination of the use of persistent toxic pesticides should be the goal."²³ The panel also noted with concern a 1962 FDA study which had shown that liver tumors were induced in mice by feeding them with 10 ppm of A/D. On the basis of this review, the FDA appointed an Advisory Committee which in 1965 recommended that the tolerances for dieldrin in foods should be reduced, and that further carcinogenicity tests be undertaken on A/D, as it found that the existing information was inconclusive. Accordingly, Shell withdrew some of its A/D registrations, including foliar application to corn, and initiated further

extensive carcinogenicity studies, known as the Tunstall 1 tests, in its Tunstall Laboratories in England. The results of these tests, which were completed by June, 1967, and transmitted to the FDA in 1968 though not published until 1973, confirmed the carcinogenicity of A/D contrary to the conclusions earlier claimed by Shell.²⁴ The FDA, however, took no action and did not seem anxious to share the information with anyone, including a blue ribbon HEW advisory committee appointed by Secretary Robert Finch in 1969 to examine the relationship between pesticides and health and to consider whether DDT should be banned (the Mrak Commission). At one meeting of the Carcinogenicity Panel of the Commission, a senior FDA scientist, O. Garth Fitzhugh, jocularly remonstrated with some members of the panel,* "I don't know why you should be so concerned about the carcinogenicity of DDT, you should see what we have on dieldrin." When asked what the FDA "had" on dieldrin, the answer was, "That's confidential," presumably referring to Shell's mouse data, the publication of which was withheld for six years.

The Mrak Commission was nevertheless able to conclude, on the basis of the 1962 FDA test in which Fitzhugh had been involved, that A/D were carcinogenic and should be banned.²⁵ Under pressure from the environmentalists, armed with this fresh support for their position, USDA reluctantly agreed in March, 1970, to cancel "non-essential" uses of A/D, including its application in aquatic environments.

EPA came into existence by order of President Nixon on December 2, 1970. The next day, the Environmental Defense Fund filed a petition to ban all uses of A/D on the grounds of its adverse ecological effects and its carcinogenicity. One month later, EPA Administrator William Ruckelshaus received the decision of the D.C. Circuit Court to ban DDT and to develop policies for cancellation of other toxic pesticides, whenever their use raised "substantial questions of safety." It was against this background of events that the regulatory struggle on A/D began in earnest.

In March, 1971, EPA announced its intent to move to the cancellation of A/D registrations for agricultural purposes by hearings before an administrative law judge. This action was taken under the authority of the 1947 Federal Insecticide, Fungicide,

* Including the author.

and Rodenticide Act, which allows the agency to move against pesticides by cancellation or suspension.[†]

Like all compromises, the cancellation decision did not please anyone. The Environmental Defense Fund promptly appealed, arguing that the cancer risks of A/D posed an "imminent hazard." The industry demanded their rights, under the terms of the 1947 Act, to have the matter referred to an advisory committee appointed by the National Academy of Sciences-National Research Council, which based on the past track record of such committees could have been expected to be sympathetic to the industry position.[‡] The NAS advisory committee released its report in March, 1972, endorsing the continued major uses of A/D.²⁸ The section of the report dealing with carcinogenicity written by Sternberg, who was later to appear as a principal witness for Shell, is puzzling. Sternberg only discussed the then unpublished Tunstall 1 study, which had concluded that A/D were not carcinogenic, and ignored the published 1962 FDA study, on the basis of which the Mrak Commission had previously concluded that A/D were clearly carcinogenic. Sternberg concluded that "if there is a carcinogenic action in dieldrin, it is likely a weak one at a level much like DDT."

In response to a ruling of the appeals court, EPA reaffirmed the cancellation decision in June, 1972, and requested public comment as to whether the agency should proceed to suspension. Shell responded by demanding a public hearing, again its right under the terms of the 1947 Act. Preparation for the trial began.

[†] Cancellation proceedings are often protracted over several years, while suspension, which is more rigorous and resembles a preliminary injunction in that it bans continued manufacture and distribution during the proceedings, is much more expedited, and can be justified only on the grounds of "imminent hazard." Suspension orders are, however, only temporary bans, pending the final outcome of more definitive cancellation proceedings.

[‡] See also discussion on the National Academy of Sciences Committee on Toxicology 1976 report on "Health Effects of Benzene," the Food Protection Committee 1972 report on Red #2, and reports on a wide range of other topics. It should be noted that membership of many such NAS committees has often reflected dominance by industry representatives or their consultants, who are appointed by NAS staff. Scientific members of the academy have not been commonly involved in these committees. It must, however, be recognized that the NAS, prompted by vigorous external criticism, now recognizes these problems and over the last two years or so has instituted various internal reforms which have improved the quality and independence of some of its reports.

On the government side, the litigation team was headed by Anson Keller and John Kolojeski of the Office of General Counsel. This team started work in virtual isolation, as the Office of Pesticide Programs, where the supposed scientific expertise on pesticides was located, was and still is highly sympathetic to agrichemical interests, quite apart from resenting the Office of General Counsel's apparent policy-making trends and ease of access to the administrator. The Office of Pesticide Programs was actually hostile to the proceedings. While this office was largely staffed by transfers from the FDA and the Pesticide Regulation Division of the USDA, the Office of General Counsel was staffed by young, environment-minded lawyers. The bitter schism which developed, known as the "scientists v. the lawyers," largely reflected the fundamental political ambivalence between environmental activism and traditional pro-industry conservatism, which had existed in the agency since its inception, rather than focusing on specifics of the A/D proceedings.

The failure of the Office of Pesticide Programs to provide scientific assistance in the proceedings opened the door for the Office of General Counsel to go outside the agency for help. This, however, turned out to be not so easy. Most university agricultural economists and entomologists receive research support from the industry and were unwilling to help the government position. The majority of experts on toxicology and carcinogenesis who were approached were either in a similar position or unwilling to take the time to help. The government case had then to rest on the efforts of the small litigation team and a handful of independent outside scientists. These were pitted against the resources of one of the largest and most powerful law firms in Washington, Arnold and Porter, under the direction of William D. Rogers, supported by a profusion of consultants from universities all over the world. In the government case against Shell conducted by EPA, Shell was supported in court by another branch of government, the USDA. The legal fees of Shell amounted to approximately \$1 million. These were more than amply repaid by their annual profits of \$10 million from continued sales of A/D during the proceedings, which it was to Shell's advantage to protract.

After months of unsuccessful negotiations, the cancellation hearings began on August 7, 1973. News of the Mississippi

chicken massacre of February, 1974, interrupted the leisurely pace of the proceedings.²⁷ This triggered an EPA announcement that it was again considering suspension. It asked Shell to agree to discontinue its intended A/D manufacture for the 1975 crop year, scheduled to begin around September, 1974. Shell refused. EPA then dropped its plans for suspension, presumably out of deference to Congressman Whitten, whose House Appropriations Subcommittee was then reviewing the EPA budget.

The reluctance of EPA to proceed more aggressively on the suspension of A/D was beginning to draw unfavorable comments from the press. On August 2, 1974, the new EPA administrator, Russell Train, announced his decision to suspend on the grounds of "imminent hazards," noting that production and use of A/D had recently increased, that environmental and body burdens of A/D were also increasing, and that further evidence of carcinogenicity had developed. In spite of the acknowledgment of "imminent hazard" in the suspension order, Train allowed the continued sale of existing A/D stocks. It was no secret that EPA had little option but to permit this or be faced with the statutory requirement of indemnifying Shell for unused stocks.

The cancellation record, consisting of about 24,000 pages of transcript and 950 exhibits comprising another 11,000 pages, was then incorporated into the suspension proceedings, which began on September 1, 1974. Because of the urgent nature of the suspension hearings, only fifteen days were allowed for opposing arguments. The final EPA brief was submitted on September 16,²⁸ and Judge Perlman submitted his decision to the administrator on September 20, recommending suspension.²⁹ This was subsequently confirmed by the administrator on October 1, 1974.³⁰

Of particular importance was the incorporation of the "nine cancer principles" in the final EPA brief as "established principles of carcinogenicity which can be applied to individual substances to determine their human cancer hazard." These principles, which were similar to the "seven cancer principles" used by EPA in the DDT cancellation proceedings, were developed by Kolojeski of the Office of General Counsel, based on the testimony of its "acknowledged cancer experts," Umberto Saffiotti of the NCI in particular. These nine principles, which were backed up by extensive supporting documentation and references and also by refutation

of contrary Shell evidence, were implicitly incorporated in both the recommended decision of Judge Perlman and the subsequent decision of the administrator. These principles were also to become the salient point of contention in the subsequent C/H hearings.

The principles aroused the strident opposition of industry. Industry objections were largely channelled through a task force of CAST composed of seventeen trade and largely captive scientific associations. The CAST task force consisted of thirteen scientists, including Newberne, the Shell witness, and Jesse L. Steinfield, Professor of Medicine at the University of California and previously U.S. surgeon general. The task force reports reaffirmed the industry position that the burden of proving the safety of a pesticide was the responsibility of the public, and recommended that rodents were too sensitive for carcinogenicity tests and should be replaced by monkeys.³¹ Not only is the latter suggestion economically prohibitive, but given the longer life span of monkeys it would also mean that any carcinogenicity test would take over ten years, rather than the two years required with rodents.

Both sides appealed the administrator's decision, the Environmental Defense Fund on the grounds that the suspension order still allowed use of existing A/D stocks, and Shell and USDA on the grounds that it objected to the basis of the ruling. There was considerable jockeying as to where the appeal should be heard, the Environmental Defense Fund favoring the D.C. Circuit Court, and Shell favoring the more sympathetic climate of the Fifth Circuit in New Orleans. The case was heard in D.C., and the decision of the administrator was affirmed in a unanimous decision of the court. In April, 1975, Shell announced that it would no longer manufacture A/D for use in the United States. A West Coast firm now manufactures aldrin for those relatively small uses exempted in the original cancellation order, including domestic termite treatment and "closed-system" moth-proofing of fabrics. It is difficult to comprehend why such uses have not also been banned, as they pose at least equal "imminent cancer hazards to man" as agricultural applications which were banned. As Shell not unreasonably asked: "How did the agency decide that 1½ pounds of aldrin under an acre of corn in the Midwest . . . leads to an unacceptable cancer hazard for man, when a rate of up to several hun-

dred pounds per acre in the soil under a human dwelling does not.”³²

Dieldrin, meanwhile, continues to be sold and used for agricultural purposes in most countries outside the United States. The EPA decision banning A/D was rejected in Britain on the grounds that “experts not trial judges were competent to judge the issue” of carcinogenicity. The British experts who concluded that dieldrin is not carcinogenic are members of a Pesticide Safety Precaution Scheme committee of the Ministry of Agriculture and Fisheries, which meets behind closed doors. The ministry is closely linked with industrial and agricultural interests.*³³

Summary

Aldrin/dieldrin (A/D) are highly persistent organochlorine insecticides which have been used mainly for the prevention and treatment of corn infestation, in spite of evidence that the complex of insects involved have become largely resistant. Use of these insecticides has resulted in extensive environmental contamination of air, soil, water, fish, wildlife, and meat products, resulting in major economic losses to the agricultural and fishing industries, and also contamination of the human body.

The carcinogenicity of A/D was established in animal tests by the FDA in 1962 and subsequently confirmed in tests by the manufacturer, Shell Chemical Company, in spite of their claims to the contrary. In regulatory proceedings against these insecticides by EPA, beginning in 1971, Shell and an extensive array of its academic consultants attempted to argue away the findings of carcinogenicity in its own and other tests by developing a set of scientific myths, escalating to the assertion that mice are unsuita-

* Such linkages, which permeate the scientific establishment, industry, and government, are commonplace in Britain where the opportunity for independent inquiry is restricted by a parliamentary system devoid of any public forum where civil servants can be held accountable (such as the U. S. Congressional committee system). Additional restrictions include a draconian “Official Secrets Act,” which can be invoked to protect information held to be “secret” by industry (such as levels of discharge of toxic pollutants into surface waters), crippling libel laws which inhibit investigative journalism, and the virtual absence of an effective public interest movement.

ble animals for carcinogenicity tests. Shell's confidence in these positions did not seem shaken by the fact that they had regularly used negative results in mouse carcinogenicity tests as proof of the safety of a wide range of their other chemical products, and also by the fact that A/D were carcinogenic in rats, besides mice. As a fallback position, Shell argued that even if the animal tests were positive, these should be discounted, as there was no evidence of carcinogenic effects in workers involved in the manufacture of A/D. However, the number of workers exposed was so few and the period of time over which they were observed was so brief that any possibility of detecting even a powerful carcinogenic effect was virtually excluded.

The success of the regulatory proceedings against A/D, resulting in their 1975 ban on the grounds of imminent carcinogenic hazard, was due to the combined efforts of a public interest group and the EPA's Office of General Counsel aided by a small team of independent experts. These were pitted against the massive legal and scientific resources of Shell and the USDA, which supported Shell's position, aided by the politically powerful Southern congressional network and the EPA's own Office of Pesticide Programs, which was hostile to the proceedings.

Chlordane/Heptachlor

Chlordane and heptachlor (C/H) are two closely related organochlorine pesticides of the same general cyclodiene subclass as A/D. Both chlordane and heptachlor are transformed in the environment and in the body to persistent and stable epoxide derivatives, oxychlordane and heptachlor epoxide, respectively. Technical formulations of chlordane contain about 7 to 12 percent heptachlor, besides various other related impurities.

Sales and Uses

Chlordane and heptachlor have been sold since the late 1940s and are exclusively manufactured by the Chicago-based Velsicol

Chemical Corporation, a subsidiary of Northwest Industries Inc. (Chlordane is manufactured at Marshall, Illinois and heptachlor at Memphis, Tennessee.) Their major agricultural uses have been as corn soil insecticides. They have also been used for treatment of termite infestation and as general insecticides around the home, lawn, and garden. Even prior to their suspension in 1975, the agricultural uses of C/H were on a gradual decline due to increasing insect resistance and the emergence of alternatives, particularly organophosphate and carbamate insecticides, which are more effective and do not pose comparable problems of environmental contamination. This decline was, however, temporarily arrested between 1973 and 1975, when the regulatory proceedings against A/D created demands for alternative corn soil insecticides.

Environmental Contamination¹

Chlordane and heptachlor and their principal derivatives are highly persistent, mobile, and fat soluble. Like A/D, their use in accordance with recommended agricultural practice has led to widespread environmental dissemination and the pollution of soil, air, and water. This, in turn, has led to accumulation and concentration of C/H in the food chain and resulted in substantial human contamination.

Residues of C/H are found in soil more than ten years following application.² Although the highest levels occur in agricultural areas of the corn belt states, residues are also high in urban soils, with average recorded values in the early 1970s of 0.16 ppm resulting from use around the home and garden. C/H are also highly volatile and escape into the air, whether applied to the soil surface or injected into the subsoil.³ In addition, C/H are transported as dust, particularly in areas where soil erosion is high. Dust levels of chlordane ranged up to 135 ppm in homes of pesticide formulators, and to about 40 ppm in homes of people who have no occupational exposure. Based on EPA monitoring data, the daily respiratory intake of an average adult would be in the order of 0.6 μg chlordane and 0.2 μg heptachlor, levels of the same order of magnitude as those from food.

Residues of C/H are found in surface waters all over the United States. Stream sediments containing chlordane residues as high as 800 ppb have been found in corn belt states. Chlordane residues are also found in fresh and saltwater fish, with levels reaching as high as 24 ppm. Laboratory experiments have shown that even very low levels of C/H cause mortality and reproductive failure in fish. Significant residues of heptachlor epoxide and oxychlordane have been found in eggs of many birds, including fish eaters. Much wildlife has been killed as a result of using C/H to control fire ants.

Diet is probably the most important source of human contamination by C/H.⁴ Once applied to soil, these insecticides begin a continuous movement up the food chain. Root crops grown on land treated with C/H as long as ten years ago absorb measurable quantities of these insecticides. FDA market basket surveys in 1973 and 1974 have shown that C/H, and particularly heptachlor epoxide, are found in the majority of dairy products, meat, poultry, and fish; the data on oxychlordane, while more recent and limited, also indicate extensive food contamination. The calculated total daily intake of heptachlor and its epoxide in the diet of a normal adult, excluding other environmental sources, is about 0.7 µg.

Residues of heptachlor epoxide and oxychlordane are found in virtually all body fat samples, each at levels from 0.1 to 0.2 ppm but ranging as high as 10 ppm for the former and 2 ppm for the latter.⁵ Levels in the United States are lower than in France and Italy, where agricultural use of C/H is more intense. Residues are also found in umbilical cord blood and in mothers' milk. It is important to note that human fat residues of heptachlor epoxide are roughly the same magnitude as levels in rats following feeding with the lowest level tested and found to be carcinogenic (0.5 ppm).

Nearly all available information on environmental contamination with C/H is related to agricultural use. It is remarkable that there seem to be no published reports on contamination of air, dust, drapes, textiles, food, and the human body following home and garden use, especially following treatment for termite infestation.

Carcinogenicity of C/H

As was the case with A/D, the regulatory battle to ban C/H largely focused on questions of carcinogenicity. C/H have been extensively tested for carcinogenicity in rats and mice in a total of some eleven studies, most of which have never been published.⁶ One exception is a 1965 FDA mouse study on the basis of which the Mrak Commission in 1969 concluded that heptachlor and its epoxide were carcinogenic.⁷ Apart from this study and more recent ones by the NCI, the results of which first became available in 1975,⁸ the main body of information on the basis of which C/H were claimed to be non-carcinogenic and safe was generated under contract to Velsicol by two commercial testing laboratories, the Kettering Laboratories of the University of Cincinnati, Ohio, and the International Research Development Corporation, Mattawan, Michigan. Studies in the latter laboratory were based on feeding C/H and heptachlor epoxide to mice and concluded that these insecticides were non-carcinogenic, although they noted a dose-related incidence of "liver nodules" in treated animals. Similar negative conclusions were reached in the Kettering rat studies.

In view of the uncertain validity of the conclusions of these various carcinogenicity tests, particularly those of the Kettering and the International Research Development Corporation, EPA decided that the liver sections should be reexamined by a team of independent pathologists headed by Melvin Reuber. Reuber undertook an extensive examination of most available liver sections, and these were spot-checked by four other pathologists in the team, who in general confirmed Reuber's findings.⁹ Where the International Research Development Corporation and Kettering had reported either normal conditions or non-malignant nodular liver lesions in C/H-treated mice and rats, Reuber and his team found a high incidence of unequivocal liver cancers. Reuber's results in many cases were statistically analyzed, showing that the incidence of liver cancers induced by C/H were highly significant. An honest difference of opinion, you might say, but for the fact that there were no discrepancies between the diagnoses of the industry laboratories and the EPA team in untreated control animals. Nor

were there discrepancies in diagnoses of the positive control animals treated with the known potent carcinogen acetylaminofluorene, as a check on their sensitivity, which resulted in a high incidence of liver cancers. An additional obstacle to the "honest difference of opinion" theory is that two Velsicol consultants who reviewed the liver sections of the International Research Development Corporation concluded that these showed cancers in the C/H-treated animals. They informed Velsicol of this by letter in December, 1972.¹⁰

C/H were also tested in the NCI bioassay program, the preliminary results becoming available in 1975 and the final published results in 1977. These studies confirmed the carcinogenicity of C/H in mice, although the results in rats were less clear-cut.¹¹

Taken together, the results of all these tests, particularly following independent reevaluation of the industry-generated data, clearly proved that C/H and heptachlor epoxide were carcinogenic in mice. These conclusions were subsequently confirmed by a 1977 Pesticide Committee report of the National Academy of Sciences, which agreed that there was unquestionable evidence of carcinogenicity in mice, and that accordingly, C/H represented a carcinogenic hazard to humans.¹² The rat data, while less extensive, again proved the carcinogenicity of heptachlor and its epoxide. While the results of chlordane testing in rats were equivocal, all the positive data on heptachlor and its epoxide are also applicable to technical chlordane, since heptachlor is a major component of technical chlordane.

As was the case in the A/D hearings, the industry minimized the human relevance of the carcinogenicity findings in rodents.†

† The scientific and emotional demeanor of some industry witnesses was unusual. William J. Butler, an English pathologist, in response to a question as to whether the induction of liver cancer in rats by C/H in the NCI Tests constituted evidence of carcinogenicity, responded, "This would slightly raise my suspicions."¹³ Another consultant, John Rust of the University of Chicago Medical School, responding to a question on the occurrence of metastases in the lungs of rodents from liver cancers induced by C/H, extrapolated, "I would like to say right now [gesturing towards respondent's counsel] that Judge Perlman ought to throw you bastards out for bringing this to court."¹⁴ Other industry consultants, such as Klaus Stemmer and Frank Cleveland of the Kettering Laboratories, who had undertaken carcinogenicity tests for Velsicol purporting to show that C/H were not carcinogenic, admitted in court that they had no training or expertise in chemical carcinogenesis.¹⁵

Industry further asserted that great weight should be attached to the human epidemiological studies which had failed to demonstrate the carcinogenicity of C/H. Three such unpublished studies have been recently conducted on behalf of Velsicol, two on pest control operators, and one on workers involved in the manufacture of C/H.¹⁶‡ All these studies suffered from the major defects of inappropriate methodology, too few workers exposed, too brief duration of follow-up, lack of exposure records, and lack of appropriate controls. As a result, it is impossible to make any valid inferences on safety or carcinogenicity.

Over the last twenty years there has been an accumulation of scattered reports of aplastic anaemia and leukaemia, besides other malignant disease, in humans exposed to C/H, under a wide range of conditions. There have also been recent reports of cancer and leukaemia in infants and young children born to mothers exposed to chlordane during pregnancy following house-proofing for termites.¹⁷ Recent product liability suits filed by workers who have developed cancers of various sites against Velsicol and exterminating companies have been settled out of court, presumably to avoid the possibility of a successful legal precedent.

The "Banning" of C/H

On November 18, 1974, EPA announced its intent to cancel all agricultural and domestic uses of C/H, excluding termite control, on the basis of carcinogenicity and widespread environmental contamination.

In the agency's first pretrial brief of April 1, 1975, the "nine cancer principles" developed during the A/D suspension hearings, were presented as "the most advanced research findings and pol-

‡ Typical of these studies was one presented by a Velsicol consultant, Brian MacMahon, Professor of Epidemiology at the Harvard School of Public Health, in testimony at the cancellation proceedings (FIFRA Docket 33, EPA, 1977). Based on a preliminary study of about 16,000 males with some occupational exposure to C/H during 1967-76, MacMahon concluded that there was no evidence of increased cancer mortality, while admitting the relatively short duration of follow-up of this study. The small number of workers who had been exposed for more than five years also invalidates the conclusion of non-carcinogenicity.

icy of both national and international cancer experts and agencies," in support of the proposed cancellation.¹⁸ Velsicol objected on a broad overall basis, particularly challenging principles number two, which deals with the essential similarity of benign and malignant tumors following administration of carcinogens, and number seven, affirming scientific inability to set thresholds or safe levels for carcinogens.¹⁹ Velsicol attempted to have the validity of these principles referred to a committee of the National Academy of Sciences for review. EPA opposed this motion on the grounds that "benign" and malignant tumors have synonymous scientific and regulatory implications in carcinogenicity testing. The appeal was denied by Judge Perlman, as was a subsequent appeal by Velsicol on more narrowly defined grounds. In these exchanges, Velsicol took the position that any burden of uncertainty in the carcinogenicity data should be borne by the agency and the public, not by industry.

On June 27, the EPA litigation team, led by Jeffrey H. Howard, Frank J. Sizemore III, and William E. Reukauf, moved to have some thirty-eight facts officially noted and incorporated in the hearing record. The first seventeen facts were an amplification of the nine cancer principles and were developed with the assistance of Umberto Saffiotti, on whose testimony the original nine principles had been largely developed in the A/D hearings.

On July 29, 1975, Administrator Train issued a further notice of intent, this time to suspend all uses of C/H other than those exempted in the cancellation order. Train cited new confirmatory evidence on carcinogenicity based on reevaluation by the EPA team of independent pathologists of previously claimed negative carcinogenicity tests, and declared an "imminent hazard of carcinogenicity" as the basis for his ruling. In his order, the Administrator discussed the seventeen cancer principles as "the basis for evaluation" of cancer risks, and thus ensured their adoption in the suspension proceedings.*

In a move apparently intended to neutralize the seventeen principles, William M. Upholt† wrote to NCI, then under the directorship of Frank Rauscher, asking for their reevaluation. This

* The author was involved in these proceedings as an EPA expert witness.

† Senior Science Advisor to the acting administrator for Water and Hazardous Materials, EPA, previously of the Pesticide Regulation Division of USDA and now an EPA consultant on pesticides.

matter was handled in NCI by Gary Flamm.[‡] Flamm referred the matter to the Subcommittee on Environmental Carcinogenesis of the National Cancer Advisory Board chaired by Philippe Shubik, Director of the Eppley Cancer Research Institute, of the University of Nebraska. Shubik, then and still a member of the National Cancer Advisory Board, is a well-known industrial consultant who has recently faced charges including mishandling federal funds and conflict of interest.²⁰

The Shubik Committee discussed the seventeen cancer principles at a meeting on November 10, 1975, and in principle was sympathetic to them. The transcript of the meeting also makes it clear that the committee was anxious to avoid reversal or criticism of the principles. Shubik, however, prepared an unsigned "working draft," which had neither been reviewed nor approved by his committee, and released it through Flamm to Judge Perlman.²¹ The draft not only gave the impression that the NCI committee had rejected cancer principles, but also perpetuated the alleged distinctions between "benign and malignant tumors."^{*} The draft report was immediately picked up by the trade journals and publicized as a formal NCI rejection of the cancer principles.^{†22}

The draft report had its presumably intended impact on Judge Perlman, who had been saturated by argument and counter-argument on questions of the carcinogenicity of C/H. Not unnaturally, Perlman was inclined to give weight to the findings of what appeared to be a top-level NCI report.²³

As news of this intervention leaked out, Shubik and Flamm sent a telegram to Perlman in late November asking that the draft should "not be misinterpreted or used prior to its completion." Additionally, Flamm has since claimed that they were forced to release the draft under the requirements of the Federal Advisory Committee and Freedom of Information Acts. However, there is

[‡] Then assistant director of the Division of Cancer Cause and Prevention, a geneticist recently recruited to the NCI from FDA and noted for his public speeches on the need to develop tests to "exculpate chemicals from carcinogenicity, rather than to indict them."

^{*} This and other current positions of Shubik on chemical carcinogenesis are in contrast to the views he previously expressed in a government document in 1970 (See Appendix II).

[†] The final report of the NCI Subcommittee on Environmental Carcinogenesis, issued in June, 1976, is however, essentially consistent with the 17 cancer principles.

no record of any such demand for the document under the terms of these Acts.

On December 12, 1975, Judge Perlman submitted his conclusion to EPA, that he was "hesitatingly unwilling at this time to find that heptachlor and chlordane are conclusive carcinogens in laboratory animals . . . [and that he could] not find an 'imminent hazard'."²⁴ This decision was rejected on December 24 by Administrator Train, who emphasized that while Judge Perlman did not find the evidence on imminent hazard from use of C/H to be conclusive, it certainly was not the agency's burden to establish risks, but rather the registrant's burden to establish safety, and this Velsicol had clearly failed to do.²⁵ Velsicol appealed the decision to the D.C. Circuit Court of Appeals, which upheld the EPA suspension ruling on November 10, 1976. The suspension created the authority for a temporary ban, pending the final outcome of the cancellation proceedings. These began in June, 1976, and opposing briefs were filed in January, 1978.

The three years of administrative litigation ended on March 6, 1978, with the announcement by EPA that a settlement had been reached between the litigants, including the Environmental Defense Fund, to phase out all agricultural uses of C/H over a five-year period ending in September, 1982, to allow agricultural users to shift to alternative crops and pest control technologies.²⁶ The settlement allows the production of no more than 7.25 million pounds of C/H annually, compared to the 20 million pounds prior to the EPA restrictions. All uses during the phase-out are restricted to certified applicators and commercial seed-treating companies.

The settlement is no victory for public health. It was apparently forced on a reluctant Environmental Defense Fund by the alliance of industry and EPA, whose Office of Pesticide Programs has been clearly adversarial to the objectives of effective pesticide regulation since its inception and to the efforts of the public interest movement in this regard. The settlement allows continued public exposure to excessive amounts of these carcinogenic and widely disseminated pesticides. Additionally, the language of the settlement clearly underestimates the human health hazard posed by the continued use of C/H. The settlement contains no legal finding of fact that C/H are carcinogenic and is thus open to subsequent

challenge by industry other than the litigants.[‡] Finally, the settlement in no way limits continued domestic use of C/H for termite control.

Criminal Indictment of Velsicol

On April 4, 1977, it was reported that a special grand jury in the Federal Court of Chicago was investigating Velsicol on charges that the company had criminally conspired to conceal information on the carcinogenicity of C/H. Specifically, Velsicol was charged with withholding the findings of carcinogenicity arrived at by its own consultants in 1972 on the basis of their review of the liver sections in tests done by the International Research Development Corporation. In announcing the indictment, EPA general counsel stated:

Velsicol Chemical Co. may have violated the reporting requirements of §6(a)(2) of the Federal Pesticidal Statute [which states that] "if at any time after the registration of a pesticide the registrant has additional factual information regarding unreasonable adverse effects on the environment of the pesticide, he shall submit such information to the Administration."

In December, 1977, the federal grand jury handed down an eleven-count felony indictment, naming six present or former company executives, all of whom face prison terms, charging:

From August 1972 to July 1975 the defendants . . . conspired to defraud the United States and conceal material facts from the United States Environmental Protection Agency by failing to submit data which tended to show that Heptachlor and Chlordane induced tumors in laboratory animals and thus might pose a risk of cancer to humans.²⁷

[‡] Velsicol's position on this is understood to reflect their intent to limit the scope of future legal actions brought against the company by pest control operators or householders developing cancer following use of C/H for termite control. This position is further strengthened by the language of the settlement, which asserts that the previous suspension decision by the EPA against C/H should not be considered as findings of fact under federal rules of evidence—an assertion of questionable legality.

A series of motions to dismiss the indictment were filed by Velsicol in March, 1978. These included technical pleadings and allegations of conflict of interest and prosecutorial misconduct based on the fact that an EPA attorney, Bingham Kennedy, had worked on the case with the grand jury on behalf of the Department of Justice. Following an evidentiary hearing in the fall of 1978 with respect to the motion to dismiss the hearing record was closed. Oral arguments were presented to Judge George Leighton in January, 1979. The case was dismissed on procedural grounds on April 20, 1979, without reaching the merits of the original issues of conspiracy raised by the indictment.

Summary

Chlordane and heptachlor (C/H), like aldrin and dieldrin (A/D), are highly persistent organochlorine insecticides used on corn, around the home as general lawn and garden insecticides, and also for treatment of domestic termite infestation. Like A/D, their use in accordance with recommended agricultural practice has resulted in extensive environmental contamination.

The carcinogenicity tests on C/H were made under contract to their manufacturer, Velsicol Chemical Company, by a commercial and a university laboratory, both of which reported negative results. During subsequent EPA proceedings against C/H, samples of the histological sections from these tests were reviewed by an independent team of experts who proved that these insecticides were in fact carcinogenic and had induced a high incidence of liver cancers. The impact of these findings was, however, blunted by the intervention of Philippe Shubik, chairman of a National Cancer Advisory Board subcommittee, and a well-known industrial consultant who at this writing faces major charges, including conflict of interest; Shubik sent EPA a working draft of his subcommittee's report, which challenged the nature of the carcinogenic effects induced by C/H but which had not been seen or approved by committee members. The subsequent refusal of the administrative law judge to suspend the insecticides was, however, reversed by Administrator Train.

Bowing to congressional and industry pressures, EPA subsequently reorganized its internal policies to exclude the possibility

of initiation of further litigation against pesticides by its Office of General Counsel and to place this responsibility, instead, largely in the hands of its Pesticide Regulation Division, which has been hostile to the proceedings against both C/H and A/D. (Since this reorganization, EPA has failed to initiate and conclude successful regulatory actions against any pesticides, and has developed regulations allowing the provisional registration of pesticides which have not been tested for carcinogenicity and other chronic toxic effects.)

Faced with an EPA now apparently hostile to pesticide regulation, a settlement to phase out major agricultural uses of C/H over the next five years has been developed between Velsicol, EPA, and the Environmental Defense Fund, which had prompted the original proceedings against C/H. The settlement excludes any legal "finding of fact" as to the carcinogenicity of C/H, and also permits their continued use for termite treatment. Termite treatment results in exposure of pest control operators and also householders to C/H. Case reports on the development of aplastic anaemia, leukaemia, and cancers following such exposures are now accumulating.

Nitrosamines

Although several classes of agents, including synthetic organic chemicals, metals, fibers, and radiation, have been shown over the past few decades to induce a wide range of human cancers, there are many types of cancers for which no such carcinogenic agents have been identified.

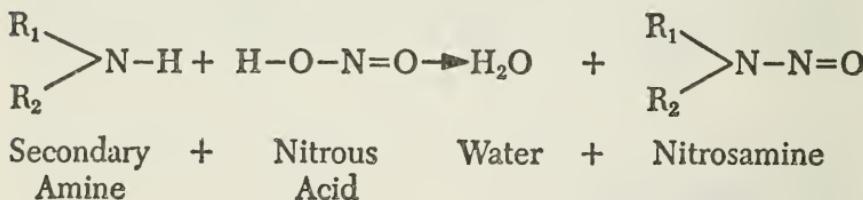
Over the last decade, there has been growing interest in the possibility that nitrosamines and other N-nitroso compounds may be a major class of universal carcinogens responsible for a substantial number of human cancers and cancers in other forms of life, under the widest possible range of conditions and circumstances, including preindustrial societies.¹

Nitrosamines are a large group of chemicals, many of which are found in air, food, and water, and most of which are highly carcinogenic to a great range of organs in all animal species tested.²

A more important reason why nitrosamines qualify as prime candidates for human carcinogens is that they can be simply and rapidly synthesized by a process called nitrosation, both in the environment and in the body, from two types of common and extensively distributed compounds, amines and nitrites or nitrogen oxides.³ In addition to naturally occurring amines, a wide range of consumer products, drugs, pesticides, and industrial chemicals are also amines, and can thus be nitrosated to form nitrosamines.

Basic Chemistry

Nitrosamines are characterized by a terminal N-nitroso, N—N=O, group. They are typically formed by the interaction of amines and nitrites or oxides of nitrogen, which are therefore called *precursors* of nitrosamines.⁴



Chemical analysis and measurement of nitrosamines, particularly at environmental levels in the ppm to ppb range, has until recently been difficult and time-consuming, thus limiting progress in investigating their presence in the environment. These problems have been resolved with the introduction of a highly specific and sensitive instrument, the Thermal Energy Analyzer, developed by the Thermo Electron Cancer Research Center, Waltham, Massachusetts, which is capable of rapid routine analysis of nitrosamines below the ppb level.⁵

Carcinogenicity

Of about 130 different nitrosamines so far tested, 80 percent have been shown to be carcinogenic.⁶ Nitrosamines are carcinogenic in

more than twenty different animal species tested, and no species has been found to be resistant. Individual nitrosamines produce various types of tumors in many organs of various animal species. Among nitrosamines are some of the most potent known carcinogens: dimethylnitrosamine (DMN), diethylnitrosamine, nitrosopyrrolidine, and dipropylnitrosamine, all of which produce cancers in test animals following administration at the ppm level in food, water, air, or by other routes. The lowest daily level of DMN which has been so far tested in rodents and found to be carcinogenic is 50 $\mu\text{g}/\text{kg}$, which is equivalent to an entire lifetime dose of less than 30 mg.

Formation of Nitrosamines in the Environment⁷

The growing realization that nitrosamines are ubiquitous environmental carcinogens largely reflects the widespread distribution of amines and nitrites or nitrogen oxides. Amines are chemical derivatives of ammonia, and are classified as primary, secondary, tertiary, or quaternary, depending on their increasing degree of chemical substitution. Amines, particularly dimethylamine and diethylamine, are well known constituents of many foods, particularly meat and fish, in which they are found at the 10 ppm range. Many common drugs and pesticides are also amines. Other important sources of amines include nicotine in tobacco smoke, ethanolamines used as emulsifying agents in cosmetics, detergents and pesticides, and air and water pollutants. Finally, amines are a major class of industrial chemicals and are used, for example, as catalysts in the manufacture of plastics, antioxidants in the manufacture of rubber, and fuel additives.

Nitrites are the reduction products of nitrates, the most common form of inorganic nitrogen in the environment. Nitrate/nitrite are present in a wide variety of foods, particularly leafy vegetables, and are also common food additives. Nitrate/nitrite are also normal constituents of drinking water and human saliva. Oxides of nitrogen, often referred to as NO_x , are major air pollutants emitted from all combustion sources, including incinerators and automobiles, and are present at high concentrations in cigarette smoke.

Amines can be nitrosated by nitrite or NO_x to form nitrosamines. These reactions occur in the test tube, air, food, and water—even in the stomach or other organs. A wide range of factors can alter the rates of synthesis of nitrosamines. Rates are increased in acidic conditions, such as those found in the stomach, by bacterial enzymes, and by salts such as thiocyanates, levels of which are particularly high in the saliva of smokers. On the other hand, some chemicals, such as vitamins C and E in high doses, can retard but not block nitrosamine synthesis.

Air

Nitrosamines have been detected by use of the thermal energy analyzer in the air of several American cities, particularly in the vicinity of chemical plants manufacturing or handling amines. In the summer of 1975, levels ranging up to about 0.05 ppb DMN were found in the downtown areas of Belle and Charleston, West Virginia.⁸ These were traced to a large Du Pont Chemical complex in Belle, which manufactures a wide range of chemicals and is the largest alkyl amine producer in the United States. Du Pont subsequently reported that they had isolated and plugged the source of the leakage.

DMN levels of about 0.1 ppb have been found in downtown Baltimore, originating two miles away at an FMC Corporation plant which manufactured dimethylhydrazine as a rocket fuel for military purposes. Plant levels were over 300 times higher, ranging up to 36 ppb; levels in an adjacent residential community were about 1 ppb. The rocket fuel production section of the FMC plant was ordered closed in February, 1976.*

It is difficult to translate air levels of DMN into daily human exposures. Making some reasonable assumptions on the average volume and rate of breathing, an atmospheric concentration of approximately 1 ppb DMN in air corresponds to a daily intake of about 14 µg or 0.21 µg/kg for an average adult male; this is only about one hundredth of the lowest dose of DMN which has been shown to be carcinogenic in conventional rodent tests. Such in-

* There is no information available as to where this operation was relocated.

take levels are in excess of DMN concentrations in tobacco smoke and in nitrite-preserved meats.

Among the significant potential sources of amine air pollutants is automobile exhaust. Of approximately seventy registered fuel additives, more than half are amines. These can be nitrosated by NO_x in automobile exhaust or subsequently in the air to form nitrosamines; another common air pollutant, ozone, has been recently shown to catalyze the rate of nitrosation. NO_x are a major class of air pollutants, originating from a wide range of stationary sources, such as municipal incinerators, industrial furnaces and domestic space heating units, besides mobile sources, such as automobiles. Levels of atmospheric NO_x are steadily increasing. According to a recent report of the Council on Environmental Quality, they are the only major pollutants whose concentrations in air have increased since the passage of the Clean Air Act in 1970. Relatively high levels of NO_x, ranging up to 0.4 ppm, are found in the air of large U.S. cities. In a non-industrial city, mobile and stationary sources contribute about equally to atmospheric levels of NO_x, with the relative proportion from mobile sources increasing during rush hours. In an industrialized city, the contribution of stationary sources is proportionately greater. It may be noted that a current EPA standard regulates automobile emissions of NO_x to levels of 1.5 g/mile, with the goal of reducing emissions to below 0.4 g/mile after 1981. EPA also regulates atmospheric levels of NO_x to an average annual standard of 0.1 ppm, based on short-term acute irritant effects, and without reference to problems of possible long-term effects, including nitrosamine formation. The importance of these problems is further indicated by two recent epidemiological studies, suggesting an association between high atmospheric levels of NO_x and excess cancers of all sites, including breast and lung. Commenting on one of these studies, the National Academy of Sciences concluded:

The consistent relation postulated by Hickey between cancer death rates and nitrogen dioxide are of enormous potential importance. Hickey reported an association in 38 metropolitan areas for breast, lung and total cancer over a nitrogen dioxide concentration range of 0.08–0.116 mg/m³ (0.04–0.06 ppm), concentrations that are frequently encountered in the ambient air of large cities.⁹

It should be appreciated, however, that such attempted correlations between a single pollution index, NO_x, and several types of cancer may be simplistic, and not necessarily implicate that specific pollutant. Rather, the correlations may reflect an overall increased exposure to a wide range of environmental pollutants. Regardless of possible limitations in these epidemiological studies, recent evidence on environmental synthesis of nitrosamines, and on high levels of atmospheric nitrosamines, lends still further urgency for a long-term NO_x exposure standard reflecting these considerations.†

Water

There has been relatively little work on the detection and measurement of nitrosamines in water. High concentrations have been found in a limited number of samples of sea and river water, and effluents from sewage plants treating wastewater from industries using or manufacturing amines or nitrosamines. DMN levels as high as 9 ppb have been detected in effluents from sewage treatment facilities handling wastewater from the FMC plant in Baltimore and the Du Pont plant in Belle, West Virginia. The intake for the drinking water supply of the Du Pont plant was about 500 feet downstream from where it discharged its effluents into the Kanawha River.

Food

Since time immemorial, nitrate has been used to preserve and cure meat. In fact, early European cave paintings show the use of salt-peter for this purpose by the Cro-Magnon man. The typical pink-red color of cured meat is due to the interaction of nitrite, formed by the reduction of nitrate, with myoglobin—a muscle protein related to the blood pigment hemoglobin—to form colored derivatives.

† Recent studies in the author's laboratories have demonstrated biosynthesis of nitrosamines in rodents following inhalation of NO₂ at levels below 10 ppm.

Nitrite has a general anti-bacterial action, besides being particularly effective in inhibiting the outgrowth of spores of *Clostridium botulinum*.

For these reasons, nitrite is used to prevent the production of the heat-labile toxin responsible for botulism (which is deactivated by heating to 185° for about 15 minutes). Botulism is a rare and often fatal "food poisoning" mainly occurring following production of the toxin under anaerobic conditions, such as in cold cuts and other processed meats, and particularly in home canning of low acid foods such as beans.

Over the years, the meat packing and processing industries have found that certain nitrate/nitrite ratios were ideal both for preserving meat and also producing the reddish color which consumers have grown to expect as visual proof of so-called "freshness." As the necessity for preservation has diminished, largely owing to modern refrigeration methods, the "cosmetic" use of nitrite has assumed greater importance to the meat industry and involves a \$12.5 billion cured meat market. Until recently, USDA and FDA standards have allowed addition of nitrite to meat and fish up to residual levels of about 200 ppm, regardless of whether its use is preservative or, as is mainly the case, cosmetic.

Nitrosamines have been found in many different meat and fish products, as expected from their content of natural constituent amines and nitrite food additives.¹⁰ The highest concentrations of nitrosamines in food are found in cooked bacon, with DMN levels as high as 10 ppb, and nitrosopyrrolidine levels as high as 50 ppb. Nitrosamine carcinogens have also been found in various other foods such as cheese, salami, hot dogs, nitrite-cured sable fish, salmon, and shad.

Nitrosamine formation in food can largely be avoided by banning the use of nitrite as a food additive for all purposes except when otherwise required by proven risks of botulism. Even then, minimal levels should be used, and whenever feasible nitrite should be replaced by other effective preservatives, including common salt.

On September 19, 1977, a USDA advisory committee on nitrosamines recommended that the meat industry be given up to three years to find replacements for nitrite in all circumstances

where addition of nitrite leads to formation of nitrosamine in meats. However, Carol Tucker Foreman, Assistant Secretary for Food and Consumer Services, USDA, in a statement of October 18, 1977, requested the industry to develop information within six months on the prevention of formation of nitrosamines in cooked bacon, either by finding suitable replacements for nitrite, or by reducing nitrite to levels at which no nitrosamine synthesis can be detected. It must be understood that the USDA proposals are based on prevention of nitrosamine formation in the meat itself, and not in the human stomach, a more difficult and possibly a still more important problem.

As a further move to encourage the sale of nitrite-free meat products, on April 28, 1978, USDA announced plans to propose new rules that would allow use of the name "bacon" on bacon-like meat products that differ from traditional bacon in that they contain little or no nitrite or nitrate. The same new rules will apply to corned beef, frankfurters, ham, and similar products. USDA also proposed the elimination of nitrite and nitrate in baby, toddler, and junior meat foods. Foreman followed this up by another proposal on May 15, 1978, reducing levels of nitrite which may be added to bacon to 120 ppm (together with 550 ppm of ascorbate or erythorbate), effective June 15, 1978, and to 40 ppm by May, 1979. These requirements were intended to reduce to less than 10 ppb the levels of nitrosamines in cooked bacon.¹¹

Foreman has been criticized by the industry for wanting to ban bacon. Her intent, of course, is to ban nitrosamine formation in bacon. How this objective is reached is clearly up to the industry.

In August, 1978, the FDA released a report by Paul M. Newberne of MIT (Final Report on Contract FDA 74-2181, "Dietary Nitrite in the Rat," May 18, 1978), which claimed that feeding nitrite to groups of rats, at levels ranging from 250 to 2,000 ppm, induced a low incidence of lymphomas.‡ For reasons which

† In the wake of the ensuing publicity, HEW and USDA developed plans for a gradual phasing out of the nitrate additives. At Secretary Califano's request, the plan was submitted to the Justice Department for approval, which ruled it illegal in March, 1979. As an alternative to a politically vulnerable immediate ban, HEW and USDA drafted legislation for Congress that would delay regulatory action until at least May, 1980, and would schedule a timetable for complete phasing out of nitrates by May, 1982, as acceptable alternatives are developed. The basis for these proposals, however, rests on concerns over nitrosamines, rather than on the validity of the questionable Newberne study.

Newberne did not explain, he maintained that these carcinogenic effects were due to the nitrite itself, rather than to the possibility of nitrosamines being synthesized from nitrite in the diet or in the stomach of the rats. In spite of the considerable publicity which this study received, its significance is questionable. Informal review by NCI scientists in December, 1978, challenged the accuracy of the histological diagnoses, and concluded that there was no statistically significant increase in the incidence of tumors in the test animals over controls which had an unusually high incidence of spontaneous tumors. Following the May, 1978, reduction in bacon nitrite levels to 120 ppm, the USDA initiated a series of tests in about ninety plants to check on nitrosamine levels in the product (the tests were based on the use of the thermal energy analyzer, positive results being checked by mass spectroscopy). While the USDA has indicated that the results of the tests were generally consistent, in that the substantial majority of the plants were in compliance (with nitrosamine levels under 10 ppb), on January 8, 1979, the agency nevertheless refused a request under the Freedom of Information Act from consumer groups and the news media for their specific findings. The agency based its decision on the grounds that the act allows investigatory records to remain private (and requested confirmation of this by the Department of Justice), and on the grounds that disclosure "could be misleading and result in erroneous conclusions."

Pesticides

Many common pesticides can be nitrosated to form nitrosamines. This happens either if the pesticide is formulated as a basic salt, dimethylamine or ethanolamine, or if the pesticide itself contains amine groups. In either circumstance, the common practice of coating metal containers with nitrite to inhibit rusting further contributes to nitrosation.

Very high concentrations of nitrosamines have been recently found in randomly selected commercial samples of pesticide formulations commonly used around the home and garden, as well as for agricultural purposes. These include Trysben (or Benzac), manufactured by Du Pont as an herbicide designed for use on

highways and rights-of-way but also generally available to homeowners, and Treflan, the commercial formulation of Trifluralin, manufactured by Eli Lilly, one of the nation's most commonly used herbicides with an annual market of \$230 million, mainly used on cotton, vegetables and soybeans. Trysben was found to be contaminated by DMN in concentrations up to 640 ppm, and Treflan was found to be contaminated by dipropylnitrosamine up to 154 ppm.

At hearings on September 20, 1976, before Congressmen John Moss (D-Calif.) and Andrew Maguire (D-N.J.), the industry admitted to these high nitrosamine levels in their products.¹² Du Pont had already recognized the problem and discontinued the practice of adding nitrite to Trysben containers. Lilly agreed to modify their manufacturing process, thereby reducing nitrosamine levels in Treflan approximately tenfold.

The industry, however, attempted to minimize the public health significance of the contamination of their products.¹³ Du Pont insisted that Trysben was not used on food crops nor by homeowners, but only by "professional applicators." In fact, Trysben can be purchased in most hardware stores. Lilly asserted that the "trace levels" of nitrosamines in Treflan posed "no hazard to human health" because they are unstable and rapidly "dissipated and degraded in air" and because "the average farm applicator comes in contact with far less nitrosamines [from Treflan] than from other sources" such as eating bacon and smoking cigarettes. Du Pont gave similar assurances, quoting the views of the Haskell Laboratory of Industrial Toxicology that "there was no imminent hazard." This prompted Congressman Maguire to ask, "Who pays their salary?" The reply was, "Du Pont Corporation."¹⁴

Farm workers were also not impressed by these assurances. In the spring of 1977, the Migrant Legal Action Program filed suit demanding the banning of Treflan and Trysben on the grounds of imminent hazard to field workers using agricultural sprayers and field cultivators. The suit included statements from several workers, presumably considered by the industry as "professional applicators," complaining that they had been heavily exposed to herbicide spray during application and that they were not warned of possible hazards nor given protective equipment.

In addition to the few pesticides tested and found to contain

high concentrations of nitrosamines, EPA admitted at the hearings that similar contamination was probable in as many as 1,000 pesticide products on the market.¹⁵ Exposure to these levels of nitrosamines, by routes including inhalation, ingestion, and skin contact, poses major carcinogenic hazards to occupational groups involved in their manufacture, formulation, and application. Hazards are also posed to the general public using such pesticides around the home and garden. These exposures are avoidable. First, industry should discontinue the practice of formulating pesticides as basic salts, and instead formulate them as acid salts. Second, industry should take precautions to avoid nitrosation of amine-containing pesticides, during both manufacture and application. Third, the use of nitrite rust inhibitors should be abandoned whenever there is any possibility of nitrosation. Fourth, pesticides labeled for use by "professional applicators" should not be made available to unskilled operators or to the general public. Finally, greater control should be developed to prevent hazardous occupational exposure at manufacturing, formulating, and application stages.

Drugs¹⁶

Many common over-the-counter and prescription drugs contain amine groups which can be nitrosated, particularly under acidic conditions in the stomach, to produce high levels of nitrosamines. Many of these drugs are prescribed or taken voluntarily at high doses for prolonged periods: aminopyrine, an analgesic, chlorpromazine, a tranquilizer extensively used to treat psychoses, and methadone, the heroin "substitute" distributed free to addicts in many cities, all of which yield DMN upon nitrosation; Disulfiram, or Antabuse, used to treat alcoholism, which yields diethylnitrosamine; and phenmetrazine, an amphetamine-type drug prescribed to control obesity, and Tolazamide, an oral hypoglycemic agent used in the treatment of diabetics, both of which yield nitroso derivatives.

Various recommendations have been made to cope with this difficult problem. These include incorporation of high doses of vitamin C in drug formulations, and the use of encapsulated time-

release formulations, from which the active amine-containing ingredient will be released in the small intestine rather than in the stomach. At best, these can only reduce nitrosamine yields, but not prevent nitrosation. The ideal solution would be the development of new classes of drugs containing no amines for use in all except life-threatening or terminal diseases. The ingenuity of the pharmaceutical industry can surely meet this challenge.

Cosmetics

Lotions and shampoos are major classes of cosmetics whose function is in part to moisten and soften skin. Many cosmetics contain ethanolamines as wetting agents, which emulsify the oily ingredients and increase their retention and absorption on the skin. Nitrosation of these amines to form the carcinogenic nitrosodiethanolamine has been recently demonstrated. Nitrosamine levels up to 48 ppm have also been identified in common commercially available cosmetics, including baby lotions (Table 7.5).

Excess risks of cancer, particularly of the lung and bladder, and leukaemia have been suggested by recent epidemiological studies on beauticians, who would be expected to be heavily exposed to a great variety of cosmetics. Whether these are related to exposure to nitrosamines or to other carcinogens in cosmetics, such as oxidative hair dyes or VC (used until recently as an aerosol propellant) has not been determined. In any case, it is clear that cosmetics should be formulated without ethanolamines, possibly using non-nitrogen-containing glycerol derivatives instead, and certainly without known carcinogens.*

Tobacco Smoke¹⁷

Tobacco smoke contains high concentrations of NO_x, at levels from 240 to 1,600 ppm, which are acutely irritating to the lung and which are almost completely absorbed during inhalation. Ad-

* In April, 1979, the FDA asked for "voluntary industry action" to reduce nitrosamine levels in cosmetics by product reformulation, failing which the possibility of future regulation was implied.

Table 7.5 Nitrosodiethanolamine Levels Reported in Common Cosmetics

Product	Concentration, ppb
Max Factor, Ultrallucent Whipped Creme Makeup	48,000
Revlon, Moon Drops	3,700
Helena Rubinstein, Silk Fashion	1,200
Clairel, Herbal Essence Shampoo	260
Scholl, Rough Skin Remover	140
Johnson's Baby Lotion	100
Avon, Topaz	100

Source: "N-Nitrosamines Found in Toiletry Products," *Chemical and Engineering News*, March 28, 1977, p. 7.

ditionally, NO_x can nitrosate the wide range of amines present in smoke to form nitrosamines. The smoke from a typical American cigarette contains various nitrosamine carcinogens, particularly DMN and N-nitrosonornicotine; the mainstream smoke from twenty U.S. blended cigarettes contains about $2 \mu\text{g}$ of the former and $3 \mu\text{g}$ of the latter. French cigarettes are likely to contain still higher nitrosamine levels because of their greater nitrate content.

A recent study has shown that the concentration of DMN in the sidestream smoke emitted from the glowing tip of a cigarette is much greater than the mainstream smoke directly inhaled by smokers.¹⁸ A non-smoker at a crowded, smoke-filled bar inhales in one hour approximately the same amount of DMN as that inhaled by the smoker of about sixteen non-filter or twenty-five filter cigarettes.[†] These facts lend urgent emphasis to the assertion of the rights of non-smokers to breathe air unpolluted by tobacco smoke, which could be accomplished by the segregation of smokers in restaurants, bars, and other public places.

The Workplace

Countless organic chemists, technicians, and students, in industry and universities, have been involved in the synthesis and use of

[†] One commercial 85-mm non-filter cigarette, for example, produced 680 ng of DMN in its side-stream smoke.

nitrosamines. Such exposure is a suspected cause of the excess cancer rates, especially pancreatic and lymphatic, found by the NCI in a 1969 survey on organic chemists.

Several nitrosamines have been used extensively as accelerators and antioxidants in the manufacture of various types of rubber. Approximately a million and a half pounds of nitroso-diphenylamine, involving exposure of up to 1,000 workers, are now synthesized each year in the United States. This is used as a retardant in the rubber curing process, involving exposures of an additional 5,000 workers. Preliminary studies on the rubber industry have recently revealed marked excesses of cancer of the stomach, prostate, and lymphatic system. What role nitrosamines play in these excess cancers has not yet been determined.[‡] This may well prove difficult, since workers in this industry are also exposed to benzene, a known leukemogen, as well as other carcinogens such as benzo[a]pyrene.

Levels of up to 10,000 ppm (1 percent) nitrosodiethanolamine have been recently reported in commercial cutting oils, used by machine operators in innumerable industries for purposes including cooling, grinding, and lubricating.¹⁹ According to NIOSH estimates, approximately 750,000 workers are exposed to cutting oils. Exposure to nitrosamines from these oils occurs via skin contact and inhalation of mists and vapors. The nitrosamines are formed from nitrite and triethanolamine, which are normal constituents of cutting fluids. NIOSH has recommended the omission of these nitrosamine precursors from cutting fluids and introduction of engineering controls and protective equipment.

The finding in August 1975 of relatively high DMN levels in the air of Belle, West Virginia, in proximity to the Du Pont chemical complex stimulated concerns as to possible hazards from occupational exposure to nitrosamines.²⁰ In December, 1975, Thermo Electron, working under an EPA contract, sampled the workplace air and found DMN levels comparable to those found outside the plant. Du Pont subsequently challenged these findings. Thermo Electron repeated the tests in February, 1976, but this

[‡] Recent findings on nitrosamines as occupational carcinogens include high levels of nitrosomorpholine in the rubber curing areas of tire factories, where a high incidence of lung cancer has been observed, and high levels of DMN in leather tanneries, which have not as yet been investigated epidemiologically (D. Fine et al., in press, 1979).

time found no nitrosamines in the plant except in one unrepresentative location. The mystery was apparently solved when Du Pont explained that the earlier findings of nitrosamines resulted from a side reaction in a small-lots manufacturing operation which management had subsequently recognized and controlled.

These events led to congressional hearings in New Jersey on May 28, 1976, which were filmed by CBS. Du Pont representatives were invited to testify, but declined to do so on grounds of "short notice." Du Pont management quietly attended the hearings as spectators, however, and were obliged to testify when they were found passing notes to the press offering to "field questions . . . at the noon recess."²¹

An additional issue raised at the hearings was the occurrence of an excess risk of cancer in the Du Pont plant in Belle, particularly cancer of the eye and the kidney, and to a lesser extent the lung.²² Cancer of the eye is exceptionally rare. The occurrence of five cases in a relatively small group of fifty workers, some of whom had cancers of other sites, is of sentinel importance. Based on Connecticut tumor registry data, this is about forty-four times higher than the incidence of cancer that would be expected in a matched control population. Whether the eye cancers are due to a nitrosamine-like carcinogen such as ethylnitrosourea, which induces similar cancers in experimental animals, has not yet been determined. Du Pont has denied the existence of an excess cancer risk in its workers, but refused to make available to NIOSH the necessary records to substantiate its claims, alleging a need to protect the privacy of its workers. In December, 1977, the courts upheld the rights of NIOSH to these records.

In addition to problems of excess cancer risk in Du Pont employees, it should be noted that Kanawha County, where the Belle Du Pont plant is located, is among the highest in the United States in incidence of lung cancer and leukaemia. The same county also has a high rate of central nervous system birth defects.

The Nitrosamine Balance Sheet

It is difficult to compare the relative amounts of all major possible sources of exposure to nitrosamines. Table 7.6 attempts to give some idea of the relative orders of potential exposures involved.

Table 7.6 Possible Daily Human Exposure to Nitrosamine Carcinogens

Exposure	Nitrosamines*, μg					
	DMN	NDEA	NPYR	NNN	NMOR	Other
Cooked bacon, 100 g	1†		5
Tobacco smoke, 20 cigarettes	2		3	...
Bacon and spinach meal, with synthesis of nitrosamines in the stomach	7
Drinking water, New Orleans	8
Air, Baltimore residential community, 1975	10
Cosmetics, Max Factor, 10 g	...	480
Herbicide spill, Trysben, 1 ml	640
Leather Tannery	630
Tire Factory	92	...

Source: Based on D. H. Fine et al., "Human Exposure to N-nitroso Compounds in the Environment," pp. 293-307, in *Origins of Human Cancer*, Book A., eds. H. H. Hiatt, J. D. Watson, and J. A. Winsten, Cold Spring Harbor Laboratory, 1977; J. M. Fajen et al., Paper 78, Air Pollution Control Association Annual Meeting, Houston, Texas, June 26, 1978.

* DMN=dimethylnitrosamine; NDEA=nitrosodiethanolamine; NPYR=nitrosopyrrolidine; NNN=nitrosonornicotine; NMOR=nitrosomorpholine.

† No data.

There are many problems involved in such comparisons, including the fact that some exposures occur by eating, others by inhalation, and by skin contact. Perhaps a more important limitation still is the fact that, with one exception, all the exposures listed

are based on levels of nitrosamines found in the product itself, rather than on the higher levels that can be expected to be synthesized in the body. In the case of the bacon and spinach meal, the exposure level is based on expected yields of DMN formed by interaction of precursors in the stomach. As can be seen, DMN levels in the stomach are higher than in cooked bacon itself.

A recent preliminary report (based on six volunteers), highly publicized by the meat industry, demonstrated substantial synthesis of nitrite and nitrate in the intestine (presumably by nitrification of ammonia or organic nitrogen compounds).²³ Based on this report, the industry claimed that levels of dietary nitrite are insignificant compared to the available body pool. These claims ignore the fact that dietary nitrites, particularly in cured meats, react with amines to form nitrosamines in the food, and that such levels will be further increased in the stomach. They also ignore the fact that there is no evidence that fecal nitrite is available for interaction with intestinal amines to form nitrosamines.

The ubiquity of nitrosamines makes it imperative that environmental levels be reduced to the smallest limit possible. Methods for achieving this goal depend almost exclusively on rigorously restricting the further introduction of nitrosamine precursors into the environment, especially under conditions of potential interaction.

Summary

Nitrosamines are a large group of chemicals, most of which are carcinogenic, producing tumors in a wide range of organs of a wide range of test animals. Although there is no direct epidemiological evidence, nitrosamines are considered to be major human carcinogens in both non-industrialized and industrialized countries, particularly because of their ubiquity in the environment. This is due to the fact that they can be easily and rapidly synthesized by the interaction of common precursors, nitrites or oxides of nitrogen and amines, in a process called nitrosation.

Regulatory control of nitrosamine formation can be achieved

by avoidance of the use of amine-containing products, such as pesticides, drugs, detergents, cutting oils and cosmetics, and avoidance of adding nitrite to amine-containing materials, including foods such as bacon, particularly under conditions in which nitrosation can occur.

Cancer in its many forms is undoubtedly a natural disease. It is probably one of nature's many ways of eliminating sexually effete individuals who would otherwise, in nature's view, compete for available food resources without advantage to the species as a whole.

F. J. C. Roe, Consultant to the American Industrial Health Council.
February, 1978.

Chapter Eight *How to Improve* *Industry Data*

The overwhelming bulk of benefit and risk data, on the basis of which most regulatory decisions are based, comes from the industries being regulated. These data are either generated and interpreted by in-house scientists or by commercial laboratories and universities under contract. In-house scientific staff are not immune to pressures from research and development and marketing departments anxious to hurry their product or process into commerce. Industrial contracts with commercial laboratories and universities are usually awarded secretly, without bids having first been solicited on the open market, a practice hardly consistent with the ethos of competitive capitalism. The contractee, anxious about the award of future contracts, is also not immune to unspoken pressures to produce information or interpretations consistent with the perceived interests of the contracting industry. Consultants, generally from prestigious universities or research institutes, provide data with an additional mantle of authority. The

industrial interests of these consultants, often unknown to the public and to their own institutions, are either not disclosed to the agencies they advise, or, if disclosed, are usually kept confidential. A similar tendency operates in testimony before law courts and congressional committees.

Faults with Industry Data

Constraints on data, from gross inadequacy, biased interpretation, manipulation, suppression and outright destruction, are commonplace, especially when profitable products or processes are involved.¹ Evidence of such constraints now justifies *a priori* reservations about the validity of data developed by institutions or individuals whose economic interests are affected, especially when the data base has been maintained as confidential at industry's insistence.

Decision-making at all levels of government presupposes the availability of a body of information, on the basis of which the merits of alternate policies can be analyzed. If this data base is constrained or invalid, resulting decisions will also be constrained or invalid. This threatens the very fabric of democratic government.

Constraints in the information base will be illustrated in three general areas relating to its generation, interpretation, and suppression or destruction, with particular reference to problems of occupational and environmental cancer.

Constraints in the Generation of Data

The most common problem with industrially generated data is its poor quality. Complementing this are faults of design and performance consciously or unconsciously built into toxicological and epidemiological studies. These tend to produce results influenced or predetermined by short-term marketing considerations.²

Deeply concerned by the inadequacy of data submitted in 1967 to the FDA by industry in support of food additive petitions, Commissioner Herbert Ley complained:

Almost half of the food additive petitions originally submitted to the Food and Drug Administration have been incomplete or have not adequately supported the regulation requested and, therefore have required subsequent supplementation, amendment, withdrawal or denial.³

There is substantive evidence that the situation has not improved over the last decade.

Problems related to improper initial design of animal cancer tests include:

1. Using too few animals
2. Exposures in excess of the maximally tolerated dose, resulting in premature animal deaths before onset of cancer
3. Doses too low for the size of the animal test group, resulting in failure to obtain a statistically significant incidence of tumors
4. Deliberate premature sacrifice of animals for other "studies" during the course of the main test, thus depleting the number of animals remaining alive and at risk for cancer
5. Premature termination of the test before sufficient time has elapsed for the animals to develop tumors.

A second set of performance problems relates to husbandry. These include:

1. Poor housing, diet, and care, resulting in infections, sickness, and premature death
2. Failure to insure that each test and control group receive appropriate prescribed treatments as originally intended
3. Failure to inspect cages regularly so that dead animals become decomposed, resulting in the possibility that tumors may be missed at autopsy
4. Inadequate autopsies

5. Failure to examine appropriate tissues and organs for histological (tissue) study
6. Poor record keeping
7. Alteration, falsification, and even destruction of records.

The following examples illustrate common patterns of experimental deficiencies and misconduct. A 1969 review of seventeen industry-sponsored studies on the carcinogenicity of DDT by consultants to the Carcinogenicity Panel of the Mrak Commission on Pesticides concluded that fourteen of these studies were so inherently defective as to preclude any determination of carcinogenicity.⁴

Having spent \$500,000 on the carcinogenicity and toxicological testing of the cosmetic food additive Red #40 by Hazleton Laboratories, which concluded that it was safe, Allied confidently submitted these data to FDA in 1970 and embarked on an ambitious advertising and marketing program. Not only had Hazleton failed to perform the customary mouse carcinogenicity test, but their rat test was of little value, as most animals died early in the test from intercurrent infection, not leaving enough alive to have revealed any but a massive carcinogenic effect.⁵

Carcinogenicity tests in rats of aldrin/dieldrin sponsored by Shell and of chlordane/heptachlor sponsored by Velsicol produced results that were claimed negative by the sponsors. In fact, these results were hardly interpretable because such high and toxic doses of both pesticides were fed the animals that many died early in the experiments, before they could have developed cancer.⁶

Other data submitted by Shell and Velsicol were used to claim that their pesticides were not carcinogenic in mice, and that the liver lesions induced in them were not really cancers, but just non-malignant nodules. Review by independent experts, however, proved just the contrary.⁷ Faced with such major discrepancies and under pressure from Senator Kennedy's Subcommittee on Administrative Practice and Procedures, EPA finally reviewed other industry data on pesticides. Twenty-four currently used pesticides were selected on the basis of their highest permissible residues (tolerances) on common foods. Their extensive toxicological files, which had been previously submitted to EPA by a

variety of manufacturers, were then independently reevaluated. In an EPA report of April 9, 1976, it was concluded that with one possible exception these data were so inadequate that it was not possible to conclude whether any of the pesticides were safe or whether there would be any hazard in eating common foods with now legal residues.⁸

These and other grave deficiencies in the EPA data base on pesticides were discussed in a recent Congressional Staff Report:

EPA almost exclusively rules upon data submitted by the pesticide companies. This data is the informational lynchpin in the Agency's regulatory program. Yet in spite of repeated warnings, beginning at least 5 years ago, EPA has failed to take corrective action designed to discover and supplement further data.⁹

More serious than inadequacies of data are the numerous examples of fraud, such as those described in the *Congressional Record* of July 30, 1969.¹⁰ Manipulation of data has been established with such drugs as MER/29, for which officials of Richardson-Merrill Company were criminally convicted; Dornwall, for which Wallace and Tiernan Company were found guilty of submitting false data; and Flexin, about which McNeil Laboratories omitted toxicity data on drug-related liver damage, including eleven deaths, in their submissions to the FDA.

On January 20, 1976, then FDA Commissioner Schmidt testified before Senator Edward Kennedy (D-Mass.) that Hazleton Laboratories (Vienna, Va.), under contract to G. D. Searle Company, reported on non-existent histological findings in carcinogenicity tests on the drug Aldactone.¹¹ Hazleton was also charged with falsifying data on the artificial sweetener Aspartame.*

Schmidt further testified on April 8 that investigation of Hazleton tests revealed a wide range of problems including ". . . large numbers of autolyzed tissues; failure to assay test substances; failure to assay treatment-diet mixture; failure to adequately review records and verify their accuracy; the use of a statistical method

* Following approval of Aspartame in July, 1974, FDA issued a stay after questions were raised on the reliability of the data. In May, 1979, FDA rejected a request by Searle to remove the stay on marketing approval pending an adjudicatory hearing.

that included autolyzed tissues, on which no observation had been made in the denominator for determining the number of lesions found; lesions reported at necropsy for which slides had not been made; tumors reported microscopically for which slides have never been made.”†

A striking example of inept design is the fiasco of nitrilotriacetic acid (NTA).¹² In 1970, Monsanto and Procter and Gamble were poised to launch a new type of detergent onto the market, based on NTA instead of phosphates. This would have resulted in the annual discharge of approximately five billion pounds of the new detergent into the surface waters and ultimately into the drinking waters of the United States. The industries concerned had spent about ten years investigating the toxicological and ecological effects of NTA, concluding that it was non-carcinogenic and that it degraded in water into harmless constituents. In fact, the industries had not done a single test to determine the mechanism of degradation of NTA in water, nor of the possible interaction of such degradation products in water with other water pollutants. The industry had also failed to appreciate that degradation was incomplete over a wide range of operating conditions with the resulting likelihood that drinking water could become contaminated with the detergent. These and other considerations led to the “voluntary” withdrawal of NTA from the market with a loss of some \$300 million to the industries concerned.‡ The detergent was subsequently shown in studies sponsored by the National Cancer Institute and the National Institute of Environmental Health Sciences to produce cancer of the kidney and ureter in mice and rats.

There are similar examples throughout the field of safety test-

† Following similar statements by the author in a recent article, “Polluted Data” (*The Sciences*, July/August, 1978, pp. 16–21), despite the written Congressional record, Roy M. Dagnall, Vice President and Director of Research Hazleton Laboratories, wrote to the editors of *The Sciences* protesting that “this is not true and at no time have any such charges been made by anyone except Epstein in the article in question,” *The Sciences*, May/June, 1979, pp. 2–28.

‡ The major precipitating event to the withdrawal of NTA from the market was the report that the author prepared as a consultant to the Senate Committee on Public Works which raised substantial questions on safety of the new detergent, besides challenging the claim that its use would prevent eutrophication in lakes, which was the main basis for its proposed large-scale use as an alternative to phosphate detergents.

ing, whether of drugs, pesticides, food additives, industrial chemicals—even motor cars. For instance, in 1972 Ford Motor Company manipulated emission control certification tests on their new fleet of cars. With approval of the Nixon administration and Department of Justice, the industry managed to ward off a subsequent criminal prosecution and jail sentence by paying a \$7 million fine.¹³

Industry has manipulated economic as well as scientific data. It is now common practice for an industry “threatened” by an impending regulation or standard designed to protect against occupational cancer, environmental pollution, or some other adverse effect to protest first that the measure is unnecessary and then that it is so expensive it will put them out of business. In this they are supported by economic consultants whose analyses apparently confirm the industry contention. For example, the economic impact analyses of the anticipated costs of meeting the proposed “no detectable level” vinyl chloride standard in the workplace, undertaken by Foster D. Snell and Arthur D. Little in the summer of 1974, estimated costs of up to \$90 billion and job losses of 2.2 million, supporting the industry claim that the standard would be too expensive and impractical.¹⁴ These estimates have turned out to be grossly exaggerated, quite apart from neglecting savings to industry from recovery of VC that would otherwise be lost to the outside air, and also major costs to society from VC-induced cancer and other diseases in the workplace and surrounding communities.

Spearheaded by the Manufacturing Chemists Association and Dow Chemical Company, an essential strategy in the industry attempt to block toxic substances legislation, which had been languishing in Congress for six years prior to its passage on October 11, 1976, was the claim that it would cost too much. In 1975, industry asserted that these costs would be in the range of \$2 billion a year. In contrast, EPA and the General Accounting Office estimates ranged from \$80 to \$200 million.

Constraints in Interpretation of Data

Explaining away awkward data is part of the now familiar scenario of constraints. Over the years, the industry position on

carcinogenicity data has crystallized into a set of five defensive propositions.

These have been aired on two major occasions:¹⁵ at the 1973 meetings of the Department of Labor Advisory Committee on Occupational Carcinogens, by industries including Dow, Du Pont, Rohm and Haas, and Esso Research, in addition to the Manufacturing Chemists Association and the Synthetic Organic Chemical Manufacturers Association; and at the cancellation/suspension hearings on aldrin/dieldrin, by Shell Chemical Company, and on chlordane/heptachlor, by Velsicol Chemical Company. These five propositions are:

1. "*Tumorigens are less dangerous than carcinogens.*" This argument was used at the pesticide hearings to explain away the allegedly "benign liver tumors" induced by DDT, aldrin/dieldrin, and chlordane/heptachlor which were hence claimed by industry to be "tumorigens," not carcinogens. Independent review established that these "tumors" are in fact cancers, which in some cases metastasized to the lungs; it was also shown that they produced cancers in a wide range of sites other than the liver and hence are clearly carcinogens. There is no conceivable basis for drawing any scientific and regulatory distinctions between allegedly "benign tumors" and cancers induced by administration of carcinogens.

2. "*Animal carcinogens are less dangerous than human carcinogens.*" In other words, the results of animal tests must be validated by deliberate and continued human exposure before instituting rigorous controls. This argument was vigorously proposed for occupational carcinogens such as dichlorobenzidine and ethyleneimine, for which there are as yet no human data, and is still pressed, even though the activity of most recently recognized "human" carcinogens, such as diethylstilbestrol and vinyl chloride, was first demonstrated in animal tests.

3. "*Most chemicals are carcinogenic when tested at relatively high concentrations.*" This is not consistent with available information. Mice or other animals can be fed with massive doses of most chemicals and they will not develop cancer. For instance, in an NCI contract study by Litton Bionetics from 1963 to 1969, approximately 140 industrial compounds and pesticides, selected be-

cause of strong suspicions of carcinogenicity, were tested at maximally tolerated doses in two strains of mice. Less than 10 percent of these chemicals were found to be carcinogenic.¹⁶

Further, of a total of some 7,000 compounds listed in the NCI's "Survey of Compounds which Have Been Tested for Carcinogenic Activity" only about 1,000 have been reported to be carcinogenic. By current standards only half of those tests are estimated to be valid, and a total of about 700 compounds are now accepted as carcinogenic. The compounds on the NCI list were selected on the basis of known similarity to proven carcinogens.

4. "*Safe levels of exposure to carcinogens can be determined.*" It is alleged that no or negligible risks result from exposure to "low levels" of occupational or environmental carcinogens. These low levels are generally determined on the basis of the sensitivity of available monitoring techniques, technical expediency, or other poorly articulated concepts. The American Conference of Governmental Industrial Hygienists has in the past assigned acceptable "threshold limit value" levels for carcinogens such as asbestos, BCME, and nickel carbonyl, but expert national and international scientific committees and regulatory agencies are agreed that there is no mechanism for setting thresholds or safe levels for any chemical carcinogen.

5. "*Human experience has demonstrated the safety of occupational exposure to 'animal carcinogens' or to 'low' levels of human carcinogens.*" These claims are generally based on a lack of positive evidence of excess cancer deaths, or on the basis of undisclosed or partially accessible records covering small working populations at risk, with undefined turnover rates and short periods of follow-up. Clearly, such data do not permit development of valid inferences, and fail to recognize inherent limitations of epidemiological techniques.

Dow and Du Pont were insistent at the 1973 Department of Labor Advisory Committee meetings on occupational carcinogens that their own experience had proved the safety of three widely used "animal carcinogens," ethyleneimine, 1-naphthylamine, and methylene-2-bischloroaniline (MOCA).^{*} After repeated chal-

* In September, 1978, Du Pont announced its intent, based on economic and safety considerations, to phase out the manufacture of MOCA by the end of the year.

lenge to produce the underlying epidemiological data, the industries finally admitted that they had destroyed the workers' records after ten years exposure as a matter of company policy, thereby making it almost impossible to detect a human carcinogenic effect.¹⁷

While these assertions cannot withstand elementary scientific scrutiny, they have nonetheless been vigorously and effectively asserted in various public forums and adjudicatory proceedings. They are myths, spawned by pressures on industry scientists and academic consultants to develop and interpret safety data on chemical carcinogenesis consistent with short-term marketing interests, and are calculated to minimize the significance of the effects of human exposure to occupational carcinogens.

Apart from explaining away carcinogenesis, attempts have also been made to explain away other chronic toxic effects, including birth defects (teratogenicity). An example of this is a 1971 Dow publication on the teratogenicity in rats of the herbicide 2,4-D.¹⁸ The summary and text of the publication state that it was tested in pregnant rats and found to be non-teratogenic while tabular data indicates the production of a wide range of congenital defects of the skeleton. However, since some of the affected progeny were shown to be capable of surviving in early infancy, Dow decided that the defects were of no particular consequence and could be dismissed. To bolster this position, Dow redefined the standard term teratology as congenital defects that are fatal or preclude optimal function. If generally applied, this definition would exclude thalidomide-type defects and most congenital heart defects.

Suppression or Destruction of Data

Occasionally data that can't be designed out of existence or interpreted away are suppressed or even destroyed. Known instances of this are legion. The carcinogenicity of the organochlorine pesticide kepone, besides its toxic effects on the reproductive and central nervous systems, were discovered by studies sponsored by

the manufacturer, Allied Chemical Co., in the early 1960s.¹⁹ Allied suppressed this information for about a decade, until workers at Life Sciences in Hopewell, Virginia, an Allied spinoff corporation, developed crippling neurological and other diseases from exposure to very high levels of kepone in grossly deficient working conditions.

In December, 1972, Velsicol was informed by its own consultants that chlordane/heptachlor were carcinogenic.²⁰ However, the company suppressed this information, resulting in their criminal indictment by a Chicago federal grand jury in December, 1977.²¹

Reserve Mining Company testified in court in the early 1970s that there were no alternate sites which could be used for the daily disposal of 67,000 tons of asbestos-laden taconite tailings into Lake Superior. In fact, the company had previously developed detailed plans for land disposal sites.

The carcinogenicity of vinyl chloride in the liver of rats was discovered in late 1972, but the Manufacturing Chemists Association (and Maltoni) withheld this knowledge for more than eighteen months, until the human evidence could no longer be ignored.²²

In the course of meetings of the Department of Labor's 1973 Advisory Committee on Occupational Carcinogens, Dow and Du Pont admitted routine destruction of workers' records, including those exposed to occupational carcinogens.²³

Industrial Biostest Labs, Northbrook, Illinois, a subsidiary of Nalco Chemical Company, faced with federal investigation in April, 1977, for fraud and submission of questionable test data, destroyed files dealing with toxicological and carcinogenicity testing of thousands of federally approved products including drugs, pesticides, food additives, and industrial chemicals.²⁴ The president of the company, A. J. Frisque, has admitted that he ordered the shredding of laboratory documents immediately prior to the initiation of the investigation, but claimed that this was due to a "misunderstanding."

FDA and EPA investigators have established that Industrial Biostest submitted falsified data on potential carcinogens to the government. It has also been established that at least four unidentified major pesticide manufacturers were aware of this

fraud when they submitted the test data in product registration applications.²⁵

Industrial Biotest has also been charged by Rep. Thomas Downey (D-N.Y.) with having mismanaged toxicological tests by "shoddy amateurish" laboratory practices on irradiated food in a U. S. Army project dating back to 1953, which has so far cost the taxpayer about \$51 million.²⁶ More recently, Industrial Biotest and Nalco have been sued by former industrial clients, including Syntex Pharmaceutical and Wesley-Jesson, Inc., for alleged breach of contract and misrepresentation of test data.† On September 23, 1978, the Swedish EPA banned eight pesticides, including captan and metabromuron, that had been registered on the basis of tests conducted at Industrial Biotest. According to Miljöcentrum, the major Swedish public interest movement headed by Björn Gillberg, the Swedish EPA had been aware for many years of problems of misconduct at certain American laboratories, but failed to take action until finally forced to do so by the Ombudsman in response to a complaint of a coalition of environmental groups. The EPA and other concerned U.S. regulatory agencies have not yet revealed the identities of the pesticides and other products registered on the basis of tests at Industrial Biotest Laboratories, nor has there yet been any indication as to whether or when such registrations will be revoked or cancelled.‡

As recently divulged in the asbestos "Pentagon Papers," the asbestos industry, under the leadership of Johns-Manville, has for decades successfully suppressed and manipulated information on the carcinogenicity and other hazards of asbestos. Involved in this conspiracy network were senior industry executives, their medical staff, attorneys, insurance companies, trade associations, scientific consultants, and commercial laboratories. Apart from detailing the mechanics of data suppression, these documents are the most revealing insight of corporate mores yet.

† Nalco has been attempting to sell the Industrial Biotest facilities in Northbrook and Wedges Creek, Illinois, since June, 1978. The third IBT facility in Decatur has been purchased by Whittaker Corporation and renamed Toxigenics.

‡ In July, 1978, IBT established a Validation Assistance Team (VAT) in cooperation with EPA, FDA, and its industry sponsors in attempts to salvage possibly-useful data from remaining records of past studies.

Extremely grave questions are being raised about the moral standards or ethical behavior of the business world today.

W. Michael Blumenthal, ex-President Bendix Corp., Treasury Secretary, May 25, 1975.

How to Improve Industry Data

What Not to Do

The reaction of industry to recently escalating evidence on the constraints of their data base has been one of angry denial followed by grudging acceptance of the possibility of an occasional unfortunate "slip-up." The present response, from which we can probably expect only "more of the same," is to increase their own toxicological and carcinogenicity testing capabilities. One of the earliest manifestations of this approach was the creation in 1974 of the Chemical Industry Institute of Toxicology, supported by the leading chemical industries. The Institute has recently moved to a new \$10 million facility in Raleigh, North Carolina. The institute is headed by Leon Goldberg, a long-time industrial consultant dedicated to such standard myths as the "benign" nature of liver tumors induced by carcinogenic pesticides. Goldberg, asserting that the institute is oriented toward the "public good," is highly critical of EPA for their "crisis approach" to toxic chemicals and of the NCI because their carcinogenicity testing procedures are "likely to produce false positives."²⁷ The institute's current research activities are being done by outside consulting

laboratories, prominent among whom has been Industrial Biotech Laboratories.

Industry is responding to the recent passage of toxic substances legislation with a massive expansion of its facilities.²⁸ Du Pont recently enlarged its toxicological capabilities in Newark, Delaware, by about 70 percent. Dow increased its Midland, Michigan, facility by 50 percent, and Monsanto, which until now has contracted out its testing to independent laboratories, is building a new facility in St. Louis. Shell recently announced the creation of a new toxicology laboratory in Westhollow, Houston, to be headed by Donald Stevenson, the leading figure of the Shell toxicology team who attempted to discount the liver cancers induced by mice by aldrin/dieldrin at the 1974 EPA hearings.

There is no apparent basis for assuming that any of these new ventures will be less constrained by their direct linkage to industry than any of their predecessors, or any less a threat to long-term industrial interests.

What to Do

Approaches now being considered and developed by FDA, EPA, NCI, and other agencies include formalization of protocols or guidelines, formalized inspection, selective auditing and monitoring, licensing of testing laboratories, and unannounced sample testing, with increased penalties for manipulation or suppression of data.* Congress has recognized this problem by allocating an extra \$16.6 million to the FDA in 1977 to insure quality control of the data submitted to the agency in support of the products it regulates. But contracts still seem to be awarded to laboratories found guilty of such practices, and products registered on the

* A recent move in the direction of providing guidelines for epidemiologic studies has been made by the Guidelines Committee, Epidemiology Work Group, of the Interagency Regulatory Liaison Group. The committee issued a draft "Documentation Guidelines for Epidemiologic Studies: Cohort Studies," on May 31, 1978. These guidelines, while flexible, recommend minimum criteria for satisfactory epidemiologic studies to be used in investigating environmental and occupational health hazards. These include availability of full supporting documentation and definition of follow-up procedures and methods of statistical analysis, discussion of potential bias, and disclosure of sponsorship and source of funding.

basis of their prior tests have not been banned or otherwise restricted. These approaches, however helpful, do not address the inherent conflict of interest, which remains unchanged. Another useful approach developed by Senator Gaylord Nelson (D-Wisc.) with particular reference to drug testing is based on the concept of "third party testing" by federal laboratories at cost to the industry concerned.

Radical approaches are clearly required to free testing from the crippling constraints of corporate influences. One possible approach is based on the introduction of the following type of neutral "buffer" between those who test and those whose product is being tested:

There is a growing consensus of opinion on the need for legislation to ensure impartial and competent testing of all synthetic chemicals for which human exposure is anticipated. The present system of direct, closed-contract negotiations between manufacturing industries and commercial and other testing laboratories is open to abuse, creates obvious mutual constraints, and is thus contrary to consumer, and long-term industrial interests. One possible remedy would be the introduction of a disinterested advisory group or agency to act as an intermediary between manufacturers and commercial and other testing laboratories. Various legal and other safeguards would have to be properly developed to avoid or minimize potential abuses and conflicts of interest in the operation of this intermediary group. Manufacturers would notify the advisory group or agency when safety evaluation was required for a particular chemical. The advisory group would then solicit contract bids on the open market. Bids would be awarded on the basis of economics, quality of protocols, and technical competence. The progress of testing would be monitored by periodic project site visits, as routine with Federal contracts. At the conclusion of the studies, the advisory group would comment on the quality of the data, make appropriate recommendations, and forward these to the regulatory agency concerned for appropriate action. . . . Additionally, quality checks during testing would ensure the high quality and reliability of data, and minimize the need to repeat studies, and thus also reduce pressure on involved federal agencies to accept unsatisfactory data and *post hoc* situations. This approach would not only minimize constraints due to special client interests, but would also serve to up-

grade the quality of testing in commercial and other testing laboratories.²⁹

Industry could be protected from the possibility of incompetent work by requiring a contractee to post an indemnifying bond, should tests have to be repeated because they were bungled or for any other reason. Some form of limited liability provisions could also be built into a buffer system. This could insure that industry complying with these requirements would be protected from possible open-ended future testing needs, and also from legal responsibility for future adverse effects not predicted by properly conducted tests.

These proposals seem more consistent with the avowed industrial practice than is the present practice of secret award of unbidded contracts to commercial testing laboratories.† It would also free top-level corporate management from the influence of those in the lower corporate structure who are over-responsive to short-term marketing interests at the expense of long-term stability and growth.

Finally, there must be greater appreciation of the enormity and public health consequences of the manipulation or suppression of toxicological, epidemiological, and other data on health, safety, and exposure. Mechanisms should be developed for banning products registered on the basis of tests by commercial or other laboratories indicted of malpractice. Medical malpractice suits are now commonplace; the strong threat of laboratory malpractice suits is clearly needed to police the practice of industrial toxicology and safety assessment. Homicide or assault by toxic chemicals is a serious variant of white-collar crime. The recognition and social stigmatization, including maximum criminal penalties, of those involved in these crimes is long overdue.

† This problem has been clearly recognized in a November, 1978, Congressional report on "Cancer Causing Chemicals in Food" (Subcommittee on Oversight and Investigations of the House Committee on Interstate and Foreign Commerce):

EPA should develop a system for pesticide safety testing which removes testing from the manufacturers' own labs and places it in the hands of independent, impartial laboratories.

Future Trends

With increasing recognition of the questionable validity of the scientific data base of industry, it is likely that their future strategies will become more sophisticated (such as performing carcinogenicity tests with low test doses on the grounds that this is "realistic," and challenging the significance of carcinogenicity results in mice and of allegedly "benign" tumors). However, there has been a recent, more fundamental shift in industry tactics. It has now become less useful to minimize (in various ways) scientific evidence of hazardous effects, than to argue for the acceptance of these effects on the basis of economic and cost/benefit considerations (such considerations generally reflect exaggerated compliance costs, while failing to adequately, if at all, recognize externalized costs of failure to regulate). Industry has found massive support for this new strategy of economic manipulation in the recent anti-inflation policies of the administration, whose Council on Wage and Price Stability depends largely on industry economic analyses as a basis for policy. Further support for the industry position has also come from the October, 1978, Fifth Circuit Appeals Court decision, overturning the new OSHA benzene standard, largely on economic grounds.

Industry is now better equipped to play the economics game rather than the science game, particularly as there is very little expertise on industry economics outside of industry. The ability of federal agencies to estimate compliance costs of abatement technologies is poorly developed. Academic economists, with traditional myopic preoccupations with the GNP, and often with close consulting ties to industry, have little comprehension of or interest in the concept of externalized costs. A new breed of economic activists oriented toward disease prevention and public health has yet to emerge, although there are isolated spokesmen for these considerations.‡

‡ See the recent exchange on cost-benefit analysis between Murray L. Weidenbaum (Center for the Studies of American Business, Washington University, St. Louis), expressing traditionalist industry positions, and Nicholas A. Ashford (Center for Policy Alternatives, MIT), expressing broader societal concerns.³⁰

PART III
THE POLITICS OF
CANCER

Chapter Nine

Governmental Policies

Environmental and occupational cancer are now becoming prime topics of national concern. Their underlying political and economic determinants are at last becoming appreciated. The data base of past decision-making is now known to have been massively distorted, or constrained, and responsive to narrowly defined special interests. Accordingly, policy and decision-making are at last moving from closed discussions between the executive branch of government and industry into the open political arena.

Congress

Congress is both initially and ultimately responsible for all agency policies and priorities. Congressional control is exercised in the Senate and in the House through committees serving three basic types of functions. *Legislative committees* hold hearings on a particular bill and report out the bill, which is voted up or down on

the floor. If voted up, the bill becomes law and provides overall authority to research and regulatory agencies. The *appropriations committees* decide how much money and staff each agency will receive each year. And both types also have an *oversight function*: they examine the administration of a law by the agency concerned and otherwise monitor its performance to see whether the Congressional intent is being met.

The most concrete generalization that can be made about the government policy on carcinogens is that there is no single such policy yet. Rather, policies and responsibilities are distributed over many diverse agencies and institutes, with widely differing philosophies, priorities, and practices and often with overlapping and poorly defined jurisdictions. While these differences reflect such factors as external pressures, historical background, and personalities, the most substantive determinants are the confused and often inconsistent authorities governing regulatory controls over air, water, food, drugs, cosmetics, industrial chemicals, and the workplace. These authorities have been created piecemeal by Congress over the last few decades and now form a legislative patchwork quilt. Rather than resolving legislative ambiguities and stalemates, such as those allowing the continued use of carcinogenic cattle feed additives, Congress has often abdicated its authority and relegated it to regulatory agencies, using vague, value-laden terms such as "unreasonable risks" or "feasibility." The subsequent actions of the regulatory agencies are then open to challenge in the courts, as is failure to take any action. Congress has thus allowed decision-making to evolve into an uneasy triangular relationship, involving besides itself the executive and the courts.

Federal Agencies

Broadly speaking, there are two types of federal agency: those primarily engaged in research, and those primarily engaged in regulation and enforcement.

Legislative inconsistencies aside, federal priorities in research on cancer prevention and on the regulation of environmental and

occupational carcinogens have been, and still are, low. This has been reflected in administrative failure to ensure that the various environmental programs of federal agencies function in an effective and coordinated manner, and in the personnel ceilings imposed by successive recent administrations. These ceilings, even more than budgetary limitations, have had and still have a crippling effect on the functions of both research and regulatory agencies.*

In contrast with personnel limitations, there has been major growth in federal expenditures on environmental and occupational health during the last decade. A 1972 congressional report which contrasted the then \$215 million total federal effort in environmental health with the \$82.5 billion value of products regulated in 1970 by one agency alone, the FDA.¹ But even the \$215 million figure was misleading, for it included biologic agents such as vaccines. When these are eliminated, the total shrinks to a \$96 million effort for chemical and physical pollutants, of which only about \$24 million was spent for carcinogenesis research. By 1976, however, federal expenditures in environmental health and carcinogenesis research had more than doubled, totaling \$485.7 million and \$76.8 million, respectively; nevertheless they are still small compared to the value of the products and processes regulated by federal agencies. As reflected in 1979 budgetary figures, this rate of growth has been sustained, over and above inflationary increases. It is, however, also clear that these expenditures are relatively trivial compared to the overall costs of environmentally induced disease and cancer, and to the 1978 total national health

* Since the Johnson administration, in a series of running battles with Congress, the executive has imposed ceilings on the numbers of personnel that can be hired by federal agencies. This has not, in fact, reduced the size of government, but instead has forced agencies to contract out federal work to non-federal employees. This has created overwhelming administrative problems for federal agencies, particularly those concerned with environmental and occupational health. In the fiscal 1979 Appropriations Bill for the Departments of Labor and HEW, Congress specifically mandated personnel increases in specific program areas, including environmental and occupational health. The administration is challenging that action and refusing to lift the personnel ceilings. It is anticipated that the General Accounting Office (GAO) will make a final determination on this matter in the spring of 1979 which, if unfavorable to the administration, will be implemented by sending Congress a notice of impoundment, on the basis of which the Courts could force the ceilings to be lifted.

care expenditures of \$185 billion. In this connection, HEW Secretary Califano, in his September, 1978, address to the national AFL-CIO conference on occupational safety and health, stressed that of the \$48 billion federal expenditures on health care, fully 96 percent is directed at treatment, and only 4 percent (under \$2 billion) is earmarked for programs to prevent disease.

The National Cancer Institute

The National Cancer Institute (NCI) is the lead agency for cancer research.

Early History Created in 1937 under the National Cancer Act, the NCI is the only federal institution with exclusive responsibility in cancer research.² Although incorporated into the National Institutes of Health in 1944, the NCI has always been considered by Congress and the public as a semi-autonomous agency. This sense of independence was further consolidated by the 1971 National Cancer Act, which assigned managerial responsibility to the director of the NCI, who reports to the President, through the Office of Management and Budget, bypassing the director of the National Institutes of Health and the HEW Secretary.³

When the first annual NCI budget of \$400,000 was established in 1937, scientific interests in cancer largely focused on problems of treatment, with little concern for prevention. Congressional and public opinion then reflected this attitude. Although considerable research was being conducted in the United States and elsewhere on chemical carcinogenesis, this was largely viewed as basic science, with little relevance to the prevention of human cancer. This background is important to understanding how NCI priorities have evolved over the subsequent four decades.

Attempts were made to challenge these priorities, particularly by the late Wilhelm C. Hueper, a German-born physician and distinguished researcher on the carcinogenic effects of radioactive agents and aromatic amine dyes at the Haskell Laboratories of Du Pont, who was appointed chief of the Environmental Cancer Section of the NCI in 1948. Hueper's outstanding research on environmental and occupational carcinogenesis was matched by his

Table 9.1 *Federal Expenditures in Environmental Health and Carcinogenesis Research*

Agency	Total 1976 Research Budgets (\$ million)	
	Environmental Health	Carcinogenesis Research*
Department of Health, Education, and Welfare (total)	301.1	70.3
National Cancer Institute	(149.5)	(47.5)
National Institute Environmental Health Sciences	(49.1)	(8.4)
National Institute Occupational Safety and Health	(48.8)	(8.4)
National Center for Toxicological Research†	(12.9)	(6.0)
Other agencies	(40.8)	
Environmental Protection Agency	51.4	1.0
Department of Energy‡	60.7	5.5
National Science Foundation	4.7	NA
Army	14.1	NA
Department of Labor	16.8	NA
National Aeronautics and Space Administration	1.6	NA
Department of Transportation	18.0	NA
Department of Housing and Urban Development	1.8	NA
Department of Interior	7.1	NA
Department of Defense	8.4	NA
TOTAL	485.7	76.8

Source: NIEHS, Report to the Senate Appropriation Committee on Federal Support for Environmental Health Research, 1977.

* NA (not available) means there is no line item on cancer research in the agency's budget.

† Excludes \$4 million from EPA.

‡ Excludes radiation carcinogenesis.

integrity, obduracy, and the energy of his advocacy. Although he was supported by Rod Heller, then NCI director, Hueper ran afoul of the federal establishment, particularly the Atomic Energy Commission and the FDA, quite apart from drawing the concentrated wrath of the chemical industry.⁴ Attempts were made to silence him, to censor his reports and block his research. In 1952, Hueper was refused clearance to testify before Congressman James J. Delaney's (D-N.Y.) Select Committee Investigating the Use of Chemicals in Food and Cosmetics, a move that Hueper countered by testifying as a private citizen. In the same year, he was ordered to discontinue his epidemiologic studies on occupational and community cancer.⁵

To Hueper, harassment came early and recognition late. Hueper is now widely appreciated as the leading pioneer in the concept of cancer prevention.⁶ Among other recent distinctions, Hueper was presented with the first Annual Award of the Society for Occupational and Environmental Health in March, 1975.† The concluding remarks of the citation read:

To Wilhelm C. Hueper, M.D., Head of the Environmental Cancer Section, National Cancer Institute, Department of Health, Education and Welfare, in recognition of his role in pioneering and fostering the study of occupational and environmental cancer and in establishing the scientific and public awareness that most human cancers are caused by environmental factors and can be prevented.⁷

Hueper, in fact, had little visible impact on NCI priorities. The annual budget of the NCI in 1948 was \$14.5 million, of which Hueper's section received \$90,000, a sum which had not materially increased when he retired sixteen years later, despite a tenfold increase in the NCI's total budget.⁸

By the late 1950s, research in the treatment of cancer had produced some interesting leads, particularly the finding that drugs inhibiting folic acid metabolism could produce remissions in childhood leukaemias and other forms of malignant disease. The significance of these findings was exaggerated and hailed as the dawn of a new era when cancer could be cured by the "magic bullet" of chemotherapy. In fact, the basis for such optimism was

† The award was made by the author, then president of the society.

slender. The "cancer cure lobby," headed by cancer clinicians, notably Solomon Garb of the American Medical Center in Denver, and the late Sidney Farber, politically astute director of the Children's Cancer Research Foundation, Boston, and including the American Cancer Society and Mary Lasker,[‡] a New York philanthropist who had close contacts with the administrations of successive Presidents, exerted a powerful influence on Congress and the public. Both were exhorted and persuaded by hard-sell techniques that the cure for cancer was just around the corner, and only needed more support and funding for the American Cancer Society and the NCI. In the optimistic search for "magic bullets" the NCI financed a huge Cancer Chemotherapy Program for mass-screening of hundreds of chemicals for anticancer activity in tissue culture and animal tumor systems.

The National Cancer Program The 1971 National Cancer Act (42 U.S.C. 282), embodying the Senate Conquest of Cancer Bill and the House National Cancer Attack Bill,⁹ had as its principal objective the launching of the National Cancer Program to cure cancer.¹⁰ The Act reflected a Senate report of the National Panel of Consultants on the Conquest of Cancer, of which Farber and Garb were leading members, which sounded a clarion call to attack and eradicate cancer. In a full-page advertisement entitled MR. NIXON, YOU CAN CURE CANCER in the *New York Times* of December 9, 1969, paid for by the "Citizens Committee for the Conquest of Cancer," whose leaders included Farber, Garb, and Lasker, Farber is quoted as follows: "We are so close to a cure for cancer. We lack only the will and the kind of money and comprehensive planning that went into putting a man on the moon . . . Why don't we try to conquer cancer by America's 200th birthday."¹¹

The Consultants' Report which was presented to the Senate Committee on Labor and Public Welfare on December 4, 1970, effectively misled the Congress into believing that the cure for

[‡] Mary Lasker is the widow of Albert D. Lasker, the multimillionaire advertising tycoon, who handled American Tobacco's Lucky Strike account and who coined what has been called the most successful slogan in American salesmanship "Reach for a Lucky Instead of a Sweet," aimed at inducing women to smoke.

cancer was imminent, needing only a massively funded national effort.* The report also insisted that NCI had to be removed from the "bureaucracy" of NIH and be given autonomy in order to find the cure for cancer.¹²

The 1971 legislation itself is poorly drafted and naive. It reflects the bias of the Consultants' Report and emphasizes immediate possibilities for the cure of cancer without attaching any significance to prevention. The Act also authorizes the establishment of National Cancer Centers "for clinical research, training, and demonstration of advanced diagnostic and treatment methods relating to cancer." The centers were not assigned any responsibility for establishing carcinogenesis or epidemiological programs, nor for any other problem-solving activities relating to cancer prevention.

The National Cancer Advisory Board and Panel The 1971 Act mandates major changes in the NCI by establishing strong links with the President and giving it virtual autonomy, while formally retaining it within the parent National Institutes of Health. This move was consistent with the general policy of the Nixon administration in obtaining direct control over Federal agencies.

The NCI Director is authorized to submit his annual budget for approval to the Office of Management and Budget, thereby bypassing the National Institutes of Health and HEW.[†] In addition to personally appointing the NCI Director, the President also appoints a National Cancer Advisory Panel of three which meets monthly and establishes NCI priorities and policies.[‡] Executive functions for the panel is provided by a Presidentially appointed

* Only a few members of Congress were not persuaded by the cancer lobby, particularly Sen. Gaylord Nelson and Cong. Paul Rogers who tried to fight the separation of NCI from the NIH.

† While the national policy-making influence of OMB was formally pivotal, it is becoming increasingly supplanted by an enlarged White House staff and by a resurgent and restive Congress that has created its own budget office to do much of the analytic work once performed exclusively by OMB.

‡ The lack of checks and balances in Presidential control of the executive and advisory functions of the NCI were periodically emphasized by Benno Schmidt's transmittal of White House policy positions (during Republican administrations) as a means of influencing Board decisions. The nature of these past policy linkages between Schmidt and the White House is yet to be revealed.

advisory board of twenty-three members, five from government and eighteen from the public sector, which meets quarterly. The National Cancer Advisory Board is executive, in contrast to its Advisory Council predecessor, which had only advisory functions.

The chairman of the Cancer Panel was and still is Benno Schmidt, a New York investment banker and a friend of the Nixon and Ford administrations, with ties to the oil, steel and chemical industries through J. H. Whitney and Co., of which he is managing partner. Schmidt has, with substantial success, attempted to dictate NCI policies over the last eight years. Membership of the Advisory Board has also included industry representatives, such as the late Elmer Bobst, Warner Lambert, and Clark Wescoe of the drug industry, but no representatives of labor or the public interest movement. Scientific membership of the board largely reflected expertise in basic science, cancer diagnosis, and treatment. The National Cancer Advisory Board and Cancer Panel have had close interlocking relationships with the leadership of the American Cancer Society.*¹³

Conflicts of Interest on the National Cancer Advisory Board One long-time member of the board is Philippe Shubik, an accomplished carcinogenesis researcher. In November, 1975, as chairman of the Subcommittee on Environmental Carcinogenesis, Shubik played a major role in attacking the "cancer principles," leading to the refusal of the EPA administrative law judge to suspend the registrations of chlordane and heptachlor.¹⁴

Shubik's influence on the Advisory Board has further weakened the regulation of environmental carcinogens. Apart from attacking the cancer principles, Shubik in November, 1975, argued successfully for abandonment of the system of Memoranda of Alert, by which the NCI warned the community of early findings in its bioassay program (designed for large-scale carcinogenicity tests on chemicals to which humans are likely to be exposed).†

* Some of these relationships have been fruitful, such as the NCI-ACS 1974 Conference on "Persons at High Risk of Cancer," and its subsequent publication (ed. J. F. Fraumeni, 1975).

† General Foods, to whom Shubik consults, is known to have been particularly incensed by the results of a bioassay program test on trichloroethylene, used to decaffeinate coffee, which was found to be carcinogenic and which resulted in claimed losses to the company of \$20 million.¹⁵

Shubik worked closely with then NCI Director Frank Rauscher and roadblocked the bioassay program over the objections of the associate director of the Carcinogenesis Program, Umberto Saffiotti. On some occasions, Shubik attended NCI meetings representing his personal industrial interests. At a 1971 meeting to discuss the carcinogenicity of Procter and Gamble's detergent ingredient nitrilotriacetic acid, Shubik argued for the continued use of the product. When asked by Saffiotti, "Would you for the record identify what capacity you are here under?" Shubik replied, "Procter and Gamble."¹⁶

Shubik's membership on the board poses problems of conflict of interest with respect to his involvement in NCI policy-making while being a major recipient of NCI research funding.‡ Shubik's list of consulting clients was first disclosed in the 1976 NCI budget hearings when Congressman David Obey (D-Wisc.) asked Rauscher who his chief advisor on environmental cancer was. Rauscher replied that it was Shubik. Obey then asked Rauscher if Shubik also consulted for industry. Rauscher replied in the affirmative, while expressing ignorance as to which industries were involved. When pressed further, Rauscher agreed to supply the list of industries, but, following the hearings, asked that this be excluded from the public record. Rauscher's request was denied. It was then revealed that Shubik consulted for Royal Crown Cola, Abbott Laboratories, Miles Laboratories, General Foods, Procter and Gamble, Colgate Palmolive, the Flavor and Extract Manufacturer's Association, and the Calorie Control Council.*¹⁸ It has

Methylene chloride, now widely used as a substitute for trichloroethylene with permissible levels of 10 ppm in roasted beans, is currently under test in the NCI Bioassay Program. However, since January, 1979, Coffex Ltd. of Switzerland has been marketing coffee decaffeinated by a hot-water process, using no chemical solvents.

‡ Shubik's potential for conflict of interest is not unique on the NCI Advisory Board. In this, he has been joined by Frank J. Dixon, a consultant for Eli Lilly and Co., and Jonathan E. Rhodes, then Chairman of the Board and Director of Penwalt Corp., a chemical manufacturer, quite apart from the industry representatives on the board.¹⁷ (Henry Pitot is current chairman of the Advisory Board.)

* Shubik is also president of the Toxicology Forum, an industry-sponsored colloquium. The secretary of the Forum is David B. Clayson, Deputy Director of the Eppley Cancer Research Inst., principal investigator of the NCI contract to the Eppley, and executive member of the NCI Clearinghouse on Environmental Cancer.

since been discovered that Shubik's Eppley Cancer Research Institute operation in Omaha has numerous other industrial clients, including the cosmetic industry, and oil and chemical companies.

Shubik is also involved in a direct conflict of interest over multimillion-dollar contracts from the NCI to the Eppley Cancer Research Institute, University of Nebraska, Omaha, which he directs.[†] As a member of the National Cancer Advisory Board, Shubik had considerable influence over NCI staff, and normal review mechanisms were waived for his contracts which, apart from being awarded non-competitively, were instead handled by special *ad hoc* procedures (contracts, unlike grants, are monitored by staff of the agency concerned).¹⁹ In spite of what in July, 1977, Congressman Obey said were "strongly negative comments by a number of reviewers," Shubik's contracts continued to be renewed.²⁰ Shubik has been the subject of a Congressional inquiry and a GAO investigation which raised serious questions about poor administrative practices and accounting of \$12 million of contract expenditures dating back to 1973, including the use of federal funds to support industrial research.²¹ The GAO investigation also questioned the scientific value of this multimillion dollar contract, as evidenced by "NCI's inability to cite more than a few notable accomplishments." According to an article in the Omaha *World-Herald*,‡ based on the results of a more recent HEW investigation, the government is demanding refund of \$1 million from the University of Nebraska for NCI contract funds which it is claimed that Shubik "used for unauthorized purposes." The Eppley Institute, however, claims that only \$85,000 of federal funds are unaccounted for. And HEW audit released in November, 1978, repeated the demand for the \$1 million refund. Simultaneously, it was announced that the Office of Investigators of the HEW Inspector General was pursuing an inquiry on a "non-audit matter," which, it was stressed, does not

† In the last 10 years the Eppley has received about \$23 million in grants and contracts from NCI. The major project officer for these contracts was Gio B. Gori, proponent of the "practical threshold" concept for cigarettes, now on leave of absence from the NCI.

‡ Prior to this article, all criticisms of Shubik and his conflicts of interest which have appeared in the national press were ignored or toned down in the Omaha *World-Herald*, the leading Nebraska daily, and in other Nebraskan press in general. This may possibly reflect recognition of the substantial federal research dollars Shubik has brought into the state

necessarily mean that criminal charges will be pressed. In December, 1978, it was revealed that the University of Nebraska was conducting its own investigation of Shubik, following the request of Senator Larry D. Stoney (D-Omaha) who presented the administration with a "list of concerns" by Eppley employees, including allegations of misuse of state funds.*²²

Shubik continues to exert considerable influence through various channels, including membership on the National Cancer Advisory Board, which in the absence of his prior resignation will extend until 1982.†

The NCI Budget and Priorities Over the years, the NCI budget has climbed by leaps and bounds from a 1938 level of \$400 thousand to a 1958 level of \$56 million, and to a 1968 level of \$183 million. Passage of the National Cancer Act, with its strong emphasis on cure rather than prevention, led to a 1971 budget of \$223 million, which by 1979 quadrupled to almost \$1 billion (See Table 9.2). The rapid rate of growth of the NCI budget from 1971 through 1975, however, has now leveled off. For the last seven years the NCI budget has accounted for about 30 percent of the total NIH budget. It is, however, clear that the early rapid growth of the NCI budget was achieved largely at the expense of basic research in other NIH institutes, particularly the National Institute of General Medical Sciences, rather than by an increased overall federal commitment to biomedical research. This has not unnaturally polarized the biomedical scientific community into pro- and anti-NCI camps. This polarization has been further compounded by the growing recognition of the questionable track record of the NCI in overall administration and fiscal management.

* Shubik was placed on leave of absence from Eppley in July, 1979, and Norman Cromwell (Professor of Chemistry at the University of Nebraska), who had been involved in recruiting Shubik in 1968, was appointed acting director.

† On March 3, 1978, Shubik was given the 27th Annual Bertner Award by the University of Texas M.D. Anderson Hospital and Tumor Institute for "distinguished contributions to cancer research" for scientific work done jointly with Israel Berenblum about thirty years ago. In receiving the award, Shubik acknowledged the warm support of Lee Clark, President of the M.D. Anderson Hospital and University of Texas Cancer System, and then President of the American Cancer Society and member of the NCI Cancer Panel.

Table 9.2 *Growth of NCI Budget from 1971 to 1979 in Comparison with that of NIH*

Year	Budgets (\$ millions)		NCI Budget As a Percentage of NIH Budget	Percent Increase NCI Budget over Previous Year
	NCI	NIH		
1971	\$223	\$1,183	18.9	29
1972	379	1,467	25.8	70
1973	492	1,713	28.7	30
1974	527	1,745	30.2	7
1975	692	2,044	33.9	31
1976	762	2,201	34.6	10
1977	815	2,500	32.6	7
1978	872	2,828	30.8	7
1979	937	3,197	29.3	7

Source: National Institutes of Health, 1979.

Under the control of the Cancer Panel and Director Rauscher, the budget of the NCI was skimpy on prevention. In testifying before Congress in 1976, Rauscher admitted that only 20 percent of the NCI budget went to environmental carcinogenesis, while agreeing that 85 percent of cancers are environmental in origin. But even this low figure of 20 percent was inflated. To be sure, the budget of the Division of Cancer Cause and Prevention was about 18 percent of the NCI total, but this included programs such as virology, constituting almost half the entire budget of the division, which apart from their intrinsic scientific importance have only limited, if any, relevance to environmental carcinogenesis (Table 9.3). Thus, the percent of the NCI budget devoted to chemical carcinogenesis, comprised by the programs in Carcinogenesis and Field Studies and Statistics, amounted to about 12 percent of the total NCI budget of \$762 million, rather than the 20 percent claimed by Rauscher.

What have been the returns for all the billions of dollars spent on cancer treatment? In the last four decades there has been little overall improvement in our ability to treat and cure most cancers. The modest improvement from the 20 percent overall five-year survival rates in the mid-1930s to about 33 percent in the mid-1950s reflects advances in surgery, blood transfusion, and antibi-

Table 9.3 *Analysis of the NCI 1976 Budget*

Division	Amounts (\$ millions)	Percentage of Total
Cancer Research, Resources and Centers	332.0	43.6
Cancer Biology and Diagnosis	57.8	7.6
Cancer Treatment	119.2	15.7
Cancer Control and Rehabilitation	56.5	7.4
Cancer Cause and Prevention	135.3	17.8
Office of Division Director	(13.0)	(1.7)
Virus Cancer Program	(62.0)	(8.2)
Task Forces Program	(5.4)	
Field Studies and Statistics Program	(12.3)	(1.6)
Carcinogenesis Program*	(42.6)	(5.6)
Office of NCI Director	37.7	4.9
NIH Management Fund	23.0	3.0
TOTAL	761.5	100.0

Source: National Cancer Institute, 1976.

* This figure reflects institute-directed research (intramural, contracts, and Cancer Research Emphasis Grants), but excludes investigator-initiated extramural grants.

otic treatment, rather than specific advances of cancer treatment. Over the last two decades, there has been little or no further significant improvement in overall cancer survival rates, nor in survival rates, for major cancer sites such as lung, stomach, pancreas, and brain, which are still virtual death sentences, nor for breast, colon-rectum, cervix, and uterus, whose five-year survival rates continue to range from 45 percent to 75 percent, with little or no change as yet (Table 1.4).²³ These facts in no way diminish the critical importance of recent striking improvements in treatment and survival of some relatively rare cancers, especially Hodgkin's disease, Wilm's tumor, choriocarcinoma, and childhood leukaemia.

In 1976, an Environmental Epidemiology Branch with a budget of \$2.6 million was created in the Field Studies and Statistics Pro-

gram. Funding has approximately doubled in 1978, now representing about 20 percent of the overall epidemiology program budget.

Of the 1976 Carcinogenesis Program budget of \$40.1 million, only some \$11 million, less than 2 percent of the total NCI budget, was spent on the bioassay program, which was formally initiated in 1968 to undertake large-scale carcinogenicity tests on industrial and consumer product chemicals to which populations are currently exposed.[‡] Most testing since 1974 was done by subcontractors under the management of a prime contractor, Tracor Jitco, Inc. (on a cost-plus-award fee basis), thereby diffusing the responsibility of the NCI. Rauscher neglected this program, and with the approval of the Advisory Board and its Subcommittee on Environmental Carcinogenesis, chaired by Shubik, gave it low priority for manpower and resources, gradually bringing its activities to a near halt. In 1973, about seventy new compounds were tested each year, but within three years this number had declined to only seven (Table 9.4). In spite of a major increase in the overall NCI budget during this period, there was no parallel increase in the bioassay budget.* In fact, in 1976, a total of only five professional staff were allotted to select test chemicals, define test protocols, oversee the contractors, analyze the data, and prepare technical reports. Additionally, the limited bioassay program staff were subjected to bureaucratic roadblocks, including frequent temporary reassignments to other responsibilities. As a result, only one report was published up to 1976, and a backlog of over two hundred bioassays, over half of which had been completed more than twelve months previously, had accumulated.

[‡] However, a wide range of carcinogenesis testing activities, such as the Litton Bionetics contract, preceded the bioassay program.

* Deficiencies of these early bioassays include the failure to have an adequate number of matched controls and the failure to make proper initial determination of the maximum tolerated dose (MTD) so that in many bioassays test animals died prematurely from acute toxicity and dosages had to be lowered during the course of the tests. However, it must be borne in mind that NCI devoted paltry resources to these activities, and that such large-scale tests must necessarily go through developmental phases. (For a critique of the inadequacies in Tracor Jitco's management, see G. J. Ahart, G.A.O. Report to Congressman H. A. Waxman, March 30, 1979.)

Table 9.4 *Analysis of the NCI Bioassay Program*

Year	Number of Compounds in Bioassay Program		
	Entered	Terminated	In Print or Preparation
1969	30	0	0
1970	2	1	0
1971	34	14	0
1972	83	17	0
1973	71	2	0
1974	14	73	0
1975	19	71	0
1976	7	52	1
1977	40	25	17
1978	76	9	156†
Total	376*	264	174

Source: National Cancer Institute, 1978.

* Excludes a few assays judged to be "incomplete."

† Includes all Technical Reports in print or in preparation, but excludes about fifty compounds yielding "insufficient data." Also excludes about 223 Bioassays not reported to Congress (G. J. Ahart, G.A.O. Report to Congressman H. A. Waxman, March 30, 1979).

Criticisms of Rauscher Criticisms of Rauscher's administration, low NCI priorities on environmental carcinogenesis, and the gross inadequacy of the bioassay program gradually surfaced. These were expressed in a report by the Comptroller General of the United States²⁴ and by Congressman Obey in House Appropriations hearings in 1976.²⁵ Rauscher was given additional appropriations and instructed to increase emphasis on environmental carcinogenesis. Specifically, he was told by Congress to create sixty new positions in the Carcinogenesis Program and seventeen new positions in the newly formed Epidemiology Branch in 1977.† He was also instructed to make \$3 million NCI funds available to NIOSH to support a projected \$8 million program on occupational carcinogenesis, an instruction ignored in 1976. The criticisms of Rauscher received further dramatic support on April

† About twenty-eight of these positions have been eliminated as a result of the freeze on federal employment instituted in October, 1978.

14, 1976, with the resignation of Saffiotti from the associate directorship of the Carcinogenesis Program, and his transfer to the Experimental Pathology Branch of the program, a position in which (as of May, 1979) he continues to serve. In a memorandum subsequent to his letter of resignation, Saffiotti protested against NCI policies in the following terms:

- (1) Lack of manpower to operate a rapidly expanding program of major national importance; (2) Inadequate support for carcinogen bioassay operations and for cancer prevention; (3) Inadequate participation offered to staff scientists in the development of NCI policies in this field; (4) Removal of integral components from the program with resulting fragmentation of program direction; and (5) Administrative action and managerial policies.²⁶

Saffiotti's resignation was shortly followed by the resignation of other staff from the Carcinogenesis Program. The program was further emasculated in July, 1977, by being split into two administratively distinct units, the Carcinogenesis Testing Program and the Carcinogenesis Research Program. This move essentially deprived the bioassay activities of needed scientific backup.

In an effort to further diffuse responsibility and head off burgeoning criticisms of the Bioassay Program, Rauscher, in February, 1976, proposed the formation of an extramural Clearinghouse on Environmental Carcinogens. Its main function was intended to be the cleaning up of the backlog of unpublished bioassay reports, and to serve as a standing peer review group for their evaluation. Additional proposed functions were the nomination of chemicals for test, improvement of the scientific base and methodology of the Bioassay Program, and increasing the public understanding of the issues involved. Membership of the Clearinghouse, which first met in November, 1976, under the Chairmanship of Arnold Brown (who a few months later opposed the FDA saccharin ban on the grounds that the positive animal carcinogenicity data should be negated by the alleged negative human data), was selected from a wide range of interests in academia, industry, labor, and public interest groups, and represented a heterogeneous amalgam of scientific and social perspectives and adversarial viewpoints, which were nevertheless expected to decide by vote on largely scientific issues. In spite of

such maneuvers, it had become clear that Rauscher was not only crippling any possibilities for using the vast resources of the NCI to prevent cancer, but that he also failed to understand why he should do so. Criticisms against Rauscher escalated, and he resigned from the NCI on November 1, 1976, to assume his present position as Vice President for Research of the American Cancer Society.[‡] His deputy, Guy R. Newell, became acting director of NCI and continued to perpetuate previous policies of low priorities for environmental carcinogenesis, and to starve the Bioassay Program of essential resources.

In spite of its earlier failure to take a leading role in shaping federal research programs on cancer prevention, NCI in the past few years has made some limited but notable achievements. Its contributions have included: supporting research programs on chemical carcinogenesis; developing criteria for application of animal carcinogenicity data to human experience; funding the International Agency for Research on Cancer in Lyon, France, for the production of an excellent series of monographs summarizing the carcinogenicity and related data on major classes of industrial compounds;* the publication of guidelines on carcinogenesis testing in rodents; and providing advice and guidance to regulatory agencies and congressional committees. Saffiotti has served the latter advisory functions with major distinction.

Recent Developments Present NCI Director Arthur Upton was appointed in July, 1977, with the backing of the scientific commu-

[‡] Rauscher attributed his resignation to financial needs. His salary at the American Cancer Society is substantially more than he received in government.

* These monographs which have been produced on an ongoing basis since 1971 by the secretariat of the agency, under the direction of Lorenzo Tomatis, supported by *ad hoc* teams of international experts are the best available compendia of comprehensive carcinogenicity data (see Lorenzo Tomatis et al., *Cancer Research* 38 (1978), pp. 877-85). So far, 368 chemicals selected on the basis of evidence of human exposure and suspicions of carcinogenicity, have been evaluated, the results of which are published in the first sixteen volumes of the IARC Monographs. For 26 chemicals, there is both epidemiological and experimental evidence of carcinogenicity (Appendix 1); for 221 chemicals, evidence of carcinogenicity is found in at least one species of experimental animal; and for the remaining 121 chemicals, available human and experimental data are inadequate for the evaluation of carcinogenicity.

nity and with the support of labor and public interest groups. Upton, a scientist with particular expertise in radiation carcinogenesis, expresses deep concerns on problems of environmental cancer, and on the urgency of needs for the NCI to institute more effective programs for the prevention of cancer, which he maintains is, or should be, the primary function of the NCI.

So far, Upton's main achievement has been to establish a climate of integrity and openness at the NCI. Upton has initiated a review of the entire range of NCI programs and activities, and has established the reasonable policy that contracts, particularly large ones, should generally be restricted to supporting applied mission or service needs, rather than basic research. To this end, there has been a substantial shift in research support from contracts to grants (Table 9.5).

Upton has shown sensitivity to problems of conflict of interest within the NCI. A vexing problem has emerged over the past few years among certain NCI branch chiefs and division heads with regard to the award of research contracts in the millions of dollars range to commercial laboratories, particularly in virology and immunology programs.[†] This practice had its genesis in the early days of the National Cancer Program, when the NCI's newly increased budget outstripped the size of its scientific staff. These "captive contracts" allowed some NCI scientists to build up large research empires in outside laboratories, which were then closely directed to pursue research goals consistent with the career objectives of the scientists concerned. In some instances, the award of captive contracts, particularly in virology, appears to have been accompanied by the restriction of competitive contract awards to outside scientists in universities or research institutes. Upton has essentially resolved this issue by reorganizing the Division of Cancer Cause and Prevention into administratively separate intramural and extramural activities, and by strengthening external peer review for contracts. This separation has also created a mechanism whereby extramural services and resources, such as animal facilities and histology, can now be made available to

[†] An outside review of the Special Virus Program in 1974 (the Zinder report) characterized it as "a self-serving bureaucracy, full of conflicts of interest. . . . [Those running it come] from a narrow section of the scientific community." The leadership of this program is now well represented among the senior scientific staff of the Division of Cancer Cause and Prevention.

Table 9.5 *Analysis of NCI Budgets in terms of Research Grant and Contract Support*

Year	Research Grants*			Research & Resource Contracts†		
	Budgets (\$ million)	Total (\$ million)	Percentage of Budget	Total (\$ million)	Percentage of Budget	
1976	762	312	41	221	29	
1979	937	409	44	236	25	
1980‡	1,055	492	47	234	22	

Source: National Cancer Institute, 1979.

* Excludes construction, training, and cancer control (educational and demonstration) grants.

† Excludes construction and cancer control contracts.

‡ Based on January, 1979, projections.

intramural scientists. Upton has also moved to resolve another internal problem in the NCI with regard to policy positions. Hitherto, ill-informed statements and publications by NCI staff minimizing the dangers of environmental cancer, on topics ranging from carcinogens in drinking water to saccharin, have been presented to the public under the mantle of NCI authority, rather than as individual opinions. Only the office of the Director is now authorized to issue such policy statements. (Marvin Schneiderman's recent appointment to Upton's office as Associate Director for Science Policy is likely to be of further help in this regard.) Upton's awareness of the cancer prevention concerns of the public interest community has also been strengthened by the appointment of Charles Wurster, Professor of Biology at Stonybrook University, New York, and founder of the Environmental Defense Fund, as consultant to the Director's office.

NCI has finally become responsive to the needs of regulatory agencies. Upton strongly endorsed the EPA's proposal for regulation of carcinogens and other organic pollutants in drinking water, and OSHA's proposal for "generic" standards for occupational carcinogens. Upton was also a prime mover into the establishment of the NCI-NIEHS-NIOSH task force that produced the September 15, 1978, report on "Estimates of the Fractions of Cancer in the United States Related to Occupational Factors" that has led to more clear understanding of the full impact of occupational carcinogens.

In December, 1977, James Sontag, Assistant to the Director of the Division of Cancer Cause and Prevention and Executive Secretary of the Clearinghouse (in an internal NCI memorandum), expressed dissatisfaction with the performance of the Clearinghouse and recommended its dissolution. Sontag made it clear that the Clearinghouse had outlived any possible useful original purpose (of wiping out the bioassay program backlog and compensating for the meager resources allocated by Rauscher to the program). Sontag pointed out that there was no longer any need to "bolster the scientific base of the program." Other criticisms by Sontag included: the Clearinghouse discussions "have tended to obfuscate issues rather than clarify them"; the Clearinghouse has nominated only one chemical for test; the Clearinghouse has "made few, if any, concrete suggestions on improvement in testing

methodology"; and the Clearinghouse has cost the NCI about \$150,000, for little if any returns other than possibly increasing the openness of the program operation. Additionally, Sontag pointed out that the heterogeneous composition of the Clearinghouse resulted in confusion between scientific and societal problems, in that societally adversarial groups are obligated to vote along "party lines" on scientific issues, such as the definition of a carcinogen. Other problems that Sontag failed to discuss include substantive questions of conflict of interest affecting several senior members of the Clearinghouse. An outstanding example is David B. Clayson, Shubik's Deputy Director at the Eppley Cancer Research Institute, who is a member of the executive committee of the Clearinghouse and Chairman of a key committee deciding on the selection or rejection of chemicals for test. Clayson is also principal investigator of a major NCI Bioassay Program contract, in which the Eppley uses test methods that still fail to conform to standard procedures and guidelines long established by the NCI. Results of the Eppley bioassay activities also come under review of the Clearinghouse. Finally, Clayson is a consultant to various industries including the Calorie Control Council, and has testified for industry on repeated occasions with regard to environmental and occupational carcinogens.

Upton rejected Sontag's recommendation, and the Clearinghouse is still operational. In May, 1978, the Clearinghouse issued a report on the "Review of the Bioassay Backlog and Data," which factually reported recent progress in eliminating the backlog (Table 9.4), but without any reference to Sontag's criticisms.[‡] Additionally, Upton has improved the overall operation of the program, systematized the basis for future compound selection, and has planned to increase the testing to about 120 compounds in 1979. (The practical importance of the Bioassay Program is illustrated by reference to the types of chemicals tested in Table 9.6.) In spite of these recent improvements, it nevertheless had be-

[‡] For a recent critique of the Bioassay Program, see G. J. Ahart, G.A.O. Report to Congressman H. A. Waxman, March 30, 1979. This report emphasizes that (as of March, 1979) only 139 of the 207 backlogged assays have been published. G.A.O. identified at least 223 additional bioassays, including those performed by Frederick Cancer Research Center, the Eppley Institute, and NCI's in-house programs, that have not been reported to Congress and published.

come clear that the bioassay program was proving an embarrassment to the NCI. In January, 1978, congressional testimony, Upton raised questions on what should be the future role and responsibility of the NCI in the Bioassay Program:

The role of government will need to change over the next decade from one of providing major support for chronic toxicity testing to one of primary concern with the development and validation of new test methods and quality control of testing conducted by industry.²⁷

Table 9.6 Bioassay Results Recently Announced by the NCI

Use Category	Positive	Negative	Inconclusive	Total Tested
Dyes and Dye Intermediates	13	3	1	17
Chlorinated Hydrocarbons, Solvents, and Intermediates	7	2	1	10
Other Industrial Chemicals	3	5	1	9
Pesticides and Agricultural Chemicals	13	7	2	22
Drugs	11	11	2	24
Food Components and Natural Toxins	1	1	1	3
Total	48 (56%)	29 (34%)	8 (9%)	85

Source: NCI Press Release, June, 1976, to September 1978 (not based on draft or final reports).

Meanwhile, discussions at top HEW levels to coordinate federal toxicology programs culminated in November, 1978, with the creation of the National Toxicology Program (NTP) under the program directorship of David Rall, Director of the National Institute of Environmental Health Sciences. While NCI continues to be fiscally liable for the Bioassay Program to up to \$22 million for its first year of operation, its scientific direction is now the re-

sponsibility of the NTP.* A future role for the Clearinghouse, as presently constituted, appears questionable.

In April, 1978, Gregory T. O'Connor, a pathologist with expertise in geographical influences on cancer, was appointed Director of the Division of Cancer Cause and Prevention, a post he had held on an acting basis since September, 1977. O'Connor abolished problem-oriented programs in carcinogenesis and virology, and reorganized the division on fiscal lines into intramural and extramural programs, in neither of which is there now clear program identification with cancer cause and prevention. The intramural program is a collection of separate laboratories and branches without overall focus on cancer prevention, and the intramural scientists have little opportunity for shaping the overall thrust of extramural activities. O'Connor is on record as stating that the main function of his division is good basic research, rather than good research on the scientific basis for cancer prevention, and he directs major emphasis on virology and molecular biology research programs. Intramural and extramural resources are now divided into three major program areas: biological carcinogenesis or viral oncology; epidemiology; and chemical and physical carcinogenesis. In the fall of 1978, NCI appointed a board of fifteen scientific counselors, representing a wide range of interests and expertise in areas including immunology, virology, and molecular biology, as an outside review group for the Division. Less than five of the group, however, have any identification with chemical carcinogenesis or with problems of cancer prevention.

Unresolved Dilemmas Historically, the NCI has operated as a collection of semi-autonomous programs, each with its own set of objectives, priorities, loyalties, and outside peer pressure groups, and often working in conflict with each other in the virtual absence of overall coordination and integration. Outside of government, the basic science and clinical communities regard the NCI as their fiscal and political territory, and believe that the prime responsibility of the NCI is to support and promote their respective interests. The basic science and clinical communities, and their committee representatives on the National Cancer Advisory Panel

* Administratively, NTP appears to be in a state of limbo between NCI and loosely defined interagency collaborative mechanisms.

and Board, generate strong pressures to further influence already sympathetic senior NCI staff to support these narrowly defined professional perspectives.[†]

It must be recognized that the low priority which the NCI has accorded to research on environmental carcinogenesis in the past has been an important factor in limiting possible regulatory initiatives for cancer prevention and control. The absence of adequate information on carcinogenicity testing of suspect carcinogens and on epidemiological investigations on environmental and occupational carcinogens is one of the most common arguments used by industry to oppose regulatory controls. Notwithstanding Upton's sincere protestations that he believes that the prime function of the NCI should be to prevent cancer or reduce its incidence, it is clear that he has so far been unable to summon the necessary aggression to translate this into operational practice by appropriate budget and personnel allocations at division levels. The 1979 NCI budget (Table 9.7) still reflects the major imbalance of Rauscher's 1976 budget (Table 9.3), with regard to the paucity of definable allocations for carcinogenesis and prevention activities, in contrast with disproportionately high expenditures in areas including treatment, cancer centers, and virology.[‡] In fact, there has not been any proportionate increase in fiscal or personnel allocation in the Division of Cancer Cause and Prevention, or any definable shifting of funds for this purpose within the division.*

[†] The continued retention of Guy R. Newell as Deputy NCI Director helps to foster, at least, the perception that NCI is not primarily committed to problem-solving. Newell has a key role in Upton's office and acts as a filter between Upton and division heads. Newell bears a large measure of responsibility for the bioassay backlog, and his track record is of indifference, if not hostility, to environmental concerns. Newell's responsibilities were further extended in December, 1978, by his assignment as Program Director of the Program on Nutrition and Cancer, budgeted for \$18 million in 1979.

[‡] The 1979 Carcinogenesis Program Budget (\$56 million) is approximately 30 percent greater than the 1976 level (\$43 million), while the total 1979 NCI budget (\$937 million) is 23 percent greater than the 1976 equivalent (\$762 million). This proportionate decrease, from 1976 to 1979, in Carcinogenesis Program funds (which in part reflects a shift from contract to extramural grants) should be further contrasted with a 92 percent increase in Division of Cancer Cause and Prevention funding over the three years (which in part reflects transfer of the grants programs from the Cancer Research, Resources and Centers).

* For a recent critique of the National Cancer Program, see G.A.O. Reports to Congressman H. A Waxman of July 26, 1978, and March 30,

Table 9.7 *Analysis of the NCI 1979 Budget**

Division	Amounts (\$ millions)	Percentage of Total
Cancer Research, Resources and Centers	72.9	7.8
Cancer Biology and Diagnosis	169.4	18.1
Cancer Treatment	236.3	25.2
Cancer Control and Rehabilitation	70.3	7.5
Cancer Cause and Prevention	240.5	25.7
Office of Division Director	(20.1)	(2.1)
Virus Cancer Program	(54.9)	(5.9)
Task Forces Program	(5.8)	(0.6)
Field Studies and Statistics Program	(23.1)	(2.5)
Carcinogenesis Program†	(56.2)	(6.0)
Research Grants	(80.5)	(8.6)
Office of NCI Director	45.3	4.8
Cancer Center Support	67.1	7.2
NIH Management Fund	35.0	3.7
Total	936.8	100.0

Source: National Cancer Institute, 1979.

* These budgetary categories are not comparable with those in Table 9.3 as they reflect recent NCI reorganization involving transfer of the grants programs from the Cancer Research, Resources and Centers to other respective divisions.

† This figure reflects institute-directed research (intramural, contracts, and Cancer Research Emphasis Grants), but excludes investigator-initiated extramural grants.

The pressures on Upton not to increase NCI resources on cancer prevention at the expense of other program areas are complex and

1979. According to the 1979 report, the proportion of NCI resources allocated to "carcinogenesis activities" has remained virtually unchanged since 1972. See also testimony of the author at the Oversight Hearings of the Senate Subcommittee on Health and Scientific Research, March 7, 1979, for an analysis of NCI priorities and a discussion of the claimed NCI expenditures on obligations of \$175 million on environmental carcinogenesis in 1979.

come from powerful and well focused constituencies. These include: the "cancer cure lobby," particularly outside clinical research scientists, cancer centers, and the American Cancer Society; the outside basic science community; and the NIH establishment, as expressed by the position of Director Donald Fredrickson that NIH has little responsibility for problem-solving, but only for excellent basic research; and indirect pressures from the industry lobby. These influences are in no way balanced by the "prevention lobby," represented by the diffuse and relatively weak activities of public interest groups and labor, and Congressional concerns, now expressed mainly by Congressmen Obey and Maguire. The absence of a powerful national cancer-prevention constituency, in the final analysis, is probably the major constraint on Upton. Meanwhile, it is unlikely that there will be major shifts in NCI priorities without an explicit and detailed congressional mandate.

The ability of the NCI, as of any other federal agency, to function effectively depends critically on its ability to attract and retain competent scientists, besides administrators, willing to cope with the problems of the bureaucracy for the sake of participating in critical national research programs. Whether the sense of purpose and direction of the NCI is sufficiently defined for this goal seems questionable. The shrinking availability of outside research funds may, however, aid future recruitment plans.

Future Policies Upton has already expressed the intent that the NCI should exercise a major role in problem-solving approaches to cancer prevention, over and above preserving excellence in basic and clinical sciences. Just as the primary role of the entire USDA is to encourage the production of food and fiber, so should the primary role of the entire NCI be to reduce the incidence of cancer. It is, however, clear, that this intent has not been reflected at division levels in the NCI by appropriate fiscal and personnel allocations.

It is likely that the next major reauthorization of the NCI budget will be enacted by May 15, 1981, for fiscal years 1982 and beyond. This review will provide a timely opportunity for critical review of the first decade of the National Cancer Program, and an accounting of its approximately \$8 billion expenditures.

It is clear that the hard-sell of the 1970 Senate Panel of Consultants has now been replaced by more somber appreciation of the realities. In Benno Schmidt's 1977 report to the President, he stated, "We are still far away from being able to put either a date or a price tag on the ultimate conquest of cancer."²⁸ A full accounting of the accomplishments of the National Cancer Program is overdue. This could be undertaken by one or several of the appropriate Congressional committees aided by a special staff established for the review, with additional support from the General Accounting Office. The programs of the NCI should be examined, using a wide range of criteria, in relation to its achievements in cancer prevention, cancer treatment, and basic sciences. Its programs should also be examined in relation to other research agencies and to regulatory agencies.

On a more immediate level, a series of substantive policy changes should be implemented that would improve the responsiveness of the NCI to the need for cancer prevention. For the purpose of illustrating how such changes could be reflected at the operational level in NCI, the following changes in policies may be considered:

1. *Amendments to the National Cancer Act.* First, consideration should be given to the need to insulate NCI from direct Presidential influence, and to restore it to administrative control of NIH. Second, the dictatorial authority of the Senate Panel of Consultants and the executive role of the National Cancer Advisory Board should be replaced by a more conventional advisory function of a council of committee that would be subject to the public checks and balances of the Federal Advisory Committee Act,²⁹ including attention to needs for disclosure of special interests of its members.† Third, senior NCI appointments should be

† As presently constituted, the National Cancer Advisory Board is top heavy with clinicians and basic scientists. Prior to 1979, there were no problem-oriented epidemiologists or statisticians on the Board or Panel, let alone recognized authorities with activist reputations in environmental and occupational carcinogenesis. (However, new appointees to the Board in April, 1979, include Irving Selikoff and Sheldon Samuels.) There are also critical needs on the Board for representation from the Department of Energy. Public members of the Board are appointed as political pay-offs rather than as a reflection of deep commitment to cancer prevention; industry is well represented, unlike labor and public interest groups. Board or

upgraded by recruiting qualified scientists with commitment to problem-solving and cancer prevention, in addition to basic and clinical sciences. Fourth, strong emphasis should be given to the development of high priority programs designed to identify causes of cancer and its prevention. An NCI division with an exclusive commitment to environmental carcinogenesis should be authorized, which should have a clearly defined budget commensurate with its importance.[‡] Finally, legislative provision must be created for the reimbursement of NCI by industry for costs of testing profitable chemicals incurred in the bioassay program.

A useful initiative in the attempt to focus NCI priorities on problem-solving has been provided by Congressman Andrew Maguire's (D.-N.J., and member of the House Health and Environment Subcommittee) 1978 Cancer Prevention Act (H.R. 10190), an amendment to the National Cancer Act of 1971. Key elements of the Maguire bill were incorporated into Chairman Paul Rogers' (D.-Fla.) (House Health and Environment Subcommittee) Biomedical Research and Training Act. The essence of this bill became law in November, 1978 (P.L. 95-622).

The Maguire amendments (which received strong support from the Industrial Union Department of the AFL-CIO and the Oil, Chemical and Atomic Workers Union) are a major and unique contribution to the drive to refocus NCI's attention on the occupational and environmental causes of cancer. They direct the NCI to conduct "an expanded and intensified research program for the

Panel membership should exclude those scientists who receive, or whose institutes receive, major NCI contracts. Although Benno Schmidt's tenure expired in March, 1978, as of January, 1979, he still serves as Panel Chairman in spite of a long record of disinterest in cancer prevention. (In spite of the fact that his credibility as a senior science advisor is in question as in view of his track record at the NCI, in December, 1978, Schmidt expressed interest in membership of the Senior Advisory Committee of NIH. According to a July 26, 1978, G.A.O. Report to Congressman H. A. Waxman, "Since the first meeting of the President's Cancer Panel in 1972, there has been minimal discussion of cancer prevention and carcinogenesis research at its meetings."

[‡] At hearings on the National Cancer Program before Senator Kennedy on March 7, 1979, Upton announced intent to create a new formal division of environmental carcinogenesis. Upton also claimed that NCI obligations for environmental carcinogenesis in 1979 totalled \$175 million, although this was not supported by the budgetary details. It may thus be reasonably anticipated that the proposed new division will be funded at a minimal annual level of \$175 million.

prevention of occupational or environmental exposure to carcinogens." They also require the HEW Secretary to publish an annual report containing a list of all substances known, or reasonably anticipated to be carcinogens; an estimate of the number of people exposed to each of these carcinogens; a statement identifying those carcinogens for which there is no effluent, ambient, or exposure standard; and a statement on the extent to which existing standards will decrease the cancer risk from such exposures.* This provision, designed to assess the effectiveness of existing regulatory standards, drew last minute fire from Benno Schmidt, who (during the House-Senate Conference between Chairman Rogers and Senator Ted Kennedy, who heads the Senate Subcommittee on Health and Scientific Research) engaged in unsuccessful lobbying to have the annual report requirements stricken from the bill. Schmidt admitted that this represented "a head-on defeat."

The Maguire amendments also require the NCI to develop demonstration programs designed to protect occupational and other groups at high risk, and to insure that cancer centers develop an emphasis on prevention. Another amendment requires that at least five of the eighteen-member National Cancer Advisory Board be "individuals knowledgeable in environmental carcinogenesis," and that the heads of all concerned regulatory agencies be *ex officio* members.

2. *Comprehensive cancer centers.* Continued funding of the nineteen centers should be made explicitly contingent on their developing strong programs in cancer prevention, with particular emphasis on carcinogenesis and epidemiology, in addition to their present, almost exclusive, emphasis on treatment. Centers should also be required to establish tumor registries, with particular interest in identifying environmental and occupational carcinogens, and with special emphasis on the surveillance of occupational populations at high risk of cancer.

3. *The bioassay program.* This should be singled out as a high priority in the NCI and NTP, with adequate budget and personnel. Besides selecting compounds and supervising their testing in

* While Maguire originally proposed that the NCI be directed to prepare the annual carcinogen report (the first of which is due before the end of 1979), in deference to Upton's wishes the Secretary of HEW has assumed this responsibility which will be implemented through the NTP.

contract and sub-contract laboratories, with particular emphasis on industrial chemicals, the program should emphasize critical evaluation of the test data and early development of reports, which should also summarize information relevant to problems of human exposure. The bioassay program should be closely related to programs in epidemiology and biostatistics in the NCI, and in all agencies involved with the NTP, as well as to basic research in carcinogenesis, and should be extended to cover problems of synergistic and other interactions, especially when clues on such interactions are afforded by epidemiology. Consideration should also be given to requiring the contract laboratories, with appropriate supervision, to prepare bioassay reports rather than maintaining this as a direct NCI responsibility. Some system of interim cancer alerts should be restored to give public warning pending publication of the reports.

Careful thinking and planning are needed for the conduct of future bioassay tests. These should be designed as chronic toxicity tests, in which the discovery of carcinogenicity is a major but not exclusive end. Tests should more clearly recognize other important manifestations of chronic toxicity (including toxic effects on the central nervous and reproductive systems, liver, and kidney) by observation and functional studies during the test and histological studies following its conclusion. Methods exist to elicit a wide range of neurobehavioral effects in animals during routine handling. Chromosome and some reproductive studies can be made in animals without prejudicing the two-year bioassay test. There are a wide range of such possibilities for improving the quality and quantity of information that can be derived from the standard two-year bioassay test, leads from which can be followed up by more specialized procedures.³⁰

4. *Tobacco research programs.* The major emphasis should be placed on meeting the needs for aggressive epidemiological and other research on smoking and cancer and to develop explicit antismoking educational campaigns. NCI programs on smoking and cancer must be commensurate with the role of tobacco as a major cause of cancer.† Future programs must be segregated from

† NCI tobacco program expenditures in all areas including research and education were under \$7 million in 1977, \$8.9 million in 1978, and are projected to be \$12.8 million in 1979. Thus, approximately 1 percent of the

the dominant influence of industry (exercised in the past through the NCI Tobacco Working Group) and protected from past patterns of conflict of interest in its award of research support. There must also be increased emphasis on problem-oriented research, including development of improved test methods, analytic and monitoring procedures for environmental and occupational carcinogens, and carcinogenesis research at the cellular level.

5. *Environmental cancer research programs.* NCI should, with the highest possible priority, develop active, large-scale internal programs on environmental and occupational carcinogenesis research and also fund such research by outside scientists, to whom all appropriate internal resources of NCI should be made available. These activities should encompass experimental carcinogenesis, epidemiology, surveillance of high risk groups, and analytic and monitoring techniques for chemical carcinogens. Basic scientists should be encouraged to develop interest in these problem-solving activities. NCI should also fund the training of scientific investigators in these various fields.†

6. *Relation of NCI and regulatory agencies.* NCI should preserve its primary function as a research agency, with emphasis on problem-solving, and should not become directly involved in regulatory specifics. NCI should, however, develop special formalized large-scale resources for providing guidance and counsel to regulatory agencies on all scientific matters relating to chemical carcinogens in the general environment and workplace.

A critical resource which NCI should develop is a documentation and analysis center, to collate and systematize available carcinogenicity data from sources including the Bioassay Program with particular reference to potential environmental and occupational exposure. Such a center should be directed by a scientist with recognition in chemical carcinogenesis and with experience and sensitivity to the needs of regulatory agencies, and should be adequately staffed with biometrists, statisticians, and epidemiologists so that it can also be capable of performing risk estimates.

NCI budget is allocated to an agent associated with up to about 20 percent of total U.S. cancer deaths.

† Although NCI recognized the need to establish training programs in toxicology and veterinary pathology in testimony before the Senate Appropriations Committee in 1977, no such programs have yet been established in spite of appropriate legislative authority.

Finally, the center should be capable of analyzing the impact of failure to regulate a particular carcinogen in terms of total costs from induced or associated cancers and other diseases. The current failure of NCI to have developed such a resource was critically noted in a recent United Nations document (*International Register of Potentially Toxic Chemicals Bulletin 1*, June, 1978, p. 4):

The National Cancer Institute of the National Institutes of Health, U. S. Department of Health, Education and Welfare, has certain program elements that relate directly or indirectly to concerns about exposure to specific agents that are environmental carcinogens. However, there is currently no identifiable program that assesses, on a holistic basis, the potential hazard from the carcinogenic insult of air and water pollutants, diet contaminants, and other composite stresses.

7. *Overall management.* Questions have been raised by Congressman David Obey (D-Wisc.) and others as to whether the administrative skills of the NCI are adequate to sustain its expanded budget, especially in the absence of adequate personnel and an adequately defined sense of mission and priorities. The apparent relief of the NCI in recently surrendering scientific direction of the Bioassay Program to NIEHS may well express tacit admission of NCI's desire to further divest itself of mission research and other problem-solving activities relating to cancer cause and prevention. This seems to be resulting in a perpetuation of the Rauscher era of predominant emphasis on clinical research and basic science programs unrelated to cancer prevention which could more appropriately be handled in other NIH Institutes. However, it is unlikely that such a pattern of activity would exert adequate appeal to Congress, besides to the broad scientific biomedical community, to justify anything like the approximately \$1 billion NCI budget.

Other Research Agencies

The National Institute for Occupational Safety and Health (NIOSH). This institute was created within the Department of

HEW by the 1970 Occupational Safety and Health Act (P.L. 91-596), and incorporated the previous Bureau of Occupational Safety and Health. Organizationally, NIOSH was originally located in DHEW's Health Services and Mental Health Administration but, following the dissolution of that Administration in 1973, was transferred to the Center for Disease Control (CDC), a HEW agency with primary responsibility for infectious diseases within the Public Health Service, where it remains today. The NIOSH Director, headquartered in Rockville, Maryland, thus reports to the CDC Director, headquartered in Atlanta, Georgia, who in turn reports to the Assistant Secretary for Health, HEW, headquartered in Washington, D.C. Most of NIOSH's personnel are located in Cincinnati, Ohio, and Morgantown, West Virginia. From a budget of \$26 million and a complement of 745 positions in 1972, NIOSH has grown to a 1978 budget of \$64 million with 913 positions.

NIOSH has exclusive responsibility for research into all aspects of occupational health and safety. This research is designed to provide a critical basis for the development of regulatory standards by OSHA. A critical activity of NIOSH is its conduct of epidemiological surveys, and its development of Health Hazard Evaluation Reports for industries, where major problems of occupational health and safety are suspected. Apart from the fact that NIOSH has only carried out about 150 of these evaluations each year, their quality, in general, has been unsatisfactory. Until recently, they seemed to be falling under the increasing operational control of CDC, especially in politically "sensitive" situations.* NIOSH is also responsible for funding outside research activities, administers a program for establishing Educational Resource Centers at major universities throughout the country, and has developed educational and training programs for industrial hygienists and other professionals. NIOSH periodically issues Current Intelligence Bulletins to alert the occupational health and safety communities to emerging critical problems, and it publishes an annual Registry of Toxic Effects of Chemical Substances,

* An example of this is the usurpation by CDC of a 1976 request to NIOSH for evaluation of a Becton-Dickinson plant in Puerto Rico, where workers making thermometers were found to be suffering from mercurial poisoning (Charles Edwards, formerly FDA Commissioner, was then a Senior Vice President at Becton-Dickinson).

which in 1976 listed 25,000 different chemicals. Included in this is a list of about 2,000 suspect carcinogens.

The major objective of the various research functions of NIOSH is the development of criteria documents recommending new updated and revised standards to OSHA. The development of these documents is the responsibility of the Division of Criteria Documentation and Standards Development, one of NIOSH's eight divisions. The proportion of the NIOSH budget allocated to criteria documents doubled from 1972 to 1973, but has remained constant at about 10 percent since then. Currently, the division employs about 80 people, and while no major increase in personnel is planned for activities under the Occupational Safety and Health Act in 1979, an increase has been requested to meet the requirements of the 1977 Federal Mine Safety and Health Act.

The criteria documents, some 85 percent of which are developed by outside contractors at a cost of about \$300,000 each, review and summarize the toxicological, epidemiological, industrial hygiene, and control technology information on specific chemical and physical agents and industrial processes. The documents make recommendations on regulatory standards, work practices, and medical surveillance.³¹ By April, 1979, over one hundred documents had been transmitted to OSHA. These were generated at an average rate of eleven a year since 1972, and about double that number since 1976. Only in one case, arsenic, was a NIOSH criteria document the initial stimulus for OSHA action, although in four other cases (asbestos, benzene, cotton dust, and vinyl chloride), OSHA issued standards for hazards described in criteria documents. Even before promulgation as regulatory standards, criteria documents are widely distributed and used by industry and labor as a basis for control practices.

The quality of these documents, in general, has been unscientific and unsatisfactory, and their conclusions appear to have been improperly influenced by undefined economic and feasibility considerations.† With the notable exceptions of the asbestos and coke oven documents, few other documents, many of which were prepared by outside contractors with clear conflicts of interest,

† The documents fail to reflect quantitative consideration of health benefits that could be reasonably anticipated from reduction in exposure levels envisaged in the proposed standard, and fail to consider the range of available control technologies.

have survived the OSHA hearing and standard-setting process. To some extent, the NIOSH track record on criteria documents reflects difficulties imposed on agencies that bridge research and regulatory functions. Responsive to these criticisms and with a view to improving the process, in September, 1978, CDC initiated an in-depth review of the criteria documentation program, including the validity of its data base and its utility to OSHA (Policy Research Inc., Baltimore, Md., "Evaluation of the NIOSH Criteria Documentation Program," CDC Contract #210-78-0048).‡ In addition to criteria documents, Current Intelligence bulletins and Health Hazard Evaluation reports, NIOSH also produces two other emergency-type documents, Special Hazard Reviews and Recommendations for an Emergency Temporary Standard.

The NIOSH budget for carcinogenesis programs had increased from \$1.8 million in 1975 to \$6.9 million in 1976, reaching \$10.7 million in 1977, including \$3 million in "pass-through" funds from the NCI.³² Carcinogenesis funding thus represents approximately 20 percent of NIOSH's total budget. The occupational carcinogen program includes laboratory studies, field surveillance, and industry-wide epidemiological studies.* The surveillance studies, which focus on groups at high risk of developing cancer, have been particularly important. The groups to be studied are identified on the basis of industrial practices, epidemiological data, and information from labor and other sources. Industries recently surveyed by NIOSH include printing, milling and mining, coal gasification, plywood, pulp and paper, steel, metal smelting, and pesticide formulation. NIOSH has also undertaken epidemiological investigations on industries using various carcinogens, including benzene, trichloroethylene, VC, vinylidene chloride,

* In March, 1979, NIOSH announced plans to direct future emphasis to the production of criteria documents dealing with control technology, encompassing across-the-board processes at the expense of traditional single-agent documents.

† Probably the most successful of these were directed by Joseph K. Wagoner (ex-chief of the Division of Field Studies and Clinical Investigations by NIOSH and now Special Assistant for Occupational Carcinogenesis at OSHA), who has pioneered a wide range of important epidemiological investigations on occupational carcinogenesis. Wagoner has also been an articulate and well-informed witness at various Congressional hearings.

chloroprene, styrene-butadiene, epichlorhydrin, polychlorinated biphenyls, and asbestos-containing talcs.³³

An important undertaking of NIOSH has been the National Occupational Hazard Survey from 1972 to 1974,³⁴ covering nearly 5,000 plants and close to one million workers, the results of which were later summarized in a document entitled, "The Right to Know."³⁵ The survey spelled out the extent and potential costs of exposure of workers to carcinogens:

One in every four American workers (approximately 21 million) currently may be exposed on either a full or part-time basis to OSHA-regulated hazardous substances. Upwards of 40 to 50 million persons or 23 percent of the general population in the United States may have had exposure to one or more of OSHA-regulated carcinogens or hazardous substances during their working lifetime.

The annual costs to society of monitoring workers with either full or part-time exposures to all OSHA-regulated hazardous substances including carcinogens could range between \$675 million and \$2 billion.³⁶

Besides monitoring, it was estimated that lifelong, surveillance costs for just those few carcinogens currently regulated is in the region of \$8.5 billion.† Such cost estimates ignore possible additional employer liability resulting from discovery of compensable impairment during examination, entitlement under various federal and state programs, recovery for damages under third-party legal action brought by workers, and even greater costs from past exposures to carcinogens not regulated by OSHA.

"The Right to Know" also confirms the fact that a substantial number of workers in industry are exposed to chemicals the identification of which the industry has refused to disclose; over 70 percent of all exposures were found to arise from trade name products of undisclosed composition. According to the document, "A major stumbling block to identifying exposed workers is the failure of chemical re-packagers and primary producers to show the chemical composition of their product."³⁷ Beyond knowing who has been exposed to what, "There is currently no effective mechanism for locating and notification [of workers]."

† Additionally, the cost of physical examinations would be about \$230 million a year.

Concerns have been growing over the inability to identify workers today who have been exposed to carcinogens in the past. Responding to these concerns and to an amendment to the Internal Revenue Service Code offered by Senator Gaylord Nelson (D-Wisc.), President Carter authorized NIOSH in November, 1977, to obtain from the Internal Revenue Service addresses of workers whom it suspects of having been exposed to carcinogens. Among the first workers targeted for notification are the many who may have been exposed to asbestos, arsenic, benzene, and benzidine.

The previous administration did not give NIOSH high priority. President Ford's request for the 1976 NIOSH budget was \$32 million, the same amount as appropriated by Congress in the previous year. His Office of Management and Budget eliminated a proposed line item for occupational carcinogenesis, a move that was countered by Congressman David Obey (D-Wisc.) of the House Appropriations Committee, resulting in an increase in total NIOSH appropriations to \$48 million. (Obey has played a major role in overseeing carcinogenesis and related programs and priorities in NCI as well as NIOSH.)

One of the major problems of NIOSH, apart from critical shortages of funds, has been and still is its relatively low political visibility and stature. Since NIOSH reports directly to CDC, the NIOSH director has no direct access to the HEW secretary (in contrast to the Assistant Secretary of Labor for Occupational Safety and Health, Eula Bingham, who reports directly to the Secretary of Labor). In spite of these and other problems, NIOSH has made significant strides in its research, epidemiological surveys, training programs (including establishment of Educational Resource Centers), and development of criteria documents.

The previous director of NIOSH was John F. Finklea, who resigned in January, 1978. Prior to Finklea's NIOSH tenure, he was in charge of air pollution biomedical research activities at EPA, where he made important contributions. While at NIOSH, Finklea had to struggle against crippling fiscal limitations imposed by unsympathetic Republican administrations, a Department of Labor more responsive to interests of commerce than health and safety, and the low bureaucratic status of NIOSH. Finklea's resignation resurrected latent questions as to the future of NIOSH and

its appropriate position within the Federal bureaucracy. Possibilities, each of which had proponents, included upgrading of NIOSH within HEW to an agency level (reporting directly to Secretary Califano or Julius Richmond, HEW Assistant Secretary for Health), a move endorsed by organized labor; the transfer, intact, of NIOSH to the Department of Labor; and, the preservation of the NIOSH *status quo* as advocated by CDC. These speculations, fueled by the protracted failure of HEW to replace Finklea, were eventually resolved with Califano's announcement at the September, 1978, AFL-CIO convention in Washington, D.C., of the appointment of Anthony Robbins, Director of the Colorado Health Department and Labor's candidate, to head up NIOSH, an appointment formalized by the Civil Service Commission in December, 1978.

Reflecting still unresolved ambiguities, and possibly foreshadowing events to come, in November, 1978 (pending ratification of the Robbins appointment), CDC moved to appoint W. Clark Heath, a staff epidemiologist, to a key NIOSH position.[‡] In view of Robbins' known opposition, this move appears to reflect undue CDC influence in NIOSH policies, and also insensitivity to the concerns of labor, by whom Heath is viewed as ultraconservative, if not hostile.* Responsive to labor's protest and Congressman Obey's intervention, Califano blocked Heath's appointment. (Instead, Philip J. Landrigan, another CDC epidemiologist was appointed in April, 1979.)

The tensions between NIOSH and CDC appear to reflect territorial, rather than conceptual, considerations. CDC can no longer justify its present budget and personnel levels on the basis of its

[‡] This position, Director of the Division of Surveillance, Hazard Evaluation and Field Studies in Cincinnati, had just been vacated following the unrequested transfer by CDC of Bobby Craft, the previous Division Director, to the Educational Resource Center at the University of Utah.

* As an example, contrary to established NIOSH policy of open joint involvement of management and labor in planning and undertaking field investigations, in 1974, unbeknown to NIOSH and labor, CDC met privately with management of a Union Carbide plant in South Charleston, West Virginia, to discuss the medical examination of workers exposed to vinyl chloride. Following discovery, protests by the Industrial Union Department of AFL-CIO forced cancellation of the CDC plans, and NIOSH was authorized to conduct the evaluation elsewhere (at the Firestone, Pottstown, Pennsylvania, facility).

anachronistic mission of infectious disease control, but only by subsuming the occupational health and safety missions of NIOSH.[†] Forcing the NIOSH tail to wag the CDC dog may well ensure continued low federal priority for the missions of NIOSH. However, it is also possible that Robbins' personal contacts at HEW and elsewhere in Washington may be adequate to counterbalance bureaucratic formalities. It also seems likely that NIOSH could benefit from the recognized professionalism and administrative skills of CDC.

A series of initiatives, now under consideration, would develop greater consistency in the interpretation and discharge by NIOSH and OSHA of their respective mandates under the terms of the 1970 Occupational Safety and Health Act. In October, 1978, the Department of Labor requested the cooperation of HEW in improving the relationships between OSHA and NIOSH, and in the creation of a NIOSH "Planning Group Activity" within the Labor Department, under the direction of Assistant Secretary Eula Bingham, but including representation from the Mine Safety and Health Administration and the Employment Standards Administration, both of which have close working relationships with NIOSH. The Department of Labor, in order to ensure appropriate priority for its research needs, also requested authority from the Office of Management and Budget to participate in NIOSH budget-setting for fiscal 1981. Irrespective of the precise outcome of these initiatives, it is clear that the primary and explicit function of NIOSH must be to undertake research that will more effectively enable OSHA to discharge its responsibility in improving occupational health and safety.

Robbins appears to have a good grasp of the more pressing problems of NIOSH. His well-attuned political instincts coupled with integrity and dedication should enable him to cope with the bureaucratic ambiguities and complexities he has inherited. Within a few days of his appointment, Robbins expressed intent to upgrade the quality and quantity of Health Hazards Evaluations, to improve the quantity, quality, and utility of criteria documents and synchronize them better with OSHA's needs, and to

[†] This motivation was admitted at a private discussion between a senior CDC official and Labor in July, 1978.

improve professional skills at NIOSH, particularly in clinical and engineering areas.‡

The National Institute for Environmental Health Sciences (NIEHS) Created in the fall of 1966 and located in Research Triangle Park, North Carolina, this is the only NIH Institute located away from the Bethesda, Maryland, Campus.* NIEHS supports basic research on the toxic effects of environmental pollutants and on ways to predict such future crises.

Although one of the youngest and smallest NIH Institutes, NIEHS has taken the lead in several major areas of research, particularly mutagenesis, which is important because of the promise of mutagenesis as a short-term test for carcinogenicity, quite apart from intrinsic public health problems of mutagenicity. A second major field is the development of improved statistical methods for extrapolating from animal tests to humans, and from high-dose to low-dose responses. (Institute statisticians have been prominent in reaffirming the scientific basis of the Delaney law, and the inability of science to determine threshold levels for carcinogens.) An additional area has been study of the rate of absorption, distribution, metabolism, and excretion of toxic and carcinogenic substances in the body. The Institute has also served as a major supporter of a number of critical areas of extramural research, including Selikoff's pioneering work on asbestos, and the studies of Norton Nelson's group at New York University, which led to the identification of BCME, dimethyl carbamoyl chloride, and epichlorhydrin as major industrial carcinogens.

Probably the most important contributions of NIEHS have been in the development of national recognition of toxicology as a major field of scientific endeavor, and in the organization of a broad forum for discussion of the scientific basis of important regulatory issues. Such activities have included the establishment of two Task Forces on research planning in environmental health,

‡ A recent expression of this perception is the Control Technology Program, budgeted for \$4.2 million in 1979, in which selected industries involving carcinogenic exposures are being assessed from the standpoint of control and process technology. Similar control technology programs are being developed at EPA.

* Long an occupant of limited rental laboratory space, NIEHS will be moving into adequate research facilities in Research Triangle Park in 1980.

which focused the attention of policy makers and scientists on research and manpower needs in this field, and the creation of a new journal, *Environmental Health Perspectives*, which has served as a key instrument in the rapid communication of proceedings of conferences convened by the Institute.

The NIEHS budget has grown from \$49 million in 1977 to about \$69 million in 1979.[†] Of the current budget, approximately \$19 million is allocated to "Disease Prediction," \$11 million to "Disease Mechanisms," \$15 million to "Manpower Development," and \$21 million to "Intramural Research." Research funds are evenly divided between intramural and extramural activities.

There are clearly some ambiguities and areas of jurisdictional overlap between the functions of NIEHS on the one hand and NCI and NIOSH on the other. This is illustrated by the recent shift in scientific responsibility for the NCI's Bioassay Program to NIEHS by the creation of the National Toxicology Program (NTP) on a two-year experimental basis. NTP was set up as an interagency department-wide cooperative program (including NCI, NIEHS, CDC/NIOSH, FDA, and other members of the Interagency Regulatory Liaison Group) under the direction of David P. Rall, Director of the NIEHS, who will report to the Assistant HEW Secretary for Health. The avowed objective of the NTP is "to strengthen the Department's activities in the testing of chemicals of public health concern, as well as in the development and validation of new and better integrated test methods." In its first year, the approximately \$41 million budget of the NTP is comprised of the following contributions: NCI \$22 million; NIEHS \$10 million; FDA \$7 million; and CDC/NIOSH \$2 million.

Rall is both skilled and enthusiastic, and has emerged as one of the leading scientific protagonists of the hazards of toxic and carcinogenic environmental pollutants. He has also been involved in critical public issues, such as defending the Delaney Amendment from industry attacks and in backing the proposed FDA ban on saccharin. Rall additionally serves as Chairman of the DHEW

[†] Congressman David Obey (D-Wisc.), in particular, has recognized the contributions and potential of NIEHS, and has been a key supporter of its sustained growth.

Committee to Coordinate Toxicology and Related Programs, which draws together the DHEW agencies (and observers from non-DHEW agencies) for the purpose of improving information flow and program coordination of toxicology research.

The National Center for Toxicological Research (NCTR) This center, in Pine Bluff, Arkansas, was established in 1971 by President Nixon, is administered by the FDA, and is jointly funded by the FDA and EPA. Its stated objectives are the development of methodologies for chronic toxicity and carcinogenicity testing, studies on exposure to low levels of carcinogens, and extrapolation of carcinogenicity data from animals to humans. The track record of the NCTR illustrates how research functions are subverted by political considerations. From its inception, senior FDA officials made it clear that they intended using the center to develop data for the purpose of challenging the scientific basis of the Delaney Amendment so as to allow the FDA to set tolerances for carcinogens deliberately added to food. At hearings before Congressman Whitten's Subcommittee on Agriculture and Related Agencies of the House Appropriations Committee in April, 1971, then Commissioner Edwards stated in congressional hearings that "the Pine Bluff testing facility will provide FDA with the scientific basis on which the Delaney anti-cancer clause may be changed," reiterating his view that the agency is "locked into an all or nothing" position because of the Delaney box. "The FDA didn't want to make it more difficult by recommending changes until it has the scientific data to justify a modification."³⁸ Four years later FDA made it clear that it had not changed its position of fundamental hostility to the Delaney anti-cancer clause.³⁹

The research programs developed by the NCTR were poorly conceived. The most widely touted of these was the "Mega Mouse" experiment, in which hundreds of thousands of mice were to be tested in attempts to find safe levels for profitable chemical carcinogens, such as DDT, that had been or were about to be banned. Not only did this approach suffer from major statistical problems, but there were not enough personnel available to undertake the necessary autopsies. The center (apparently

seriously) suggested instead that they would spot-check animals at the end of a carcinogenicity test, rather than autopsying them all.[‡]

Responding to mounting criticisms and at the request of HEW, NCI Director Rauscher appointed an expert committee under the chairmanship of the distinguished pathologist, Harold L. Stewart to evaluate the center's programs. The committee's unanimous report in August, 1973, concluded:

The program will not contribute materially to progress toward its stated objective, viz., improved capability for assessing the carcinogenic hazard for man on the basis of data obtained in laboratory animals.⁴⁰

Morris F. Cranmer, then director of the center, reacted hostilely, asserting that the critics were not familiar with his programs and had failed to understand his objectives. Apparently interested in avoiding embarrassment to the FDA, Rauscher rejected his committee's report. Four years later, however, a National Academy of Sciences committee came to essentially the same conclusions.⁴¹ The immediate problem was resolved in December, 1977, when Cranmer was relieved of his post following investigations by the General Accounting Office and the FBI resulting in charges of conflict of interest and major mishandling of federal funds.⁴² As of May, 1979, completion of formal action to terminate his FDA appointment is still pending and Cranmer is contesting the charges.

The Energy Research and Development Administration (ERDA) ERDA was created in 1974 by the Energy Reorganization Act and is now part of the Department of Energy. Its Biomedical and Environmental Research Program, budgeted at \$122 million in 1977, is responsible for investigating the public health and environmental effects of developments in energy technology, including nuclear power and coal gasification. Most of ERDA's health effects research is on radiation, but \$5.5 million is

[‡] In spite of these problems, results of recent large-scale NCTR tests on the potent carcinogen acetylaminofluorene are consistent with the no-threshold concept of carcinogenesis, as evidenced by a linear extrapolation through zero. In other words, they confirm the extreme difficulty, if not impossibility, of setting "safe levels."

budgeted for other aspects of environmental carcinogenesis. Ruth C. Clusen, past president of the League of Women Voters, is Assistant Secretary for Environment of the Department of Energy.

Office of Technology Assessment (OTA) Following years of deliberation and public debate, Congress passed the Technology Assessment Act creating OTA in 1972. The bill was guided through Congress by Representative Emilio Daddario (D-Conn.) and Senator Edward Kennedy (D-Mass.). OTA began operations in late 1973 with Kennedy as the first Board Chairman and Daddario (by then no longer in Congress) as the Office's first Director, to be succeeded by Russell W. Peterson in January, 1978.* From initial funding of about \$2 million in 1974, the OTA budget increased to about \$8 million in 1978, with an estimated 1979 projection of \$11.2 million.

The Office of Technology Assessment is intended to serve Congress as a non-partisan think tank on issues relating to science and technology, and to assess the impacts of technological change on society. The concept of "technology assessment" first originated with the House Committee on Science and Astronautics in the mid-1960s, as Congress wrestled with scientific and technical issues whose consequences were unclear or on which there was sharply polarized opinion. These include the impacts of supersonic transport, new transportation systems, anti-ballistic missiles, and toxic chemicals. While the original perception of OTA was that of Kennedy's "Brain Child" and answer to Nixon's Office of Science and Technology (currently transformed into the Office of Science and Technology Policy), Congress now appears to accept it as a useful resource for "scientific foresight." It is, however, questionable whether Congress interprets "technology assessment" in terms of secondary and tertiary impacts, rather than as merely assessing the soundness of a particular technology.

OTA currently operates in eleven principal areas: energy, food, genetics and world population, health, materials, national security, oceans, R&D policies and priorities, technology and world trade, telecommunications and information systems, and trans-

* Peterson resigned on March 31, 1979, and was replaced by John Gibbons, a physicist from the University of Tennessee.

portation. Within these areas, OTA studies involve consultants, contractors, and citizen advisory panels to augment the in-house professional staff of scientists, engineers, lawyers, and policy analysts. In the past, OTA responded principally to requests from congressional committees or OTA Board members. However, during 1978, OTA launched a broad outreach effort to determine the general perception of the most important issues warranting OTA study, on the basis of which new priorities were established.

In the health area, OTA reports have addressed issues such as drug bioequivalence (the first report issued by OTA), the need for assessing the safety and efficacy of medical technologies such as the computerized axial tomography (CAT) scanner, the carcinogenicity of saccharin, and methods for carcinogenicity testing. While past reports have been restricted to assessment of the benefits and risks of various policy alternatives, OTA is considering moving in the direction of making specific recommendations which, subject to approval by Board majority, are authorized by the enabling legislation of the Technology Assessment Act. OTA reports have often been the basis for congressional action, or for programmatic changes by Federal agencies, besides serving as a useful resource for the scientific and technical community and the general public.

The Council on Environmental Quality (CEQ) The first official act of President Nixon was the signing of the National Environmental Policy Act, dedicated to improving environmental quality.⁴³ The Act also established CEQ in the executive office of the President, where its primary duty is to give Congress an Environmental Quality Report each year, setting forth the status and conditions of the nation's environment.† Under the successive leadership of Russell Train and Russell W. Peterson, the council

† The Act requires environmental impact statements when proposed projects within the jurisdiction of federal regulatory agencies may significantly affect "the quality of the human environment." CEQ has recently proposed extending the requirements of the Act to the international activities of agencies. Hearings on this proposal were held in June, 1978, by Senator John Culver's Resource Protection Sub-Committee of the Environment and Public Works Committee.

has played an important role in developing critical analyses of environmental pollution problems, in emphasizing the urgent need to develop preventive approaches to environmental problems, particularly cancer, and in stressing the importance of interagency collaboration in meeting these objectives. Under the chairmanship of Charles Warren, who was appointed in March, 1977, the council is living up to the promise of past performance. Warren came from the California State Assembly, where he built up a sound record on energy and environmental concerns. The second member of the three-person council is Gus J. Speth, appointed in April, 1977, an attorney who was one of the original founders of the Natural Resources Defense Council and who has strong interests in problems of nuclear power, water pollution, and corporate policy.

Regulatory Agencies

The function of regulatory agencies is to regulate. This entails not only developing standards but enforcing them as well. The former is cosmetic without the latter. The regulatory function of every agency is mandated by statutory legislative authority, and confusion or ambiguity in the mandate will be reflected in agency practice.⁴⁴

As illustrated in the various case studies in chapters 5, 6, and 7, the track record of federal agencies in regulating carcinogens in the workplace, in consumer products, and in the general environment has been unsatisfactory. Of the few regulatory actions that have been undertaken against carcinogens in the past decade, the great majority have been formally initiated or instigated by public interest or labor groups (Table 9.8).‡ (See Appendix III for a comprehensive list of substances regulated as carcinogens.) It is clear that the fundamental problem with the regulatory agencies

‡ It is possible that Table 9.8 does injustice to regulatory agencies which, in some instances, were developing the legal basis for action when labor or public interest groups intervened. For a recent discussion of "Chronic Indecisiveness" in regulatory agencies and their inadequate track records, see R. J. Smith, "Toxic Substances: EPA and OSHA are Reluctant Regulators," *Science* 203 (1979), pp. 28-32.

Table 98 Standards Promulgated by Regulatory Agencies to Control or Ban Carcinogens

Legislative Authority	Carcinogen	Agency Action	Action Initiated by Public Interest or Labor Groups*
Occupational Safety and Health Act (Section 6, Workplace standards)	Asbestos Package of 14 carcinogens Vinyl chloride Coke oven emissions Benzene Acrylonitrile Beryllium Asbestos	OSHA, 1972 OSHA, 1973 OSHA, 1974 OSHA, 1976 OSHA, 1978 OSHA, 1978 EPA, 1973 EPA, 1973-1976 EPA, 1976 EPA, 1977 EPA, 1977 EPA, 1977 EPA, 1977 EPA, 1977 EPA, 1977	AFL-CIO, 1972 OCAW and HRG, 1973 AFL-CIO and URW, 1974 URW, 1976 EDF, NRDC, CBE, etc.
Clean Air Act (Section 112, Hazardous Air Pollutants)	Vinyl chloride DDT Endrin Aldrin/dieldrin Benzidine PCB	
Federal Water Pollution Control Act (Section 307, Toxic Pollutants Effluent standards)			

(continued on following page)

Table 9.8 (continued)

Federal Insecticide, Fungicide, and Rodenticide Act	DDT	EPA, 1972	EDF, 1969
	Cyanamide	EPA, 1972	• • •
	Aldrin/dieldrin	EPA, 1974	EDF, 1970
	Vinyl chloride	EPA, 1974	HRG, 1974
	(aerosols)	EPA, 1974	
	Chlordane/ heptachlor	EPA, 1975	EDF, 1974
	Mirex	EPA, 1976	EDF, 1973
	Kepone	EPA, 1976	• • •
	Octamethyl- phosphoramide	EPA, 1976	• • •
	Safrole	EPA, 1977	• • •
Federal Food, Drug, and Cosmetic Act	Violet #1	FDA, 1973	CSPI
	Vinyl chloride	FDA, 1974	HRG
	(aerosols)		
	Chloroform	FDA, 1976	HRG
	(cosmetics)		
	Red #2	FDA, 1976	HRG
	Vinyl chloride	CPSC, 1974	HRG
	(aerosols)		
	Asbestos	CPSC, 1977	NRDC
	Tris	CPSC, 1977	EDF
Consumer Product Safety Act			

Source: S. M. Wolfe, "Standards for Carcinogens: Science Affronted by Politics," in *Origins of Human Cancer*, Book C, eds. H. H. Heath, J. D. Watson, and J. A. Winsten, (Cold Spring Harbor Laboratory, 1977) pp. 1735-48.

* OCAW=Oil, Chemical, and Atomic Workers Union; HRG=Health Research Group; URW=United Rubber Workers; EDF=Environmental Defense Fund; CSPI=Center for Science in the Public Interest; NRDC=Natural Resources Defense Council; CBE=Citizens for a Better Environment.

has not been a shortage of laws or ambiguities in the laws, but an unwillingness or inability of the agencies to enforce them.*

Statutory Authority There are two major types of statutory authority governing control of toxic agents and environmental and occupational carcinogens: *product legislation* and *media legislation* (Table 9.9). Product legislation governs the manufacture, distribution, and use of particular products, such as pesticides, food additives, cosmetics, and drugs. Media legislation governs quality of environmental "media," such as air, water, and the workplace.

Product legislation arises from recognition of the basic obligation of a manufacturer to provide a product of "merchantable quality" which has no harmful effects on the consumer other than those explicitly stated on the label.⁴⁵ Over the years, the government's authority has extended from simple labelling to the entire composition and manufacture of a product. More important, the burden of proof has gradually been shifted to the manufacturer, who now must prove the safety of his products rather than demanding that the government or public prove it harmful.

Media legislation attempts to regulate the discharge or emission of toxic and carcinogenic pollutants into the community and workplace environment, as recognized by the subsequent identification of those agents. As such, media legislation is retrospective rather than anticipatory in nature. It says, "By all means use the carcinogen, but don't let any of it or too much of it escape into the environment." Media legislation is specifically addressed to one particular environmental component, air, water, or the workplace, without consideration of the essential unity of the environment. In contrast, toxic substances legislation, while generally considered to be product rather than media in type, insofar as it relates to specific chemicals, is unique in that it can exercise multimedia control over chemicals in air, food, and water in the general environment, home, and workplace.

* An important exception to the adequacy of current legislation is its failure to require the retention of exposure and employment records in the absence of any known or suspected environmental or occupational hazards. This deficiency is all the more critical in view of the prolonged latent period of many cancers.

Table 9.9 Legislation Conferring Regulatory Authority for the Control of Environmental Carcinogens

Type of Legislation	Specific Authority	Regulatory Agency*
Product	Federal Insecticide, Fungicide, and Rodenticide Act	EPA
	Federal Food, Drug, and Cosmetic Act	FDA
	Consumer Product Safety Act	CPSC
	Safe Drinking Water Act	EPA
	Toxic Substances Control Act	EPA
Media	Federal Water Pollution Control Act	EPA
	Federal Clean Air Act	EPA
	Occupational Safety and Health Act	OSHA
	Federal Mine Safety and Health Amendment Act	MSHA

* EPA=Environmental Protection Agency; FDA=Food and Drug Administration; CPSC=Consumer Products Safety Commission; OSHA=Occupational Safety and Health Administration, Department of Labor; MSHA=Mine Safety and Health Administration, Department of Labor.

There is considerable overlap and inconsistency between the authorities of the various regulatory agencies. As an example, VC has been regulated separately on five different occasions by four different agencies: in 1974 by OSHA as an occupational carcinogen; in 1974 by EPA as a pesticide propellant; in 1974 by the Consumer Product Safety Commission in various household products; in 1975 by FDA in food and drug products; and in 1976 by EPA as a hazardous air pollutant.

While regulatory agencies depend on research institutes, such as NCI or NIOSH, for providing the essential data base and advice on which standards are developed, most regulatory agencies also have backup research and scientific resources of their own.

Burden of Proof The ability of an agency to regulate carcinogens and other toxic agents effectively is substantially

influenced by whether or not the burden of proof has been determined by statute to be its responsibility as opposed to that of the manufacturer, who may be required to provide the regulatory agency with information on safety prior to marketing and to update such information after marketing. Exceptions to such requirements in product-type legislation are chemicals in consumer products, regulated by the Consumer Product Safety Commission, and cosmetics, regulated by the FDA, where the onus is on government.

In media-type legislation, the burden of proving hazard for carcinogens and other pollutants, in community air and water and in the workplace is placed on the government. Toxic substances legislation offers EPA the discretionary authority to shift the burden of proof to the manufacturer. An exception to the general burden of proof rule can be made when an agency is petitioned to regulate, for instance, a particular carcinogenic chemical. Then the burden rests not with government or the manufacturer, but with the petitioner, almost invariably a public interest or labor group.

The Occupational Safety and Health Administration OSHA was created in 1970 as an agency within the Department of Labor after considerable lobbying by AFL-CIO and other labor organizations to create an Act that would "assure so far as possible every working man and woman in the nation safe and healthful working conditions" (P.L. 91-596).†

After the establishment of OSHA, it was delegated additional responsibility for a variety of health and safety programs within the Department of Labor (including the Walsh-Healey Public Contracts Act of 1936; the Service Contract Act of 1965; the Construction Safety Amendments of 1969; the Maritime Safety Amendments of 1958; the National Foundation on the Arts and Humanities Act of 1965; and the Federal Safety Program). Unlike its predecessor, the Bureau of Labor Standards which had

† A major deficiency in the Act is its failure to provide transfer and wage retention (rate retention) rights for workers whose health has been impaired or who are at increased risk from exposure to OSHA-regulated substances. Consequently, workers may hesitate to seek medical care or to remove themselves from dangerous exposures unless they are prepared to risk job loss or demotion. (This is in striking contrast to the Coal Mine Health and Safety Act which guarantees rate retention.)

mostly advisory power, OSHA has major regulatory authority, extending to about 2 million workplaces and 75 percent of the U.S. work force. Federal, state, and local government workers, and some other non-federal employees already regulated by the government, are excluded from OSHA jurisdiction. However, the Act allows individual states to administer their own occupational safety and health "state plans," provided these set standards and enforcement levels at least as stringent as the federal, and provided their administration is evaluated and approved by the OSHA Office of Federal State Operations.

In addition to its Washington, D.C., headquarters within the Department of Labor, OSHA has several directorates and regional offices through which it exercises local authority. From 1972 to 1979, OSHA's staff grew to an approximate total of 3,000, with a commensurate budgetary increase from \$37 million to \$163 million. Of the 1979 budget, about \$9.3 million are allocated to Safety and Health Standards, \$745,000 to the Occupational Cancer Information and Alert Program, and \$178,000 to the Experimental Technology Incentives R&D Program. In October, 1978, OSHA announced award of "New Direction" training grants totalling \$6.4 million (divided approximately equally between fiscal 1978 and 1979 funds) to 86 business, employee, and educational organizations for developing institutional competence in job safety and health.

The Occupational Safety and Health Act authorizes OSHA to establish and enforce three types of standards.⁴⁶ The first type are the approximately 400 initial (interim) consensus standards, established under Section 6(a) of the Act, previously developed as threshold limit values by industry or quasi-industry organizations, such as the American National Standards Institute. These were largely designed to protect against immediate toxic effects rather than delayed toxic and carcinogenic effects. In 1974, NIOSH and OSHA developed in a collaborative effort a "Standards Completion Process" to supplement and update the original 400 consensus standards (with the exception of carcinogens and certain other selected substances for which NIOSH is preparing individual criteria documents), which can all be covered by a single HEW standard.

The second type are the new permanent (complete) standards,

or modification of old ones, which are authorized under Section 6(b) of the Act and designed to assure "to the extent feasible that no employee will suffer material impairment of health." This is the language of compromise which reflects industrial determination of technological and economic feasibility, rather than the goals of health protection. Although NIOSH supplied OSHA with about one hundred criteria documents, the agency, burdened by fiscal constraints and intense political pressures under the Nixon and Ford administrations, has so far passed only ten new final standards of which eight deal with carcinogens: asbestos in 1972; vinyl chloride in October, 1974; a package of fourteen carcinogens without monitoring requirements in January, 1974; coke oven emissions in 1976; and benzene, acrylonitrile, DBCP, and arsenic in 1978 (See Table 9.10).‡

The third type of standards are the Emergency Temporary Standards, authorized under Section 6(c) of the Act, which may be imposed without the formal hearing requirement of the Administrative Procedure Act for a maximum of six months on grounds of "imminent hazard." Also embodied here is the ability of OSHA to abate these hazards without feasibility considerations. Emergency standards must be followed by proceedings to establish new standards or they are voided. Six sets of emergency standards, all based on carcinogenicity, have been developed over the last six years: in 1972, a standard for asbestos of 2 million fibers per cubic meter of air; also in 1972, regulation of a group of fourteen carcinogens without monitoring requirements, the permanent standard of one of which, MOCA, being subsequently successfully challenged on procedural grounds; a standard of 50 ppm for VC in April 1974; a 1 ppm standard for benzene in May, 1977; an emergency standard for dibromochloropropane in Sep-

‡ Probably the most important, precedential, and technology-forcing standard promulgated by OSHA was the November, 1978, lead standard, reducing permissible exposure levels from $200 \mu\text{g}/\text{m}^3$ to $50 \mu\text{g}/\text{m}^3$. (Major responsibility for drafting the standard belongs to John Froines, who in January, 1979, was appointed Deputy Director of NIOSH.) The Steelworkers Union immediately sued OSHA in the Philadelphia Third Circuit Court of Appeals on the grounds that the standard does not provide an ample margin of safety, that the lead time for compliance is excessive, and, presumably, to pre-empt the exclusive jurisdiction of the standard in the Fifth Circuit court in New Orleans, where it was known that the Lead Industry Association had planned suit.

Table 9.10 Final Standards Issued by OSHA

Standard	Date Issued	Number of Exposed Workers	In Effect
Asbestos	6/7/72	1,600,000	Yes
Carcinogens (14)	1/29/74	11,000	Mostly*
Vinyl chloride	10/4/74	10,000	Yes
Coke oven emissions	10/22/76	30,000	Yes
Benzene	2/10/78	600,000	Vacated
DECP†	3/17/78	2,000	Yes
Arsenic	5/5/78	12,000‡	Yes
Cotton dust	6/23/78	600,000	Stayed
Acrylonitrile	10/3/78	125,000**	Yes
Lead	11/14/78	835,000	Effective 2/79

Source: T. B. Clark, "Cracking Down on the Causes of Cancer," *National Journal* 10 (1978): pp. 2056-60.

* Regulation vacated for the most widely used of the fourteen carcinogens. There is no requirement for monitoring, nor are there any prescribed analytical techniques for this package of fourteen carcinogens, in contrast to the other carcinogen standards.

† This standard was issued primarily to protect against sterility, rather than carcinogenicity.

‡ Exact numbers unknown; 660,000 workers are involved in the "commercial cycle of arsenic."

** 10,000 are "most directly exposed."

tember, 1977; and an emergency standard for acrylonitrile in January, 1978.

Under the Nixon and Ford administrations, OSHA was subverted in a number of ways, including an inducement by Assistant Secretary of Labor George Guenther to stall standards-setting procedures in exchange for business support of the 1972 presidential election campaign.

The past record of OSHA has been one of extreme inactivity.⁴⁷ Inspections concentrated on such trivia as misplaced ladders and split toilet seats rather than seriously attempting to assess blatant health hazards from such substances as lead and asbestos. Fines averaged around \$50 per inspection, were often suspended on the company's promise of eventual abatement, and provided little economy incentive for compliance.

Under the leadership of Secretary Ray Marshall, and Assistant Secretary Eula Bingham, appointed to head OSHA in March,

1977, there has been considerable improvement in the activities of the Department of Labor for protecting workers against occupational carcinogens and other toxic agents. The standard-setting process has been strengthened and speeded up, and new policies on carcinogens and other health hazards have been proposed.* Inspectors have been instructed to overlook trivia and instead pursue obvious health hazards. Bingham has launched an aggressive recruitment campaign to secure committed and capable specialists, and is transforming OSHA into an effective agency.

Bingham has assigned top priority to promulgating "generic" standards for occupational carcinogens, drafted by Anson Keller, now Special Assistant for Regulatory Affairs at OSHA, during the latter part of the tenure of the previous OSHA Director, Morton Corn.⁴⁸ These standards lay down procedures for categorical rule-making to be followed once a chemical is shown to be a carcinogen, and are designed to obviate the virtually impossible task of separate rule-making for each individual carcinogen—an effort characterized by Secretary Marshall as "trying to put out a forest fire one tree at a time." While determination of carcinogenicity in these proposals is generic, as in the Delaney Amendment, subsequent rule-making for each carcinogen is, however, clearly individualized and not generic and likely to remain a protracted and difficult process. Public hearings and informal rule-making on the proposals commenced on May 16, 1978.[†]

Broadly speaking, three categories of carcinogens are recognized in the OSHA proposals. Category I substances are unequivocal carcinogens, as proven by human evidence, or two independent animal tests, or in one animal and one short term test. Category I classification must be accompanied by the issuance of an emergency temporary standard. Exposure to Category I car-

* The very low rate of promulgation of OSHA standards has been a critical rate-limiting factor in the control of occupational carcinogens. However, in addition to specific workplace exposure standards, other regulations which can be used to limit carcinogen exposure include standards requiring the removal of exposed workers and product-safety standards; besides OSHA, EPA and the Consumer Product Safety Commission are involved in the latter. Although only eighty carcinogen exposure standards have so far been promulgated, it is likely that these are beginning to influence the overall approach of big industry to the handling of other carcinogens and highly toxic substances.

† The author testified on behalf of OSHA on May 26.

cinogens would be allowed only at the lowest levels technically feasible, under controlled conditions with sensitive monitoring procedures, and with due warnings to all concerned. If safe substitutes are available, then continued use of the carcinogen could be banned completely. While emphasizing the goal of zero exposure, the OSHA proposals are flexible and include a wide range of regulatory options. These include continued use of the carcinogen with add-on pollution control devices, closed-system technologies, personal-control devices (in restricted conditions), product or process substitution, or ban.

Category II "suspect" classification is extended to chemicals found to be carcinogenic in a single animal test, in suggestive epidemiological studies, or in short term tests.[‡] Continued use of these carcinogens will be allowed in the workplace subject to standards designed to limit but not prevent exposure. Category III is for chemicals about which there is suspicion but insufficient evidence of carcinogenicity. These will not be regulated, but will be listed in government documents for public information. Category IV is for any chemicals not used in the American workplace.

Preliminary review by OSHA of the 2,415 chemicals on the NIOSH list of suspect carcinogens indicates that about 270 fall into Category I. These include some exotic laboratory curiosities which are unlikely ever to be used in industry, and other various derivatives of the same carcinogen, such as various nickel salts. It is, however, likely that the number of carcinogens which will require regulation will be in excess of 100. It must be appreciated that workers are being currently exposed to such carcinogens in the absence of substantive regulatory controls. It is also estimated that there are about 196 carcinogens in Category II, many of which will require permanent standards, and about 300 chemicals in Category III.

While the proposed OSHA regulations are clearly a move in the right direction, not only for the protection of workers, but also the general public, they clearly do not go far enough. The burden of proof for elucidating the status of Category II carcinogens appears to fall on government and the worker, and continued exposure is permitted during the interim period. Additionally, the pro-

[‡] OSHA is given discretion as to how results from short-term tests can be used.

posals contain broad "rebuttal" powers that allow OSHA to decide on a wide range of poorly defined grounds whether the carcinogenicity data are appropriate and relevant.*

Industry has reacted negatively to these proposals, criticizing the scientific basis of the standards and invoking the familiar specter of impossibly high costs. Industry reaction, however, has been far from uniform. Rohm and Haas and Hardwicke Chemical Company have both agreed that the policy is generally "feasible and workable."⁴⁹

In a concerted effort to fight these proposals, the Manufacturing Chemists Association has set up a special task force, the American Industrial Health Council, that represents some hundred and twenty companies and sixty trade associations and has raised funds in excess of \$1 million.† In January, 1978, the council produced a misleading and anonymous document which minimizes the significance and extent of cancer due to industrial chemicals (ignoring the fact that the majority of industries have not been evaluated for carcinogenic hazards), backed by voluminous statements from other industry and its academic consultants, attempting rebuttal of the OSHA position.⁵⁰ The apparent intent is to preclude effective regulation of occupational carcinogens and to play down the public health impact of carcinogenic industrial chemicals in the workplace and general environment.

On September 15, 1978, HEW Secretary Califano released a blue ribbon HEW draft document, "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors," prepared by ten internationally recognized and leading scientific

* The latitude allowed by the regulations is so wide that, in reality, few issues can be totally excluded from rule-making. Additionally, OSHA plans to conduct an individual notice and comment procedure for each of the 270 Class I carcinogens prior to the issuance of emergency temporary standards.

† Approximately one quarter of the Council's budget has been directed to "scientific" activities, and about one third to an economic impact analysis (by Booz, Allen, and Hamilton) of the "generic" regulations. Dow Chemical Company is exercising a role of leadership in the Council's activities similar to that it assumed on behalf of the chemical industry in attempts to defeat Toxic Substances legislation. The Council is chaired by Dow's Orrefice, and the treasurer, Keith McKennon, is also a Dow executive. The Council has made no secret of its intent to fight any attempt by EPA and the Consumer Product Safety Commission to establish "generic" type cancer standards.

authorities in chemical carcinogenesis, epidemiology, and biostatistics in the NCI, NIEHS, NIOSH, and the International Agency for Research on Cancer. The document concludes:

1. The estimates that only 1–5 percent of total cancers in the United States are attributable to occupational factors have not been scientifically documented and have little meaning for estimating even short-term future risks.
2. Most cancers have multiple causes: It is a reductionist error and not in keeping with current theories of cancer causation to attempt to assign each cancer to an exclusive single cause.
3. Because cancer incidence is strongly dependent on age and duration of exposure, and because most cancers occur late in life, many industrial epidemiological studies detect only a small fraction of cancers (i.e., those developing early).
4. Past exposure to asbestos is expected to result in up to 2 million excess cancer deaths in the next three decades: This would correspond to roughly 13–18 percent of the total cancer mortality expected in that period.
5. Reasonable projections of the future consequences of past exposure to established carcinogens suggested that at least five of them (benzene, arsenic, chromium, nickel oxides, and petroleum fractions) may be comparable in their total effects to asbestos.
6. These projections suggest that occupationally related cancers may comprise as much as 20 percent or more of total cancer mortality in forthcoming decades. Asbestos alone will probably contribute up to 13–18 percent, and the data (on the other five carcinogens) suggest at least 10–20 percent more. These data do not include effects of radiation, or effects of a number of other known chemical carcinogens.
7. Although exposure to some of the more important occupational carcinogens has been reduced in recent years, there are still many unregulated carcinogens in the U.S. workplaces; a number of occupations are characterized by excess cancer risks that have not yet been attributed to specific agents.
8. There is no sound reason to assume that the future conse-

quences of present-day exposure to carcinogens in the workplace will be less than those of exposure in the recent past.

9. Patterns and trends in total cancer incidence (and mortality) in the U.S. are consistent with the hypothesis that occupationally related cancers comprise a substantial and increasing fraction of total cancer incidence.

10. The conclusion that a substantial fraction of cancers in the United States are occupationally related is not inconsistent with conclusions that a substantial fraction of cancers are also associated with other factors, such as cigarette smoking and diet.

11. Occupationally related cancers offer important opportunities for prevention.

The HEW document (whose publication in final draft form is anticipated in 1979), is the first scientifically supported and detailed estimate of the importance of occupational carcinogens. This is in contrast to the undocumented earlier "guesstimates" of others, including the American Industrial Health Council, which have consistently failed to supply any data base on the numbers of carcinogen-exposed workers in U.S. industries. The statistical basis for the exposure calculations in the HEW document is derived from the NIOSH 1972 National Occupational Hazards Survey, based on a sample of 4,700 establishments out of an approximate 5 million total.

The document fully recognizes the importance of known non-occupational carcinogens (especially tobacco). The document also clearly recognizes the following considerations: that the major impact of occupational carcinogens is still in the future; that multiple factors (such as asbestos or uranium and smoking) may be involved in certain occupational cancers (and therefore the document analyzes associations between carcinogens and cancer, rather than necessarily implying exclusive causality); that relatively few epidemiological studies on cancer risk have been undertaken on an industry-wide basis; and that of the few epidemiological studies that have been done and published, the majority underestimate cancer risk as their cohorts have been followed for relatively short periods (as opposed to workers' lifetimes). However, the HEW document itself clearly underestimates the cancer

risk from occupational carcinogens. It fails to take into account radiation; carcinogenic exposure of agricultural workers; a wide range of epidemiologically known occupational chemical carcinogens other than just the six considered quite apart from a wider range still of carcinogens identified in animal tests; and cancer in the general public (community cancer) occurring as a result of discharge or escape of occupational carcinogens into the air, water, and hazardous waste disposal sites of the surrounding community.

Another important action by OSHA has been the proposal of a labeling standard which would require industry to identify by trade and chemical name, hazardous chemicals to which workers are exposed. A chemical would be considered hazardous that appears on any list such as the NIOSH list of suspect carcinogens. However, identification would not be required for untested chemicals, to which exposure could continue without the workers' knowledge. NIOSH has estimated that 90 percent of the chemicals in trade-name products to which workers are exposed are not identified by the industries concerned. The chemical manufacturers have "fought tooth and nail" to insist that this is the concern of industry and nobody else.⁵¹ There is, in fact, ample basis in the General Duty Clause and other sections of the 1970 Occupational Safety and Health Act to mandate disclosure and to develop appropriate safeguards in those rare instances in which trade secrets may be involved.

The failure of the Occupational Safety and Health Act to fully address the issue of access to proprietary data (on product ingredients and process technology), although several provisions of the Act such as the record-keeping requirements relate to it, is compounded by a longstanding body of state and federal law which impedes efforts at disclosure. Furthermore, while NIOSH may by subpoena require disclosure of product ingredients during hazard investigation,[‡] it is unclear whether these data can be made available to OSHA for regulatory purposes. In an effort to resolve these ambiguities, in July, 1978, OSHA issued a "Proposed Rule of Access to Employee Exposure and Medical Records" which requires that the employer shall make available to each employee,

[†] See *E. I. Du Pont de Nemours and Co. v. Finklea* (S.D.W.Va., December 20, 1977), 6 OSHC 1167.

former employee, or designated representative all relevant exposure and medical records. Such information should enable more clear recognition of the nature and identity of particular occupational hazards, and thus allow OSHA and labor to attempt their control. Industry has protested on several grounds, including that the rule will involve them in excessive paper work and that making the required information available will create confusion and alarm. Irrespective of OSHA initiatives, Toxic Substances legislation, once fully implemented (particularly in its pre-market notification and testing requirements), is likely to be the major regulatory method for identifying occupational carcinogens, though not necessarily in tracking them through the pipeline from manufacture to trade name products.

Bingham has also developed close working relationships with EPA, FDA, and the Consumer Product Safety Commission with whom, in October, 1977, she set up an interagency agreement to develop consolidated approaches to the regulation of toxic chemicals, including sharing resources and instituting compatible testing and compliance procedures.

In May 1978, Bertram Cottine, former attorney for the Health Research Group and assistant to Eula Bingham for the last year, won Senate confirmation as one of three members of the Occupational Safety and Health Review Commission following prolonged debate and vigorous opposition from national industrial organizations.

Outstanding problems which OSHA still has to resolve include the major difficulties in enforcing the Occupational Safety and Health Act in small businesses, as well as problems of employee-initiated inspections in non-unionized shops. Industry has fought hard to penalize employees who invoke their OSHA rights, docking their pay for time spent accompanying inspectors or firing them outright. An additional problem that OSHA must now contend with is posed by the Supreme Court (Barlow) decision of May 23, 1978, requiring OSHA inspectors to obtain search warrants before making "surprise" inspections in those instances where an employer does not voluntarily agree. However, OSHA will not have to show "probable cause" when it suspects that an employer is guilty of some violation. Surprisingly enough, the Barlow decision has not yet had any impact on plant inspections.

From May 23 until September 15, 1978, only about 612 of 59,171 inspections (1 percent) initiated by Federal and state health and safety compliance officers have been refused entry, presumably because of a lack of warrant. The decision has, however, imposed an increased administrative burden on the Solicitor's office.*

Another major problem posed to OSHA is the recent Fifth Circuit Court's decision (now under appeal to the Supreme Court) overturning the 1 ppm benzene standard, that economic feasibility is a prime determinant in standard setting, and that the government must make a specific "estimate of benefits supported by substantial evidence," before any standard can be promulgated. This ruling is in conflict with a wide range of previous legal decisions in which the courts have sustained standards even though OSHA had been unable to determine the precise effect of low-level exposure and thus to make the finding required by the Fifth Circuit (but not by the other Circuits) as to the extent of benefits that will result from reducing exposure to the lowest feasible level. The conflict created by the Fifth Circuit's decision requires immediate resolution. As of January, 1979, there are pending before Courts of Appeals three challenges to OSHA standards: inorganic arsenic (Ninth Circuit); cotton dust (Fifth and Third Circuits); and lead (D.C. Circuit). The validity of these standards, affecting hundreds of workplaces and thousands of workers, is at stake. Additionally at stake is the future of OSHA's proposal for "generic" regulation of occupational carcinogens. If the Supreme Court fails to resolve this conflict in OSHA's favor, industry by filing first with the Fifth Circuit will be able to use the benzene decision to defeat any new OSHA standard. Industry, however, will be unable to do this if the first petition is filed in other Circuits upholding the right of government to set standards without first proving benefits. As pointed out in the December, 1978, In-

* The American Conservative Union, which paid more than \$100 thousand in legal fees for Ferrol G. Barlow (a master plumber from Pocatello, Idaho) in his battle to bar OSHA inspectors, has contacted 170,000 employees previously inspected by OSHA in their *Stop OSHA* project, suggesting that they demand warrants before allowing inspections. In May, 1979, Melvin Booher, owner of a small lead-recycling company in Toledo, Ohio, was jailed for seven days for refusing entry to inspectors; three of his twenty employees had blood lead levels over 118 $\mu\text{g}/100 \text{ ml}$.

dustrial Union Department, AFL-CIO, benzene petition to the Supreme Court:

The mischief created by this situation was recently highlighted by a courthouse race which ended in a dead heat when those who thought the new standard governing occupational exposure to lead ($50 \mu\text{g}/\text{m}^3$) went too far filed in the Fifth Circuit while those who felt the standard did not go far enough simultaneously filed in the Third Circuit.

OSHA's ability to implement the Occupational Safety and Health Act is also critically limited by a shortage of trained personnel (particularly industrial hygienists, epidemiologists, and clinicians). Of a total of 1,000 OSHA inspectors, only 250 are trained occupational hygienists capable of conducting full-scale safety and health inspections; 85 percent of all 1977 inspections were for safety, and 17 percent for health. This contrasts with the approximately 4,500 trained hygienists working for industry (approximately one tenth of which number work for organized labor). Personnel problems aside, OSHA also lacks adequate instrumentation to monitor carcinogens effectively in any but a very small number of the numerous workplaces covered by OSHA regulations. OSHA's compliance and enforcement abilities are similarly restricted by lack of intramural resources in industrial technological innovation (such as product and process substitution), and by inadequate allocations for R&D in new technologies for carcinogen control (\$178,000 in 1979). The New Directions Program does, however, offer OSHA the possibility of developing extramural resources in pollution control R&D. NCI's contribution to this critical area is similarly meager, and is restricted to a few contracts on pollution control R&D (Stanford Research Institute has produced three documents on carcinogens (DES, vinyl chloride, and asbestos) under contract to NCI, which include analyses of control strategies for occupational and non-occupational exposures). EPA, however, does support considerable research on pollution control technology, some of which is relevant to occupational exposures. It is, however, clear that (for reasons that include limited federal resources, the concentration of such resources in industry, and the large number of workplaces

to be regulated) OSHA must rely on voluntary compliance and the affirmative duties of industry, both under the Occupational Safety and Health Act and Toxic Substances legislation.

The Environmental Protection Agency (EPA) The current administrator, Douglas M. Costle, was appointed on March 11, 1977. Costle, formerly a member of the Congressional Budget Office staff and head of the Connecticut Department of Environmental Protection, also served in 1969 on the Presidential Ash Committee, which had a major role in designing the EPA.

EPA has extensive legislative authority to control carcinogens under six separate statutes. This includes three media-type laws, the Clean Air Act, the Federal Water Pollution Control Act, and the Resource Conservation and Recovery Act, and three product-type laws, the Federal Insecticide, Fungicide, and Rodenticide Act, the Safe Drinking Water Act, and the Toxic Substances Control Act.

1. *The Clean Air Act.* This 1970 Act provides broad authority for establishing primary ambient air quality standards for dispersed pollutants from stationary and mobile sources, performance standards for stationary sources, regulations for fuel additives, and emission standards for hazardous air pollutants. Section 112 to the Act is designed for the strict and uniform regulation of hazardous air pollutants, those which pose risks of serious adverse effects, particularly cancer, at relatively low exposure levels.⁵² While EPA has discretionary authority for listing an air pollutant as hazardous, it has shown a strong reluctance to do so, as opposed to achieving controls through more flexible provisions of the Act. Once a substance is designated as a hazardous pollutant, mandatory rule-making procedures are put into effect within one year. (This is the shortest time required by any pollution legislation, involving preparation of a criteria document and proposing and promulgating a standard.)

Emission standards have been developed for only four hazardous air pollutants including mercury, and three carcinogens, beryllium and asbestos in April, 1973, and VC in October, 1976. In addition, EPA proposed a benzene standard in 1977. How-

ever, it is questionable how meaningful these standards really are. That for asbestos is based only on visible emissions and the use of work practices, such as wetting down buildings during demolition, and tends to be more honored in the breach than in the performance. The VC standard is supposed to limit emissions from all sources to the limits of best available technology, but excludes the innumerable PVC fabrication plants scattered all over the country. Recognizing these various problems, the Environmental Defense Fund petitioned EPA in June, 1977, for more stringent standard setting, with the goal of zero emissions for carcinogenic hazardous pollutants.

2. *The Federal Water Pollution Control Act.* This 1948 law, amended in 1972 and 1977, is one of the most complex and extensive pieces of environmental legislation ever passed, and perhaps the most difficult to administer.⁵³ Its philosophy is that all water pollution is undesirable and should be reduced to the extent technology allows, rather than to the extent dictated by health considerations alone. Like the Clean Air Act, the Water Pollution Control Act contains a wide range of provisions: new source standards (Section 306), oil and hazardous substances regulation (Section 311), water quality standards (Section 303), water quality related effluent standards (Section 302), and toxic effluent standards (Section 307).

Toxic effluent standards are aimed primarily at limiting the industrial discharge of toxic pollutants that can induce cancer and other serious effects.† The standard takes into account problems of persistence and pollutant degradability in water. However, there is a built-in contradiction in a standard which must be set, regardless of economic considerations, at a level which provides an "ample margin of safety," knowing full well that there is no known safe level for any carcinogen.

In 1973, EPA listed nine pollutants under Section 307 and, following a consent agreement stemming from extensive litigation with public interest groups and industry, promulgated standards for six carcinogenic toxic water pollutants in 1977: DDT, aldrin,

† Industrial discharge from point sources are regulated by the National Permit Discharge Elimination System. This system, however, cannot be used to regulate non-point sources of pollution such as agricultural runoff of pesticides and fertilizers and municipal stormwater runoff.

dieldrin, toxaphene, endrin, PCBs, and benzidine. Zero effluent limits were set for DDT and aldrin/dieldrin, which EPA had already banned, while numerical limits were set for effluents of benzidine and PCB. Under the consent agreement, EPA has designated about 140 other toxic pollutants subject to control by "best available technology" in 21 priority industries.

3. *The Resource Conservation and Recovery Act.* This 1976 Act, which amends the Solid Waste Disposal Act, creates a regulatory framework to control hazardous wastes. The Act is designed to comprehensively regulate hazardous wastes, particularly those contaminated by carcinogens, from generation through transport to disposal, and management of disposal sites. The Act does not, however, consider proximity of these sites to inhabited areas or potential adverse effects of toxic run-off to water. The Act aims to systematize the chaotic and inconsistent regulation of hazardous waste-disposal sites at a state level. Currently, forty-six states have some regulatory authority over hazardous waste disposal, although only California fully implements a hazardous waste program. Only fourteen states have designated hazardous waste-disposal sites, of which there are estimated to be over 1 000 nationwide, and only one of these sites (in Massachusetts) is located in an eastern state, where over 40 percent of the nation's hazardous wastes are generated. The proposed regulations containing minimal criteria for determining which solid waste land disposal facilities shall be classified as having no reasonable probability of adverse effects on health or the environment were published by EPA in the Federal Register on February 6, 1978, followed by a notice of proposed rulemaking on December 18. EPA was required by the Act to have promulgated these standards by April 1978. However, it is unlikely that they will be issued prior to January, 1980.‡

A November, 1978, EPA study was undertaken for an in-

‡ In September, 1978, Illinois Attorney General William J. Scott filed suit against EPA for having failed to issue these regulations, asking that EPA be required to develop these within the next 30 days. ("Wilsonville Battles a Landfill." Special Staff Report, Illinois Issues, August, 1977, pp. 4-6.) In his suit, Scott stated that disposal of toxic wastes in Illinois, which he has repeatedly called the "dumping ground of the nation," is going to become one of the biggest problems in the country in the near future unless it can be controlled.

teragency task force created to investigate the Love Canal crisis (R. P. Whalen, New York State Commissioner of Health, "Love Canal: Public Health Time Bomb." A Special Report to the Governor and Legislature of the State of New York, September, 1978). This reported that there are more than 30,000 sites, many of which since abandoned by their owners, where toxic wastes may have been improperly dumped. EPA also identified 103 specific sites, including municipal landfills, industrial dumps, and abandoned mining sites, where potential health hazards have already been documented. The agency report concludes that improper disposal of hazardous and carcinogen-containing wastes may be widespread and "constitutes an extremely serious environmental problem." Administrator Costle further commented that such improper disposal affects as much as 90 percent of all hazardous wastes.*

4. *Federal Insecticide, Fungicide, and Rodenticide Act.* Passed in 1947, this Act was designed to protect consumers from ineffective products and to warn with appropriate labels against toxic effects, without consideration of carcinogenic and other chronic toxic or ecological effects. The Pesticide Regulation Division of USDA failed to enforce even these minimal requirements. This contributed to the decision to transfer regulatory authority for pesticides to EPA after its creation in 1970.⁵⁴ The thrust of this move was, however, blunted by the simultaneous transfer to EPA of USDA Pesticide Regulation Division personnel. These personnel were regrouped in the EPA Office of Pesticide Programs, where they have perpetuated USDA traditions of excessive protection of agrichemical interests at the expense of other considerations. In this, they have been further aided by the USDA, which has supported industry against EPA in all major proceedings to ban carcinogenic pesticides.

* Stimulated by the Love Canal disaster, two bills to amend the Resource Conservation and Recovery Act were introduced in October, 1978, by Rep. John L. LaFalce (D-N.Y.): H.R. 14338, which establishes a program for identification and reclamation of abandoned hazardous waste sites and provides for a process for the selection of future sites for hazardous waste disposal; and H.R. 14301, "Toxic Pollution Compensation Act," designed to provide non-exclusive Federal relief to all persons injured as a result of toxic pollutants and to ameliorate the burden of proof and statute of limitation requirements, while retaining the fault concept that will enable recovery of compensation payments from individuals or industries responsible.

An additional serious problem which has adversely influenced EPA pesticide policies was and is the congressional jurisdiction which the House and Senate agriculture committees continued to exercise after the transfer of regulatory authority for pesticides from USDA to EPA.⁵⁵ The agriculture committees have traditionally been preoccupied with narrowly focused agrichemical interests and have failed to grasp the need to regulate pesticides to protect public health and the environment. On occasions when EPA seems about to deal decisively with a pesticide problem, the agriculture committees threaten to cancel its authority over pesticides and to transfer it back to USDA.

An example of the power exercised by the House Agriculture Committee is the 1976 bill H.R. 8841, amending the 1947 Act, which, as passed in a somewhat modified form by Congress, severely restricts the authority of EPA to regulate pesticides. The thrust of H.R. 8841 is to give the Secretary of Agriculture virtual veto power over EPA's suspension and cancellation decisions. EPA is required to notify USDA at least sixty days prior to proposing any pesticide regulations and also to similarly notify the House Committee on Agriculture and the Senate Committee on Agriculture and Forestry. EPA is further required to publish any comments of the USDA in the Federal Register at the same time of publication of final regulations. These seemingly harmless provisions carry the implicit threat of political reprisals if EPA ignores unfavorable comments by USDA on proposed pesticide regulations.

The exclusive jurisdiction of the agriculture committees over pesticide regulation by EPA is further anomalous in view of the fact that about half of all pesticide usage in the United States is for non-agricultural purposes (See Table 7.2). Strong public support is needed to ensure that the House and Senate commerce committees, which represent more broadly based interests, be given a share in the congressional authority over pesticides.

The 1947 Act was substantively amended in 1972, by the Federal Environmental Pesticide Control Act (FEPCA).⁵⁶ The amendments express the intent of protecting against "unreasonable adverse effects on man or the environment," and place the burden of producing evidence of safety on the manufacturer. The manufacturer is required to produce evidence of safety and

effectiveness when petitioning EPA for registration of products. Pesticides can then be classified for general use or for restricted use by trained applicators only. Registrations are automatically cancelled after five years, unless the manufacturer reapplies with updated information. EPA has the power to suspend manufacture on an emergency interim basis if "imminent hazard" can be proven. Otherwise, banning is by a protracted adjudicatory hearing that can stretch over years, during which the pesticide can be used without hindrance. EPA also has responsibility for setting tolerance levels of pesticide residues on foods, which are then enforced by the FDA.

Over the past eight years, EPA has taken regulatory action against only a handful of pesticides. Some of these were no longer in production at the time of the action, such as octamethylphosphoramide, and some of these actions were initiated at the manufacturer's request, as was the case with safrole (also used as a flavoring agent in root beer). The agency has undertaken successful proceedings only against DDT, aldrin/dieldrin, Mirex chlordane/heptachlor, and VC (used as a propellant in pesticide aerosols). However, all these latter actions were only initiated under threat of legal action by public interest groups (Table 9.5).

These limited regulatory actions taken by the EPA aroused intense opposition from industry, supported by the congressional agriculture committees. In July 1975, EPA announced new regulations for re-registration of all currently used pesticides and for registration of new pesticides.⁵⁷ This move coincided with an internal reorganization of pesticide policy in EPA in November, 1974, which effectively wiped out any authority for the Office of General Counsel and gave almost exclusive authority to the Office of Pesticide Programs. The new regulations defined EPA's understanding of "unreasonable adverse effects on man or the environment" in terms of chronic toxic, mutagenic or carcinogenic effects. Pesticides producing these effects are subject to a "Rebuttable Presumption Against Registration" (RPAR). The manufacturer is given ninety days to rebut this presumption on grounds that include the risks being outweighed by the benefits, following which EPA is required to take final action within six months. While in principle this approach may be sound, the agency's im-

plementation of the new regulations can only be regarded as public window dressing. So far, EPA has initiated RPARs against about forty-five pesticides, none of which however, has yet been brought to final action.[†] In three instances, the pesticides concerned, endrin, chlorobenzilate, and chloroform (an "inert" pesticide ingredient) are carcinogenic.

EPA's record on regulation of pesticide residues in food is as gravely deficient as its record of pesticide regulation.⁵⁸ EPA is responsible for establishing all tolerances for pesticide residues on the basis of data submitted by industry as to the nature, level and toxicity of the residue. Any residue on food is considered unsafe unless a tolerance has been established and the remaining residue

[†] With the exception of voluntary cancellations of kepone and DBCP, EPA has initiated no cancellation proceedings against any pesticide since November, 1974. An illustrative example of non-action on an RPAR candidate is the case of the herbicide 2,4,5-T, a chemical with a tortuous regulatory history. In 1969, the Mrak Commission recommended that this (and its related derivatives, including 2,4-D), be banned because it induced birth defects (teratogenic). Even though a petition for suspension (followed by a law suit) was subsequently filed with the USDA in 1970 by Nader's Center for the Study of Responsive Law, it was not until 1974 that the EPA canceled most uses of 2,4,5-T. However, the day before the adjudicatory hearing was to have begun, EPA withdrew the cancellation notice and postponed the hearing indefinitely on the grounds that they did not have adequate monitoring data for TCDD, the toxic contaminant of 2,4,5-T, in the environment and human tissues. While EDF denounced this move, as the EPA's assumption of the legal burden of proof which should properly rest with the manufacturer, EPA has continued the stance of not being able to take action on this herbicide until indisputable evidence of human contamination exists. However, every time monitoring programs reveal TCDD residues, be it in beef fat or in human breast milk, industry takes exception to the findings and EPA announces that it will perform yet another test, a procedure that takes one or two more years. While independent scientists and environmentalists claim there is currently more than adequate evidence to suspend, 2,4,5,-T under the RPAR procedure and hence eliminate exposure to TCDD (the most potent carcinogen known to man, one hundred million times more potent than saccharin and ten times more potent than aflatoxin), EPA seems to be waiting for further indisputable evidence of human toxicity. Following disclosures of excess numbers of miscarriages in Alsea, Oregon, women who had been exposed to repeated spraying with 2,4,5-T and 2,4-D by the Forestry Service, on March 1, 1979, EPA announced emergency suspension of 2,4,5-T and Silvex, but not of 2,4-D, for major agricultural uses, excluding rice fields and cattle rangelands. While emphasizing the hazards of TCDD as a contaminant of 2,4,5-T and Silvex, EPA, however, failed to make any reference to 2,4-D and the probability of its incrimination in the miscarriages. On April 2, a federal court in Flint, Michigan, denied a request by Dow Chemical to delay the suspension.

is within the limits of tolerance. Authority is shared with the FDA, which is responsible for enforcing pesticide tolerances by testing food samples. FDA can remove from interstate products any food containing residues in excess of established tolerances.

A 1975 report to Congress entitled "Federal Pesticide Regulation Program: Is It Protecting the Public and the Environment Adequately from Pesticide Hazards?" showed that EPA established many tolerances without sufficient test data to determine levels of pesticide residues on crops and the potential of the pesticide to induce carcinogenic and other toxic effects.⁵⁹ Further, EPA registered pesticides for use on food and feed crops without setting tolerances.

As of May, 1976, EPA had examined about 890 of the approximately 1,400 active ingredients of over 40,000 pesticide products.^{‡⁶⁰} Only about 419 ingredients examined had sufficient backup data to allow any assessment of risk, and of these, about 238 fell in a high risk category, 80 percent of which were "suspect carcinogens." These suspect carcinogens are incorporated in about one-third of all pesticide products currently on the market.

In 1976, an EPA consultant reviewed carcinogenicity test data on twenty-four pesticides with the highest tolerances on common foods. His report concluded that, with the possible exception of data on one pesticide, all other data which EPA had used to set tolerances were so inadequate and defective that no reasonable conclusions could be drawn from them.⁶¹

EPA seems to have effectively eliminated oversight of its pesticide policies at the agency level by disbanding the Federal Working Group on Pesticides and the Pesticide Policy Advisory Committee. However, in April, 1977, EPA informed the General Accounting Office that its Science Advisory Board had been asked to study the tolerance-setting program. A subcommittee appointed for this purpose met first in February, 1978, and submitted a sharply critical preliminary report in October, 1978.*

[‡] Twenty-five basic ingredients account for about 75 percent of total agricultural sales. The Office of Pesticide Programs, in a misleading numbers game, has claimed that as many as 40,000 pesticides (formulations) will need to be reviewed for the registration process, rather than just the few hundred (active ingredients) properly requiring review.

* At this meeting, the author (as a member of this subcommittee) raised questions as to the validity of the industrial data based on pesticide toxicol-

Meanwhile, EPA has made little serious attempt to rectify the deficiencies in its tolerance setting programs as indicated in a 1978 General Accounting Office report which concluded "that the American public had not been adequately protected from the potential hazards of pesticide use because of inadequate efforts to implement existing Federal laws."⁶²

During the 1977-78 congressional proceedings to reauthorize EPA's pesticide authority, the Office of Pesticide Programs, with enthusiastic industry support, formulated and successfully advocated a series of weakening amendments to the 1972 Pesticide Act (the Federal Pesticide Act of 1978, P.L. 95-396). EPA now has authority to grant three types of conditional registrations: to pesticides identical or substantially similar to current registered pesticides (many of which have been previously registered on the basis of inadequate or defective data); to pesticides with new ingredients not contained in currently registered pesticides; and to pesticides that are registered, but for which new uses are sought. Public health concerns on "conditional registration" largely reflect the broad and virtually unrestricted authority given the agency.[†] As such, this amendment could effectively negate the registration requirements of the 1972 Act in that it permits potentially hazardous and extensive public exposure from continued or new uses of pesticides for which safety and related data have not yet been generated or, if on file with the agency, have not yet been reviewed for adequacy and validity. "Minor Use Registration" is another weakening amendment that allows considerations of "economic factors" relating to costs of providing safety, residue chemistry, and related data to influence the agency's requirements for registration of pesticides for "minor uses." Such registration would subsidize the industry at the expense of potential public health costs, particularly for those segments of the population with heavier than average consumption of minor crops. Perhaps the most dangerous of all amendments are those that grant new

ogy. In a private letter of November 30 to EPA Administrator Costle, Jack Early, President of the National Agricultural Chemicals Association, complained that this was insulting and harassing to industry scientists.

[†] For an effective critique of conditional registration, see "Statement of the Environmental Defense Fund and the National Audubon Society at the November 6, 1978, Public Hearings on EPA's Interim Final Regulation of FIFRA as Amended, September 30, 1978."

powers to states to register pesticides with minimal EPA supervision, and to enforce their regulation.

Even taking into account legislative ambiguities and pressures from industry and the congressional agriculture committees, the record of EPA on pesticides has been and continues to be unacceptable. The strictures of an earlier congressional report seem at least as apt now as when they were written:

. . . pesticide regulation in the United States is fundamentally deficient. Pesticide regulation has failed to include many obvious and prudent steps to better protect public health and the environment. Moreover, the severe inadequacies of pesticide regulation are not attributable in any significant way to deficient legislation. Rather, the principal cause lies with EPA's poor administration of the program, including its failure to recognize and correct serious program deficiencies as they arose.⁶³

5. The Safe Drinking Water Act. While the Federal Water Pollution Control Act is media-type legislation designed to limit the discharge of toxic pollutants into surface and other waters and to control pollutant levels, the Safe Drinking Water Act is a product-type legislation specifically designed to regulate the purity of treated drinking water. As pollutants discharged into surface water are likely to eventually find their way into drinking water unless they are unstable or infinitely diluted, it is unfortunate that there is not a greater consistency in the language and intents of the two laws.

The Safe Drinking Water Act was passed in 1974 in response to pressures by the Environmental Defense Fund and public alarm at the high levels of carcinogens and organic pollutants found in the drinking water of New Orleans. According to the Act, every community water supply serving twenty-five or more people must meet certain minimum standards of purity, thus involving a national total of about 40,000 community water supply systems. "National Interim Primary Drinking Water Regulations" went into effect in 1977, and cover ten chemicals, including the carcinogens arsenic, cadmium, chromium, endrin, lindane, toxaphene, and methoxychlor. Strangely, EPA's current informational pamphlet "Is Your Drinking Water Safe?" claims that

"radioactivity is the only contaminant for which standards have been set that has been shown to cause cancer."

Concerns have been expressed about the finding of high levels of the carcinogenic chloroform in drinking water treated by chlorine. Chloroform and much higher levels of other related (trihalomethane) compounds, most of which are toxicologically active though still unidentified, are produced following chlorination of water heavily contaminated with organic pollutants.‡ The answer is not necessarily to stop chlorination, but to limit discharge of toxic and carcinogenic pollutants into surface waters, which ultimately reach drinking water supply systems, and also to effectively treat drinking water by passage through activated carbon filtration systems prior to its chlorination.

Responding to further pressures from the Environmental Defense Fund, in January, 1978, EPA proposed to regulate four of the main trihalomethanes, of which chloroform is typical, produced from organic pollutants by the chlorination of water, in order to reduce total levels of trihalomethanes to below 100 ppb.⁶⁴ EPA also proposed that all cities with more than 75,000 people should be required to design and operate a treatment system which uses granular activated carbon filters or an equivalent technology in order to reduce levels of synthetic organic pollutants to the maximum extent feasible. Variances can be granted only if it can be demonstrated that such treatment is unnecessary. Estimated household costs for treatment range from \$7 to \$26 a year.

These proposals are part of a phased implementation program which, over time, will be expanded to cover all public water supplies in the United States. The proposals represent the most significant advances in drinking water treatment since passage of the 1976 Act. They represent the first serious attempt to control contamination of drinking water with synthetic organic contaminants.* It should be recalled that over 700 synthetic organic

‡ Resulting levels of chloroform and trihalomethanes in drinking water in general far exceed concentrations of other synthetic organic pollutants. Chloroform levels are approximately correlated with total organic carbon levels in water.

* Apart from chloroform and other trihalomethanes which are often found in the 100 ppb range, the other organics most commonly found in the low ppb range are pentachlorophenol, dichlorobenzene, trichloroethylene, carbon tetrachloride, and 1,2-dichloroethane.

chemicals, including many carcinogens such as chloroform, carbon tetrachloride, benzene, vinyl chloride, lindane, aldrin, and bischloroethylether, have been identified in drinking water. The organic chemicals so far identified represent only a small fraction of total organic material in drinking water.

Illinois and some other states, backed by the American Water Works Association, are opposing these regulations on various grounds.⁶⁵ These include questioning the significance and public health relevance of the carcinogenicity of chloroform and other organic contaminants in water and asserting that the costs of carbon treatment are exorbitant. The position of the states reflects lack of appreciation of fundamental principles of environmental carcinogenesis and of the fact that failure to regulate creates costs greatly in excess of those of regulation.

6. *Toxic Substances Control Act.* Passage of the Act on October 11, 1976, culminated six years of bitter struggle during which a powerful industry lobby pulled out all stops to defeat this legislation.⁶⁶ The resistance was spearheaded by Dow Chemical Company and the Manufacturing Chemists Association, which formed a semi-autonomous standing committee empowered to lobby without checking back to individual industries for approval. This striking change from previous practices indicates the mood of crisis within the industry.

The legislation authorizes the EPA administrator to require information necessary for standard-setting on new chemicals and for chemicals in current use, with the exception of chemicals covered by other legislation.^{†67} The legislation, while not authorizing the routine need for information, shifted the burden of proof away from the government and public and placed it firmly on the manufacturer. While the legislation is specifically directed to chemicals, it reflects patterns of use and distribution in the environment, water, air and the workplace, and is thus multimedia as well as product in type. Key provisions of the law are:

- Industry must give EPA ninety days notice before marketing a new chemical, including proposing "significant new uses" of existing chemicals. Data must be provided on structure, composition,

[†] As consultant to the Senate Committee on Public Works, the author developed the first draft of a bill, "The Environmental Protection Act of 1971," which formed the basis of subsequent toxic substances legislation.

uses, quantity to be produced, byproducts of manufacture, health or environmental effects, and numbers of workers expected to be exposed. While some guidelines are offered on data that may be required on health effects, no such information is provided in the Act for environmental effects.

- EPA must draw up an inventory of existing chemicals to be exempted from premarketing notification requirements, but not necessarily from later challenges.‡
- Each year, an intergovernmental agency group (known as the Committee of Eight) will select no more than fifty potentially hazardous chemicals, particularly chemicals suspected of being carcinogens, and recommend priority for their testing to the administrator.
- Industry must keep records of significant adverse health effects caused by any chemical for thirty years and of environmental damage for five years.
- Chemicals produced in small quantities for research and development will be exempted from premarket notification. So also will be small businesses, i.e., those with fewer than thirty employees at any one time.*
- Pesticides, tobacco, drugs, cosmetics, food additives, and nuclear materials are exempt from the law, since they are covered by other regulations.
- The Act allows petitions and suits from citizen and public interest groups who wish to challenge EPA decisions.

The main thrust of the law is that if, based on pre-market data, EPA believes a new chemical to be hazardous, within forty-five days the agency must give industry notice of intent to ban. EPA can also seek a court injunction restricting or banning chemicals it believes are "imminently hazardous," and can also take appropriate action against chemicals it considers "unreasonable risks."

‡ Import of toxic chemicals is covered by the law, but inadequately so.

* This exemption allows the license to small business to handle toxic and carcinogenic chemicals and products with virtually no control other than that theoretically available under the Occupational Safety and Health Act. This highest risk group in the chemical industry is generally non-unionized and often transient and ethnic labor.

This legislation is potentially the most important single preventive public health measure of the century.⁶⁸ For the first time, there is the opportunity of controlling industrial chemicals and anticipating carcinogenic and other adverse effects, rather than reacting to their occurrence.[†] However, there is little indication yet as to how well this potential for control will be exercised.

Congress initially allocated a first-year budget of \$10 million for the Office of Toxic Substances in EPA, created to implement the new legislation. About 10 percent of the 1979 EPA budget (\$5.63 billion) is allocated to the Toxic Substances program (\$56.7 million), of which \$4.2 million is for "Abatement and Control," \$10.5 million for R&D, and \$4.6 million for Enforcement. Even this increased figure is small compared to the \$150 million budget of the first year of the Clean Air Act.

The costs to industry of toxic substances legislation were estimated in 1975 by EPA and the General Accounting Office to range from \$80 to \$200 million. These estimates contrast strikingly with estimates of \$2 billion by the Manufacturing Chemists Association and Foster D. Snell. The maximal government estimate of \$200 million, based largely on costs of carcinogenicity and chronic toxicity testing, represents about 0.3 percent of the chemical industry's total 1975 sales of \$72 billion and 3.6 percent of its net profits after taxes of \$6.5 billion.

Enforcing toxic substances legislation is probably the most complex and ambitious task any regulatory agency has ever had to face.[‡] EPA has been slow to respond, and its toxic chemical program is still embryonic, although it is now attempting to scale up recruiting efforts for much needed professional personnel. So far, EPA has failed to encourage adequate public participation in its planning and activities.

The administration's concerns with inflation, together with the apparently waning interest of Congress, are now emerging as possible threats to the toxic chemical program, particularly in view of

[†] For instance, this legislation affords a comprehensive basis for control of industrial uses of toxic and carcinogenic chemicals by setting occupational standards, with the concurrence of OSHA, and also regulating their emission into the surrounding community.

[‡] A further example of the unresolved complexity of the legislation is the problem of alleged trade secrets and the interagency sharing of such secrets. Invoking trade secrecy is a key element in evolving industry strategies to fighting the legislation.

the legislative requirements of the Act to consider the costs and benefits of proposed regulation. Illustrative of the administration's position are the emphasis by Commerce Secretary Juanita M. Kreps and Robert Strauss, Special Presidential Counsel on Inflation, on the high costs of regulation to industry. Recent estimates by Chase Econometrics concluded that total costs of EPA programs add less than 0.4 percent annually to the consumer price index. However, as Costle recently pointed out, such estimates do not take into account improvements to public health, reduced property damage by air pollutants, increased crop yields, and many other benefits that result from pollution control spending.

Consumer Product Safety Commission The Commission was established in 1973 by the Consumer Product Safety Act (CPSA), incorporating the Federal Hazardous Substances Act, the Flammable Fabrics Act, the Poison Prevention Packaging Act, and the Refrigerator Safety Act. The Commission was given responsibility for some 10,000 consumer products, excluding those (such as tobacco, drugs, pesticides, cosmetics, and foods) over which other agencies have jurisdiction. The Commission does not have authority to require pre-market registration of consumer products, and must therefore meet the burden of proving hazard due to "unreasonable risk of injury" before it can regulate.

Prior to the CPSA, Congress enacted product safety legislation haphazardly, reacting to specific hazards rather than adopting a broad product safety statute. With the passage of CPSA, responsibility for overall product safety was consolidated within a single agency and many more consumer products became subject to regulatory authority than were previously covered by safety legislation. The Commission is specifically mandated by the CPSA to protect the public against unreasonable risks of injury from consumer products, to assist consumers in evaluating product safety, to develop standards for consumer products, to minimize conflicts of these standards at the Federal, state, and local level, and to promote research into the causes and prevention of product-related deaths, illnesses, and injuries. However, the Act is a poorly conceived attempt to fill in legislative "cracks." It is anachronistic in shifting the burden of proof from the manufacturer to the government, which must prove hazard before it can

regulate. Statutory limitations aside, the Commission, in its early phases, has not been an aggressive regulator.

The Commission has become increasingly involved in the regulation of chronic, as well as acute, hazards posed by consumer products. In 1974, the Commission was petitioned by the Health Research Group to ban VC propellants in household aerosol products. However, the final order effectively banning such products was delayed until March, 1978, because an earlier order was successfully challenged in court on procedural grounds. In April, 1977, following a petition from the Environmental Defense Fund, the Commission banned the use of Tris as a flame retardant on children's sleepwear. While a court ruled against this action on procedural grounds, the Commission, however, proceeded against Tris garments in individual enforcement actions, and a federal appeals court has sustained this approach in an October, 1978, decision. The court additionally affirmed the Commission's authority to seize without first having a formal hearing in the district court, and also affirmed that the statute does not authorize post-seizure export. In December, 1977, the Commission issued a final regulation banning consumer patching compounds and artificial emberizing materials (embers and ash) containing respirable free-form asbestos. Reacting to a May, 1977, petition from the Health Research Group and the Center for Occupational Hazards, in the following year the Commission proposed a ban of benzene-containing consumer products, except gasoline and laboratory benzene. The public comments on the proposal are currently being analyzed by Commission staff prior to a possible ban.

In June, 1978, the Commission issued an interim cancer policy statement based in general on the OSHA "generic proposals" concerning the classification, evaluation, and regulation of substances that, if present in consumer products, pose a carcinogenic risk to consumers. A court decision in November, 1978, however, enjoined the implementation of the classification aspect of the proposal, pending issuance of a final policy.

The Commission had come under substantial criticism from consumer groups and from some Congressmen for its regulatory tardiness. In December, 1977, the General Accounting Office issued a report criticizing the Commission for dragging its feet in developing and issuing safety standards and in setting priorities,

and for keeping inadequate records on product-related injuries.⁶⁹ On February 8, 1978, the embattled chairman of the five-member Commission, S. John Byington, announced his resignation effective June 30, charging that he had been a victim of political harassment by the Carter administration.* His resignation was applauded by Rep. John E. Moss (D-Cal.) as "a very significant public service," and by Senator Wendell E. Ford (D-Ky.) as "in the best interests of the Agency."⁷⁰

On July 1, 1978, Susan B. King succeeded Byington as Chairman, declaring her commitment to make the Commission a fair, but tough and effective regulatory agency. Chairman King has emphasized the need for the Commission to focus its efforts on carcinogenic and other such hidden hazards to which populations are involuntarily exposed in consumer products. In addition to a new Chairman, two of the other four sitting Commissioners were appointed in 1978, and another vacancy will be created early in 1979. One indication of the Commission's new stance was the 1978 reversal (with respect to Tris-treated sleepwear) of its previous statutory interpretation that it lacked authority to ban export of hazardous substances.

Speculations as to the Commission's future were cut short on November 10, 1978, when President Carter signed into law a bill reauthorizing the Commission for three years. The Congress and the Administration have thus indicated their support for the new Commission leadership. A key test now facing Chairman King is her ability to attract quality talent to senior openings in her health sciences program.

Food and Drug Administration The major regulatory authority of the FDA is mandated by the 1938 Federal Food, Drug, and Cosmetic Act, which gives the FDA authority over food additives, cosmetics and drugs, all of which are regulated with distinct and differing philosophies and practices. The Act prohibits the marketing of food that contains a "natural or added substance which may render it injurious to health." The Act permits the addition of toxic substances to food within prescribed tolerance levels, but shifts the burden of proof to the manufacturer to show that the additive is safe under the conditions of proposed use.⁷¹

* Byington was appointed chairman by President Ford in June, 1976.

The 1938 Act was extended by the 1954 Pesticide Amendments, the 1958 Food Additive Amendments, including the Delaney Amendment, the 1960 Color Additives Amendments, and the 1962 Animal Drug or Feed Additive Amendments. The overall laws resulting from these various amendments are complex and inconsistent, especially with regard to the regulation of carcinogens.⁷²

The 1958 Delaney anticancer clause is a straightforward piece of legislation, stating that

no additive shall be claimed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found after tests which are appropriate for the evaluation of safety of food additives to induce cancer in man or animal.⁷³

This law reflected the then and currently prevailing scientific consensus that there is no known method for setting safe levels for human exposure to carcinogens.⁷⁴ The FDA is given authority only to determine whether the carcinogenicity tests are appropriate, then after these limits of bureaucratic discretion are reached an automatic set of rule-making procedures are invoked leading to a ban of the carcinogenic additive. The requirement for appropriate test methods can be used to exclude carcinogenic effects induced in animals from subcutaneous or intravenous injection of food additives. However, it would seem inappropriate on these grounds to try to exclude carcinogenic effects of additives administered to animals by gastric intubation, a standard practice in carcinogenicity tests, rather than in diets. Nevertheless, the FDA concluded in 1975 that such exemption could be valid.

Although invoked on several occasions, the Delaney anticancer clause has only been formally used twice or so for the purpose of banning a carcinogen: in 1967 for Flectol H and in 1969 for MOCA, both used in food packaging adhesives. The FDA has, however, used the broad statutory authority of general safety provisions of food law to ban several other carcinogens, including: the sweetener dulcin in 1950; coumarin, in Tonka Bean Extracts, in 1954; safrole in 1960; oil of calamus in 1968; the sweetener cyclamate in 1969; diethylpyrocarbonate in 1972; the animal drug

DES in 1972; mercaptoimidazoline in 1973; Violet #1 in 1973; and FD&C Red #2 in 1976.

There are many loopholes in the legislative definition of a food additive that exempt a wide range of carcinogens from the requirements of the Delaney Amendment.†

1. Pesticide residues: These are not defined as food additives. EPA has authority to set tolerances in food for carcinogenic pesticides.

2. Unavoidable or unintentional contaminants: Like pesticides, these are exempt. Most common examples are PCBs, benzo[a]pyrene and other such polycyclic compounds formed during broiling, and chemicals migrating from food packaging materials. Additionally, FDA does not require carcinogenicity testing of unintentional additives derived from packaging materials, some 10,000 of which have been approved for use, unless they are present in concentrations over 1 ppm, and unless the FDA believes there is valid reason to suspect carcinogenicity.

3. Prior-sanction additives: By a "grandfather clause," additives sanctioned by the FDA prior to September 6, 1958, are exempt.

4. GRAS additives: Additives "generally recognized as safe" by experts prior to January, 1958, are not regarded as additives from the Delaney standpoint.

5. Color additives in use before July, 1960: Under a "grandfather clause" of the 1960 Color Additive Amendments, color additives in prior use can be provisionally listed for a period of two and a half years to allow completion of tests. The FDA is allowed to extend this period "in good faith" if necessary. Using this stratagem, FDA extended the provisional listing of Red #2 fifteen times from 1960 to 1965, before its final ban in January, 1976.

6. Animal drugs without prohibited residues: The 1962 Feed Additive Amendment (or the DES clause) allows administration

† In spite of such regulatory flexibility, the FDA announced in February, 1979, that it plans to seek relaxation of the Delaney Amendment and other federal food safety laws to allow the setting of "acceptable low levels of (carcinogenic) risk (in a) very small" number of cases on the basis of benefit-risk considerations.

to cattle of carcinogenic drugs or feed additives, such as DES, provided no residues can be detected in meat or animal food products. This special-interest legislation was exploited to the utmost by successive FDA commissioners to allow continued use of DES even though residues were consistently detected from the late 1960s until its ban in 1973, a ban which was, however, overturned on procedural grounds.

The 1938 Act created a specific exemption for coal-tar dyes, provided they are appropriately labeled. The FDA cannot now ban them, even though their carcinogenicity has been recently proven. However, congressional moves which will probably abolish this exemption are now pending.

FDA also has authority for enforcing tolerances on foods set by EPA for pesticides and toxic chemicals. It accomplishes this by testing samples of food to determine if there are residues exceeding tolerance levels, in which case the food can be banned and penalties on violators can be imposed. However, a 1975 General Accounting Office Report criticized the FDA tolerance program for failing to test food for residues of 179 out of 233 pesticides for which tolerances were set.⁷⁵ A subsequent General Accounting Office Report in 1978 demonstrated that the FDA had failed to rectify these serious deficiencies.⁷⁶ Of 268 pesticides with a total of 5,872 individuals' tolerances on various foods, only 38 percent can be detected by currently used FDA multi-residue techniques. Also, 940 of these 5,872 tolerances are for pesticides which are either carcinogenic or suspected of being carcinogenic. About 70 percent of these carcinogens or suspect carcinogens cannot be detected by FDA monitoring techniques. FDA Commissioner Kennedy in subsequent testimony on February 24, 1978, recognized various of these deficiencies in FDA's monitoring program. He indicated his intent to institute various reforms, including more effective coordination with USDA and EPA.

Cosmetics are treated differently from food additives under the Federal Food, Drug, and Cosmetic Act. The burden of demonstrating carcinogenic or other hazards is placed on the FDA. Following petitions by the Health Research Group, the FDA banned the use of VC as a propellant in cosmetics in 1974 and of chloroform as an ingredient in cosmetics in 1976, both on grounds of

carcinogenicity. While there is no requirement for manufacturers to undertake toxicological testing of cosmetic ingredients prior to marketing, current labeling laws of the FDA require untested products to be clearly labeled as such.⁷⁷

Drug law is as different from food law as is cosmetic law.⁷⁸ Unlike food law, which is based on hazard alone, drug law allows consideration of matching benefits. The 1938 Act requires that drugs be "adequately tested to show that they are safe for use under conditions of use prescribed in their labeling." The 1962 Kefauver-Harris Amendments require formal proof of effectiveness and authorizes banning on grounds of "imminent hazard." There are, however, no formal requirements for carcinogenicity testing of drugs before clinical trials are undertaken. Carcinogenic drugs can be used for both medical purposes, such as Flagyl for trichomonas vaginal infections and griseofulvin for athlete's foot and other superficial fungal infections, and for non-medical purposes, such as oral contraceptives.

The current commissioner, Donald Kennedy, was appointed to the FDA on April 8, 1977. Kennedy, a Stanford University biologist, has already made significant impact on an agency whose past record of protection of consumer interests has been grossly deficient.‡ Under Kennedy's direction, FDA moved in the direction of greater concern for consumer safety and interests. Kennedy has taken sound positions on various issues such as dangers of saccharin and nitrite, promoting the use of lower-priced generic drugs, and the labeling of alcoholic beverages (with warnings to pregnant women that too much alcohol may cause birth defects). In May 1978 the FDA announced plans to launch a "cyclic review" of food additives by December. This would include a priority list of about 2,300 substances (some 350 direct additives, 620 natural flavors and spices, and 1330 synthetic flavors) that FDA wants tested now or in the near future.

U. S. Department of Agriculture The regulatory authority of the USDA over carcinogenic and other contaminants in agricultural products and meat is limited.* The Food Safety and Quality

‡ On April 17, 1979, Kennedy announced his resignation to take a top administrative position at Stanford University, effective August 1, 1979.

* This authority is granted by the 1906 Federal Meat Inspection Act, the 1967 Wholesale Meat Act, and the 1968 Poultry Products Inspection Act.

Service conducts programs to protect wholesomeness of meat and poultry products for human consumption. USDA is responsible for preventing the marketing of adulterated raw meat and poultry, including that containing residues in excess of tolerances set by FDA and EPA. As part of this program, USDA samples and monitors meat and poultry, generally at the time of slaughter, for illegal residues. These illegal residues include excessive residues of non-carcinogenic animal drugs, pesticides and environmental contaminants above tolerance levels, and prohibited residues of any detectable level of carcinogenic drugs such as DES. Apart from these, tolerances or action levels have been set for residues of pesticides and other carcinogenic environmental contaminants, even though a safe level cannot possibly be scientifically established for them. These include the banned carcinogenic DDT and dieldrin, residues of which persist in meat and poultry as a result of their agricultural uses several years ago.†

According to a recent congressional report, the USDA monitoring program is seriously deficient.⁷⁹ There are at least 143 known drugs and pesticides, including 40 carcinogens and 18 teratogens, besides an unknown number of environmental contaminants which may leave residues in food-producing animals.‡ USDA's monitoring program tests for only 46 drugs and pesticides, and 8 environmental contaminants. Using USDA data, on the basis of which an overall estimated rate of 2 percent violation with illegal residues was claimed by USDA, the General Accounting Office report showed that from 1974 to 1976 the violation rate may have ranged from 2.6 percent in sheep and goats to almost 16 percent in swine. The actual violation rate is probably very much higher, as USDA fails to test for most drugs and pesticides likely to leave

† DDT has an official tolerance (5 ppm), which by legal definition is a "safe" level. The current dieldrin action level (0.3 ppm) was agreed upon as part of the EPA ban on agricultural uses of aldrin/dieldrin. In both instances, human exposure levels and the rate of decline of residues reflect environmental factors that, apart from determination of action levels, are beyond regulatory controls. In 1976, USDA tests showed that 82 percent of about 900 poultry tested for DDT and 52 percent of 1800 cattle tested for dieldrin had measurable residues, which in most instances, however, were below tolerance levels.

‡ These inadequacies generally reflect the lack of appropriate analytic methods that FDA and EPA should have required from manufacturers prior to their original registration of the animal drugs and pesticides, respectively.

residues. Among pesticides and drugs which are not included in USDA monitoring programs are the carcinogenic drug furazolidone, ethylene-bis-dithiocarbamate fungicides, which break down to the carcinogenic ethylene thiourea, chlorophenoxy herbicides such as 2,4,5-T and Silvex, which are teratogenic and contain the highly persistent and carcinogenic tetradiroxin contaminant and 2,4-D which is teratogenic.

High violation rates of carcinogenic and other contaminants in meat and poultry are further compounded by the fact that most illegal residues are discovered only after the meat and poultry have been marketed. Furthermore, FDA and EPA fail to follow up on most residue violations and to take appropriate corrective action.

USDA authority for inspection of illegal and potentially harmful residues in raw meat and poultry is shared with FDA and EPA. Cooperation on enforcement policies has been reached by administrative agreements between these agencies. FDA is responsible under the Federal Food, Drug, and Cosmetic Act of 1938 (as amended) for ensuring the safety of drugs given to food-producing animals, setting tolerances for animal drugs or environmental contaminants allowable in food, and preventing the marketing of raw meat and poultry containing residues that exceed established tolerance levels. EPA is responsible for regulating the introduction of pesticides and toxic substances into the environment. Under the Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (as amended), EPA must approve pesticide products for safety and effectiveness before they can be marketed. Additionally, under the Federal Food, Drug, and Cosmetic Act, EPA must establish safe tolerance levels for pesticides likely to leave residues in food. Finally, under the 1976 Toxic Substances Control Act, EPA regulates the introduction of toxic substances into the environment which can contaminate meat and poultry. Both FDA and EPA are responsible for requiring manufacturers to provide suitable, practical, and sensitive test methods for the detection of chemical residues.

USDA also sets tolerances for nitrate and nitrite in meat, though not in fish, which is an FDA responsibility. The authority of the USDA over nitrate and nitrite in meat is due to a legislative quirk by which these two additives were given a prior sanction

under the 1907 Meat Inspection Act and were thus exempt from the 1958 Food Additive Amendments.

Assistant Secretary for Food and Consumer Services of the USDA, Carol Tucker Foreman, has taken steps to ensure that the meat industry reduce nitrite in bacon to levels at which no nitrosamines can be detected. In congressional testimony on February 24, 1978, Foreman endorsed the general criticisms of USDA's monitoring program contained in the 1978 General Accounting Office report. Foreman also announced plans of the USDA to improve its sampling and monitoring programs.⁸⁰

It is clear that USDA procedures for meat inspection and monitoring are out of date and inadequately responsive to the grave problems of the modern petrochemical era. Additionally, the fragmentation of authority and responsibility for setting tolerances and food inspection between the USDA and the FDA and EPA is an anachronism which leads to regulatory complexity and diffusion of authority.* In a limited effort to resolve this problem, in December, 1977, the Senate Governmental Affairs Committee recommended that the regulatory function of the USDA over chemical contaminants in food be transferred to the FDA.

Secretary of Agriculture Bob Bergland has shown an apparent sensitivity to toxic and environmental problems of pesticide uses. In March, 1977, he expressed the intent of USDA to wean farmers away from dependence on pesticides and to encourage integrated pest management instead. USDA has not yet implemented such intent.

Other Regulatory Agencies

The Federal Trade Commission, through the 1964 Federal Cigarette Labeling and Advertising Act, requires cigarette packages to be labeled with the familiar warning that smoking "is dangerous to your health." The FTC spends about \$125,000 annually to measure the tar and nicotine content of commercial domestic cig-

* OMB is formulating plans for investigation of current national food policies with regard to production, distribution, nutrition, and safety. This project will also examine the authorities of concerned federal agencies, FDA, EPA, and USDA, for overlap and consistency.

arettes, requiring the findings to be printed on the packages. Without this modest pressure, the tobacco industry would have no incentive to reduce the tar and nicotine yield of its products. As it is, the industry has cashed in on the low-tar concept with massive media campaigns to win smokers to the lower-tar brands. Industry efforts to move the testing from the FTC to private concerns were thwarted in 1977. Similar attempts will, however, probably be made in the future. Efforts to regulate the tobacco industry now seem futile in view of its strong support by the administration and a powerful network of Southern congressmen. If there are any possible remedies, they seem to rest in the courts.

The current FTC commissioner, Michael Pertschuk, former chief counsel of the Senate Commerce Committee, is a dedicated consumer activist. He has brought in new staff and has overnight transformed the FTC into an agency aggressively dedicated to protect the interests of the consumer.[†]

Under the 1974 Hazardous Materials Transportation Act, the Department of Transportation has authority to regulate transportation of various categories of materials, such as flammable liquids or explosives, but not specifically carcinogens.

The Bureau of Mines of the Interior Department has authority under the Federal Coal Mine Health and Safety Act of 1969 and the Federal Metal and Nonmetallic Mine Safety Act of 1966 to enforce federal health and safety in mining operations. The bureau has adopted the 1972 OSHA standards for asbestos and the 1973 threshold limit values for other airborne pollutants.

The Federal Mine Safety and Health Amendments Act of 1977 supercedes the 1966 Mine Safety Act. The 1977 Act established a Mine Enforcement Safety Administration, separate from OSHA, in the Department of Labor.

The "New Look"

The last two years have witnessed the emergence of significant new trends in federal agencies. An important element is the over-

[†] In May, 1978, Pertschuk was charged with bias in his regulation of TV advertising for children by the Toy Manufacturers of America, the American Association of Advertising Agencies, the American Advertising Foundation, and the Association of National Advertisers.

all and explicit emphasis of the Carter administration on integrity and openness.[‡] This has also put new teeth into recent laws governing agency conduct. These laws include the 1973 amendments to the 1967 Freedom of Information Act, making it possible for concerned citizens to obtain copies of documents on the basis of which agencies make decisions and regulatory policies,^{§1} and the 1972 Federal Advisory Committee Act, governing the conduct of these committees, with particular reference to the needs for balanced representation, disclosure of special interests, and public announcement of meetings.^{§2*} The administration has also introduced new policies designed to limit conflicts of interest and the "revolving door" between industry and federal agencies.^{§3} Senior agency officials are now forbidden to accept positions in those industries they have regulated for one year after resignation from government. A bill approved by the Senate in 1977 mandates an even stricter two-year ban in certain cases.

There is no question that the overall quality of new appointments of agency heads under the Carter administration has been outstanding from the point of view of their past records. While it is too early to make definitive assessments, it is possible to observe some emerging trends in performance. In general, these trends are favorable. Bingham at OSHA, Foreman at USDA, Claybrook at Transportation, Kennedy at FDA, and Pertschuk at the Federal Trade Commission, have all transformed their agencies much for the better. As part of their reforms, they have recruited much needed fresh and skilled new personnel into senior positions. Additionally, Upton at NCI, Costle at EPA, and King

[‡] While there is no evidence that the Carter administration, which came to Washington pledging "open government" and protection for "whistleblowers," has taken measures similar to those used in the Nixon administration, it has mounted a range of internal inquiries, tightened the National Security Council regulations on interviews, opened the prosecution of an espionage case, filed a breach of contract suit against a former CIA employee who wrote an unauthorized book, and required Justice Department lawyers to sign affidavits about their contacts with reporters as a part of leaking inquiries. Attorney General Griffin Bell has taken still stronger positions on news leaks, and his department had conducted most of the investigations on unauthorized disclosures, including a recently closed investigation on the *Washington Star*, which refused to disclose its sources of information about alleged corruption in the Interstate Commerce Commission.

^{*} It should be recognized, however, that the National Academy of Sciences, a major source of technical advice to Congress and regulatory agencies, has so far successfully resisted legal challenge to require compliance with the Freedom of Information Act.

at the Consumer Product Safety Commission have also made a substantial impact at their agencies by virtue of their integrity and openness.

Problems of overlapping jurisdictions and regulatory inconsistencies are now being recognized.⁸⁴ Attempts are being made to correct this and to develop better coordination of efforts at the fact-finding and regulatory levels. Among the more important cooperative moves that have been made are the formation of an Interagency Regulatory Liaison Group (IRLG), involving EPA, OSHA, FDA, and the Consumer Product Safety Commission, the formation of an EPA Toxic Substances Strategy Committee, an overall coordinating group which reports directly to the President, an HEW Committee to coordinate toxicology and related programs, and more recently the National Toxicology Program.

The likelihood for success of these new cooperative ventures is increased by the close contacts and understanding that have developed between Bingham, Costle, and Kennedy, which have been reinforced by similar contacts with heads of research agencies, particularly Upton and Rall. Some of these cooperative moves, particularly the IRLG and the NTP, may well foreshadow the emergence of more extensive and formalized consolidation, probably within HEW, of the functions of the several different agencies now dealing with various aspects of environmental pollution and public health.

Economic Policies of the Administration

In March, 1978, President Carter issued executive order 12044 requiring regulatory agencies to develop "regulatory analyses" of all major proposed standards with particular attention to their economic impact on business.[†] The order was promptly endorsed by the U. S. Chamber of Commerce. Since then, the administration has imposed increasing restrictions on health and environmental regulation, particularly through the Regulatory Analysis Review Group of the Council on Wage and Price Stability (COWPS).[‡] As an agent of the President, COWPS is now pitted

[†] This order replaced President Ford's Executive Order 11821, which required "inflationary impact statements"; the name of this requirement was changed to "economic impact statements"; on December 31, 1977.

[‡] The inequity of these restrictions is further emphasized by reports of soaring corporate profits in the first quarter of 1979.

against the regulatory agencies in their discharge of Congressionally mandated policies.

As OSHA was concluding review of the post-hearing comments on its "generic" cancer policy, COWPS issued a report in October, 1978, sharply critical of the proposal on both economic and scientific grounds. COWPS, which draws freely on affected industries for staff work, cited the economic impact analysis prepared for the American Industrial Health Council by Booz, Allen & Hamilton, admitted by the Council to be "seriously flawed," as its authority for stating that the total costs of the proposed regulations will be well over \$1 billion annually. The Council was equally critical of the OSHA benefits analysis for its failure to address the cost-benefit question on a carcinogen-by-carcinogen basis, and for failing to determine incremental benefits over and above those achievable by alternate methods of regulation. This criticism was buttressed by reference to the October, 1978, decision of the Fifth Circuit Court overturning the benzene standard on grounds including economic feasibility, and cost-benefit considerations. The Council was also critical of OSHA for disregarding potency and risk assessment in their essential classification of chemicals into carcinogens and non-carcinogens.

On October 24, 1978, President Carter announced his new anti-inflation program, concluding that inflation is the nation's No. 1 problem, and that prompt remedial action, including round-the-board austerity measures, must be immediately taken.* However, the program embodies budgetary cuts, which are likely to in-

* Current inflation is poorly understood. Neither classical nor Keynesian economic theory can explain the combination of unemployment or stagnation and inflation (stag-flation) that has characterized the 1970s. In the absence of firm theory, inflation fighters are groping with traditional empiricism for possible solutions and scapegoats, a role that regulation seems to fit well, especially as it also appeals to the national mood of resurgent conservatism. The issues have been further clouded by the action of the administration in terminating monopolistic airline practices by their deregulation, the success of which has been exploited by both administration economists and industry as further argument for environmental deregulation. Environmental regulation is claimed to be inflationary on various grounds including: It makes technology prematurely obsolete; it fails to promote productivity of future new standards; the regulations are especially hard on small business who may be driven out of the market, resulting in industry concentration; and it is difficult to prove benefits from a regulatory action.

crease unemployment, and further restrictions on regulations designed to protect workers and the environment. The new measures, however, fail to protect consumers from runaway price increases in the four basic necessities of life—food, energy, housing, and medical care—those areas where inflation hits hardest.

Following preliminary skirmishing between the Office of Management and Budget and the heads of the major regulatory agencies, President Carter created a Regulatory Council, headed by EPA Administrator Costle, to implement the new regulatory policy. The Council held its first meeting in November, 1978, with twenty-five attendees representing all Cabinet and thirteen independent agencies. The Council established five work groups—health and safety, finance and banking, economics, social justice, and resource development. Federal agencies were asked to submit an immediate list of all planned major regulations with an impact of over \$100 million on industry. Besides economic impact, each regulation lists eleven descriptive items, including title, legislative authority, alternatives to regulation, background documentation for the standard, an analysis of the needs for regulation, and an agency contact. The Council was required to submit this to President Carter by February 1, 1979, before publication of the Calendar (containing about 200 regulations), which is intended to provide a regulatory cost-benefit analysis.

The Regulatory Calendar concept has come under vigorous attack, particularly from consumer and minority groups and organized labor, the basic constituency that elected Carter. Congressman Rogers, (D.-Fla.) in a November 15, 1978, speech to the newly formed National Coalition for Disease Prevention and Environmental Health, characterized the Calendar philosophy as saying, "if getting sick is cheaper, then maybe we should not try to prevent illness." The AFL-CIO Executive Council criticized the proposal as "inequitable and unfair."

A portent of the new economic policies of the administration appears to be reflected in the January, 1979, decision of EPA Administrator Costle to weaken the Clean Air Act by allowing reduction in the ozone (smog) standard from 0.08 to 0.12 ppm (which is routinely exceeded in many large cities, such as Houston and Los Angeles). EPA claimed that the new standard will save industry approximately \$1.5 billion annually. While Costle

acknowledged talking to White House economists before announcing his decision, he insisted that the new standard is justified by "careful re-evaluation of medical and scientific evidence" (although no details of this re-evaluation were provided), and would not lead to adverse health effects in the general population, nor in hypersusceptible groups such as asthmatics. Richard Sinsheimer, president of the American Lung Association, however, called the new standard "dangerous" and warned, "we're playing Russian roulette with our health."

The new administration initiatives raise important constitutional and legal issues, particularly as they appear to represent direct executive usurpation of legislative authority. (This usurpation is over and above the personnel ceilings imposed by the administration which have prevented agencies from functioning adequately within approved budgetary limits.) Regulatory responsibilities have been created by Congressional Acts to implement specific programs under specific legislation. The Occupational Safety and Health Act, for example, mandates "safe and healthful working conditions" without reference to economic and technical feasibility or cost-benefit considerations. The intervention of White House staff in the regulatory process, in the name of fighting inflation, is not authorized by statute.[†] Constitutional and legal issues aside, there are serious problems and flaws inherent in the administration's approach to regulation from myopic and narrowly defined cost-benefit perspectives.

First, most cost-benefit analyses do not adequately reflect the economic and other costs of deregulation or failure to regulate in terms of disease and death, and environmental degradation. This is especially so in view of the substantial uncertainties involved in such costing. Quantitative risk costing or assessment is a premature science fostered by pressures to express public health hazards in economically simplistic terms. The uncertainties inherent in this approach are illustrated by the 10 million-fold

[†] In November, 1978, the Environmental Defense Fund sent to the White House a forty-page legal memorandum, arguing that the President has no more authority to intervene in regulatory proceedings after the public comment period has closed than anyone else, unless that authority is explicitly granted by the statute under which the rule is written. The extent to which Congress is likely to resist legislative moves further extending Presidential authority in this direction remains to be seen.

range in current estimates of the carcinogenic hazards of saccharin (Table 9.11). Additionally, such estimates ignore even greater uncertainties due to potential synergisms and multiple exposures that, in general, cannot be anticipated let alone quantitated.[‡]

Quite apart from these uncertainties, costings based on medical treatment and income or productivity losses, seem inadequate or inappropriate estimates for pain and suffering and loss of life. For instance, the recognized annual costs of cancer are in the region of \$30 billion, and particularly with occupational cancer, there are still larger currently unrecognized and externalized costs. As the burden of environmentally induced cancer and disease has progressively increased, total national health expenditures have soared from \$30 billion in 1960 to \$185 billion in 1978, and are expected to reach \$230 billion by 1980. Health-care costs in 1978 were roughly 9 percent of the G.N.P., and \$55 billion more than the defense budget. Health care leads the nation's inflationary spiral, and has been growing at the rate of 15 percent or more for the last five years. The contrast between runaway health-care spending and the resistance of the administration, besides industry, to invest in environmental health protection is striking.⁸⁵ Apart from recognized health-care costs, there are related costs that can no longer be externalized, such as the pending multimillion dollar law suits on asbestos. As recently pointed out,⁸⁶ even the conservative economist Paul Samuelson warns that conventional estimates on the impact of regulation on economic growth and the gross national product are meaningless, unless—

we adjust for any such "bads" that escape the G.N.P. statistician whenever society is both failing to prevent pollution and failing to make power [or water or air or cotton] users pay for the full costs of the damage they do. [Once we make these adjustments] we see that net economic welfare grows more slowly than [conventionally measured] G.N.P.

[‡] These grave limitations do not appear to be recognized by the chemical industry and the proponents of deregulation, who are proposing that quantitative risk assessment should be used as a basis for regulation (See, for instance, Cong. J. G. Martin, "Where Does Science Fit In?" address to the Manufacturing Chemists Association, Washington, D.C., September 12, 1978).

Table 9.11 *Estimated Human Risks from Saccharin Ingestion of 0.12 g/day*

Method of high- to low-dose extrapolation	Lifetime cases/million exposed	Cases per 50 million/yr.
<i>Rat dose adjusted to human dose by surface area rule</i>		
Single-hit model (Hoel, 1977)	1,200	840
Multi-stage model (with quadratic term) (Hoel, 1977)	5	3.5
Multi-hit model (Scientific Committee of the Food Safety Council, 1978)	0.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	450	315
<i>Rat dose adjusted to human dose by mg/kg/day equivalence</i>		
Single-hit model (Saccharin and Its Salts, 1977)	210	147
Multi-hit model (Scientific Committee of the Food Safety Council, 1978)	0.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	21	14.7
<i>Rat dose adjusted to human dose by mg/kg/lifetime equivalence</i>		
Single-hit model (Brown, 1977)	5,200	3,640
Multi-hit model (Scientific Committee on the Food Safety Council, 1978)	0.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	4,200	2,940

Source: "Saccharin: Technical Assessment of Risks and Benefits," Report No. 1, Committee for a Study on Saccharin and Food Safety Policy, National Academy of Sciences, Institute of Medicine, November, 1978.

Second, there are similar problems in evaluating the costs of regulation.* Compliance strategies involve large degrees of uncertainty and generally ignore treatment of positive externalities arising from innovation associated with add-on devices (as interim measures) and product or process substitution, or alternative technologies. Compliance may achieve substantial economies by recovering and recycling valuable chemicals otherwise lost as air and water pollutants. Cost analyses also rarely reflect the creation of new pollution-control industries which provide employment besides goods and services. According to a November, 1978, report prepared for EPA by Arthur D. Little, Inc., the air-and-water-pollution-control industry (manufacturing equipment, instrumentation, and chemicals for pollution control from industrial plants, and for municipal solid-waste recycling plants) had record sales of \$1.8 billion in 1977, accounting for about 36,000 jobs. These new industries are growing about twice as fast as the rest of U.S. industry, and are projected to grow even faster over the next decade. Another important consideration is the fact that industry has a virtual monopoly on data needed to assess costs of compliance. Industry estimates on the cost of regulation are often exaggerated, sometimes by several orders of magnitude, as was shown to be the case for the vinyl chloride occupational standard. OSHA does not have adequate resources to scrutinize such alleged costs and must often rely on consulting firms with close industry ties for economic and technical advice.

Finally, there is the question of equity. The penalties of failure to regulate carcinogens are usually long delayed and impact on different sets of people than those who profit from the manufacture or processing of the carcinogen and who resist bearing the immediate costs of compliance (recognizing also that much of these costs could be redistributed through tax write-offs and price pass-throughs). It would seem reasonable to require that the interests of a worker exposed to hazardous conditions receive substantially more protection than now afforded by the regulatory process, and still more than that envisaged by regulation further attenuated in the name of inflation fighting.

* These costs, which are immediate, are weighted heavily, while delayed health benefits of regulation are almost invariably discounted.

Constraints on Agencies

The performance of Federal agencies, both research and regulatory, is influenced by an interplay of technical and political considerations of such complexity as to discourage simplistic assessments. Besides attempting to resolve inherited legislative ambiguities, agencies must deal with a growing range of constraints.[†] The most limiting include those imposed by the administration, such as long-standing personnel ceilings, and the new anti-inflationary policies, particularly the narrowly defined cost-benefit analyses demanded by COWPS as a prerequisite to the discharge of congressionally mandated regulatory action. These constraints have been reinforced by the October, 1978, decision of the Fifth Circuit Federal Court of Appeals in New Orleans (now under appeal before the Supreme Court) overturning OSHA's new benzene standard on economic grounds, and placing on government the burden of proving that the costs[‡] of compliance are outweighed by health benefits.

The unique pre-emption by Congress of the FDA's regulatory authority on saccharin, reflects manipulation of the public perception of public health issues by powerful special interests exploiting poorly restricted control of the media, coupled with the failure of regulators to adequately inform the public as to the underlying realities. Notwithstanding the recent impact of organized labor and public interest groups, perhaps the most crippling of all constraints on agencies is the lack of a disease and cancer-prevention national constituency to balance the pressures of industry and the indifference or hostility of the "cancer cure lobby" and the medical establishment or industry.

[†] According to R. J. Smith, *Science* 203 (1979), pp. 28-32, "chronic indecisiveness" or "chronic avoidance" has emerged as the most recent characteristic of regulatory agencies, accounting for the extreme paucity of their regulatory actions. However, both OSHA and EPA are now attempting to build public constituencies to counterbalance pressures from regulated industries.

Future Trends

Future events will be critically shaped by the outcome of an emerging power struggle between Congress and the administration, not only with regard to the new economic policies of the President, but also with regard to the personnel restrictions imposed on federal agencies. Another critical determinant is the ability of agencies to attract established scientists into key positions in the bureaucracy, besides recruiting lower rank professionals.

Past Republican administrations have achieved more effective environmental regulation with weak agency heads than has been or is likely to be achieved by the present Democrat and liberal administration aided by strong and progressive agency leadership. Determinants of this paradox include emerging fiscal conservatism, increasing pressures by the administration and industry for deregulation in the name of anti-inflation, the public and congressional perception of major uncertainties or confusion in the scientific base of environmental decision making (as illustrated in the mishandling of saccharin) and in risk assessment, and the false issue of freedom of choice being pitted against regulation. Inflation forces are clearly in control in the executive. There is a strong decline in the environment and anti-cancer forces in Congress, with the recent retirement of Congressmen James Delaney (D-N.Y.), John E. Moss (D-Calif.), and Paul Rogers (D-Fla.), and with the emergence of the new fiscal conservatives.‡

‡ Exemplified by Congressman James Martin (R-N.C.), whose Ph.D. in chemistry seems to have invested him with a role of scientific authority in environmental and health issues. Martin is a strong advocate of the revocation of the Delaney Amendment on the grounds that it is "unscientific," and of the saccharin ban on the grounds that it is only "a weak carcinogen," whose (alleged) benefits outweigh the risks he seems to feel that the consumer is or should be willing to bear. However, Rogers and Moss have been succeeded as chairmen of the key House Commerce Committee's Subcommittee on Health and the Environment and Oversight and Investigation by the liberal Henry A. Waxman (D-Calif.) and Bob Eckhardt (D-Tex.), re-

The future role of labor has been made uncertain by recent wage limitations imposed by Carter, and it is unclear whether organized labor will make wage or environmental controls their main priority. The likelihood of success of the deregulation trend seems enhanced by the absence of an effective national environmental and anti-cancer constituency.

Initiatives emerging at the state government level represent additional new trends of major potential importance which are being pioneered by California.⁸⁷ The 1976 California Occupational Carcinogen Control Act (SB 1678) requires that all industries using designated carcinogens register with the newly created Occupational Carcinogen Control Unit, which has the authority to inspect facilities and levy civil penalties for violation of standards. Other bills introduced to the California legislature in 1978 include AB 3249 on Workers' "right to know" of the identity of chemicals to which they are exposed; AB 3413, which would create a repository of information on toxic chemicals; AB 3414, which would create a University of California training center for occupational health professionals in the north and south of the state; and SB 1530, which would investigate the regional distribution of cancers in Bay Area counties. The 1977 New Jersey "Cancer Control Act," introduced by Senator John M. Skevin, proposing a ban on the manufacture of sixteen known carcinogens and offering the most comprehensive state legislation on control of public exposure to industrial carcinogens, was withdrawn in response to massive industrial opposition and failure to generate adequate public support.

spectively. Eckhardt has established priorities in agency decision making and in the role and limitations of cost-benefits analysis. Waxman, who does not command a majority on his subcommittee, can be expected to strongly defend the Clean Air Act and retention of the Delaney Amendment, to oppose export of hazardous products, and to advocate a comprehensive national health insurance.

*I hope we shall crush in its birth the aristocracy of our
monied corporations which dare already to challenge
our government to a trial of strength, and bid defiance
to the laws of our country.*

Thomas Jefferson, 1816.

Chapter Ten *Non-governmental* *Policies*

Until recently, industry and labor have been the only major non-government influences on Congress and regulatory agencies in all areas of public health and safety, whether relating to the general environment, consumer products, or the workplace. In the last decade a new element has emerged, the public interest movement, which, in spite of trivial material resources compared to those of industry, has begun to transform the climate of decision making. A discussion of the three—industry, labor, and public interest groups—and also of additional influences with respect to environmental and occupational carcinogenesis follows.

Industry

American industry early gained a reputation for innovation and flexibility. These are among the qualities that established interna-

tional preeminence for the U.S. free enterprise system. Nowhere has this flexibility been better seen than in the major chemical industries, which have learned to deal with shifting supplies of raw materials and shifting demands of the market.

In spite of this, industry has failed to adequately comprehend the magnitude of health and safety problems entailed in the manufacture and handling of hazardous, particularly toxic or carcinogenic, chemicals. Industry has also failed to comprehend the enormous costs to society of the cancer and other diseases resulting from the use of toxic and carcinogenic chemicals. Industry is not alone in this failure of comprehension, which must also be shared by government and the public. Such failure of comprehension, coupled with historic imbalances reflecting industrial dominance of decision making with regard to its own products and processes, appears to be the major determinant of current industry policies. In analyzing industry policies and problems of constraints in their data, these considerations appear preferable to alternate simplistic theories based exclusively on machiavellianism.

Top management has also failed to be aware of the shortcomings in its own modes of developing health and safety information. As a result, marketing decisions and all-but-irreversible economic commitments are often made on the basis of information that subsequently proves to be defective or based solely on short-term marketing considerations. The conflicts inherent in this tend to limit the interests and incentives of industry to develop equally effective but less hazardous alternative products and processes—hence to stifle needed innovation.

Big industry faces two distinct types of problems in developing control technology. First, there are the difficulties of effectively refitting old plants with add-on devices to allow them to handle toxic chemicals more safely. It is now generally recognized that in many instances this just may not be practical. This does not exclude the possibility of materially decreasing risk by improving work practices. Part of the problem here is the fact that some industries, particularly steel, have in the past failed to plow back profits into renovating old plants.* This problem of old plants with old technology must be dealt with on an industry-by-

* The 1976 OSHA hearings on coke oven emissions made it clear that the newer Japanese coke ovens are better designed than their U.S. equivalents.

industry basis. There are no simple solutions or general formulae. It is clear, however, that old plants cannot be allowed to function as before at the continued expense of human health. While they are being phased out, at a pace influenced by industrial economics and public health concerns, improved work practices and engineering controls must be instituted on an interim basis.

The second (and relatively easier) set of problems faced by big business are those involved with the design of new plants. This is where industry can be expected to exhibit bold innovation. Health and safety considerations must be designed into plants at the earliest possible stages. The substitution of safer products and processes must be exploited to the fullest to avoid the use of carcinogenic chemicals. If it can be proven that there are no practical alternatives to the use of a carcinogen, then closed systems must be devised and engineered with all possible precision and safeguards, including constant monitoring with highly sensitive instrumentation. Costs of such controls are a useful incentive to the innovative development of safer alternatives.

The problems of small industry are probably the most difficult and complex. Many of these operate marginally and cannot afford to install expensive engineering controls.† Many also employ poorly educated and transient, non-unionized labor. While some improvement in work practices to reduce risks is feasible, there are clearly practical limitations as to what can be done in the small plant. To add to these pressures, large corporations have historically sided with government in efforts to regulate and destroy competition from small business. It is clear that small business must be gradually weaned away from handling hazardous chemicals. It is also clear that they should be encouraged in this direction and in the direction of improved work practices by special treatment, including tax subsidies and interim variances.

Industry, like labor, represents a heterogeneous array of interests and objectives. Such diversity, however, tends to be replaced by a common front of intransigence in response to proposed regulation of toxic and carcinogenic chemicals. A complex of in-

† It must be stressed that most epidemiological investigations that have so far demonstrated carcinogenic hazards in the workplace, have been undertaken in large chemical corporations that have some degree of protective controls, as opposed to small industry.

terrelated factors seems involved in this posture. These include the near-automatic rejection of federal controls (without a parallel rejection of tax subsidies and other forms of corporate protectionism); preoccupation with short-term marketing interests (often in conflict with needs for hazard controls) rather than consideration of long-term growth and stability; excessive reliance on narrowly based, self-interested recommendations of in-house marketing and scientific staff and their consultants on problems of health and safety; and a tendency to wait for health and safety problems to arise (which they then deal with defensively) rather than developing anticipatory strategies based on long-term considerations.

Strategies

In support of the status quo, industry has evolved a complex set of strategies to use individually or in concert to meet the needs of any particular circumstance. These are illustrated by the various case studies discussed in this book. The essence of all of them is to minimize the reality of risks due to a particular product or process, to maximize the social benefits, and to exaggerate the costs and difficulty of regulation. The elements of these strategies are sometimes presented frankly as industry positions, but they often come to us from industry spokesmen and academic consultants as "professional" viewpoints, with no hint of who employs the professionals.

Minimizing the Risk This standard ploy is exemplified by the Quebec Asbestos Mining Association's position. The association has publicly asserted that asbestos disease is a reaction of poor working conditions in the past which have been so improved that there is now little or no risk. Similarly, the Manufacturing Chemists Association and the academic consultants of industry have testified that benzene-induced leukaemias and other toxic effects reflect high exposures in the past and that now, based on the relatively low exposures encountered under modern working conditions, there is no cause for concern. As a further example, Rohm and Haas, as recently as 1974, denied that exposure to BCME has

caused any worker deaths following exposure at their plant. Other illustrative positions include the claim, by such organizations as the Nutrition Foundation and the Council on Agricultural Science and Technology, that there is no risk in being exposed to "relatively low levels" of chemicals found to be carcinogenic in humans, and that there are no substantive risks of exposure to chemicals found to be carcinogenic in animals and for which there are as yet no human data.‡

Diversionary Tactics These are generally based on insistence on degrees of precision and legal definition that cannot possibly be met in carcinogenesis tests or in epidemiological studies. Such a demand is often coupled with rejection of experimental carcinogenicity test data and alternative proposals for long-term prospective human studies over the next few decades, pending which, it is claimed, regulatory action should be suspended.

On January 11, 1978, the day HEW Secretary Joseph Califano announced a new "war on smoking," Senator Wendell Ford (D-Ken.), on behalf of his tobacco-producing state, told a news conference that Califano should instead direct the earmarked antismoking funds "into well-founded scientific research. The American people can make their own decisions," implying that still more research was needed and that government should do this research but should not set policy based on its results.

A December 13, 1977, meeting of the Toxicology Forum, an industry-sponsored group of toxicologists and geneticists, decided that saccharin should be given top priority for new studies. These new studies, the group concluded, should be directed to identify "impurities" in commercial saccharin, which members apparently

‡ Paralleling the attempts of the petrochemical industry to minimize the hazards of its products and processes are the skyrocketing insurance premiums and the growing difficulty of the industry in obtaining product liability insurance. Some industry trade associations are now considering establishing their own insurance companies in the Bahamas. Another proposed solution, especially favored by the asbestos industry, is the establishment of a no-fault insurance, possibly based on federal subsidies and akin to the limited liability secured for the nuclear power industry by the Price-Anderson Act. Such a move would perpetuate for the consumer the double indemnity of contracting cancer from industrial chemical carcinogens and paying for its costs.

had convinced themselves were responsible for the carcinogenic and mutagenic activity of saccharin.

Propagandizing the Public The media blitz orchestrated by the Calorie Control Council following the FDA's proposal to ban saccharin was unprecedented in regulatory history. The payoff obviously was worthwhile, for the unexpected and tumultuous public response led to a moratorium on its regulation. The council's use of such high-priced public relations firms as Hill and Knowlton reflects the determination of an industry faced with potential control. The council's propaganda is an outgrowth of an evolving media campaign, in which the chemical and oil industries are striving to improve their public images with all the techniques of modern mass advertising.

"Assuming a leadership role" on behalf of the chemical industry, Monsanto Chemical Company has recently launched a major public advertising campaign directed to the importance and safety of synthetic chemicals. Synthetic chemicals, it is claimed, are no different from all other naturally occurring chemicals to which mankind has been exposed for millions of years, and are essentially harmless in the absence of massive exposure or careless misuse. More specifically, the campaign consists of attacks against standard uses of maximally tolerated doses, against the Delaney Amendment, and against other regulatory controls of carcinogenic chemicals, all of which are categorized as irrational and emotional. A Monsanto pamphlet called "The Chemical Facts of Life" explains that the purpose of the campaign is "to explore the benefits and risks of chemicals—to find a clear path through the labyrinth of information and misinformation about chemicals which may help or harm health and the environment."¹

Monsanto is spending about \$5 million this year and is planning to spend similar amounts annually over the next five years on spots on national television, newspaper ads, and pamphlets. Some 500,000 pamphlets have been distributed so far, even to high school children. The campaign has been well planned and seems to limit possibilities of asking for equal time under the Fairness Doctrine. Following protest by the Environmental Defense Fund, Monsanto initially agreed to limit somewhat the scope of its campaign. One sixty-second national television spot features a speaker

identified as an agricultural chemist drinking from a glass of water and asserting the dependence of the modern farmer on chemicals such as di-hydrogen oxide—water. He then goes on to discuss the herbicide Vegadex,* explaining that while one would never drink this, it benefits crop growth in several ways. The screen flashes images of weeds being killed and healthy crops growing. The speaker allows that “no chemical is totally safe all the time,” but maintains that chemicals such as Vegadex are necessary in circumstances of worldwide food shortages, and concludes that without chemicals life would not be possible.

The Monsanto campaign is not a public service. The company would do better to stress concerns that the chemicals they plan to produce should be well tested to avoid future problems such as those posed by the toxicity and carcinogenicity of its products, such as Vegadex and nitrilotriacetic acid. Monsanto should also consider the judgment of its executives and consultants, on the basis of whose advice this mass campaign was presumably authorized.

Blaming the Victim Simply stated, the argument is, “Modern industrial working conditions are so safe that if a worker gets hurt or sick it must be his or her fault and not the fault of the industry.” The culprit is either the worker’s bad habits, such as smoking, or the worker’s genetic susceptibility to effects which any normal person would shrug off. Applications of this perspective have taken many forms. Perhaps its latest variant is the stance of

* Vegadex, or sulfallate, is a chlorinated dithiocarbamate derivative used as a selective pre-emergence herbicide on vegetable crops. It is structurally similar to a number of other pesticides which were shown to be carcinogenic more than nine years ago. In January, 1978, Vegadex was shown to be positive in the Ames test,² and in the following March the NCI bioassay program published a report showing that the herbicide is carcinogenic to rats and mice, inducing breast cancers in females of both species, tumors of the stomach in male rats and of the lung in male mice.³

Recent production data for Vegadex are unknown, as this is considered proprietary information. However, a 1971 report estimates U.S. production as about 500,000 kg annually. As the NCI report points out, “The potential for exposure to sulfallate is greatest for agricultural workers, but may also be considerable for workers in sulfallate production facilities. Residents of agricultural communities may be exposed to airborne residues following spraying operations. The herbicide is readily taken up by plant roots . . . and the general population may be exposed via ingestion of residues in food crops.”

Johns-Manville's Paul Kotin, in shifting attention from what *chemicals* cause cancer to what *people* get cancer. Kotin has helped resurrect the notion of the "hypersusceptible worker," one who, by his own constitutional or genetic makeup, is at higher risk for occupational disease than fellow workers. Starting from the plausible premise that all biological organisms, including humans, vary in their response to external stimuli such as toxic substances or carcinogens, he then advances the following proposition:

The workplace, no matter how elegantly controlled, cannot assure uniformity of protection to all workers because of susceptibility variation. . . . A safe, acceptable workplace for hypersusceptible workers is as much a cultural concept as it is a scientific one. . . . It is still the responsibility of management to deny the worker the "right" to place himself at increased risk.⁴

Kotin jumps from the variability premise to the assertion of management's "right" to assign sturdier individuals to riskier jobs, overlooking the difficulty, if not impossibility, of making such judgments on scientifically sustained grounds, especially regarding carcinogenesis. However, the viewpoint has superficial appeal, as it rationalizes management's right to make arbitrary work assignments, and leaves open the possibility that management will somehow attempt to predict or decide in advance which workers are cancer-prone.

Another blame-the-victim ploy tries to shift the responsibility for workplace disability from uncontrolled exposure to lifestyle. Thus, industries (other than the tobacco industry, of course) are quick to blame lung cancer on smoking and in so doing try to absolve dusts and chemicals in the workplace from any role in the disease.

There is no question that smoking markedly increases the susceptibility of asbestos workers to lung cancer, but the risk of the non-smoking asbestos worker is also significantly greater than that of the person who does not work with asbestos. Also, smoking has no relation to other malignant diseases caused by asbestos such a pleural or peritoneal mesotheliomas.

Similarly, alcoholism programs in industry focus almost solely on family and marital problems as a cause of drinking, rather than looking into frustrations on the job as a possible factor. Re-

cent studies on heart disease are focusing on so-called Type-A behavior (characterized by a hard-driving, aggressive, competitive personality), which is considered to predispose to coronary disease. An employer may thus be provided with a rationale for blaming the disease solely on the employee, without considering that the behavior itself may also be influenced by stresses inherent in the work.

An equally insidious blame-the-victim scheme, characteristic of the cosmetic approach of some industry to occupational hazards, involves exaggeration of the known problems of small numbers of people with genetic or enzyme deficiencies. It would be useful to industry to have it proven that those workers who contract occupational illness were genetically defective and thus hypersusceptible.[†] A deficiency in the respiratory enzyme alpha-1-antitrypsin, for example, is claimed to be associated with chronic obstructive lung disease:

if susceptible subjects can be identified during pre-employment screening and are effectively excluded from hazardous occupations, some cases of chronic bronchitis may be prevented.⁵

However, a 1975 University of Arizona study demonstrated no association between deficiency of the enzyme and symptoms of chronic obstructive pulmonary disease or reduced lung function, and furthermore, found the frequency of this deficiency in the population to be trivial.⁶

Controlling Information The overwhelming majority of decisions made by regulatory agencies is based on information provided by the industries themselves being regulated. In retrospect, it seems strange that this practice has persisted so long, and that in fact it still persists. In every case study documented in this book, the relevant data base is inadequate or constrained by incompetence, biased interpretation, or even manipulation and suppression. There is no basis for believing that such examples are uncommon.

[†] Another example is the genetically determined condition of hyperinducible aryl hydrocarbon hydroxylase, affecting 10–40 percent of the general population, which appears to increase susceptibility to lung cancer.

Influencing Policy The methods by which industry influences the legislative and regulatory processes, both in the passage and enforcement of standards, are legion. Even after scientific evidence can be developed which shows that a chemical is carcinogenic, the ensuing regulatory process and development of exposure standards are strongly influenced by industrial lobbyists and trade associations. Throughout the last stages of the writing of toxic substances legislation, lobbyists from the Manufacturing Chemists Association were in daily conference with congressmen and their staffs.⁷ Out of that experience emerged a semi-autonomous lobbying group which promises to challenge the environmental legislative and regulatory process for many years to come.

Exhausting the Agencies Once an agency has determined to regulate, or has been obliged to regulate by concerns of labor or public interest groups, a common tactic of industry is to resort to protracted legal action. This is done in the full knowledge that legal proceedings on one particular chemical product or on one standard alone may extend over years, during which no regulatory control can usually be imposed. The legal costs incurred by the industry during such proceedings are usually small compared to the continued sales profits. One or two cases such as aldrin/dieldrin can exhaust the legal resources of an agency, which are small compared to the virtually limitless legal and other resources that industry can muster.

Insistence on the case-by-case approach has been a favored industry tactic. Basic questions on carcinogenesis have to be argued over again and again for every separate proceeding (such as for the chlordane/heptachlor case, which revived all the same set of problems settled before in the aldrin/dieldrin hearings). This seems the basis for industry's vigorous opposition to the "cancer principles" and to the generic approach to regulation of carcinogens proposed by OSHA.

In late 1977, the Manufacturing Chemists Association spun off the American Industrial Health Council to "assist" OSHA and other agencies in developing policies on carcinogens.⁸ Convinced that "OSHA may be developing the national standard for the identification and regulation of carcinogens" in the environment as well as the workplace, the council provides technical and eco-

nomic analysis on behalf of its member industries. Its counter-proposal to OSHA's "generic" carcinogens standard would set up two major categories of carcinogens: "human carcinogens" (Category I) and "animal carcinogens" (Category II). Within each category, it would differentiate high, intermediate, and low-potency agents. More tellingly, it would require OSHA to establish apparent no-effect levels for carcinogens, to assess both risks and benefits before setting workplace exposure levels, and to emphasize the use of controls based on personal protective equipment. This is in contrast to OSHA's and labor's policy favoring stricter work practices. The council's proposals would lay the foundation for unending legal challenges to future attempts to regulate any occupational carcinogen.

The position of the American Industrial Health Council rests on claims that there is no evidence of any recent increase in cancer incidence, that most cancer is due to smoking and diet, that the incidence of occupational cancer is low, only in the region of 5 percent,[‡] that the role of industrial chemical carcinogens in oc-

[‡] The scientific quality of the testimony of industry and its consultants is not impressive. Union Carbide's Browning, in response to a question as to whether his company had a regular ventilation inspection and maintenance program, whether they just awaited complaints of workers, or what else they waited for, jocularly answered: "Well, we pick up the bodies." James J. Jandl, Professor of Medicine at Harvard (who testified in earlier OSHA hearings to the effect that only hypersusceptible workers develop leukaemia following benzene exposure), when asked to comment on the value of carcinogenicity tests in rodents took a somewhat moderate view from Browning and responded:

. . . this is a very faulty system. First of all, these are bad seed animals. They are inbred in the most obscene way, mother and son, father and daughter, brother and sister, and this is done by people who enjoy that, for many, many generations. . . . there has to be some equity achieved by the amount of dose given to these poor little critters to compensate for their short life span. . . .

Richard Wilson, Professor of Physics at Harvard, expressed his view that "compensation or hazard pay" is a preferable alternative to government regulation of occupational carcinogens. Harry B. Demopoulos of New York University Medical School recommended that OSHA could more effectively prevent cancer by controlling smoking, besides alcohol, in the workplace (Demopoulos is author of an unpublished document "A Rational View of Cancer in New Jersey," widely circulated by the New Jersey Chamber of Commerce, which contains unsupported statements such as "only a small number of cancers are industrially related," and "asbestos is a weak carcinogen . . . handled with precautions that lead to low exposures of workers such that cancers will not develop").

cupational cancer is small, and that the costs of regulation as proposed by OSHA are excessive. These cost estimates were developed by Foster D. Snell Inc., Division of Booz, Allen & Hamilton (in a report released on February 27, 1978), whose earlier cost analyses on meeting the "no detectable level" vinyl chloride standard were shown to be grossly exaggerated. The study claimed that the cost of controlling suspect carcinogens could range between \$9 billion and \$88 billion in capital investment, and between \$6 billion and \$36 billion in annual operating expenses. However, HEW Secretary Califano, in his September 11, 1978, address to a national AFL-CIO conference on occupational health, commented:

It is in my judgment myopic to argue that programs to protect workers are inflationary . . . if we do not count in our calculations what those programs buy: safety, health, and often greater productivity.

Apart from the inherent distortions in these claims, they ignore the growing evidence of the occurrence of cancer in the general community due to discharge or release of carcinogens from the workplace to the external environment. They also ignore the likelihood of inducing cancer in the children of exposed pregnant workers, besides in the workers themselves. Finally, apart from inherent questions on the validity of economic impact analyses by industry, they ignore the much greater costs to society of failure to regulate industrial chemicals in the workplace, let alone in the general environment.

The debate as to the overall importance of occupational carcinogens as a cause of cancer was, to all intents, effectively settled with the release of the September 15, 1978, HEW report, "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors." In an anonymous October document, AIHC attempted a rebuttal on undocumented grounds including that the HEW exposure estimates were based on past exposures that were much higher than allowed in current "more responsible" industrial practices. Fred Hoerger of Dow Chemical Company

and an AIHC spokesman told a news conference on October 26 that "The whole [HEW] paper is exaggerated speculation [with] erroneous assumptions in elementary statistics and elementary epidemiology." In a subsequent interview, David Rall, one of the senior author's of the report, commented, "In general, this is what you'd expect from industry, we're comfortable with our study" (*Washington Post*, October 26, 1978). The American Petroleum Institute (API), however (in a supplemental post-hearing brief of December 19, 1978), adopted a more progressive stance:

API has always viewed the "cancer epidemic" question as irrelevant, since API supports the general goals of OSHA in improving its ability to regulate carcinogens. Whether occupational sources are partly responsible for 1 percent or 40 percent of all human cancer makes no difference in the context of developing regulatory procedures to control occupational carcinogens.

The inability of the industry during and after the hearing process to substantively challenge the scientific basis of the OSHA proposals, has become generally apparent.* This inability led to the decision by industry to shift the focus of debate from science in OSHA to economics in Congress, where the issues are clouded by other considerations including the national mood of deregulation. This reflects a more broadly based strategy that industry has recently evolved in opposition to environmental regulation.

The industry position on the allegedly heavy costs of regulation in general and occupational carcinogens in particular has gained the sympathy of the present administration. A Regulatory Analysis Review Group, with representation from the Council of Economic Advisors and the Council on Wage and Price Stability, is now requiring agencies to justify all proposed regulation that is perceived to be inflationary, even if this is unproven. The Group chaired by Council of Economic Advisors Charles L. Schultze, in September, 1978, selected the "generic" carcinogen policy as one of the handful of "very expensive regulations" it would study. On

* The overall conclusions of the HEW report were supported by two AIHC consultants, Revel A. Stallones and Thomas Downs (of the University of Texas School of Public Health). AIHC failed to include the Stallones-Downs review in its post-hearing submissions to OSHA.

October 24, the Group issued a report criticizing OSHA for proposing too inflexible a regulatory scheme, and one that did not pay adequate attention to the costs of regulation. As yet, OSHA and other regulatory agencies have failed to develop and present a sufficiently strong case for the opposing position: that the costs of regulation are trivial in relation to the costs of failure to regulate, which are highly inflationary though still largely unrecognized.

The Flight of the Multinationals In the past, when faced by the prospect of local regulatory controls, industry has moved or has threatened to move to Southern states, which have traditionally been more receptive to industrial interests and less concerned with occupational health and environmental considerations. With the passage of the 1970 Occupational Health and Safety Act, the opportunity for such evasions in the United States became more limited.[†] U.S. industry with multinational connections then shifted tactics to exporting their hazardous industries abroad. "Runaway" shops were created in lesser developed countries such as Brazil or Taiwan, where there are virtually no regulatory controls and where cheap and unorganized labor is amply available. More surprising, however, is the increasing flight of segments of the chemical industry to runaway shops in eastern Europe, where regulatory controls and opportunities for public protest are minimal compared to the United States.

The growing flight from regulation poses major threats to foreign workers, and to the environmental quality outside the United States, besides reflecting on the corporate ethics of the industries involved. It also poses two sets of threats to the U.S. economy: loss of jobs and unfair advantage in competition with those segments of industry complying with pollution control regulations in the United States. In some industries, the flight from regulation is already established.⁹ In others, it appears imminent. The greatest flight is seen in the asbestos textile industries, which are being increasingly located in Mexican border towns and in Taiwan and South Korea. There are also indications that other asbestos manu-

[†] However, the chemical industry in New Jersey, is threatening to move elsewhere if the state perseveres in attempts at regulation, with particular reference to limiting the discharge of carcinogenic chemicals into the environment of the surrounding community.

facturers, particularly of friction products such as brake linings and disc pads, will follow this course. Other flights involve arsenic-producing copper smelters and the plastics, benzidine dye, and pesticide industries.‡

Vigorous legislative initiatives, such as federal chartering of giant multinational corporations, are urgently needed.¹⁰ Federal chartering would impose specific restrictions on giant industries where four or fewer firms account for over 50 percent of sales in some major markets, and would restructure them internally to prevent such corporate abuses as bribery, illegal domestic and foreign political contributions, price-fixing, monopolistic practices, regulatory violations (including manipulation or suppression of data), and the export of hazardous products and processes. The broad objectives of the proposed federal corporate chartering would be to achieve corporate accountability to the U.S. government and people

to assure more corporate democracy by giving greater voice or authority, for example to shareholders over the decision of managers; to require greater disclosure of the social and financial performance of companies; to deconcentrate industries and restore competition; to assure employees their civil rights and liberties by a bill of rights for employees.¹¹

The recent proposal of the Council on Environmental Quality to require industry to file environmental impact statements before exporting hazardous products and processes is also an overdue approach to this problem. Patterns of flight need to be carefully monitored by federal groups and other concerned interests, including organized labor and responsible industry.* Assistance should also be requested from international organizations such as the World Health Organization and international labor groups.

An issue related to the flight of the multinational corporations is the common practice of export of products whose use is not permitted in the United States, such as the pesticide leptophos, or

‡ Following legal action by a coalition of environmental groups, the Agency for International Development announced in 1976 that it would no longer sponsor the export of pesticides banned in the U.S.

* The information available on hazard export is extremely scanty, though the trend is already well established.

products whose use has been banned in the United States, such as the pesticide dieldrin and children's sleeping garments treated with the flame retardant Tris. In January, 1978, Senator Gaylord Nelson (D-Wisc.) called for a ban on export of pesticides whose use is prohibited in the United States, after samples of imported agricultural products show residues of these pesticides. This whole area needs comprehensive legislation to prevent exposure of foreign workers and consumers to products manufactured by the U.S. industry but considered too hazardous for use here.[†] A critically related issue which demands vigorous international initiatives is the growing promotional campaign of the tobacco industry in the Third World.

Technological Innovation and Regulation

Some segments of industry have repeatedly expressed concerns that the mounting tide of federal regulation over the last two decades is impeding or stifling technological innovation. The Manufacturing Chemists Association and Dow Chemical Company have claimed that requiring chemicals to be tested prior to their introduction into commerce, in accordance with current requirements of toxic substances legislation, is acting as an obstacle to industrial innovation. (These claims have particularly involved the manufacture of pesticides and contraceptive drugs.) Such claims ignore costs to society of the failure to regulate and they do not bear critical scrutiny even on narrowly defined economic grounds. Costs of carcinogenicity and other chronic toxicity testing and costs of toxic substances legislation are small in relation to the profits of the chemical industry.

Ever sensitive to changing national moods, industry demands for deregulation have recently become more clamorous and linked to concerns on Proposition 13, inflation, alleged free-spending by runaway regulation agencies, and growing big government intrusion into free enterprise. Industry has taken out full-page advertisements in leading national newspapers complaining that "the

[†] Banned products, being exported include Tris, DDT, cyclamates, and Red #2.

spiraling costs of regulation," both compliance and administrative, are inflationary and are stifling innovation.[‡] The industry position is buttressed by articles and letters in leading journals and newspapers from prominent academic spokesmen, and by restrictions on health and environmental regulations newly imposed by the Regulatory Analysis Review Group of COWPS.¹² Apart from the self-serving nature of industry demands for deregulation, these reflect the myopia of traditional economists preoccupied with immediate costs of compliance, rather than with the usual heavier and externalized costs of failure to regulate, such as the recognized \$30 billion annual costs of cancer (apart from its much greater unrecognized costs), the multibillion dollars costs of impending law suits on asbestos, and the costs of environmental degradation.¹³

In an address to the Third National Conference on Health Policies on May 22, 1978, Congressman Rogers (D-Fla.) commented on the dichotomous attitude of industry to costs:

Yet the contrast is startling between the runaway spending for health care and the resistance of most of American business to spending for environmental health protection. At a dizzying pace, hospitals race to build new beds and new wings, acquire CAT (computerized axial tomography) scanners, open-heart surgery units, and cardiac catheterization units—all to treat disease once it occurs.

On the other hand, last year's total environmental control expenditures for all American industry totalled less than \$40 billion, that is, less than 20 percent of the Nation's total health care spending. And American industry fought every inch of the way against every environmental health requirement. Every dollar invested to reduce deadly coke-oven emissions, to control arsenic and lead from copper smelters, to block unnecessary radiation exposures, to capture chem-

[‡] Organizational inertia and vested interests in existing technology are likely to be rate-limiting factors in the development of new technologies. Additionally, it must be recognized that the immediate costs of compliance may be disproportionately great for small business which cannot usually capture the economies of scale available to big business adopting control technologies, and may thus exert monopolistic influences. It is, however, clear that advancing information on hazards of occupational carcinogens has not been paralleled by advances in process and compliance technology. (For a critical analysis of the impact of regulation on technological innovation, see N. A. Ashford, *et al.* "The Implications of Health, Safety and Environmental Regulations for Technological Change," Department of Commerce Contract No. NB-79-SAC-A0030, January 15, 1979.)

ical plants' carcinogenic discharges, to curb toxic sulfates and nitrate particles from coal combustion, has come only after protracted political and legal struggles.

Industry demands for deregulation in pollution and preventive health areas are in interesting contrast with their insistence on continued economic regulation to protect monopolistic practices.¹⁴ In spite of all the praise lavished by industry and its public-regulations machinery on the concept of free competition in a deregulated market, industry fights vigorously to foster "economic socialism" whenever its interests are threatened, as illustrated by the opposition of the trucking industry to proposed deregulation by the Interstate Commerce Commission, and the American Medical Association (on behalf of the medical industry) to advertising. As Chairman Michael Pertschuk of the Federal Trade Commission commented in October, 1978:

Such regulations are not sanctioned by law, but rather are carried on in defiance of the law—not as *government* regulation of business, but as anti-competitive and inflationary *business* regulation of business. And where these forms of business-inspired regulation do remain inbedded in the law, it is because those businesses and professions regulated have stoutly defended their ancient right to be shielded from the discomforts of free competition.

In recent Congressional testimony, Secretary of Commerce Juanita Kreps emphasized that every industry leader agitated by "government intrusion" should understand that industry cannot responsibly demand less regulation without also addressing those social issues that prompted the need for regulation.

To the extent business helps [through improved corporate social performance] to deal with issues that might otherwise prompt government regulation, it serves its own economic interests.*

* However, a December 20, 1978, draft report on "Environmental Health and Safety Regulations" of a Department of Commerce Advisory Subcommittee (of the Advisory Committee on Industrial Innovation) demonstrated lack of comprehension of Secretary Kreps' warning. The committee (which in its exclusive composition of industry appears to violate at least the intent of the Federal Advisory Committee Act) claimed that federal regulations have a severe negative impact on industrial productivity and industrial inno-

What we are involved in is a simple but meaningful thing, the commandment that in civilized society thou shall not kill. The proponents of cost-benefit analysis would have us believe that it is all right to kill if killing is not too expensive.

James Smith, United Steelworkers of America
economist, OSHA testimony, 1978.

Labor

A 1970 University of Michigan survey sponsored by the Department of Labor found that American workers rated health and safety a higher priority than increased wages.¹⁵ This helped explode the common belief that workers relegate health issues to a minor role compared with bread-and-butter and job-security issues. In fact, workers have placed a high premium on safe working conditions throughout the hundred-year history of trade unions.

Organized labor's support of child labor laws and its insistence on an eight-hour working day led to considerable industrial strife in the 1870s. The March 25, 1911, fire at the Triangle Shirtwaist Company in New York City drew public attention to the atrocious

vation on grounds including: diverted capital expenditures from productive to non-productive areas; increased cost of product development; increased product development cycle; uncertain standards; the special problem of small business; inadequate protection of trade-secret information; excessive reporting requirements; and growing costs of product liability loss protection and prevention. The report also calls for consensus standards as a preferable alternative to mandatory government regulations. As illustration of the potential of innovation if not fettered by excessive regulation, the health panel of the subcommittee opined "the 'penicillin' for cancer . . . may be just around the corner if development is encouraged."

working conditions of many young girls, and led to the enactment of corrective legislation.¹⁶

One of the unions that has long been involved in health and safety issues is the United Mine Workers, whose members are employed in the most hazardous industry in America. The record of the union on health and safety is mixed.¹⁷ During the late 1940s and early 1950s, frustrated by its inability to obtain minimal compensation for disabled workers and urged on by Lorin Kerr, Assistant to the Executive Medical Officer of the Union's Welfare and Retirement Fund (Director of the Department of Occupational Health of the United Mine Workers of America since 1969), the Fund paid for the establishment and operation of ten hospitals in mining regions of rural Appalachia and recruited its own doctors and staff.† By 1962, affected both by mismanagement and severe recession in the industry, the hospitals were sold to the Presbyterian church and the experiment ended. One of the staff physicians, Donald Rasmussen, also led an effort to have black lung recognized as a compensable illness. The union leadership, while initially hostile to the pressure which quickly developed in its ranks around the black lung issue, was ultimately forced to support federal legislation. It took a disaster, however, the 1968 explosion at a Farmington, West Virginia, mine which killed seventy-four miners, to bring about enactment of the 1969 Federal Coal Mine Health and Safety Act.

The modern era of labor concerns over health and safety and occupational carcinogenesis is a striking tribute to a handful of labor leaders who have had to overcome crippling problems. Not only have they had to emancipate themselves from the self-serving authoritarianism of industry physicians and other professionals, and to educate themselves in the relatively recent area of adverse health effects due to chemical exposures, but they have also had to develop rank-and-file support. To do this, they have sought out advice and guidance from a few independent professionals in the academic community. On a limited scale, they have also developed their own expertise and resources, particularly in industrial hygiene. Additionally, they have had to contend with economic

† The Fund was established in 1946 under a wage agreement between the Union and Coal Mine operators, and is financed by a royalty paid by the operators per ton of bituminous coal.

blackmail and threats of job loss by industry whenever they advocate or support attempts to regulate unsafe exposures. Not surprisingly, most of the focus of labor concerns on problems of chemical exposures has so far been expressed in Washington, D.C. rather than at the grass-roots level.

Most prominent among these labor leaders is Anthony Mazzocchi, Vice President of the Oil, Chemical, and Atomic Workers Union (OCAW). One of Mazzocchi's many contributions has been to extend the arena of concerns on health issues to the rank-and-file of union membership. The president of the union, Al Gospiron, has also made important contributions, particularly as chairman of the Standing Committee on Safety and Occupational Health, AFL-CIO. Another labor leader who has taken consistently strong positions on needs to regulate chemical hazards is George Taylor, executive secretary of the Standing Committee on Safety and Occupational Health. Taylor has exerted a powerful influence on the development of a wide range of occupational standards, particularly through his chairmanship of the Staff Subcommittee of the Standing Committee. Another important figure is Peter Bommarito, president of the United Rubber Workers, assisted by his industrial hygienist, Louis Beliczky. Bommarito is chairman of the Executive Committee on Occupational Health and Safety of the Industrial Union Department, AFL-CIO, and has pioneered the development of joint labor—management contracts to universities for research on problems of carcinogenesis in the rubber industry.

The Industrial Union Department of the AFL-CIO, established after the 1954 AFL-CIO merger (the current president is the labor veteran Jacob Clayman), plays a critical role in the whole area of occupational health and safety. The director of the department's Division of Occupational Safety and Health and the Environment is Sheldon Samuels, who has functioned primarily as a policy analyst and technical consultant to the industrial unions. He also monitors the performance of OSHA, NIOSH, NCI and other agencies.‡ Additionally, Samuels has developed educa-

‡ An interesting sideline on Samuels was his recommendation in July, 1978 (on behalf of organized labor), that NCI withdraw its invitation to Hans Weill, Professor of Medicine at Tulane University in New Orleans, to cochair a conference on lung-cancer surveillance. Labor's objections were based on the fact that Weill was unlikely to be neutral in view of his close

tional programs for organized labor on occupational hazards.

Major credit for the development of the 1970 Occupational Safety and Health Act belongs to Jack Sheehan, legislative director of United Steelworkers of America. Sheehan is an accomplished lobbyist whose influence has been felt on most recent major occupational standards.

George Perkel, Director of Research of the Amalgamated Clothing and Textile Workers Union, and Larry Ahern, Research Director of the International Chemical Workers Union, have both contributed materially to expressing labor's informed concerns on standards. Perkel also exercised an important influence as Chairman of the Industrial Union Department *Ad Hoc* Committee on Occupational Carcinogens on the precedential 1973 OSHA standards proceedings for fourteen occupational carcinogens.

The International Association of Heat and Frost Insulators and Asbestos Workers, whose president is Andy Haas, has also been prominent in the struggle to protect workers from exposure to carcinogenic dusts and fibers. The successes that the union has achieved in this regard reflect the important collaboration they have developed with Irving Selikoff.

AFL-CIO is now developing closer collaboration with unions outside the Federation, particularly the International Brotherhood of Teamsters and the United Auto Workers Union. In this they have been materially aided by R. V. Durham, Research Director of the Teamsters, and Dan McLeod and Frank Mirer, Industrial Hygienists of the Auto Workers.

Recent labor concerns on occupational carcinogenesis have

relationship with the American Textile Manufacturer's Institute and with the Asbestos Information Center who had contracted with him to attack the OSHA proposal to reduce to 500,000 the current 2-million-fiber-per-cubic-meter asbestos standard. Weill's position, that the current standard "should be given a reasonable trial while further epidemiologic investigation established its safety or lack of it" (submission of the Asbestos Information Association on Proposed Revision to the OSHA Asbestos Standard, April 8, 1976, Docket H-033, p. 24), is consistent with his earlier prospective studies of accelerated silicosis among poorly protected sandblasters, during which time workers dying after one and a half years exposure were observed in order to assess "rational occupational environmental standards" (National Heart and Lung Institute Grant Application, September 4, 1975). The latter studies effectively excluded OSHA inspections under an agreement reached between the industry and Weill (see S. W. Samuels, "NCI Disinvitation," *Science* 202 [1978], p. 694).

been largely spearheaded by OCAW, whose members operate many of the nation's largest refineries and chemical plants. Throughout 1969 and 1970, many of the union's nine district councils, covering much of the United States and all of Canada, sponsored workshops entitled "Hazards in the Industrial Environment." At these conferences, Mazzocchi discussed with union members the basic facts underlying health and safety problems in OCAW plants. For many, it was the first realization that problems arising from workplace chemicals could be recognized and dealt with.

Mazzocchi sought out and developed close personal contacts with a handful of professional scientists who helped him increase awareness in labor, Congress, and elsewhere in the government of the major hazards posed to workers by uncontrolled exposure to toxic and carcinogenic chemicals. Mazzocchi also sponsored the formation in 1971 of the Scientists Committee for Occupational Health, which, jointly with the United Auto Workers and other New Jersey labor groups, taught several courses at the Rutgers University Labor Education Center. Their students were workers who, instead of hearing just about ladders and fire extinguishers, found out about cancer-causing chemicals in their own workplaces, many for the first time.

In 1973, 4,000 OCAW workers went out on a five-month strike against Shell Oil in California and in four other states, demanding that their new contract embody specific measures to protect health and safety on the job. The union made four key demands:

1. Establishment of a joint union—management health and safety committee in every plant.
2. Periodic inspections of plants, by independent consultants jointly approved by labor and management, to determine whether workers are being exposed to hazards.
3. Medical examination of workers, at company expense, when indicated by plant inspections.
4. Availability to the union of all company records on worker's sickness and death.¹⁸

Impressed by the importance of the strike, a group of about twenty-five leading scientists and educators signed a statement, published by the union as a full-page advertisement in the *New York Times* on May 3, 1973.* This statement recognized that the strike was unique in labor history and prompted exclusively by concerns for occupational health:

Workers have long served as unwitting guinea pigs, providing useful toxicological data which helped to protect the public. The effects of most environmental pollutants, such as carbon monoxide, lead, mercury and also of most human carcinogens were first detected in workmen; the in-plant environment is a concentrated toxic microcosm of that outside. Additionally, many toxic agents disperse beyond the plant and pose public hazards.

The success of the OCAW strike is critical both to labor and the public. This has already been recognized by ten major environmental and public interest groups who have endorsed the Shell strike and boycott. The demand of labor to participate actively in protecting the health and safety of workers is basic and inalienable and cannot be sacrificed to narrow economic interests. It is hoped that Shell will adopt a posture more consistent with the public interest and the intent of the 1970 Occupational Safety and Health Act . . .¹⁹

Shell, which at first refused to bargain on "management prerogative" issues, was eventually forced to give in. However, the subsequent enforcement of contract terms continues to be an uphill struggle.

A key labor issue which has been strongly championed by OCAW is the guarantee of full economic protection of a worker in the event he or she is removed from a job classification on the basis of medical examination results. This is known as "rate retention" and means that the worker would, upon transfer, retain the same rate of pay allowed by the previous job classification, as well as all pay increases, seniority, and other benefits accruing to the former position. Another critical area pioneered by the union is the use of the Review Commission of OSHA to protect its members in situations where management contests citations by OSHA for violations against health and safety standards.

* The author wrote this statement.

Over the recent years, management has encouraged hostility between labor and environmentalists by threatening to close plants when there are major attempts to control in-plant pollution. In 1972, responding to demands to improve working conditions, Union Carbide threatened to shut down its Alloy, West Virginia, plant, elected one of America's ten dirtiest factories by *Business Week* magazine. OCAW President A. F. Grospiron refused to knuckle under to "environmental blackmail," and Union Carbide was eventually forced to improve work practices.²⁰ In an address to the Union convention in 1973, Sierra Club Executive Director Michael McCloskey commented, "Your Union has been preeminent in recognizing that many environmental threats originate in the workplace and affect the workers first and foremost, before they escape into the community-at-large."

Labor has gradually developed working relationships with NIOSH and OSHA. Representatives of labor, as well as management, now participate in various advisory committees of these agencies. In addition to the more long-standing association of labor with Selikoff (particularly by the International Association of Heat and Frost Insulators and Asbestos Workers), and other such associations of labor as those with Thomas F. Mancuso, occupational physician at the University of Pittsburgh, who contributes an excellent monthly health column in the newsletter of the International Union of Electrical, Radio and Machine Workers (see Appendix IV), labor has recently developed contractual arrangements with a few universities to investigate specific occupational health problems. Unions that have been prominent in this regard include OCAW, the United Auto Workers, and the United Rubber, Cork, Linoleum, and Plastic Workers of America. A major recent resource for labor besides management and government, is the Society for Occupational and Environmental Health, whose meetings and conferences have created an opportunity for independent and expert analysis of health-related issues.

Realizing the critical importance of developing its own internal scientific and technical resources, several unions have created health and safety departments or units, which are at present largely staffed by industrial hygienists.[†] OCAW and the United

[†] These include OCAW, United Steelworkers of America, United Rubber, Cork, Linoleum and Plastic Workers of America, and United Auto Workers.

Auto Workers have set up Health and Safety Offices which administer nationwide programs for their members, coordinate activities of individual locals (particularly in testing provisions of the Occupational Safety and Health Act), and help extend the parameters of the collective bargaining agreement. The only union that has had a medical director for any period of time (Lorin Kerr) is the United Mine Workers of America.

AFL-CIO for several years has been considering the creation of its own resource in occupational health and safety. Recent occupational health crises have lent further urgency to these plans and to the realization that, in the final analysis, labor must rely on its own resources.‡ Accordingly, in December, 1977, the AFL-CIO Executive Committee authorized creation of its own "institute or appropriate structure . . . [as a] permanent means of more adequately meeting our responsibilities to protect the health and safety" of workers. With the guidance of OCAW's Grospiron, this proposal was transformed from an earlier concept of an academy-like institution to a department with the on-line function of providing staff services to AFL-CIO as part of its secretariat. The department was formally created in August, 1978, with George Taylor as its head. Taylor reports directly to AFL-CIO President George Meany through his assistant Tom Donahue. It is expected that the department will hire scientific and technical staff in addition to consultants, and that its initial priorities will focus on the standard setting process in both NIOSH and OSHA.*

Another major and overdue development has been the growing awareness in labor that there is an inevitable built-in conflict of

‡ In three recently publicized occupational catastrophes (involving kepone, a carcinogenic pesticide producing neurotoxic and sterilizing effects in workers at Life Sciences Products Corporation in Virginia; leptophos, a pesticide producing neurotoxic effects in workers in a Velsicol Plant in Bayport, Texas; and DBCP [dibromochloropropane], a carcinogenic soil fumigant producing sterility in workers involved in its manufacture at Occidental Chemical Company in California), it was the workers themselves who first recognized the problem, not the plant physicians and not OSHA. It must be clearly recognized that plant health and safety committees are still the exception in the U.S. and that hygiene and occupational health services are still not available or utilized by most U.S. industries.

* Additionally, an AFL-CIO Workers Institute for Safety and Health, headed by Charles Warren, Secretary-Treasurer of the Ohio AFL-CIO, was incorporated in Columbus, Ohio, in April, 1979, with a satellite office in Washington, D.C.

interest in the present system of direct employment of occupational physicians by industry. Results of physical examinations on individual workers can thus be directly transmitted to management, with ensuing risks of job transfer or loss.

The role of industry epidemiologists, industrial hygienists, and other professionals involved in occupational health and safety demands critical evaluation. These needs are emphasized by the growing body of information on the existence and extent of constraints on health and safety data, ranging from inadequacy and biased interpretation to manipulation and fraud.

Clearly the salaries of health and safety professionals is the exclusive responsibility of industry as an essential part of the costs of doing business. This should not mean that the loyalty of these professionals must necessarily be directed to their employers. While the salaries of meat inspectors and grain elevator inspectors are in the final analysis paid for by the industries concerned, these inspectors are primarily responsible to USDA. Similarly, health professionals in industry must be primarily responsible to the worker—patient, rather than to industry. It should be a felony for an industrial physician to divulge to management the results of a physical examination. Such information is the exclusive property of the concerned principals, the physician and the worker—patient, and must not be shared with management. This is the only way by which a worker can be protected against economic penalties which management may invoke if a worker is found to be suffering adverse effects from conditions at work. Otherwise, the worker will be forced to choose the Russian roulette of exposure to occupational hazards, rather than risk job loss or transfer to a lower-paid job.

Confidential physician-worker relationships would in no way decrease the ability of an occupational physician to disclose to management and to labor the gross and anonymous results of physical examination and biological monitoring of groups of workers in specific job situations in order to allow necessary corrective action to be taken. Labor has begun to realize that the development of further occupational standards is of limited value, possibly even counterproductive, unless workers can be assured of the independence of the professionals whose responsibility is, or should be, the protection of the workers' health. The worker also

must be protected against economic penalties by guarantees of equal pay and seniority rights in the event he is moved from a job with a high level of exposure to one with a lower level.

The Public Interest Movement

The public interest movement, as a modern expression of social ethics and as an instrument of political reform, is now about a decade old. Public interest organizations have generally evolved from the initiatives of young activist lawyers and other professionals, and also from expressions of citizen and consumer concerns. In this, they have been supported by a small number of independent scientists and engineers who have helped bridge the gap between technical and societal considerations.

Public interest organizations embrace a wide spectrum of heterogeneous objectives and styles. While the most influential and best-known groups are Washington-based, citizen and consumer groups more "grass roots" in nature are found in most major metropolitan centers. Student public interest research groups are a nationwide effort. They are autonomous, student-run organizations to be found on most campuses and have a record of local activism. Such groups were inspired in large part by Ralph Nader. (See Appendix V for a summary listing of major public interest groups with particular concerns on environmental and occupational cancer.)

The public interest movement expresses the conviction that the "common good" is inadequately represented in decision making at federal and local levels, where narrow economic and political interests are joined, often at the expense of social equity. The movement also expresses the conviction that the public health and environmental costs of modern technology are poorly perceived and too readily discounted in regulatory decision making, and that the burden of proof for such "externalized" costs is too readily accepted by government, or inappropriately shifted from the private to the public sector. As recently stated:

In almost every judicial, legislative or administrative conflict or policy-making process, the law provides either implicitly or explicitly

that the burden of proof rests on one of the parties. The criteria are quite simple. The burden of proof rests on the party, that initiates the risk, that profits from the risk, and that has the greatest resources to do something about the risks.²¹

The public interest conviction of the imbalanced and unrepresentative nature of governmental decision making has been supported by evidence of major conflicts of interest in senior staff of regulatory agencies, by their unwillingness to involve qualified citizen and consumer representatives in decision making, by restrictions on public access to data on the basis of which important decisions on health and safety are based, and by evidence of major constraints and deficiencies in this hidden data base.

Broadly speaking, public interest groups are either "resource" or "activist" in nature. The resource function is well illustrated by the activities of the Rachel Carson Trust in gathering, organizing, and interpreting information on pesticides and toxic chemicals, and in disseminating this to other concerned groups and the public.[†] Activist functions include lobbying, attempting to institute regulatory reforms, monitoring agency performance, and filing legal action as a last resort. Each public interest group tends to specialize in a particular area: drugs, food additives, pesticides, air and water pollutants, or occupational health and safety, to name a few. While in the past labor has tended to resent the "intrusion" of public interest groups into the arena of occupational health, particularly because of the alleged conflict between job security and safer working conditions, informal accommodations, such as the supportive relationship between the Health Research Group and OCAW, have recently developed.

Public interest groups have faced difficulties in establishing themselves and making an impact on public perceptions and government policies, already sensitive and responsive to the massive and well-focused and financed industry lobby. The most limiting of these problems have been financial.[‡] Public interest groups

† The author is president of the Rachel Carson Trust.

‡ An important recent development is the "Public Participation in Federal Agency Proceedings Act," sponsored by Senators Edward Kennedy (D-Mass.) and Charles Mathias, Jr. (R-Md.), and Congressman Peter Rodino (D-N.J.), now pending before Congress. The bill would allow pub-

largely depend on voluntary contributions from the general public. Other problems stem from the understandable tendency of the groups to move on to other areas of concern after initial resolution of a particular issue, with resulting inadequate follow-up and the possibility of "winning the battle, but losing the war." Public interest groups have also tended to work in relative isolation from each other, for reasons which include their strong sense of independence and preoccupation with their own immediate aims, sometimes to the exclusion of broader objectives. Recognition of these limitations, in addition to the need to develop closer contact between public interest groups and concerned professionals and labor, led to the creation in 1974 of the Commission for the Advancement of Public Interest Organizations.* Current activities of the commission focus on the development of loose, ad hoc coalitions of public interest groups and labor around critical generic concerns, particularly relating to preventable cancer. These activities include supporting New Jersey citizen and labor groups in their efforts to reduce the high incidence of environmental cancer in their state; nominating qualified professionals to serve on the NCI National Cancer Advisory Board and advisory committees of other agencies with prime responsibility in control of environmental carcinogens; supporting the nomination of qualified scientific and legal professionals to senior positions in federal agencies (for example, the present NCI director, Arthur Upton); and holding "round-tables," where heads of agencies are invited periodically to interact with the public interest and labor communities on such critical questions as environmental and occupational cancer.

The past impact of public interest groups on national perspectives and on the legislative and executive branches of government has been profound and disproportionate to the small size and resources of these groups. In no area of public interest activity has

lic interest groups to participate in agency proceedings and also to file suit against agencies for unlawful acts. It would create a special treasury fund of \$15 million annually for three years which would be available for these and related purposes.

* The author chairs this commission, which is an arm of the Monsour Medical Foundation, Jeanette, Pa.

this been better exemplified than in that of preventable cancer. As illustrated in the case studies cited in this book, the great majority of all standards on environmental and occupational carcinogens developed over the last decade have been initiated by petitions and lawsuits of public interest groups and labor against the government (see Table 9.8). The past successes of public interest groups in these actions have been all the more remarkable in that they have generally had to fight on two fronts, against both industry and the regulating agency. Groups that have taken a lead role in these actions are the Environmental Defense Fund, Public Citizen's Health Research Group and Litigation Group, and the National Resources Defense Council. Important contributory roles have also been played by other groups, including the Sierra Club, Consumers Union, Consumer Federation of America, Center for Science in the Public Interest, Federation of Homemakers, Action on Smoking and Health, Migrant Legal Action Programs, Friends of the Earth, the Rachel Carson Trust, the National Audubon Society, and the National Wildlife Federation.

Recent Trends

Past contacts between public interest groups and regulatory agencies and industry have necessarily been adversarial. Adversarial tactics, whether in committee meetings or the courts and Congress, have been helpful in defining positions on environmental priorities and posing critical environmental and public health problems. Tentative moves are now being made by a few public interest groups to explore the alternative that non-adversarial dialogue with industry may prove to be mutually beneficial in defined circumstances, such as assuring industry of the essential consistency between long-term industrial growth and protection of the environment and public health.

An interesting example of these exchanges is the National Coal Policy Project, the environmental caucus of which is headed by Laurence I. Moss, former president of the Sierra Club.²² Another is the Business-Environment Project created by the Conservation

Foundation in attempts to suggest improved guidelines for toxic substances testing.[†] A draft document of the Business-Environment Project dated January 16, 1978, entitled "Approaches for the Development of Testing Guidelines Under the Toxic Substances Control Act" reveals an apparent lack of comprehension of the basic toxicological issues involved. The document has been criticized by an industry scientist as "being more concerned with birds and bees than humans." The document places major emphasis on short-term tests as indirect indicators of carcinogenicity. As a final criterion of carcinogenicity, the document recommends the "heritable translocation test," which is a highly specialized procedure that has so far only been applied to fewer than a dozen compounds.

Questions of expertise apart, there are needs to consider whether the public interest movement now has the necessary scientific resources to develop and sustain the type of rapprochement with industry envisioned in these new exchanges. There is a growing likelihood of an increase in these dialogues between industry and the public interest movement, which is encouraged by the possibility of foundation and agency funding. It seems possible that premature moves of this type may blunt the limited impact of the public interest movement, even to the point of possible co-option.

An important development has been the recruitment of some key leaders of the public interest movement to senior positions in federal agencies. These include Joan Claybrook, former director of the Public Citizen Congress Watch, currently Administrator of the National Highway Traffic Safety Administration; Carol Foreman, former executive director of the Consumer Federation of America, currently Assistant Secretary of Agriculture; Harrison Wellford, formerly of the Center for the Study of Responsive Law and chief legislative assistant to the late Senator Philip A. Hart (D-Mich.), currently Executive Associate Director for Management and Regulatory Policy, Office of Management and Budget; Gus J. Speth, formerly of the Natural Resources Defense Council, currently a member of the Council on Environmental Quality;

[†] This project is co-chaired by Karim Ahmed of the Natural Resources Defense Council and George Dominguez of Ciba-Geigy, and is headed up by Sam Gusman, just retired as Washington representative of Rohm & Haas.

David Hawkins, also of the Natural Resources Defense Council, currently Assistant Administrator Air and Waste Management, EPA; Peter Shuck, formerly of Consumers Union, currently Deputy Assistant Secretary of HEW; and Cynthia Wilson, formerly of the National Audubon Society, currently Assistant to the Secretary of Interior.

It is premature to assess the impact of this "move to government." While it is generally welcomed as a potential infusion of "new and honest young blood," a caution has been raised to the effect that not only have the slender ranks of the public interest movement been seriously depleted, but also that its unique strength lies in keeping a distance from government. Nader has been more explicit in his criticism of consumer advocates who have joined the administration.

. . . I think they've been too cautious. I think they've been too defensive, and I think to some degree they've even been apologetic about prior careers as consumer advocates. They won't admit it, but their behavior has been such that they're leaning over the other way to compensate for it.²³

The public interest movement is now at a critical juncture. It has lost some of its best leaders and most informed lobbyists to government. In the absence of new initiatives, the future financial base of the movement is precarious. Competition for public funds among the estimated 2,500 public interest organizations is now becoming keener. Direct mailing lists soliciting support for public interest groups have become so overgrazed that they are now of questionable value. Foundation support for public interest groups has sharply declined, consistent with usual foundation policies of initiating but not sustaining. This growing financial crisis has been compounded by the election of a liberal President, who has taken the steam out of left-wing social protest, which in the past has been an important source of public interest support. There has not yet been adequate articulation of this shift of the winds of fortune by public interest groups to the executive branch, Congress, foundations, or the public at large.

The public interest movement has not yet adequately shifted focus from emphasis on specific individual issues, such as a par-

ticular carcinogen, pesticide, or feed additive, to broader approaches which will embody a wider set of generic concerns. More critical still is the absence of a grass-roots consumer movement which is clearly the only practical way consumers will be able to exercise effective political influence to protect their interests.[‡] Industry, on the other hand, has mobilized on a massive and well-financed scale to propagandize the government and an already apathetic or even antipathetic public against the need for regulatory controls and to assert, on the basis of tenuous or misleading evidence, that their costs would be inflationary, while completely ignoring the much higher costs to society from failure to regulate. Industry has launched a new range of well organized and financed cooperative initiatives, such as the Business Round Table, corporate Political Action Committees,* and the American Industrial Health Council, which threaten the future effective control and regulation of industry.

The combination of well-focused intensive legislative pressures from a small army of highly paid lobbyists in Washington, national grass-roots support mobilized through Chambers of Commerce all over the country, and lavish advertisements in the press (such as those of the Calorie Control Council in opposition to the proposed FDA saccharin ban), have created major and unparal-

[‡] The absence of such a grass-roots base, together with strong pressures from big business on the House of Representatives, were critical factors in the defeat in February, 1978, of the long-embattled bill to establish a new federal consumer protection agency.

* Political Action Committees, authorized by recent changes in federal election laws, now number about six hundred, while their labor counterparts have leveled off at about 250. Massive expansion of the corporate committees is being organized and stimulated by a consortium that includes the National Chamber of Commerce, the National Association of Manufacturers, the National Federation of Independent Business, and the Center for the Study of Free Enterprise of the University of Southern California's Graduate School of Business. The avowed major objective of these new committees is to reduce government regulation and bureaucratic paper work. However, as pointed out in a recent OMB report, "Paper Work and Red Tape," much of the paper burden has been created by Congress and the courts, and most complaints mask an opposition to a particular federal program. (Also, major needs for paper work are the necessity to protect the public against fraud and to evaluate government programs.) In fact, despite a large number of new programs with reporting requirements, OMB has shown that there has been a 10 percent reduction in the time spent on report filing since January, 1977.

leled threats to the whole process of democratic decision making as well as to the public interest movement. It is now more urgent than ever the public interest groups address this crisis of imbalance in national policies. This is the critical message that must be intensively disseminated on a grass-roots level if public interest groups are to survive, let alone maintain their effectiveness.

The possibility of stronger public interest input into federal agencies was created by a memorandum of April 27, 1978, by President Carter, outlining new functions for the White House Office of Consumer Affairs, headed by Esther Peterson. It is proposed that this office should become actively involved in executive policy making on consumer problems. Existing public interest participation programs in federal agencies will be reviewed. Peterson will also be able to evaluate public interest programs in federal agencies—and other actions that impact on the public interest—and to make necessary recommendations how these may be improved.

Additional Influences on Policy Making

Independent Professionals

Among other groups influencing national policies, a handful of independent professionals of recognized expertise in fields such as toxicology, carcinogenesis, and epidemiology has been particularly important. Over the last decade, these people have been instrumental in providing a critical data base and scientific guidance to leading labor reformers, and to public interest groups and members of Congress concerned about preventable cancer and other environmental and occupational problems. These professionals have also become an important resource to leading press and science writers.

Professional Societies

On the whole, the professional community-at-large and professional organizations and societies have been indifferent, if not hostile, to environmental and occupational problems and needs for controls. The main reason for this is a not unnatural preoccupation with professional concerns, which is often compounded by conservatism, ignorance of the problems, or special interest. The role of the American College of Obstetricians and Gynecologists in joining with the Pharmaceutical Manufacturers Association in opposing the FDA's action on labeling of Premarin with a carcinogenicity warning is illustrative. Other examples include the Society of Toxicology, which has served as a professional base for the protection of industrial interests, such as by fighting against the Delaney Amendment. In a similar class, the American Conference of Governmental Industrial Hygienists has generated so-called safe exposure levels or "threshold limit values," exposure levels for a wide range of chemical agents without adequate consideration of long-term effects, particularly cancer.

On the other side of the coin, organizations such as the Medical Committee on Human Rights have exercised a useful role in informing socially conscious clinicians of needs for safe working conditions. From such activities have sprung a series of Committees on Occupational Safety and Health (so-called COSH groups) many of which continue to play an important long-term role in their communities, such as those in Chicago (CACOSH) and Philadelphia (PHILAPOS). The Environmental Mutagen Society, created in 1969, has performed and continues to perform a useful service by interesting geneticists in practical problems of genetic hazards from toxic chemicals in the general environment and workplace, and in educating the scientific and regulatory communities on such problems. The American Public Health Association is also developing a contributory role in environmental and occupational areas. The American Association for the Advancement of Science has developed programmatic coverage of major environmental and occupational problems and their social

implications in its annual meetings, and in 1976 formed a Committee on Scientific Freedom and Responsibility to examine underlying ethical considerations.

The Society for Occupational and Environmental Health, founded in November, 1972, represents an important milestone in the history of professional societies.[†] The society was created to provide a mutual context for dialogue between government, labor, industry, and academia on scientific problems and information underlying regulatory decisions in the workplace and general environment. The uniqueness of the society stems from its broad-spectrum and staunchly independent approach to problems of critical concerns on health and safety, and its promotion of occasions for focusing independent expertise on these concerns. Society meetings and workshops on such topics as occupational exposure to beryllium, lead and arsenic, occupational carcinogenesis, and reproductive hazards in the workplace provide opportunities for unusually frank discussions of scientific and regulatory problems. This is in sharp contrast to conventional practices in the usually self-congratulatory climate of industry and establishment-dominated professional societies dedicated to preserving and defending the status quo. Recognizing these particular qualities, then Senator Walter Mondale stated in an address at the annual society meeting on December 4, 1973:

You represent—more than anyone else—the best skills and experience necessary to the accomplishment of the national objective declared by the Occupational Safety and Health Act.

Another important independent organization is the Federation of American Scientists, known as "The Voice of Science on Capitol Hill." The federation is a unique lobbying group of 7,000 natural and social scientists and engineers concerned with problems of science and society. It was first organized in 1946 as the Federation of Atomic Scientists, but its current interests are now broader. It has recently taken an active and informed stand on ur-

[†] The past presidents of the society were Irving Selikoff (1972–74), Samuel S. Epstein (1974–76), and Joseph Wagoner (1976–78). The current president is Umberto Saffiotti.

gent needs for control of environmental cancer. While the federation is a high-caliber professional society, it also functions as an activist public interest organization.

Cancer is one of the most curable of the major diseases of this country.

American Cancer Society, 1976.

The American Cancer Society

The American Cancer Society is the largest private philanthropic institution in the country (besides being the world's largest non-religious charity), and is devoted exclusively to cancer. It was founded as the American Society for the Control of Cancer in 1913, and incorporated in 1922, by a small group of concerned clinicians and laypersons (mainly industrialists) in order to educate the public in the need for early diagnosis and proper treatment of cancer. Fund raising for the society was undertaken by the Women's Field Army, an association of national women's organizations with no representation on the board, which was composed exclusively of cancer clinicians and hospital administrators.

Mary Lasker's involvement in the society began in 1943, when its budget was \$356,000. She recruited Emerson Foote, a senior executive of Lord and Thomas (a Chicago advertising agency whose previous president was Albert D. Lasker), and Elmer Bobst, head of the U.S. arm of the international Hoffman La Roche drug company and honorary chairman of Warner-Lambert Pharmaceutical Company. The triumvirate transformed the society from a voluntary amateur-type organization into a highly efficient and aggressive fund-raising operation, which by 1946 had raised the budget to about \$4 million. The name of the society

was changed to the American Cancer Society, the bylaws and constitution were rewritten, and the board was reconstituted with 50 percent lay representation. The society then rapidly grew to its present strength to include 2,800 local units (organized in fifty-eight major divisions), with headquarters in New York, a paid staff of over 3,000, and an active volunteer staff of some 300,000. Of a \$176 million fund balance in 1977, \$114 million came from public contributions at the state level, largely from legacies and the annual April crusade of the society involving over two million solicitors. Direct contributions from industry were in the region of 3 percent of total donations. The national headquarters survives by taking 40 percent of each division's fund. About 60 percent of the society budget goes for staff salaries, office supplies, and other expenses; the 1977 travel budget of the society was about \$7 million. Less than 15 percent of the budget is spent on assisting patients (for purposes such as driving them to doctors' appointments, loaning wheelchairs, and donating bandages made by volunteers, rather than paying for treatment costs).

The overall governing group for the American Cancer Society is the 194-member House of Delegates, which in 1977 included one labor representative and one black, but no representative of public interest or citizen organizations. The 116-member National Board of Directors is recruited from the House of Delegates. Of the ninety-four delegates, eighteen are senior officers or directors of banks, seven are members of investment firms, and thirteen are business or industrial executives. Board members have recently included the late Elmer Bobst, and Frank J. Dixon, a consultant to Eli Lilly and Company and member of the NCI Advisory Board. At least eighteen members of the Board and delegates are executive officers or directors of banks which, as of August, 1976, held about 42 percent of the society's cash and investment, totalling \$75 million. The major decision making of the society seems to be shared between senior staff, members of the board, and a select group of thirty-two Life Members.[‡] The new presi-

[‡] Bylaws of the society require that laymen fill half the positions on its policy-making boards. These tend to be conservative and mistrustful, if not hostile, to "big government" and federal regulations. Professional representation comes from about 50,000 surgeons, radiologists, and chemotherapyists heavily concerned with treatment. As constituted, the power base of the society is overwhelmingly oriented to the diagnosis and treatment, rather than to the prevention, of cancer.

dent of the society (elected in November, 1978) is LaSalle D. Lefall, Jr., a black surgeon from Howard University. Among the life members, the banking, insurance, advertising, and pharmaceutical industries are well represented, in the absence of representation from labor or public interest groups. These lay representatives share leadership almost equally with clinicians and research scientists.

Since its inception, the society has been preoccupied by problems of cancer diagnosis and treatment, not unnaturally reflecting viewpoints which generally prevailed until relatively recently. While the society made important contributions to the smoking-cancer problem prior to 1964, its subsequent efforts to control smoking have been weak and diffuse. In fact, it has refused to endorse meaningful activist approaches such as those developed by Action on Smoking and Health, and has yet to develop any effective legislative programs.

Research programs, which are the major emphasis of the fund-raising appeals of the society, accounted for about 26 percent of its 1976 budget. Of about \$13 million spent on new research projects in 1976, \$394,000 was allotted to chemical carcinogenesis, while no new awards were made on problems of environmental carcinogenesis. Society fund raisers have routinely told the public that the society could not finance promising research "due to insufficient funds." This claim was challenged in 1976 by a report of a charity-monitoring service, the National Information Bureau, on the grounds that the society then had over \$31 million in uncommitted reserves. The society responded to this criticism by withdrawing their claim, and substituting it with the statement that it "will now place research in perspective as part of overall program needs." The audit further revealed that the research budget of the society declined from 36 percent in 1967 to the 1976 level of 26 percent, while the share given to management and fund raising increased proportionately during this time. There also seems to be evidence of conflict of interest in the award of research funds. Those same board members who decide which research projects should be funded themselves receive support. About 70 percent, \$26 million, of the 1976 research budget was

awarded to individuals or institutions with whom board members were affiliated.*

The society has supported major experimental and epidemiological research on smoking, and also some on occupational problems. These include studies on carcinogenesis and other hazards among printers, in collaboration with the Printing Pressmen's and the International Typographical Union, and studies on asbestos by Selikoff in collaboration with the Papermakers Union.

The educational programs and publications of the American Cancer Society emphasize the importance of early detection of cancer, even for those cancers with known low cure rates. The society has issued the widely publicized Seven Warning Signs of Cancer (see below). Apart from smoking, however, no reference is made to any other causes of cancer, such as Premarin as a major known risk factor for uterine cancer. By emphasizing individual responsibility for early detection, without providing information on environmental or occupational carcinogens other than tobacco, the American Cancer Society has implicitly created an impression that it endorses industry's "blaming the victim" perspective.

The Seven Warning Signs of Cancer

1. Change in bowel or bladder habits.
2. A sore that does not heal.
3. Unusual bleeding or discharge.
4. Thickening or lump, especially in the breast.
5. Indigestion or difficulty in swallowing.

* Pat McGrady, for twenty-five years the science editor of the society and the organization's main liaison between cancer researchers and medical and science writers, recently resigned in embarrassed protest over these and related issues. Of the society slogan: "Control Cancer With a Check-up and a Check," McGrady remarked:

It's phoney, because we are not controlling cancer. That slogan is the extent of ACS's scientific, medical, and clinical savvy. Nobody in the science and medical departments there is capable of doing real science. They are wonderful pros who know how to raise money. They don't know how to prevent cancer or cure patients; instead they close the door on innovative ideas. (P. B. Chowka, *East/West Journal*, July, 1978.)

6. Obvious change in a wart or mole.
7. Nagging cough or hoarseness.

The Cancer Lobby Subsequent to her transformation of the society, Lasker's interests grew to encompass the NIH. Over the ensuing decades, her close associations with successive White House administrations and with powerful political figures, such as Representative John Fogarty (D-R.I.) and Senator Lister Hill (D-Ala.), House and Senate Appropriations subcommittee chairmen, respectively, facilitated her activism and contributions to the growth of biomedical research. The death of Fogarty and retirement of Hill in 1967, together with decelerated federal support for the NIH, made her unduly receptive to the overtures of a group of cancer clinicians who had persuaded themselves that just given more funds they could cure cancer. Typical of these was Solomon Garb, a University of Missouri Medical School clinician (support for whose activities had been terminated by the NCI in 1966), whose 1968 book *Cure for Cancer: A National Goal*, with extravagant promises for an early cancer cure, made a deep impact on Lasker. (Garb is now "scientific director" of a thirty-two bed cancer hospital at the American Medical Center, Denver, and still without personal support from the NCI.) Lasker forged a powerful "cancer-cure lobby," including clinicians such as Garb and Farber, hospital administrators such as Lee Clark, and industrial philanthropists such as Foote (most of whom were already actively involved in the American Cancer Society), whose object was to force massive expansion of federal funding for cancer diagnosis and treatment.[†] To this end, Lasker enlisted the particular support of Senator Ralph W. Yarborough (D-Tex.), Chairman of the powerful Senate Health subcommittee. With Lasker's active involvement, in 1971 Yarborough appointed a National Panel of Consultants on the Conquest of Cancer, whose sixteen members were equally divided between laypersons and cancer clinicians (with virtually no basic scientists), distinguished by a complement of over 60 percent millionaires and its predominant representation of the American Cancer Society. The Panel's recom-

[†] The success of the "cancer-cure lobby" in increasing NCI appropriations has been achieved largely at the expense of other NIH institutions, particularly the National Institute of General Medical Sciences.

mendation to create a National Cancer Program, with vastly expanded funds and an autonomous NCI, aroused substantial opposition in the scientific community and Congress. This was, however, successfully muted by the propaganda machinery of the society. The society initiated a large-scale letter-writing campaign, buttressed by full-page advertisements in daily newspapers, to pressure Congress to accept the Panel's recommendations. Garb took matters further by exerting direct but counterproductive pressure on Congressman Paul Rogers (D-Fla.), one of the few congressmen who had not been persuaded by the lobby's hysteria, and who favored retaining NCI within NIH. Passage of the 1971 National Cancer Act, with massively increased financial appropriations for the NCI, but without parallel increases in personnel slots, whether an error of omission or commission, virtually ensured dependence of the NCI on the American Cancer Society for direction of its programs and priorities. Rep. David Obey (D-Wisc.) has more recently charged that the society "wants to keep the Cancer Institute strong in bankroll and weak in staff, so that it can direct its spending without too much interference."

The close links that have developed between the NCI and the society have been cemented by the personal relationships between members of the same lobby that supported both organizations, including the late Sidney Farber, Benno Schmidt (Chairman of the NCI Advisory Panel), and Mary Lasker. These interlocking relationships have also helped create a fiscal pipeline from the NCI to clinicians in leadership roles in the American Cancer Society. Certainly, the interlocking relationships between members of the NCI National Cancer Advisory Panel and Board and the American Cancer Society leadership have been important factors in maintaining high NCI priorities on problems of treatment and low priorities in problems of prevention. When Frank Rauscher recently resigned from the NCI directorship, he moved to his present position of Senior Vice President for Research of the American Cancer Society, an appointment apparently reflecting endorsement by the society of Rauscher's policies at the NCI.

In the Spring of 1978, in an effort to increase NCI appropriations, Lasker took out full page advertisements in leading newspapers in every district represented by members of the House Labor HEW subcommittee. Lasker's influence in the Senate was

exerted primarily through her friends Senators Warren Magnuson (D-Wash.), Edward Brooks (R-Mass.), and Birch Bayh (D-Ind.), whose late wife was also hired as a society lobbyist. Garb assisted these efforts by direct personal attacks in Wisconsin against Congressman David Obey (D-Wisc.) in response to his criticisms of NCI's maladministration and low priorities on cancer prevention.‡

Apart from being uninvolved in cancer prevention, other than to a limited extent tobacco, senior officials have developed for the society a reputation of being indifferent if not actively hostile to regulatory needs for the prevention of exposure to carcinogenic chemicals in the general environment and workplace. In early 1977, the past president of the society, Lee Clark, joined by Frank J. Rauscher, attacked the FDA for its proposed ban on the carcinogenic saccharin. This apparent position of the society has not yet been modified or retracted. Sidney Arje, Vice President for Professional Education, objects to the FDA proposal for inserting cancer warnings in Premarin packages. The society also objects to FDA requirements for reporting adverse drug reactions in humans receiving experimental anti-cancer drugs in NCI programs, and has demanded legislation to abolish FDA authority in this area. Over the past decade, the society has refused to endorse critical public health legislation and moves such as the Clean Water and Air Acts, and regulation of Red Dye #2, Aldrin, Tris, and the proposed FDA ban on DES in cattle feed.* Its support of

‡ Garb's strategy was developed with the initial connivance of the society's Pollster.

* In spite of Cuyler Hammond's negativism to the Clean Water and Air Acts, based on his failure to find increased cancer rates in epidemiology studies on Holland and Lincoln tunnel workers, the society initially indicated willingness to support this legislation. This position was reversed when Lee Clark was subsequently told by Texas auto dealers that it would wreck their business. Hammond has also testified on the side of industry in hearings on saccharin and hair dyes, and has been openly critical of the Delaney Amendment. In some such positions, Hammond, and other society officials, such as Lee Clark and Rauscher, claim to be representing themselves and not the society.

This negativism to critical preventive health legislation, which has generally been enacted in spite of rather than because of the society and other voluntary health organizations, aroused the unfavorable comments of Congressman Paul Rogers (D-Fla.) in an address to the Third National Conference on Health Policies on May 22, 1978:

I regret that this legislation was adopted with little or no help from

the Toxic Substances Act, probably the most important single piece of legislation of the century designed to prevent exposure to carcinogenic and toxic chemicals, was perfunctory and too late to be effective. The American Cancer Society, together with the American College of Radiologists, has insisted on pursuing large-scale mammography screening programs for breast cancer, including its use in younger women, even though the NCI and other experts are now agreed that these are likely to cause more cancers than could possibly be detected. While the traditional explanation for the position of the society on cancer prevention lies in an amalgam of conservatism and ignorance, a recent series of critical articles in the press have raised questions as to the possible influence of the wide range of industries in which society directors have financial interests.

On March 9, 1978, Rauscher told a Rutgers University audience that New Jersey's high cancer rate may be a result of personal habits rather than industrial pollution.

People are talking about a cancer hot spot here. They are blaming industry. They are blaming everybody but themselves.²⁴

Rauscher further stated that there is clear evidence that New Jerseyans smoke more than the national average, thus accounting for their excess cancer rates. However, in response to a subsequent question by Congressman Andrew Maguire (D-N.J.), Rauscher admitted that he had no evidence to support his claim.

groups or individuals involved with health care. I can think of no better example of the serious consequences of the organized health interests non-involvement than last year's Congressional battle over the Clean Water and Air law. A key part of this struggle was the auto industry's push to relax automobile pollution standards. The sweeping relaxation of standards proposed by the industry would have posed a very real threat to the health of millions of Americans over the next thirty years. Despite the obvious health implications of the auto industry's proposal, we had to work just to get the American Cancer Society and the Heart Association to take a look at the question. Eventually, after long delays, their entire political activity consisted of one letter of support. It could only be considered too little, too late. The Lung Association and the American Public Health Association were somewhat more active. While they took strong supportive positions early in the battle, and they testified in behalf of strong health protections, their support was never translated into political organization and clout.

The problems with the American Cancer Society are largely a function of its history and structure and reflect clinical bias and stodgy conservatism, coupled with a basic failure to comprehend the importance of environmental and occupational causes of cancer.²⁵ The society has declined to harness its considerable political clout to support legislation and regulation designed to prevent cancer.²⁶ The hostility or indifference it has further expressed to particular moves in this direction has been an important determinant in the failure of Congress to act more decisively on cancer prevention and even more seriously, in public apathy and confusion. Equally grievous and damaging are the society's misrepresentation of government cancer statistics as indicating that cancer death rates "are leveling off and in some cases dropping off,"²⁷ rather than in fact increasing (see for instance, Tables 1.7 and 1.8).

While the overall response of the society to emerging criticisms from quarters including the press, public interest groups, labor, and some key Congressmen, is defensive in extreme, there are nevertheless limited indications of responsiveness, such as the recent creation of a "public-issues committee." The tempo of such responses is likely to increase further only if the society feels that its public image and fund raising ability is threatened. In the final analysis, it no longer seems possible to avoid the overall conclusion that, since 1964, the American Cancer Society, spearheading the cancer cure lobby, has exercised an essentially negative if not detrimental influence on cancer prevention.

*He shall be disenfranchised who in times of faction
takes neither side.*

Solon, quoted in Plutarch Chronicles,
1st century A.D.

Chapter Eleven

What You Can Do to Prevent Cancer

By now, you will have a grasp of the basic political and scientific problems of cancer cause and prevention. Both are problems, though for different reasons. First, the objective scientific data are often not clear-cut. Second, even when they are, their interpretation is usually distorted by economic and political pressures, which have influenced or shaped regulatory policies. In the final analysis, such policies are based on some kind of risk–benefit equation whose elements are usually concealed or poorly articulated, and whose benefits are not necessarily enjoyed by those who bear the risk.¹ Understanding the risk–benefit equation should help reduce the sense of frustration which often overwhelms lay people when faced with technical discussions on cancer. Understanding should also result in shifting public focus on the cancer problem away from the narrowly scientific to the open political arena, where it clearly belongs.

It is perfectly true that we can make changes in our personal lives and habits that may significantly reduce our chances of get-

ting cancer, but the possibilities here are limited. An asbestos worker with a growing family may well have a true grasp of the dangers he is exposed to, but in all probability he is firmly locked into his particular work situation. Modern industrial society offers most people little opportunity to choose freely where to live, where to work, what air to breathe, what water to drink, what food to eat, and what advertisements to read or see. We must be willing to accept the fundamental reality that a *significant* reduction in exposure to environmental carcinogens will result only from organized political action. The system of checks and balances leading to decision-making must protect the overall interests and welfare of the public. This is the essence of democratic practice. Until very recently, congressional decisions and regulatory policy have too often reflected the overwhelming pressures and influences of industry without significant balance by consumer and labor interests.

Depending on your personal circumstances, you have two major realistic options for effective political action: by working with public interest and citizen groups or by working with organized labor. Review all the case studies presented in this book. Try to analyze the relative roles of government, labor, and public interest groups in protecting against industrial abuses and irresponsibility. Virtually every major action designed to protect consumers or workers against cancer has been initiated by public interest groups or labor (see Table 9.5). There is little basis for assuming that this pattern will change in the future. This is where we must focus our energies and efforts if we are to reduce the massive national toll of cancer. Over the last decade, Senator Edward Kennedy has repeatedly warned that democratic decision-making processes have become increasingly subverted by special interests. Cancer is a visible manifestation of such subversion.

What You Can Do on the Political Level

In order to take meaningful action, become as well informed as possible. Many books, periodicals, and newsletters of various

groups dealing with occupational, consumer, and environmental concerns are available.*

Public Interest Groups

Public interest groups have taken a key role in forcing improved regulation of environmental and occupational carcinogens. Some groups function purely in an educational or resource capacity, while others are oriented toward legislative, regulatory, legal, and community action (see Appendix V). While the larger groups are based in Washington, most large cities now have their own local citizen or consumer groups. They generally specialize in different areas, such as food additives, occupational hazards, drugs, and radiation, but there is usually overlap between these various categories. Get in touch with these groups, find out how you can become actively involved, which of them is most suitable for your particular interests and purposes, and how you can best support them with your time, energy, and money. Finally, one of

* The references given in this book should be a useful beginning. Your librarian should be able to help you further. Most universities now have adult or continuing education courses in these areas. This is, or should be, a function of the university extension service or labor education center. Make sure, by checking with others in your labor or public interest group, that your lecturer is both bona fide and well informed. For a valuable resource, see *Public Policies for the 80's: Perspectives and Resources for State and Local Action*, published by the Conference/Alternative State and Local Public Policies, 1978 (1901 Q Street, N.W., Washington, D.C. 20009). This lists federal agencies and departments; Congressional committees; state legislative committees (where information on pending legislation can be obtained); National Association of State and Local Officials; state associations of municipalities; national labor unions; state Public Interest Research Groups; state and local consumer organizations; national public interest groups based in Washington, D.C.; and Washington-based environmental groups. For a listing of environmental groups based outside of Washington, D.C., see the *Conservation Directory*, published by the National Wildlife Federation (1412 16th Street, N.W., Washington, D.C. 20036). For a listing of public interest publications, see *A Catalog of Periodicals and Newspapers of Public Interest Organizations, 1979*, published by the Commission for the Advancement of Public Interest Organizations (Appendix V). This briefly describes about 100 periodicals and newspapers under 13 major categories, including health and nutrition; environment; public interest law; energy; and appropriate technology. See also R. Nader, "A Seasonal Salute to Crusaders and Their Causes: Non-profit Civic Literature Available on Many Issues," *Washington Star*, December 27, 1978.

the best legacies you can leave your children and society is the inclusion in your will of public interest groups dedicated to the prevention of cancer. The future of the public interest movement depends on its developing adequate financial support and a national grass-roots base. Help as much as you can on all these levels.

Needs for a National Anti-Cancer Constituency

A major constraint to the development of effective political action is the virtual absence of a defined national constituency for the prevention of disease, in general, and cancer, in particular. The booming medical industry, euphemistically called "the health care system," has little if any incentive to prevent, as opposed to treat, cancer. Further, it has successfully resisted increasing recognition of the importance of disease prevention and the proportionate expenditures of federal funds for this purpose. It is questionable whether the insurance industry would profit from disease prevention as their decreased payments to the sick would be more than negated by increased payments for long-term pensions and retirement policies. While public interest groups and organized labor have emerged as the only coherent anti-cancer lobby, they have yet to impact significantly on a national grass-roots level.

Recognizing these problems, Paul Rogers, who retired last year from Congress and the chairmanship of the House Subcommittee on Health and Environment, in November, 1978, announced the creation of a National Coalition for Disease Prevention and Environmental Health, stating that "we have learned that a preventive approach is necessary in light of the spiraling human and economic costs of disease." The coalition, which has attracted the support of about 120 groups (including consumer, public interest, labor, health providers, health planning and voluntary health organizations, pollution control equipment manufacturers, and religious bodies), is hiring a small permanent staff and has set up a Washington-based information center, as the focus of its activities.

An untapped potential constituency (besides the church) are senior citizens, pensioners, and retirees, whose numbers are growing disproportionately to the remainder of the population, and

who, for considerations of latency, represent the highest cancer risk group, and one on whom the financial burdens of cancer are the heaviest. "Gray Power" could well emerge as a new and potent anti-cancer lobby.†

Organized Labor

Encourage your union to fight to strengthen OSHA. While working for tougher standards, persuade your union to follow the lead of some of the more health-conscious unions, particularly the Oil, Chemical, and Atomic Workers (OCAW) and the United Auto Workers, in lobbying for better laws, developing their own professional resources and skills, including hiring full-time industrial hygienists and trustworthy consultants, demanding OSHA inspections, and educating their own members.

The ability of your union to protect you and your fellow workers ultimately depends on your self-education and understanding of health and safety problems, particularly in high-risk industries. Work collectively with your union leadership to produce a work environment free of added cancer risk. If you feel that your union leadership is ignorant or not interested in these problems, then lobby and campaign to vote them out of office and replace them with more responsive leadership.

The OCAW has a double-barrelled strategy of working within and without OSHA. On the one hand, OCAW makes maximum use of both the "general duty" clause of the Occupational Safety and Health Act, guaranteeing a safe and healthful workplace, and the "imminent danger" clause, demanding action when life-threatening situations occur.‡ On the other hand, recognizing that OSHA has had a poor track record for rectifying dangerous health conditions, OCAW has written into many of its contracts specific health and safety language, providing for monitoring of

† Leading senior citizen national organizations include the Washington, D.C.-based American Association for Retired Persons (202-872-4700) and the Urban Elderly Coalition (202-857-0166), and the more activist, Philadelphia-based, Gray Panthers (215-382-6644).

‡ The Act has been crucial in supporting union demands that health and safety standards be included, as is now usual, in collective bargaining contracts.

workplace hazards, with results accessible to the union's representatives as well as management, and for receiving health statistics compiled by companies. The union has also won an important settlement from the National Labor Relations Board affirming its right to information on the working environment under the representation clause contained in every collective bargaining agreement. The representation clause establishes the union as the sole collective bargaining agent for the employees on matters of "wages, hours, and working conditions." Never before has this clause been used to extract health and safety data. Winning the settlement is an important victory for all organized workers. Thus, even in the absence of specific health and safety clauses, a labor bargaining unit is able to act aggressively on health and safety.

If you are a member of a union which is not health-conscious, seek assistance from any of a number of professional and public interest organizations devoted to labor education on health and safety, or from the new University Labor Educational Centers, such as Rutgers in New Jersey, Cornell in New York, and the University of Wisconsin in Madison.

One area in which an otherwise apathetic union can make an inroad is through its publications.* Ralph Nader has recently pointed out that most union newspapers or periodicals are little more than photogalleries for their officers.

The feeble state of the labor press means that 30 million union members are left in the dark about some major issues, never review or discuss them, and cannot really come to grips with many of the problems that beset labor . . .²

A number of labor publications, on the other hand, do run regular or occasional columns written by health and safety specialists (See Appendix IV), some of which should be syndicated and run nationwide.

Even the most optimistic estimate of cancer-consciousness in U.S. labor must deal with the fact that three out of four are not organized and so can have very little to say about their working conditions. While every worker is entitled in principle to OSHA

* The U.S. labor press is comprised of some 800 publications and reaches some 30 million workers.

protection, the non-union individual who complains may be ignored or, at worst, fired.

State Initiatives

Regulatory and legislative initiatives at a state level which are being pioneered in California and New Jersey are emerging trends of major importance to cancer prevention.[†] These initiatives provide a focus for education and for well directed political pressure by public interest and citizen groups.

Other Action

Encourage your local media to cover environment-related events, and to run regular columns on topics ranging from congressional legislation on toxic substances to water pollution, particularly as they impact on cancer. During the early 1970s, great sport was made of Boy Scouts bravely paddling up stinking creeks to trace the source of noxious effluents. But it was efforts such as these, particularly because of the television coverage they received, that caught the public's interest and have to some extent sustained it. Aggressive media action may also be the quickest way to uncover hidden relationships between the industrial interests of legislators and of university scientists. It is also worthwhile asking your newspaper editor or publisher some hard-hitting questions, such as why coverage of violent crimes and road accidents is so complete but coverage of tobacco-related cancer and other diseases and of suppression or manipulation of health and safety data is non-existent or disproportionately low. Also, look for hidden influences of advertising interests on the coverage of environmental issues. Is this why your local newspaper won't run the Nader column?

Find out the position of your state representative and Con-

[†] Important examples of these include recent activities of the California Campaign for Economic Democracy, in collaboration with the California Public Policy Center, and the New Jersey Chapter of the Sierra Club.

gressman on key environmental issues. Let them know of your interest and that you expect them to take vigorous action on the prevention of cancer, if they want your future vote. Pressure them to run on a ticket in which cancer prevention ranks high, if not number one. Remember that President Johnson was forced out of office by his failure to extricate the U.S. from the Vietnam war, the total U.S. death toll of which over all the war years combined was only a fraction of the annual number of cancer deaths. Cancer prevention should be made, at least, to rank with inflation in the next presidential campaign.

If you are a professional, such as a doctor, lawyer, chemist, engineer, physicist, or social scientist, you have a wider range of options. These include working actively with public interest groups and organized labor, testifying at Congressional, State, and Municipal hearings, lobbying at the local or federal levels, supporting responsible regulatory agency officials, criticizing irresponsible or indifferent officials, and pressuring voluntary health agencies, particularly the American Cancer Society, to develop more aggressive preventive programs, if they hope to retain your financial support.

What You Can Do on the Personal Level

You can reduce your own chances of getting cancer by making changes in three major personal areas:³ your lifestyle and personal habits; your choice and use of consumer products; and your work. These areas obviously overlap, as your work may be an integral part of your lifestyle. In all these overlapping areas, you have only limited options for making decisions that will affect your exposure to environmental and occupational carcinogens and decrease your risks of getting cancer. The major public interest groups publish useful reports dealing in further detail with these various problems, such as carcinogens in food and water. You are recommended to contact them (See Appendix V).

Depending on your particular circumstances, some of the rec-

ommendations offered here may possibly be impractical. But you should at least know what are your available options, even if you are unable or unwilling to exercise them.

In addition to your efforts to prevent cancer in yourself and your family, you should appreciate the importance of early detection and treatment, particularly of the curable and manageable cancers. Finally, you should be aware of possible legal remedies if you do contract cancer and have reason to believe that someone else is responsible.

Lifestyle and Personal Habits

1. *Smoking.* The most effective single action you can take is never to start smoking or, if this advice comes too late, to stop smoking as quickly as possible. Smokers develop lung cancer at about thirty times the rate of non-smokers, and about one out of ten smokers of a pack or more a day will develop lung cancer. Smoking also increases risks of cancer of the larynx, esophagus, mouth, and bladder. The additional benefits of quitting extend beyond cancer to chronic heart disease, the incidence of which becomes markedly reduced in the ex-smoker.

While many people can quit "cold turkey," most smokers are so physically and psychologically habituated that they need help. Two well-known organizations (there are others) offer structured help in classes or group therapy, and seem to have good success rates: Smoke-Enders is a private group, that charges a reasonable fee to get smokers to give up the habit in a few weeks; the American Cancer Society also conducts smoke cessation clinics in many cities for a nominal fee.

There can be no argument about the cost-effectiveness of quitting smoking. The current direct medical cost of each lung cancer case is about \$10,000, which excludes lost wages and other costs borne by the family of the patient, who rarely survives even a few years.[‡] The cost of quitting through a program such as Smoke-Enders is under \$200. At current cigarette prices, a one-pack-a-day smoker would save, on the cost of cigarettes alone, enough

[‡] From the time of diagnosis of lung cancer, the median survival for men and women is about six months.

money to pay for the program in one year. To get ten heavy smokers to quit, and thereby prevent one case of lung cancer, would cost about \$2,000, compared to about \$10,000 to treat the one who would get lung cancer.

There is no alternative to quitting. Switching to low-tar cigarettes is no substitute for not smoking. Regardless of how low the tar, if you smoke cigarettes your risk will be greater than if you don't. A major danger in changing brands rather than completely cutting out cigarettes is that some smokers compensate for the low nicotine levels in low-tar cigarettes by smoking or inhaling more. An additional problem is that levels of carbon monoxide are relatively higher in low-tar cigarettes, probably increasing the risk of heart attack.

It has been suggested that a cigarette smoker who cannot quit should instead switch to cigars or pipes, since cigar and pipe smokers have lower lung cancer rates than cigarette smokers. However, while lifetime cigar and pipe smokers inhale little of the bitter, alkaline smoke, former cigarette smokers who switch to cigars tend to inhale nearly as much as when they smoked cigarettes. This is not an effective method of preventing cancer.⁴

If you are a non-smoker, avoid smoke-filled, poorly ventilated places, particularly crowded bars. Also become more aggressive about your rights to clean air in elevators, restaurants, airplanes, and other public places.* Insist, as far as possible, that your employer provide you with a smoke-free workplace.

2. *Alcohol.* While there is no direct evidence that alcohol is itself a carcinogen, heavy drinking, particularly of hard liquor, increases the risk of developing cancer of the mouth, throat, esophagus, larynx, and liver.⁵ These risks, particularly for cancer of the mouth and esophagus, are still further increased by heavy smoking; cancer of these sites is about fifteen times higher in heavy smokers and drinkers than in abstainers.

The type of alcohol consumed also seems to influence the cancer risk. Esophageal cancer is highly correlated with both chronic alcoholism and cirrhosis of the liver in certain regions of France,

* Among many examples of the non-smoker's decreasing reticence to demand clean air is the use of the anti-smoker's spray can. Developed by Paul L. Wright, a Denver management consultant who has so far sold 30,000 cans, it drenches offending smokers with a lemon-scented mist.

particularly Brittany and Normandy, where Calvados brandy and applejack are popular. The death rate from cancer of the esophagus in France is highest in the four contiguous brandy-producing areas of Calvados, Manche, Mayenne, and Orne.⁶

The mechanism of these alcohol-related cancers is unknown. It may be due to the nutritional deficiencies which are common in heavy drinkers and which may increase susceptibility to tobacco or other environmental carcinogens. Additionally, alcohol may act as a solvent for tobacco or other environmental carcinogens and may, thereby, increase their access to tissues.

The influence of chronic alcoholism on cancer is difficult to evaluate, since heavy drinkers tend to die early of other causes, including accidents and diseases related to malnutrition. However, a 1977 study of Veterans Administration hospital patients with cirrhosis of the liver, commonly associated with chronic alcoholism, found a greatly increased risk of the otherwise relatively rare liver cancer. Additionally, patients with cirrhosis developed cancer at other sites at earlier ages than non-cirrhotic and non-alcoholic patients did.⁷ This would seem to suggest that alcoholism may increase susceptibility to cancer in general, besides also increasing liver cancer.

3. Food. Your dietary choices and habits are clearly important. Some diets may reduce your cancer risk, while others may increase it. This is, however, an area where caution and common sense must be exercised, especially as the facts are incomplete, and the consumer is caught between opposing viewpoints. Industry, on the one hand, dismisses as hysterical any questions on the safety or carcinogenicity of food,⁸ while on the other hand public interest groups emphasize the carcinogenic hazards of many food additives and contaminants.^{†⁹}

These problems are aggravated by the fact that it is difficult for the concerned consumer to know where to go to obtain reliable information on the hazards of food additives and contaminants.¹⁰

† Unequivocal support for these concerns is detailed in a November, 1978, report on "Cancer-causing Chemicals in Food," by the Subcommittee on Oversight and Investigations of the House Committee on Interstate and Foreign Commerce, which castigates the EPA, FDA, and USDA for failing "to protect the public from dangerous chemical residues in food." The report also made specific recommendations for the immediate correction of these deficiencies in the regulatory practice of the three agencies.

With a few possible exceptions, university departments of nutrition are probably the last place to go. Quite apart from the fact that most such departments have no expertise in toxicology and carcinogenesis, many of them are recipients of major support from the food industry or from industry-sponsored organizations such as the Nutrition Foundation. A joint 1976 report by Congressman Benjamin Rosenthal (D-N.Y.) and the Center for Science in the Public Interest detailed the close ties between academia and the food and chemical industry. While a dozen other universities were mentioned, Harvard's nutrition department was singled out as "riddled with corporate influence."¹¹ Particular reference was made to the intimate relationships between Harvard's previous department chairman, Fred Stare, and the cereal, sugar, and food industries. Less well known is the case of Jean Mayer, President of Tufts University and previous professor in Harvard's nutrition department. Mayer, a responsible nutritionist who writes a widely read, nationally syndicated column on nutrition, has publicly rebuked Stare for being among those "favorable to the sugar interests" who have distorted nutritional evidence, but has himself advocated the use of textured vegetable protein without mentioning that (prior to 1979) he was director of the product's manufacturer, Miles Laboratories.¹² (Mayer is also a director of the Food and Nutrition Board, which represents interests of the food industry, and a director of Monsanto, which has recently mounted an aggressive campaign to persuade the public of the essential safety of synthetic chemicals.)

Much has been made of the relationship between modern eating habits—particularly high caloric intake, high consumption of animal fats, cholesterol, dairy products, and meat; and low consumption of grain and fiber—and the twentieth century cancer epidemic.[‡] On the basis of indirect evidence, it has been suggested that a low-fiber, high-fat diet increases the risk of cancer of the colon and possibly of other cancers, including breast, while a high-fiber, low-fat diet protects against these.* As far as dietary

[‡] Bread, the high-fiber staple, has been considered the staff of life since time immemorial. Now, only 5 percent of all grain consumed in the United States is eaten by people; the remainder is fed to DES-treated cattle in feed lots, producing high fat meat.

* There is generally a high degree of correlation between mortality from colon cancer and also from coronary disease, and high consumption of ani-

fat is concerned, there is no question that a very wide range of environmental carcinogens, particularly pesticides and industrial chemicals, are fat-soluble and are likely to accumulate in the food chain. So the more animal, dairy products, and other fats you eat, the greater will be your intake of these fat-soluble carcinogens.[†] It is also known from carcinogenicity experiments that high total fat and high-calorie diets increase the incidence of cancers in animals fed known carcinogens, and that low-fat diets seem to protect against cancer. The apparent protective effect of low-fat diets may, however, merely reflect a reduced intake of the carcinogenic contaminants found in animal fats.

Many claims have been made for the protective effect of "dietary fiber," although this term describes a variety of different foods with substantially different properties. The fiber craze in America culminated in two popular recent books, one by David Reuben¹³ and the other by Carlton Fredricks,¹⁴ which advocate the consumption of greatly increased quantities of fiber. The underlying theory,¹⁵ popularized by Denis Burkitt, a British surgeon originally known for his research on childhood lymphomas in Africa, that since fiber increases fecal bulk and thereby decreases "transit time" in the colon, this will reduce the contact times of dietary carcinogens in the intestines. Fiber has also been claimed to promote growth of favorable intestinal bacterial strains, which are said to produce fewer carcinogens or promoting agents than is the case when the diet is low in fiber.

mal fats and low consumption of grains and fiber. This, however, by no means constitutes proof of causality. Berg, for example, concludes that, "Epidemiologically the case against fat is weak because there are populations that have a high fat-intake and little bowel cancer, and there is no case-control study pointing to fat as a risk factor." Berg, J. W., "Diet," in J. F. Fraumeni, Jr., ed., *Persons at High Risk of Cancer: An Approach to Cancer Etiology and Control* (New York: Academic Press, 1975), pp. 201-24.

[†] Human breast milk provides a good measure of the amount of fat-soluble carcinogens retained in body fat. A recent study has shown that vegetarians have lower levels of chlorinated hydrocarbon pesticides, particularly DDE, in breast milk than their matched meat-eating controls, and that the more high-fat dairy products eaten by vegetarians, the higher the level of pesticides in their breast milk (T. Page and S. Harris, "The Role of Diet in Breast Milk Contamination," in press, 1979). From this standpoint, a low-fat vegetarian diet, provided it is carefully balanced, would be the diet of choice for a nursing mother.

In spite of the lack of evidence supporting the cancer-preventing effects of low-fat, high-fiber diets, there is certainly no evidence that they are in any way harmful. Cancer risks apart, any diet such as the American Heart Association Prudent Diet is likely to reduce your risk of coronary and other diseases.¹⁶

The principles of low-fat, high-fiber diets are to emphasize vegetables, beans, grains, and fruits, and decreased intake of dairy products, meat, saturated animal fats, and cholesterol. Animal protein should be obtained from fish,‡ veal, and poultry, rather than from high-fat beef, lamb, and pork. If at all possible, buy the lean meat of range or grass-fed cattle rather than cattle fattened in feed lots. Lean cuts of meat should be selected, trimmed of fat, the remains of which should be drained off during cooking, and baked or stewed, rather than deep-fat fried. Soups and stews should be refrigerated after cooking, and the surface fat layer skimmed off before reheating. Egg consumption should be kept down to one or two a week, and skimmed milk and low-fat cottage and hard cheeses, margarine, and corn or soybean oils should be used in preference to whole milk, high-fat soft cheeses, and butter.

Nutritional deficiencies can cause cancer. The best-known example of this is the Plummer–Vinson Syndrome, characterized by painful difficulty in swallowing, associated with iron-deficiency anaemia and vitamin B deficiency, in which the subsequent incidence of cancer of the esophagus and pharynx is high. The disease, which used to be common in northern Sweden, where winter diets were deficient, has virtually disappeared since flour has been supplemented, in Sweden and elsewhere, with iron and vitamin B.¹⁷

Food is the most important single source of exposure to a very wide range of synthetic chemicals, either as direct additives or as accidental contaminants such as pesticides and industrial chemicals. Many of these are carcinogens, and food and beverages

‡ Deep-ocean fish are less likely to be contaminated by fat-soluble carcinogens (such as chlorinated hydrocarbons pesticides and PCBs) than fresh-water fish which, depending on the purity of the water from where they are caught, may accumulate and concentrate these carcinogens.

containing them or suspected to contain them should be avoided to the greatest possible extent.*

Avoid all highly processed "junk" foods, which are rich in additives and poor in nutrients. Hot dogs, potato chips, sugary breakfast cereals, and soda pop contain the greatest concentrations of synthetic additives. Exclude as much as possible known or suspected carcinogenic food additives, such as saccharin and Red #40, and all other synthetic coal tar dyes. Don't buy any foods or beverages containing cosmetic food additives, labeled FD&C (Food, Drug, and Cosmetic) or U.S. Certified Colors. Another major cosmetic food additive is nitrite, which combines with amines in meat and fish to form the highly carcinogenic nitrosamines. Levels of nitrosamines tend to be particularly high in bacon,† and they are present in lower quantities in sandwich meats, salami and bologna, hot dogs, and smoked meats and fish. All of these should be avoided, especially bacon. While this may sound like drastic advice, it is well founded. Nitrite-free hot dogs and, to a lesser extent, bacon are now becoming available in some supermarkets; these products must be kept refrigerated. Their availability will increase if you firmly make your preferences known to your supermarket manager or grocer.

Avoid all food products containing petroleum-derived protein, either as a flavor enhancer or as a food ingredient. As far as is known, Amoco Foods Company, a subsidiary of Standard Oil of Indiana, is the exclusive U.S. manufacturer of petroleum protein.¹⁸ Marketed under the trade name of Torutein, this is a high-protein yeast culture grown on "food grade" ethanol derived from hydrocarbons (usually ethylene), isolated from crude oil, which has been manufactured at the rate of about 15 million pounds per year since 1975. Torutein is now being sold to U.S. food processors for use in meat products, baked foods, infant foods, and fro-

* For instance, avoid coffee decaffeinated by the standard U.S. process which uses methylene chloride, currently under test in the NCI Bioassay Program. Coffex Ltd. of Switzerland now markets coffee (available through a few U.S. distributors including the White House Coffee Company in Long Island City, New York) which is decaffeinated by a more expensive pure water process which uses no chemical solvents.

† The USDA is now taking vigorous steps to reduce nitrosamine levels in bacon by ordering meat manufacturers to decrease amounts of nitrite that may be added to bacon.

zen and other prepared foods, particularly for the institutional food market—hotels, restaurants, and schools. Torutein is found in Prince's macaroni, French's croutons, Health Snacks Limited's breadsticks and cake mixes, La Choy food products, and Gerber baby foods. It is difficult, if not impossible, for the consumer to find out whether a particular product contains Torutein. Under current labeling laws, its presence as a flavor enhancer can be hidden in the catch-all term "natural flavorings." Its presence as a protein booster can be described by the term "torula yeast," without giving any indication as to whether this is natural torula yeast or petroleum-derived.

There are many unresolved questions about the safety of Torutein. The only data voluntarily submitted by Amoco to FDA are the negative finds of subacute rodent toxicity tests, on the basis of which FDA informally approved the use of Torutein in March, 1974. There are no data available on the nutritional value of Torutein (particularly with regard to its high, 10 percent content of nucleic acids), its chronic toxicity, reproductive or mutagenic effects, or carcinogenicity. While various foreign governments, including Japan, Great Britain, and Italy, have withheld approval of petroleum protein because of such questions on safety, there are no current restrictions in the United States, where its use is burgeoning.

There is a critical and overdue need for the regulation of the use of petroleum protein. In the meantime, to be on the safe side, avoid any food whose label bears any reference to torula yeast. You may express your concerns by writing directly to both the FDA and Amoco Foods Company to demand the immediate curtailment of this market until full toxicological and nutritional testing has been completed and independently evaluated.‡ Should

‡ The needs for such testing prior to the marketing of petroleum protein were in fact spelled out in detail at a tripartite meeting between the United States, Canada, and the United Kingdom at the FDA on December 16, 1974, whose recommendations were spelled out in a working document entitled "Single Cell Protein." The Protein Advisory Group of the United Nations made similar recommendations on February 7, 1972 (PAG Guideline No. 12, "Single Cell Protein"). According to the FDA, Torutein is a "likely candidate" for early consideration in their recently implemented cyclic review of GRAS food additives, with relation to its nutritional adequacy, besides carcinogenicity.

Torutein be then found acceptable, its presence in food must be acknowledged by clear and explicit labeling.

Avoid organ meats, particularly liver (even though this is high in protein and vitamins and relatively low in calories), pancreas or sweetbreads, and kidney, as these concentrate residues of both accidental carcinogenic contaminants and carcinogenic feed additives. Avoid any food, oil, or beverage sold or stored in rigid PVC containers. Although banned, these are still on the market. Residues of carcinogenic and other chemicals from the plastic are dissolved in the contents.

4. *Water.* It is now common knowledge that drinking water in most cities, particularly downstream from chemical industries, contains a great variety of synthetic organic chemicals, of which more than 700 have so far been identified, including many known carcinogens.*¹⁹ Demand from local EPA offices as much specific information as possible on the impurities of your drinking water. Do not accept unsubstantiated assurances of safety from water treatment engineers. Your personal options are limited, however. Boiling water will remove some volatile organics, but will actually concentrate others. Distilling is not particularly effective, since many organic chemicals, such as benzene, form "constant-boiling mixtures" with water and will be carried over with the distillate. Depending on source and purity, bottled water may be an improvement on your tap water, but there is no way of knowing, as bottled water labels give no information at all on levels of organic chemical pollutants.

Until polluting industries can be regulated and until municipal water treatment plants install appropriate water-purifying technologies, you have little option but to install carbon filtration or the more expensive and more efficient reverse osmosis units, preferably to your water mains supply.† Carbon units require regular and frequent replacement to reduce bacterial contamination and to prevent filter exhaustion. The efficiency of domestic carbon units in removing organic contaminants is under current study by EPA.

* The chemicals so far identified account for only a small fraction of total organic contaminants in water.

† If you have even minimal mechanical skills, your best plan is to contact the Environmental Defense Fund Washington Office (see Appendix V) and ask for a copy of their pamphlet (\$1.00 fee) on how to construct your own activated carbon unit.

5. *Drugs.* A wide range of drugs are known to be carcinogenic, as shown by human experience and animal tests.²⁰ It is unfortunate, but true, that the most effective drugs used to treat cancer can also cause it (Appendix VI). Considering the long latency period of most cancers, it may well be worthwhile taking the risk of being treated with carcinogenic drugs if you have cancer or some other equally serious disease. A possible example of such worthwhile risks is the case of kidney transplants. The recipient of a kidney transplant, for example, must be treated to suppress the immune response and to prevent rejection of the new kidney, and the drugs used for this purpose increase the risk of developing lymphomas up to thirty-five times. It is not, however, worthwhile taking carcinogenic drugs for relatively trivial conditions, such as Flagyl for trichomonad vaginal infections, griseofulvin for athlete's foot or for scalp infestation with ringworm, and Lindane shampoos for head lice. There are alternative non-carcinogenic treatments for all these conditions. Discuss this with your doctor if he appears to be well informed. If he is not, don't be lulled into false security or intimidated by reassurances such as "Those carcinogenicity data are just based on animal tests," or, "I've been using this drug for over twenty years and have never had any problems." Read the label and insert or stuffer in the packaged medicine bottle, and ask the pharmacist whether he has additional information. Check carefully for any reference to cancer.‡

If you are a menopausal woman, do not take estrogens unless your symptoms are really crippling, and if you do, take the lowest possible dose for the shortest possible time. Your risk of uterine cancer will be greatly increased by "estrogen replacement therapy" with Premarin. If you are a fertile woman who had unprotected intercourse last night, and you would rather not risk pregnancy, never take DES, as commonly prescribed in campus clinics, which apart from being highly carcinogenic may not be particularly effective.

‡ In May, 1979, the NCI announced that the following four widely used drugs were carcinogenic in the Bioassay Program: methapyrilene, an anti-histamine used in most non-prescription sleeping aids such as Nytol (Block Drug Co.), Excedrin (Bristol Myers), and Sominex (J. B. Williams Unit of Nabisco) and common nasal sprays and allergy medicines; reserpine (Ciba Geigy Co.), used for treatment of high blood pressure; selenium sulfide, an ingredient in antidandruff shampoos such as Selsun (Abbott Laboratories); and disulfiram, used as a fungicide and as the antialcholic drug Antabuse.

After tranquilizers, the most commonly prescribed drug is "the Pill." Millions of women the world over are taking it for a substantial part of their lives. This is the largest carcinogenicity test in human experience, and the answers are not yet all in. Estrogens are carcinogenic in animals, Premarin induces uterine cancer in menopausal women, and the synthetic DES induces vaginal cancer in adolescent girls whose mothers took it while they were pregnant. Epidemiological studies on users of birth control pills have so far been inconclusive, probably because most women have been taking them for too short a time for possible cancers to show up. The pill has, however, been associated with liver tumors, stroke, and other diseases. So consider other forms of contraception. And make up your own mind about this; your gynecologist or physician is likely to tell you not to worry.

6. *Cosmetics.* Under the authority of the 1938 Federal Food, Drug, and Cosmetic Act, the FDA has recently required the ingredients of all cosmetics to be listed on the label. Exemptions are granted to ingredients constituting less than 1 percent of the product, and to the names of specific flavors and fragrances. While the agency does not have the authority to require the industry to test their products for safety, it does require that if a product has not been tested, then the label must read: "Warning: The safety of this product has not been determined." Do not buy any products carrying such a warning, nor products containing known carcinogens, such as 2,4-toluenediamine or 4-methoxy-m-phenylenediamine, which are used in permanent (oxidative) hair dyes, particularly the darker colored ones. Nor should you allow your hairdresser to use these carcinogenic products on your hair.*

* Several epidemiological studies have demonstrated an increased risk of lung, bladder, and thyroid cancer, and leukaemia in beauticians. However, none of these studies specifically incriminate any known carcinogens, such as 2,4-toluenediamine or vinyl chloride propellants and nitrosamine contaminants in cosmetics and hair dyes. In February, 1979, R. E. Shore and a group of co-investigators from the New York University Institute of Environmental Medicine reported on preliminary case control studies on women using hair dyes. These studies, stimulated by the finding that the majority of oxidative hair dyes are mutagenic in the Ames system, and that several are also carcinogenic in animals, indicated that the incidence of breast cancer is increased in women who had used hair dyes for over ten years. The study controlled for other factors (such as family history of breast cancer, childbearing history, and socio-economic class) known to also influence the risk

The FDA still lacks the current statutory authority to ban the carcinogenic hair dyes, which are exempt from the requirements of the Federal Food, Drug, and Cosmetic Act. Recognizing this problem, the General Accounting Office in December, 1977, called for a legislative change to bring hair dyes under food, drug, and cosmetic regulations. This was followed in January, 1978, by the announcement of Congressman John Moss (D-Calif.) that his House subcommittee would hold hearings on whether to abolish the hair dye exemption. The dyes, however, could be regulated by OSHA, as about 400,000 workers, including hairdressers, cosmetologists, and furriers, are potentially exposed to them. Accordingly, on January 13, 1978, NIOSH urged that these dyes be handled as occupational carcinogens and proposed a 50 ppm standard. On December 12, 1977, the FDA banned further use of six color additives in drugs and cosmetics: Yellow #1, Blue #6, and Reds #10, 11, 12, and 13, the red colors mainly being used in lipsticks and soaps, but did not require these products to be removed from the market.

A small market based on cosmetics containing only natural ingredients and free from synthetic chemicals such as coal tar dyes, is now developing. You are encouraged to explore this to see if it meets your needs. If it doesn't, you may want to consider changing your needs.

7. *X-rays.* X-rays are carcinogenic. The more X-rays you submit to and the greater the dose, the greater is your risk of cancer.²¹ Avoid unnecessary X-rays like the plague. Make your doctor or dentist spell out to you in detail the benefits you may

of breast cancer. A possible limitation in this study is that no relationship was found between the color of the dye used and the degree of cancer risk, although dark dyes contain more chemical ingredients than blond dyes. While the number of women (129 breast cancer cases vs. 193 controls) involved in this study is too small and the risk estimates (1.4) too low to allow definitive conclusions, these findings add yet further information on the potential carcinogenic hazards of hair dyes. The industry, with its \$300 million market involving 25 million consumers, has responded by insisting that no chemical in hair dyes is carcinogenic. Clairol and other manufacturers have, however, recently introduced new formulations devoid of known carcinogens. John Corbett, vice-president for technical development at Clairol, made it clear that the only reason for the industry action was because it would otherwise be required to carry a cancer warning on hair dye labels. "It's not good business to have to market a product with a cancer warning on it. We don't want our product used by worried women."

get from exposure to X-rays. Are they given for "routine reasons," or for "defensive medical practice" to protect against possible malpractice suits, or because they are paid for by Medicaid and Medicare from which your physician may get a fee, or because critical choice of treatment in serious disease or injury is at stake?

You should raise these questions before you consider submitting to X-rays, even at the risk of offending "professional dignity." If you are convinced that X-rays are essential, only have them done in the office of a physician who is a specialist in radiology or in the radiology department of a hospital. Also, make sure that the technician is certified, not just "office trained," that modern equipment is used, that the smallest dose is given, and that your non-irradiated areas are protected with a lead shield.

Whatever you may be told, refuse routine mammograms to detect early breast cancer, especially if you are premenopausal. The X-rays may actually increase your chances of getting cancer.^{†22} If you are older, and there are strong reasons to suspect that you may have breast cancer, the risks may be worthwhile. Very few circumstances, if any, should persuade you to have X-rays taken if you are pregnant. The future risks of leukaemia to your unborn child, not to mention birth defects, are just not worth it.

At issue here is not the occasional obvious necessity of X-rays, but their indiscriminate use. According to U. S. Public Health surveys, over 150 million Americans are given 210 million medical and general X-ray examinations annually.[‡] The number of medical X-ray examinations per person has increased steadily from 50 per 100 population in 1964 to 56/100 in 1970, a 12 percent jump.²³ Medical uses of ionizing radiation now account for 90 percent of all uses. The number of dental X-rays per person increased from 27/100 in 1964 to 36/100 in 1970, a 29 percent jump. Not only is the number of exposures increasing, but the dosage is much larger than necessary. Many doctors and hospitals

[†] When first introduced in the 1960s, mammography exposed women to about 7 rads per examination, compared to the 0.02 rads of today's most up-to-date equipment, found only in a relatively few centers. Until very recently, the lowest amount of mammography exposure was about 2 rads.

[‡] This excludes more than 2 million Americans occupationally exposed to nuclear radiation in the last thirty years, including over 500,000 soldiers who were deliberately exposed to nuclear blasts.

use old, outdated equipment, which is not properly controlled and has not been given needed annual inspections by a qualified health physicist.*

Dentists are also often guilty of overexposing their patients.²⁴ Some dentists require a full set of sixteen to eighteen films every time a patient comes in for a routine checkup. The additional diagnostic information furnished by such a series, over and above inspection aided by a dental pick, is difficult to imagine. The American Dental Association advises that a full set need not be taken more often than every three to five years; and other authorities extend this to between six and ten years.

More than 20 million Americans consult chiropractors, instead of or in addition to physicians. Some chiropractors base entire treatments on extensive use of full body X-rays. Avoid such treatments and all chiropractors who offer them.

8. *Sex.*²⁵ Cancer of the cervix seems in some way related to sex. The earlier in life you start intercourse, the more your partners, marriages, and pregnancies, and the poorer your prenatal and postnatal care, the greater are your chances of cervix cancer. Intercourse during and immediately after menstruation is thought to increase risk, possibly accounting for the relative rarity of cervix cancer in orthodox Jewish women, who abstain during and immediately after menstruation. The relatively increased risk of this cancer in non-Jewish women has also been attributed to their sexual partners being uncircumcised. These sexual risk factors are further aggravated by poverty, possibly because of poor nutrition and limited opportunities for personal hygiene. The rate among lower socioeconomic groups, particularly low-income blacks, is double that for middle-class whites, and its incidence among other low-income ethnic groups, such as Mexican-Americans, is higher

* Federal expenditures on the health effects of ionizing radiation are trivial. The Department of Energy's annual budget for this purpose is about \$12.6 million, of which nearly two thirds is allocated to follow-up studies on Japanese atomic bomb survivors and on the Marshall Islanders, and the establishment of a radiation emergency assistance center and exposure data file. All other agency efforts total under \$9 million. Responsive to these deficiencies, the Biomedical Research and Training Act (P.L. 95-622), introduced in November, 1973, by Congressman Paul Rogers (D-Fla.), makes provision for a new major coordinated federal research effort on the biological effects of ionizing radiation within HEW, as opposed to other agencies more concerned with promotion of nuclear energy uses.

still. There is some evidence that a venereally transmitted Herpes virus is in some way responsible for this cancer.

Risks of breast cancer are increased in women who menstruated before the age of twelve, who have never had children or who had their first child after the age of thirty, who have had a history of benign cysts or breast tumors, and who have a familial predisposition.[†] If you fall into any of these high-risk categories, monthly breast self-examination is imperative.

If you are a Jewish male, your chance of getting cancer of the penis is virtually zero, as this is prevented by circumcision. If you are uncircumcised, make sure to retract your foreskin daily and wash away the secretions with soap and water.

There are also some suggestions, based on epidemiological studies, that promiscuity increases risk for prostate cancer, possibly due to a sexually transmitted virus. Rates of prostate cancer in black males are increasing at about twice those in whites.

9. *Sunlight.* This makes you feel and look good. But too much sun or exposure to ultraviolet lamps will age your skin and may give you skin cancer, especially if you have a light skin and blond complexion. You have much less to worry about if you are black. Besides avoiding too much sun, wear a good sunscreen ointment; those containing para-aminobenzoic acid are particularly effective. If you work outdoors, use sunblocking creams such as zinc oxide around your lips and nose.

The incidence of skin cancer and melanomas is greatest in farmers and fishermen, who spend a great deal of time outdoors.[‡] The incidence is also greater in southern latitudes, where sunlight is more intense. While most skin cancers are easily curable, melanomas are not, and account for approximately 9,600 new cases and 4,000 deaths a year in the United States.

10. *Where you live.* This influences your overall risks of cancer, and also the particular type you may get. For some, this advice may well be academic; but, you may nevertheless want to think about this if you are about to move or if you have the lux-

[†] Other high risk factors include living in the vicinity of petrochemical plants, particularly those manufacturing, handling, or processing carcinogens, and prolonged use of hair dyes.

[‡] The role of environmental factors other than sunlight is suggested by the striking recent increase in the incidence of melanomas in white males, from 2.6 per 100,000 in 1947 to 6.3 per 100,000 in 1975.

ury of choosing where you live. If you can possibly avoid it, do not live close to a chemical plant, refinery, asbestos plant, or metal mining processing or smelting plant, or hazardous waste disposal site, even if claimed to be well managed. Also avoid living close to major highways and expressways.

From 1969 to 1971, the NCI conducted an intensive survey of new cancers in nine regions of the country and found wide geographic variations in the incidence of different types.²⁶ Many of these patterns paralleled those previously found in the twenty-year NCI cancer death rates study in each of the nation's counties. This study led to publication of the "cancer maps," which show that an excess of many cancers are clustered in regions of heavy industrialization and concentration of petrochemical plants. The excess incidence of cancers in the heavily industrialized counties includes women as well as men, and thus cannot be mainly due to occupational exposures. Rather, it is probably also due to breathing and drinking carcinogens discharged into the air and water or dumped with chemical waste products into land disposal sites by the local petrochemical, metal mining, smelting, or asbestos plants. There is chemical monitoring information that confirms this for growing numbers of industrial carcinogens.

Among all states, for the survey period of 1950 to 1969, New Jersey leads in overall cancer mortality and in the variety of mortal cancers as well.²⁷ Every known major industrial chemical carcinogen is manufactured or otherwise handled in bulk in New Jersey²⁸ (Table 11.1). Nineteen of the twenty-one counties in the state have an incidence of bladder cancer in the top 10 percent of the nation. Salem County, New Jersey, has been singled out as having the highest national death rate from bladder cancer in both men and women, possibly related to the location there of a concentration of chemical industries, including a giant Du Pont organic chemical complex, and the fact that 25 percent of the male population in the county work in the chemical industry.* New Jersey is now attempting to control the discharge of carcinogens

* Du Pont has acknowledged compensation of 330 workers who have so far contracted bladder cancer from working in its Chamber Works Plant, Deepwater, Salem, since 1919. Most of these cases occurred prior to 1955, when production of the carcinogen primarily responsible, 2-naphthylamine, was stopped. Some new cancer cases are still developing.

from industry into the environment of the surrounding community.[†]

New Jersey is not unique. In New Orleans, there is also an excess of overall cancer mortality, as well as of cancer of the bladder and large bowel. This is probably associated with the heavy concentration of organic carcinogens in the drinking water, these being discharged from countless industries along the banks of the lower Mississippi. The increased incidence of birth defects, and possibly brain tumors, in certain Ohio counties where VC/PVC plants are located has been associated with the discovery of VC leaking from the plants into the air of the nearby communities.

Petrochemical industries are by far the main, but not the only danger. Avoid, if possible, living in the vicinity of hazardous waste disposal sites or the innumerable other sites where hazardous wastes have been improperly dumped. Love Canal, Niagara Falls, New York, is such an example. This is a sixteen-acre tract, housing about ninety families and a school which was used as a dump for disposal of hazardous wastes by Hooker Chemical Company from 1942 to 1952; the U. S. Army is also suspected of dumping during this time. In 1953, the site was sold to the board of education which built a school and sold the rest for residential construction. Since 1976, the site has been oozing chemical wastes and even containers into backyards and basements of homes. About 82 toxic chemicals including 11 carcinogens, such as benzene, chloroform, trichloroethylene, and perchloroethylene, have so far been identified in these wastes. An excess of miscarriages,

[†] Regulations effective by 1979 will require about half of all industries in New Jersey to install new anti-pollution devices designed to sharply curtail carcinogenic emissions from industry, though these regulations will initially apply to only eight known carcinogens. Questionnaires are also being sent to 12,000 companies in the state to determine whether they use any of 188 known or suspect carcinogens in their operations. Additionally, New Jersey has established a computer terminal linked to an NCI data bank which will enable rapid studies on correlation of cancer mortality rates with geographical, ethnic, and other data. Industry has responded by the usual threats to move elsewhere. A September, 1978, interim report of the New Jersey Department of Health and Environmental Protection was "unable to confirm a specific cause for the outbreak of disease, despite exhaustive analysis of a wide variety of causes." However, it appears questionable whether this conclusion is justified by the restricted monitoring undertaken, particularly as this has not yet been extended to an investigation of numerous local chemical industries for the carcinogens they manufacture, process, or emit.

Table 11.1 *Carcinogens Made or Handled at Major Facilities in New Jersey*

Carcinogens	City
Aromatic Amines	Linden, Parsippany
Arsenic	Elizabeth
Asbestos	Manville, Paterson (closed)
Benzene	Wayne, Newark, Phillipsburg, Trenton, Garfield
Benzidine	Linden, Newark, Clifton, Carteret
Beryllium	Elizabeth, Parsippany
Cadmium	Elizabeth
Carbon black	Clifton
Chromium ore and oxides	Menlo Park, Teaneck, South Plainfield, Clifton
Coal-Tar Chemicals	Linden, Paterson, Cranford, Hackensack
Epichlorhydrin	Cranford
Nickel	Elizabeth
Pitch	Cranford
Radioisotopes	New Brunswick, Lawrenceville
Tetrachloroethylene	Morristown, Clark, Cinnaminson, Monmouth Junction
Vinyl chloride	Middlesex, Lyndhurst, East Rutherford, Rahway, South Plainfield, East Orange, Moorestown
Vinylidene chloride	Haddonfield, West Orange

birth defects including mental retardation, breast cancer, and leukaemia have been reported in the local population. On August 7, 1978, the U. S. Senate approved by voice vote a "sense of Congress" amendment, stating that a serious environmental disaster had occurred, and demanded that immediate Federal aid be made available. On the same day, President Carter approved emergency financial aid for the Love Canal area.

A further, though less dramatic, example is Wilsonville, a small

county of about 700 residents in Macoupin County, central Illinois. Earthline Corporation operates a 130-acre disposal site, 90 acres of which is in the city limits and the main entrance to which is four blocks from downtown. The site is, in part, located on a disused mine, operated from 1918 to 1954 by Superior Coal Company, posing problems of surface cracking of the clay subsoil through mine subsidence, with the likelihood of waste leakage and contamination of water supplies, underground wells, and sewage systems of Macoupin County. In the spring of 1977, concerns were triggered by the discovery that Earthline had been dumping PCB wastes from Missouri and Indiana. Illinois EPA has refused to identify what hazardous wastes are being dumped at the landfill under a clause in the state Environmental Protection Act that exempts agency files constituting a "trade secret" from public disclosure requirements. Following a court order, (viewed as a national precedent) shutting down the Earthline disposal site at Wilsonville, Illinois, Attorney General William J. Scott filed suit in September, 1978, against the Federal EPA for having failed to issue regulations for hazardous waste disposal by April, 1978, as required to do so by the 1976 Natural Resources and Recovery Conservation Act. Scott cited the Wilsonville example and stated that the State of Illinois has become "the dumping ground" for the nation's hazardous wastes.‡

Avoid, if possible, living downtown in heavily air-polluted cities and live as far as you can from heavily traveled major expressways and highways. A recent Swiss study, based on a relatively small population sample, claims that there is a strong correlation between cancer incidence and proximity of residence to highways.²⁹ Quite apart from any possible excess cancer risks, levels of carbon monoxide, lead, and other automobile pollutants are also increased near major highways.

‡ A further example of what is now becoming commonplace was the discovery by EPA in April, 1977, of 600 drums of highly toxic chemical wastes dumped by Donald E. Distler, President of Kentucky Liquid Recycling, Inc., New Albany, Indiana, in a field (owned by his family) flooded by the high waters of the Ohio River. Recent heavy rains caused the drums to scatter over a widespread area and to rupture. In December, 1978, in a landmark case, Distler was criminally convicted by a federal court for discharging pollutants into a federal waterway.

11. *Your home.* Your house or apartment can expose you to hidden carcinogenic hazards. These include asbestos insulation and lining of ventilation and heating ducts, and pesticides used for termite treatment and other purposes. Make sure that the apartment house manager is not allowed to disinfect with pesticides he "is sure are safe."

12. *Race.* You should recognize that race and color are factors that may be associated with excess risks of cancer. However, these excess risks are probably due to environmental factors rather than any intrinsic or genetic susceptibility. This is the only reason why questions of race have anything to do with ways and means by which you can possibly reduce your own cancer risks.

The overall cancer risks of black U.S. males are higher than those of white men and higher than those of blacks anywhere in the world.³⁰ The incidence of lung cancer in black males is particularly high, despite the fact that substantial underreporting is suspected. This is probably due to heavy cigarette smoking, particularly of unfiltered cigarettes, among blacks. The highest incidence of lung cancer in U.S. black males in ten major national areas recently surveyed is in Pittsburgh, Pennsylvania, and probably reflects their extensive employment in the most hazardous jobs in the steel industry.

Both black men and women are experiencing an increase in the incidence of esophageal cancer at a time when this is declining in whites. Cancer of the large bowel has increased sharply in blacks, compared to a slow increase in whites. Black women have more cervix cancers than whites.

Factors which have been incriminated in the excess incidence of cancer in blacks are varied. These include discriminatory employment of black males in high risk jobs; heavy smoking, particularly of unfiltered cigarettes; the high proportion of blacks in the populations of city centers, where air pollution is greatest and where there is likely to be heavy pesticide use; living in areas near high-risk industries; and heavy consumption of dairy products and animal fats, rather than vegetables and fiber. Various surveys have shown that human fat residues of carcinogenic chlorinated hydrocarbon pesticides such as dieldrin and heptachlor epoxide are substantially higher in blacks than in whites.

Consumer Products

1. *Spray cans.* A wide range of consumer products—including insecticides, hair sprays, disinfectants, deodorants, furniture polishes, and cleaners—are marketed as aerosols. While vinyl chloride is no longer used as a propellant, existing stocks of VC-containing aerosols have not been recalled, nor has there been any clear brand identification of these stocks. Labeling may not necessarily help, for although the presence of propellants is stated their identities are not generally disclosed. The fluorocarbon Freons® are being phased out as propellants and are known to escape into the upper atmosphere and attack the ozone layer, which filters the sun's ultraviolet rays.* This will increase your chance—and everyone else's—of getting skin cancer.

Avoid all aerosols, no matter what their propellant. Every time you use one for any purpose, you will inhale high concentrations of its chemical contents, whatever they happen to be.

2. *Pesticides.* A number of common pesticides used in and around the home and garden are carcinogens. Among the more dangerous are chlordane and heptachlor, which are widely used as common garden insecticides, moth and termite proofing, and other purposes.

In the last decade, there have been major advances in the understanding of biological control of insects using integrated pest management systems. These are equally applicable for home, lawn, and garden infestations and other urban uses as for agriculture.

3. *Tris.* Until recently, children's sleepwear was treated with the flame retardant Tris. Don't buy such sleepwear. Tris is absorbed through the skin, persists in fabric even after repeated laundering, and has been recently shown to be both carcinogenic and mutagenic. Instead, try to use only inherently fire-resistant natural and semi-synthetic textiles.

4. *Cleaning agents and solvents.* Do not use *any* products containing carbon tetrachloride, trichloroethylene, perchloroethyl-

* Since December, 1978, fluorocarbons may no longer be manufactured or packaged.

ene, or benzene, which are all carcinogenic. Use alternatives based on detergents. Be especially careful to avoid all products containing benzene, particularly paint and varnish removers, adhesives, and cements.

Work

1. *Industry.* Your choice of work can greatly affect your chances of getting cancer. Workers in petrochemical, asbestos, steel, smelting, and some mining industries are recognized "high risk" groups (See Table 5.1). While risks are clearly greatest in these manufacturing industries, they also extend to industries that subsequently fabricate products derived from these carcinogens.

The conditions you will experience in different industries vary from the totally uncontrolled, especially in smaller, non-unionized plants, to the partially controlled. One of the major problems, however, has been the chemical industry as a whole, through its politically powerful trade association, the Manufacturing Chemists Association, refusing to disclose the identity of most chemicals used in trade name products in the workplace on the grounds that these are "trade secrets." The likelihood is that you will not even know the names of many or most of the chemicals you work with. Instead you will find yourself handling and breathing chemical mixtures labeled something like AB-347. If you ask your foreman or plant manager what this is, the answer may be "We don't know, we buy it like this," from such a company as Monsanto or Du Pont, who in turn will not be eager to tell you what is in their product, again claiming trade secrecy. Alternatively, management may know what is in the mix, but will tell you that "it is none of your business."

Unless you are fully and completely prepared to take the consequences, you should not go to work in an uncontrolled, high-risk industry, especially one with a bad track record. If you are already working in one, you may only have very limited options, other than leaving, at the expense of loss of seniority and other

rights, and trying to find other, safer work.[†] If you decide to stay, work with your union to make conditions safer.

If you do plan to seek work in one of the high-risk industries, try to choose a large, well-organized plant with reliable and informed union leadership, one in which carcinogens are handled in closed systems and the workplace is monitored with sensitive instrumentation. Also make sure the results of the monitoring are promptly made available to you. Avoid any non-organized industry, particularly one that refuses to give you complete information on the names of the chemicals you will be working with. Do not otherwise accept assurances of safety from the plant manager or even the company physician, who is employed by management and may not consider you his first loyalty. Finally, if you possibly can, try to find out from your union or some other independent source the record of this particular industry in the health and cancer area before you accept employment there. But be forewarned that your chances of getting such information are not good.

2. Arts and crafts. Arts and crafts are to some a full-time occupation, and to others a hobby. Whichever is the case, you should know as far as possible the composition of all your materials so that you can handle them with due care, and find substitutes for any which are carcinogenic (Table 11.2).

Some construction materials, such as plasterboard and spackle, contain asbestos. Many paints are based on carcinogenic pigments, including chromium, cadmium, nickel, and arsenic, and may also contain carcinogenic solvents, particularly benzene. Artists, especially, should take meticulous precautions when mixing dry pigments, since the dust generated is easily inhaled. Spray paints may still contain VC as propellants, even though its use for this purpose has been banned. Whether an occasional hobbyist or a serious artist, you should avoid handling carcinogenic materials. If you must handle them, do so either with complete ventilation and personal protection, such as a respirator, or with the process completely enclosed.

[†] You have legal rights to refuse work you consider to be hazardous. Your options include suing the Department of Labor to force an injunction restraining employers from exposing employees to imminent hazards; rights under Sections 7 and 502 of the Labor Management Relations Act; and rights under Section III of the Occupational Safety and Health Act.

3. *Schools.* Schools may contain hidden and unexpected hazards, including the hazard of cancer, and children spend as much time there every day as does any workman in a factory or plant. Parents should check on the location of the school, to make sure that it is not near a chemical, mining, or smelting plant, or too close to busy highways and other sources of chemical emissions. The elementary school in Saugus, California, where VC levels of about 3 ppm were found in classrooms in the summer of 1977, is a good case in point. The construction of the school building should also be examined to avoid the now common experience of schools such as those in Howell Township, New Jersey, in which friable asbestos-sprayed surfaces, such as soundproof ceilings, were found in 1976 to be liberating large quantities of asbestos fibers into the air.

The cafeteria menu may also be of concern. Through your PTA, work for the ban of "junk" or convenience foods. Encourage the sale of nuts and fruit for snacking. The trailblazing example set by the West Virginia Board of Education should be followed on a national basis:

. . . Effective with the 1976-77 school year, the sale of the following non-nutritional foods or beverages is prohibited during the school day in all public schools of the state: candy, chewing gum, soft drinks, flavored ice bars.³¹

In November, 1977, the USDA, under an amendment to the Child Nutrition Act, regained the authority it had lost in 1972 to regulate what food items can be sold in vending machines on à la carte lunch lines or at snack stands at schools. USDA Secretary Bergland subsequently initiated action to restrict "competitive (junk) foods" in schools. However, under threats of legal action from "junk" food industries, including Hershey Candy Company, the USDA announced in December, 1978, that it would postpone such action for at least a further year in order to elicit public comments on the proposal.‡

‡ In these negotiations, Hershey was represented by its attorney Peter Barton Hutt, formerly FDA General Counsel, supported by Ogden Johnson, Hershey's senior nutritionist and former Chief Nutritionist of the FDA. This is a not unusual example of the "revolving door" between agencies and industry which the Carter administration is attempting to limit.

Table 11.2 *Carcinogenic Materials Encountered in the Arts and Crafts*

Material	Process	Type of Cancer
Arsenic and alloys	Textile prints, metal alloys	Skin and lung
Beryllium	Vapors in sculpture, dust in ceramics	Lung and liver
Cadmium	Silver soldering, brazing, welding	Lung and prostate
Chromium	Paints, lithographic dyes, mordants, printing	Lung
Nickel, oxides, and carbonyl	Welding, nickel alloys	Lung
Asbestos	Mold-making, foundry welding, soldering, spackling	Lung, pleura, and peritoneum
Wood	Carpentry and cabinet making	Nasal sinus
Arsene	Etching	Lung, skin
Benzene	Solvent for resins, glues, and rubber cement	Leukaemia and aplastic anemia
Carbon tetrachloride	General solvent, cleaner	Liver cancer
Trichloroethylene	Solvent for oils, resins, dry cleaning, scouring	Liver cancer
Tetrachloroethylene	Solvent for oils, resins, dry cleaning, scouring	Liver cancer
Formaldehyde	Preserving	Produces BCME, a lung carcinogen in acid solution

Source: Based on B. W. Carnow, "Health Hazards in the Arts and Crafts," University of Illinois, School of Public Health, April 19, 1974.

Laboratory courses should not expose students to harmful chemicals.³² Wood and metal shops should avoid the use of or-

ganic cleaning fluids and solvents containing benzene, carbon tetrachloride, trichloroethylene, or other carcinogens. Ventilation must be adequate. Chemistry laboratories and stockrooms should be completely cleared of all carcinogenic and other toxic chemicals, such as benzene. Some people question whether organic chemistry should be taught at all at the high school level. If it is, all chemicals used in classroom or laboratory work should be cleared by a knowledgeable independent authority. Finally, the unsupervised use of toxic and carcinogenic pesticides by janitorial staff should be completely stopped.

Early Detection and Treatment

Early detection is no substitute for preventing cancer, but it may result in a cure, or at any rate, increase your survival time. The prognosis of a wide range of cancers, particularly skin, breast, cervix, colon, and larynx, depends on how early they are picked up and treated effectively, in which case there is a good likelihood of a complete "cure."* Cancers which are localized to their organ of origin at the time of diagnosis and treatment are more curable than cancers that have spread to regional lymph nodes or beyond (Figure 11.1). Curability is usually expressed in terms of cases surviving without apparent recurrence of disease for over five years past initial treatment.

In view of the importance of early diagnosis, particularly for some of the more curable cancers, you should be on the lookout for any warning signs or symptoms and should check for these regularly. Additionally, you should make arrangements to have the following regular screening tests:

* A specific example of the importance of early diagnosis is the mammography program of the Health Insurance Plan of New York sponsored by the NCI in the late 1960s and directed by Samuel Shapiro. This is the first and only completely controlled trial of early cancer diagnostic techniques, which proved that mammography in women over the age of 50 could lead to a reduction in mortality of breast cancer by 30 to 50 percent. (Mammography in younger women, however, is associated with increased risks of breast cancer, which may balance possible diagnostic advantages.)

- Pap smears for cervix cancer.† Women over the age of twenty, especially sexually active ones, should have this test periodically. Black women should be more insistent on this, as their risk is higher than for white women.
- Pelvic examination for uterine cancer. Women over fifty years old should have this done periodically, especially if there is abnormal discharge or bleeding.
- Proctosigmoidoscopy for colon cancer. This unpleasant but lifesaving procedure is recommended routinely for men and women over forty, especially those with a family history of high-risk precancerous diseases, such as polyposis or ulcerative colitis.
- Self-examination of breasts. Every woman from adolescence on should learn and practice this procedure monthly.
- Laryngoscopy. This is recommended regularly for smokers and drinkers, particularly if there is a history of "laryngitis" or hoarseness.

Screening is even more important if you are already at a particular "high cancer risk," several categories of which are recognized:

1. *Familial predisposition.* Certain cancers tend to run in families, for poorly understood reasons.³³ These include cancer of the lung, large bowel, uterus, stomach, and breast, and childhood sarcomas and brain tumors. Your chances of contracting any of these particular cancers seem to be two to four times higher if a close relative has previously developed one of them. The excess risk is restricted to cancers of specific sites; a family history of lung cancer will not predispose to breast cancer.

Familial predisposition to breast cancer is particularly well established. Sisters or daughters of women who developed breast cancer before menopause are known to be about nine times more likely to get breast cancer than the general population. The risk is

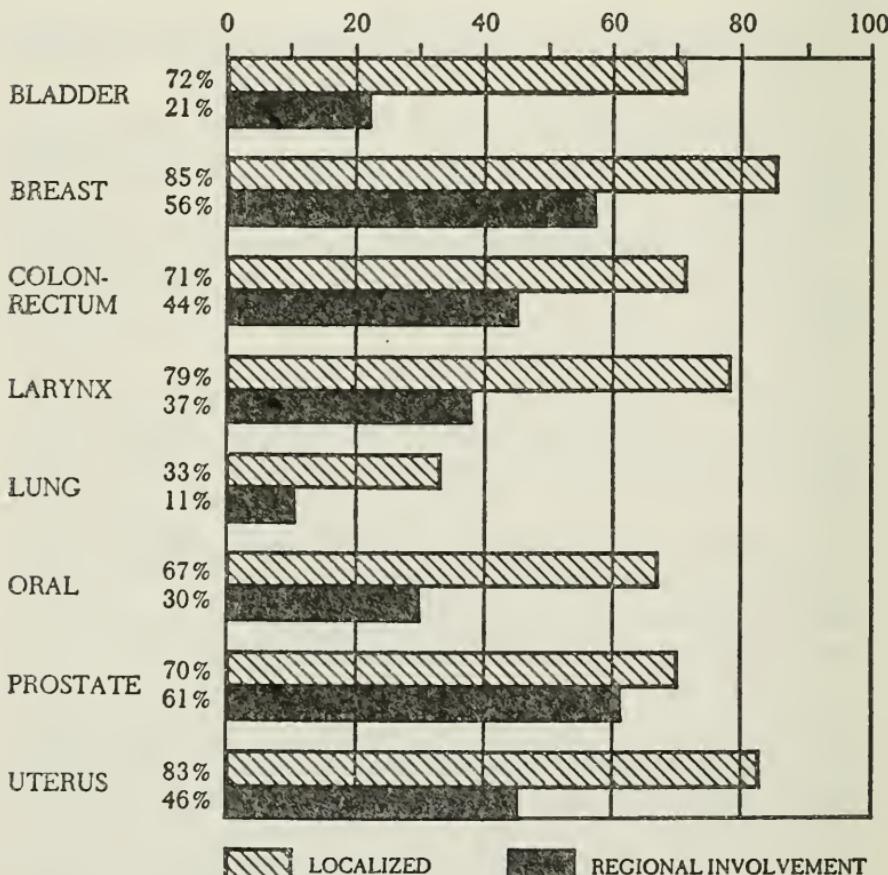
† The value of the Pap test appears to have been exaggerated. The decline of cervix cancer deaths, commonly attributed to the Pap test, began before this test was widely introduced, and more probably reflects the high rate of unnecessary hysterectomies.

still further increased if the relative had cancer in both breasts. Risks for postmenopausal breast cancers are much lower.

2. *Genetic predisposition.* Certain rare cancers or predisposing conditions can be directly inherited. These include multiple polyposis of the colon, which predisposes to colon-rectal cancer, and xeroderma pigmentosum, which predisposes to skin cancer.

3. *History of occupational exposure to carcinogens.* The degree of excess risk will depend on the nature of the carcinogens you work with and the intensity and duration of exposure.

Figure 11.1 Five Year Cancer Survival Rates for Selected Sites



*Adjusted for normal life expectancy.

Source: "1978 Cancer Facts and Figures." American Cancer Society, New York, 1977.

4. *History of treatment with carcinogenic drugs or X-rays.* As for occupational carcinogens, the excess risks depend on the degree and duration of exposure.

There are certain cancers, however, which are generally death sentences, regardless of how early they are diagnosed. Some of the claims which have been made for improved survival with early diagnosis probably reflect the extra time apparently gained before the cancer would have otherwise been diagnosed. These poorly curable cancers include lung, brain, liver, pancreas, and stomach. Early treatment may, however, improve chances of survival and increase the quality of remaining life.‡

For Hodgkin's disease and some forms of leukaemia, particularly acute lymphocytic leukaemia of childhood, complete remissions, and prolonged survival is possible with early diagnosis and treatment, particularly in specialized centers. The importance of going to such a center for these and certain other cancers is critical. It may mean the difference between survival and death, or between prolonged and short survival. Find out what are the best centers in the country, and insist on going there if you possibly can.*

Recognizing the reality that one in four of us will sometime need cancer treatment, and that the costs will not be adequately covered by conventional policies, the ever-responsive insurance

‡ It is important to note that the "cancer surveillance programs" adopted by industry for lung or liver cancer most certainly do not offer prevention, but merely the earlier diagnosis of an inevitable death.

* There are three major guides to this: accreditation by the American College of Surgeons for cancer treatment; accreditation by the Joint Commission of the American Hospital Association; membership of the Comprehensive Cancer Centers, nineteen NCI-funded national centers for advanced cancer treatment. In addition, there are certain hospitals and centers that specialize in treatment of specific types of cancer and have the best survival rates (See Appendix VII). The importance of specialized treatment and specialized centers with their highly skilled and enthusiastic oncology teams has been recently emphasized in *Strike Back at Cancer* by Steven Rapaport (Englewood Cliffs, N.J.: Prentice Hall Inc., 1978), and in *The Conquering of Cancer* by Lucien Israël (New York: Random House, 1978). While Israël's optimism appears to reflect his humanity rather than documented overall improvements in curability of the major cancer killers, the importance of "limited benefits" that can be achieved in the best modern centers, particularly the improvement in the quality of terminal life, must be clearly appreciated.

industry is now offering cancer policies which you may want to investigate. About 60 percent of these policies are written by the American Family Corporation, at a cost of about \$75 a year for individual policies. Profits and a growth rate of 35 percent are expected by this industry in 1978.

Legal Remedies

If you have developed cancer and have reason to believe that this is due to the fault of industry or possibly even government, then there are some legal remedies available to you or your heirs. Your ability to succeed in these, apart from the inherent validity of the case, will depend on your persistence and on the expertise of your attorney. Any successful legal action you take against the industry responsible for your cancer may act as an incentive to prevent further such cancers.[†]

1. *Medical or drug-related suits.* More often than not, drug companies will settle out of court when faced with an obviously legitimate claim for damages in order not to implicate a particular drug or medicine as a precedent for other suits, which would inevitably follow. As for treatment-related cancer, such as that of the thyroid which developed following irradiation of children for "enlarged thymus glands," a malpractice suit may be difficult to prosecute. Not only has it been a problem to get doctors to testify against each other, but it has also been successfully argued that a given treatment was justified provided it was considered safe and effective at that time, even if it later turned out to be harmful and useless.

[†] Pressures from the insurance business may act as similar incentives. Robin Jackson, an executive of Merret Dixey Syndicates of London (a powerful force in the Lloyd's market) has warned:

As manufacturers move into new fields of product technology, so we in the insurance markets move into new areas of liability coverage that we can't fully understand yet. It's got to the point where a number of us in the underwriting market in London are starting to question whether we'll be able to provide coverage for certain products against cancer or similar diseases. (J. H. Miller, "Jackson's Leisure Study Reinforces Policy Fears," *Business Insurance*, February 14, 1979; see also S. S. Epstein, "Criticizes Insurers," *Business Insurance*, April 30, 1979.)

2. *Product liability suits.* If you or any member of your family develops cancer following the use of or exposure to a carcinogenic product, then you have the basis for a product liability suit. The burden to prove your case is less for a food or drug than for other types of products, such as pesticides or paint strippers. In cases involving food and drugs, the courts usually assume that the seller warrants his product as fit and safe for human consumption, and the plaintiff then usually only needs to show that damages were sustained and were caused by the product in question.

For a successful product liability suit, you must prove a "breach of duty of care"; that is, the manufacturer or supplier knew, or it was general knowledge among the industry, that the product was carcinogenic. This duty, when breached, constitutes negligence when the party affected is within the "ambit of risk," and could thus reasonably have been anticipated to be exposed to the product and consequently injured. The product in question must be the proximate or immediate cause of the disease, and the disease itself must be a genuine damage, such as cancer. When all these conditions can be established, grounds then exist for an award for negligence. Some states disqualify the plaintiff if the defense can prove that he somehow contributed to the negligence, while more liberal states, such as New York and Wisconsin, permit partial judgments based upon comparative negligence of both parties.

An alternative, but less well tested, legal approach is based on contract theory. The courts have often recognized that the purchaser of a product expects and receives an implied warranty from the manufacturer that the product is fit for use, or "merchantable." This warranty cannot be waived by mere labeling. The instances where this attack has failed, cigarette suits in particular, have usually involved jury trials, where the purchaser was found to have knowingly assumed a risk. Apart from this, chances of success in product liability suits are increased if the product label contained no indication or warning of its carcinogenicity.

3. *Tobacco cancer.* Suits against the tobacco industry for lung cancer have so far been unsuccessful. There is, however, some reason for guarded optimism based on as yet untested new legal strategies, which you or your heirs may wish to explore if you

have developed lung cancer or other tobacco-induced diseases following smoking. Probably the single most effective measure for the prevention of cancer would be a series of large, successful lawsuits against the industry. This is a potential solution whose time is overdue.

4. Occupational cancer. Should you develop cancer after exposure to a known carcinogen, if you are both lucky and persistent, you may be awarded workman's compensation if you can legally prove that the exposure was work-related. This, however, is rarely sufficient to cover the total costs of your cancer, quite apart from deprivation of future earnings. It has also the added disadvantage that your acceptance of a settlement absolves the industry of all further liability from tort actions. An exception in theory may be made only if gross negligence can be proven, at best a difficult task for you when pitted against the resources of a giant industry or corporation.

State compensation systems have abjectly failed to deal with occupational health problems, particularly for diseases with long latency such as cancer.‡ Workman's compensation laws vary from state to state only in their degree of inequity. Theoretically, these laws are based on an implied trade-off in which workers surrender their rights to sue their employer in exchange for the guarantee of adequate compensation in a non-adversarial process. The courts have almost consistently upheld the legality of the denial of right to sue, but have generally failed to maintain the right to a non-contested adequate compensation. Impossibly heavy burdens are

‡ An important recent development in attempts to reform the inequities of current workers state compensation systems has been the introduction of S.3060 by the Senate Human Resources subcommittee on labor. This bill is designed to provide comprehensive reform of compensation programs, and to mandate uniform national guidelines while allowing a reasonable degree of autonomy at the state level. Industry has reacted critically. The Alliance of American Insurers testified that the bill would impose "further liberalization of benefits without curtailing the abuses—[and that it would] explode costs and create administrative chaos." John F. Burton, chairman of the 1972 National Commission on State Workers Compensation Laws, however, testified on behalf of the bill, expressing the view that "for the first time a workers' compensation bill had been introduced in Congress that deserves to be enacted." Other important proposed reforms include the Toxic Substances Pollution Victim Compensation Act of March, 1978 (H.R. 9616), which addresses problems of causality by establishing procedures of standards of proof and shifts the burden of proof of safety to industry.

placed on workers or their heirs to unequivocally demonstrate causal and exclusive relationships between their cancers or other diseases and prior occupational exposures to carcinogenic and toxic agents.³⁴ Workers are obliged to hire a lawyer on a contingency basis (most lawyers are reluctant to accept such cases because of the poor chances of success and minimal nature of awards) to represent them before compensation boards which are often both unsympathetic and poorly informed. State compensation systems further make no provisions for identification and medical examination of retired or active workers previously exposed to carcinogens, but who are not yet clinically ill. Recent surveys by the Department of Labor have shown that the average length of time from onset of disability to the first disability payment is one year for a disease claim, compared to two months for an injury case; that less than 3 percent of compensation awards are for occupational diseases; that 60 percent of disease cases which were eventually compensated were contested, compared to 10 percent of injury awards; the probability of litigation approaches 90 percent for serious diseases; 55 percent of disease claims are settled by compromise and release agreements, compared with 16 percent of injury cases; the total compensation payment for permanent occupational disease is less than \$10,000, compared to \$23,400 for similar injury cases; compensation for death caused by occupational disease averages \$3,500, compared to \$57,500 for an injury case; foreign countries settle proportionately more disease claims than do the U.S. (in the case of Sweden the disparity is about twelve-fold); and the claims determination process in most foreign countries is in the hands of a disinterested party, in contrast with the U.S.

A more practical option, which may sometimes be available, is a third-party or product liability suit. You can bring one against the manufacturer supplying a carcinogenic product or process, especially in the absence of appropriate labels and warnings, to the industry in which you worked and contracted your cancer.

The principle of the third-party suit was expanded in 1972 in *Dole v. Dow Chemical et al.* (New York Court of Appeals, March 11, 1972) by the heirs of an employee of a small exterminating company who had died of exposure to methyl bromide, a pesticide widely used in fumigation. Unhappy with the trivial

workman's compensation award, the heirs sued the third party, Dow Chemical; the manufacturer of the chemical. The grounds of the lawsuit were that the pesticide was not appropriately labeled, and that the worker had thus not been adequately warned of the hazard. Dow, while not explicitly accepting blame, sued the worker's employer for contributing to the negligence by failing to instruct him properly in the chemical's safe use. Dow thus won damages from the company, some of which it then paid the worker's family in its own settlement. The two major precedents set by this case were that liability for negligence could be shared between the defendant and a third party, and that a negligent employer could no longer hide behind workman's compensation to limit his liability for exposing workers to toxic chemicals or other hazards.

The third party principle was substantially strengthened, especially for carcinogens, when the government, late in 1977, settled a \$20 million suit brought by families and former employees of a defunct asbestos plant in Tyler, Texas. The plant, which had been literally dismantled and buried because asbestos levels were so high that it could not be cleaned up, belonged to PPG Industries, which will pay \$8 million, and before it, Union Asbestos and Rubber, which will pay \$1 million. The government itself will pay the survivors \$5 million, admitting that because of a secret agreement with the industry it had failed to warn workers of hazards of asbestos, even after several government inspections over a ten-year period turned up extremely high levels.

As the causal relationship between past exposure and delayed onset of cancer has become increasingly appreciated, the courts have more and more come to apply the doctrine of strict liability, and the prospects of success in third-party suits is now increasing. It seems likely that the recent disclosure of the asbestos "Pentagon Papers" will have a favorable impact on the multimillion-dollar asbestos cases now before the courts. While large adverse judgments may act as an incentive to manufacturers to produce carcinogen-free products and to be more candid and explicit if they persist in manufacturing carcinogenic products, the financial impact of out-of-court settlements is blunted by current IRS law, allowing the carrying forward of such costs for tax purposes.

Another important option you have is suing your company doc-

tor for medical malpractice if you can show that he failed to warn you of any findings that could have allowed you to limit further exposure or seek early treatment.* Such malpractice suits are likely to increase in the future. It is also likely that the scope of such actions will be extended to hold culpable other professionals in the workplace, such as industrial hygienists or chemists, who fail to warn workers of exposure to carcinogenic or other toxic hazards.

Another possible avenue by which a diseased worker or his heirs may circumvent the legal barricade of the workman's compensation system is based on a fraud theory. Two Northern California courts have recently rendered conflicting decisions on whether a worker can sue his employer directly if he can prove that the company deliberately concealed or manipulated information on the hazards that ultimately led to the disease and claim. These suits are precedential and, if allowed to go forward, are likely to create a powerful deterrent to future suppression or manipulation of health and safety data by industry and its consultants. More salutary still would be the successful prosecution of guilty parties for criminal acts, including manslaughter.

5. Community cancer suits. Assume you are a middle-aged or elderly non-smoking lady living in Salem County, New Jersey, who has developed bladder cancer. It should seem reasonable to take the position that there is a significant probability that your cancer was caused by discharge of aromatic amine carcinogens into your air and water from nearby plants known to be handling these carcinogens. The NCI cancer maps would be helpful in supporting your position, especially if these can be supported by evidence of the leakage of carcinogens from the industry to the outside air. This approach has not yet been tested in the courts, but when it eventually is, it will probably be done on a class action basis for

* Over ten lawsuits, totaling more than \$50 million, have been filed against Kent Wise, the former physician of a Johns-Manville plant in Pittsburg, California, on the grounds that he deliberately withheld information from workers on X-ray evidence of asbestos-induced lung disease. Wise in turn is suing Johns-Manville for \$100 million, claiming that in his original terms of employment he was "told not to have anything to do with X-rays," which would be read at the Trudeau Institute in Saranac Lake, New York. However, Wise also contends that he had no duty to report the results of the X-rays to the workers concerned but only to Johns-Manville.

high claims, because the expense is likely to be large and the case difficult to prove. The plaintiffs will also need to establish their case through arguments based on correlation in order to show proximate causes.

Finally, it must be realized that industry itself is not always legally passive. However, the recent failure of industry in the *Galaxy v. Capurro* case, besides the climate of current opinion, is likely to dampen any latent initiatives or ambitions in this direction.

The Goal of Public Action

The time has come to summarize the goals of the actions recommended in this book to reduce the national toll of cancer:

1. Cancer must be regarded as an essentially preventable disease.
2. The hidden political and economic factors which have blocked and continue to block attempts to prevent cancer must be recognized.
3. The ineffective past track record of government in cancer prevention must be recognized.
4. The critical roles in cancer prevention that public interest groups and informed labor leadership have exercised must be recognized and their further efforts fully encouraged and supported.
5. Congress must resolve the major inconsistencies in a wide range of legislation on environmental and occupational carcinogens.
6. Substantially higher federal priorities for the prevention of cancer must be developed.
7. Policies of the various federal agencies with responsibilities in cancer prevention must be effectively integrated and coordinated.
8. Top business management must recognize the essential similarities between their long-term interests and goals and those of

society. Prevention of occupational cancer and cancer in the community-at-large is of primary importance to both.

9. The American Cancer Society must be influenced to balance its preoccupation with treatment with activist programs designed to prevent cancer.

10. The medical and scientific community must accept a higher degree of responsibility and involvement in the prevention of cancer by actions on both the professional and political levels.

11. Medical schools and schools of public health must be persuaded to massively reorient their educational and training programs from the diagnosis and treatment of disease and cancer to prevention.

12. Chemicals in consumer products and in the workplace must be clearly and simply identified and labeled.

13. Additional new approaches must be developed for obtaining and for retaining honest and scientifically reliable data on the carcinogenicity and toxicity of new chemicals, besides of untested or poorly tested chemicals already in commerce; such data must be made accessible to public scrutiny. Maximum legal penalties should be directed against all those responsible, directly and indirectly, for distortion or manipulation of toxicological and epidemiological data on the basis of which decisions on human safety and risk are based.

14. Apart from actions on a political level, we all have limited personal options. To some extent, it may be possible to reduce our own chances of developing cancer by making informed changes in lifestyle, use of consumer products, and work.

15. The major determinants of preventable cancer are political and economic, rather than scientific, and as such must be addressed in the open political arena. Cancer prevention must be made, at least, to rank with inflation on the next political ticket of your local and state representative, congressman, and President.

The vigorous implementation of policies based on these goals will reverse the growing epidemic of modern cancer and restore it to its rightful role of an uncommon disease.

Epilogue

Over the past few decades, there has been a progressive escalation of available information on the chemical causes of cancer. There has also been a parallel increase in our ability to test for carcinogenic effects of chemicals in animals and also to recognize such effects in humans. Not only is the level of this information in general adequate, but there are also ample laws, in spite of their occasional ambiguities and inconsistencies, to translate such information into regulatory action. The problem is thus not one of inadequate information or inadequate laws.

So then, what is the problem? As the case studies in this book make clear, there has been and continues to be a massive failure to utilize available knowledge and to implement the law. A combination of powerful and well-focused pressures by special industrial interests, together with public inattention and the indifference of the scientific community, has created a major imbalance in decision-making and public policies. In spite of efforts by organized labor and public interest groups, this imbalance has consistently and effectively thwarted, and still continues to thwart, meaningful attempts to prevent the carnage of chemical-cancer, a carnage whose unrecognized costs run each year into the tens of billion dollars.

It is not as if there is any necessary conflict between long-term industrial growth and the prevention of cancer. Many carcinogens are used for purposes that are trivial, or under conditions where they can be replaced by non-carcinogenic substitutes. In those special circumstances where carcinogens perform critically needed and irreplaceable functions, they can be used much more safely, provided industry invests in the appropriate engineering controls.

While much is known about the science of cancer, its prevention depends largely, if not exclusively, on political action. This then is the message of the book.

Humans			
Chemicals or industrial process	Main type of exposure	Target Organ	Main route of Exposure*
1. Aflatoxins	Environmental, occupational	Liver	p.o., inhalation
2. 4-Aminobiphenyl	Occupational	Bladder	Inhalation, skin, p.o.
3. Arsenic compounds	Occupational, medicinal, and environmental	Skin, lung, liver	Inhalation, p.o., skin
4. Asbestos	Occupational	Lung, pleural cavity, gastrointestinal tract	Inhalation, p.o.
5. Auramine (manufacture of)	Occupational	Bladder	Inhalation, skin, p.o.
6. Benzene	Occupational	Hemopoietic system	Inhalation, skin
7. Benzidine	Occupational	Bladder	Inhalation, skin, p.o.

Appendix I

Chemicals Known to Induce Cancer in Humans

Animals

Animal	Target Organ	Route of Exposure*
t	Liver, stomach, colon, kidney	p.o.
h, duck, narmoset, tree hrew, monkey	Liver	p.o.
t	Liver, trachea	i.t.
ouse, rat	Liver	i.p.
ouse	Local	s.c. injection
ouse	Lung	i.p.
ouse, rabbit, dog	Bladder	p.o.
wborn mouse	Liver	s.c. injection
t	Mammary gland, intestine	s.c. injection
ouse, rat, dog	Inadequate, negative	p.o.
ouse	Inadequate, negative	Topical, i.v.
ouse, rat, hamster, rabbit	Lung, pleura	Inhalation or i.t.
t, hamster	Local	Intrapleural
t	Local	i.p., s.c. injection
	Various sites	p.o.
ouse, rat	Liver	p.o.
bbit, dog	Negative	p.o.
t	Local, liver, intestine	s.c. injection
ouse	Inadequate	Topical, s.c. injection
ouse	Liver	s.c. injection
t	Liver	p.o.
	Zymbal gland, liver, colon	s.c. injection
umster	Liver	p.o.
og	Bladder	p.o.

Humans

Chemicals or industrial process	Main type of exposure	Target Organ	Main route of Exposure*
8. Bischloromethylether	Occupational	Lung	Inhalation
9. Cadmium-using industries (possibly cadmium oxide)	Occupational	Prostate, lung	Inhalation, p.o.
10. Chloramphenicol	Medicinal	Hemopoietic system	p.o., injection
11. Chloromethylmethylether (possibly associated with bischloromethylether)	Occupational	Lung	Inhalation
12. Chromium (chromate-producing industries)	Occupational	Lung, nasal cavities	Inhalation
13. Cyclophosphamide	Medicinal	Bladder	p.o., injection
14. Diethylstilbestrol	Medicinal	Uterus, vagina	p.o.

Animals

Animal	Target Organ	Route of Exposure*
Mouse, rat	Lung, nasal cavity	Inhalation
Mouse	Skin	Topical
Rat	Local, lung	s.c. injection
Rat	Local	s.c. injection
	Local, testis	s.c. or i.m. injection
		No adequate tests
Mouse	Initiator	Skin
	Lung	Inhalation
Rat	Local, lung	s.c. injection
	Local	s.c. injection
Mouse, rat	Local	s.c., i.m. injection
Rat	Lung	Intrabronchial implantation
Mouse	Hemopoietic system, lung	i.p., s.c. injection
Rat	Various sites	p.o.
	Bladder	i.p.
	Mammary gland	i.p.
	Various sites	i.v.
Mouse	Mammary	p.o.
Mouse	Mammary, lympho- reticular, testis	s.c. injection, s.c. implantation
Rat	Vagina	Local
	Mammary, hypo- physis, bladder	s.c. implantation
Hamster	Kidney	s.c. injection, s.c. implantation
Squirrel monkey	Uterine serosa	s.c. implantation

Humans

Chemicals or industrial process	Main type of exposure	Target Organ	Main route of Exposure*
15. Hematite mining (?radon)	Occupational	Lung	Inhalation
16. Isopropyl oils	Occupational	Nasal cavity, larynx	Inhalation
17. Melphalan	Medicinal	Hemopoietic system	p.o., injection
18. Mustard gas	Occupational	Lung, larynx	Inhalation
19. 2-Naphthylamine	Occupational	Bladder	Inhalation, skin, p.o.
20. Nickel (nickel refining)	Occupational	Nasal cavity, lung	Inhalation
21. <i>N,N</i> -Bis(2-chloroethyl)-2-naphthylamine	Medicinal	Bladder	p.o.
22. Oxymetholone	Medicinal	Liver	p.o.
23. Phenacetin	Medicinal	Kidney	p.o.
24. Phenytoin	Medicinal	Lymphoreticular tissues	p.o., injection
25. Soot, tars, and oils	Occupational, environmental	Lung, skin (scrotum)	Inhalation, skin
26. Vinyl chloride	Occupational	Liver, brain, lung	Inhalation, skin

Source: L. Tomatis et al., "Evaluation of the Carcinogenicity of Chemicals: A Review of the Monograph Program of the International Agency for Research on Cancer," *Cancer Research* 38(1978): 877-85.

* p.o.=per os or oral; s.c.=subcutaneous; i.m.=intramuscular; i.t.=intratracheal; i.v.=intravenous.

Animals

Animal	Target Organ	Route of Exposure*
ouse, hamster, guinea pig at	Negative Negative No adequate tests	Inhalation, i.t. s.c. injection
ouse at	Initiator Lung, lympho- sarcomas	Skin i.p.
ouse at	Local	i.p.
amster, dog, monkey	Lung	Inhalation, i.v.
ouse at, rabbit	Local, mammary	s.c. injection
amster, dog, monkey	Bladder	p.o.
ouse, rat, hamster	Liver, lung	s.c. injection
ouse, rat, hamster	Inadequate	p.o.
ouse, rat, hamster	Lung	Inhalation
ouse, rat, hamster	Local	s.c., i.m. injection
ouse, rat, at	Local	i.m. implantation
ouse, rat, at	Lung	i.p.
ouse, rat, at	Local	s.c. injection
	No adequate tests	
	No adequate tests	
ouse	Lymphoreticular tissues	p.o., i.p.
ouse, rabbit	Skin	Topical
ouse, rat	Lung, liver, blood vessels, mammary, Zymbal gland, kidney	Inhalation

Appendix II

Evaluation of

*Environmental Carcinogens**

Report to the Surgeon General, USPHS
April 22, 1970

Ad Hoc Committee on the Evaluation of Low Levels
of Environmental Chemical Carcinogens

**Members of the Ad Hoc Committee on the
Evaluation of Low Levels
of Environmental Chemical Carcinogens**

*National Cancer Institute
Bethesda, Maryland*

Umberto Saffiotti, Chairman, Associate Scientific Director for Carcinogenesis, Etiology, National Cancer Institute, Building 37, Room 3A21, Bethesda, Maryland.

Hans L. Falk, Associate Director for Laboratory Research, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

* This report was introduced as an exhibit and published in full in both the following Senate hearings: "Chemicals and the Future of Man," hearings before the Subcommittee on Executive Reorganization and Government Research of the Committee on Government Operations: United States Senate, April 6 and 7, 1971; and the "Federal Environmental Pesticide Control Act," hearings before the Subcommittee on Agricultural Research and General Legislation of the Committee on Agriculture and Forestry, United States Senate, March 23-26, 1971.

Paul Kotin, Director, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

William Lijinsky, Professor of Biochemistry, The Eppley Institute for Research on Cancer, University of Nebraska College of Medicine, Omaha, Nebraska.

Marvin Schneiderman, Associate Chief, Biometry Branch, National Cancer Institute, Wisconsin Building, Room 5C10, Bethesda, Maryland.

Philippe Shubik, Director, The Eppley Institute for Research on Cancer, University of Nebraska, College of Medicine, Omaha, Nebraska.

Sidney Weinhouse, Director, Fels Research Institute, Temple University School of Medicine, Philadelphia, Pennsylvania.

Gerald Wogan, Professor of Food Toxicology, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts.

Staff Members: John A. Cooper, Executive Secretary, Richard R. Bates, James A. Peters, Howard R. Rosenberg, Elizabeth K. Weisburger, John H. Weisburger.

Introduction

Establishment of this Ad Hoc Committee was requested on October 24, 1969, by the Deputy Assistant Secretary for Health and Scientific Affairs.

The task of the Committee is to review the problems relating to the evaluation of low levels of environmental chemical carcinogens, to consider the scientific bases on which such evaluations can be made, and to advise the Department of HEW on the implications of such evaluations.

The Committee, in addressing itself to the problems of environmental exposures to chemical agents from all sources, has considered the scientific criteria for evaluation of carcinogenic hazards.

Many previous recommendations on the criteria to be used for evaluating environmental chemical carcinogenic hazards have been made for specific sources of exposure or for specific groups of substances (e.g., food additives, pesticides, certain occupa-

tional carcinogens). In some cases this approach has led to an uneven approach to preventive measures.

The task of this Committee covers a broader area and includes an appraisal of the scientific criteria for evaluation of chemical carcinogenesis hazards in the total environment.

I. Recommendations

In full consideration of the past and present states of carcinogenesis investigation this Committee offers the following recommendations:

1. a. Any substance which is shown conclusively to cause tumors in animals should be considered carcinogenic and therefore a potential cancer hazard for man. Exceptions should be considered only where the carcinogenic effect is clearly shown to result from physical, rather than chemical, induction, or where the route of administration is shown to be grossly inappropriate in terms of conceivable human exposure.
b. Data on carcinogenic effects in man are only acceptable when they represent critically evaluated results of adequately conducted epidemiologic studies.
2. No level of exposure to a chemical carcinogen should be considered toxicologically insignificant for man. For carcinogenic agents a "safe level for man" cannot be established by application of our present knowledge. The concept of "socially acceptable risk" represents a more realistic notion.
3. The statement made in 1969 by the Food Protection Committee, National Research Council, that natural or synthetic substances can be considered safe without undergoing biological assay should be recognized as scientifically unacceptable.
4. No chemical substance should be assumed safe for human consumption without proper negative lifetime biological assays of adequate size. The minimum requirements for carcinogenesis bioassays should provide for: adequate numbers of animals of at least two species and both sexes with adequate controls, subjected for their lifetime to the administration of a suitable dose range, including the highest tolerated dose, of the test material by routes of administration that include those by which man is exposed. Ade-

quate documentation of the test conditions and pathologic standards employed are essential.

5. Evidence of negative results, under the conditions of the test used, should be considered superseded by positive findings in other tests. Evidence of positive results should remain definitive, unless and until new evidence conclusively proves that the prior results were not causally related to the exposure.

6. The implication of potential carcinogenicity should be drawn both from tests resulting in the induction of benign tumors and those resulting in tumors which are more obviously malignant.

7. The principle of a zero tolerance for carcinogenic exposures should be retained in all areas of legislation presently covered by it and should be extended to cover other exposures as well. Only in the cases where contamination of an environmental source by a carcinogen has been proven to be unavoidable should exception be made to the principle of zero tolerance. Exceptions should be made only after the most extraordinary justification, including extensive documentation of chemical and biological analyses, and a specific statement of the estimated risk for man are presented. All efforts should be made to reduce the level of contamination to the minimum. Periodic review of the degree of contamination and the estimated risk should be made mandatory.

8. A basic distinction should be made between intentional and unintentional exposures.

a. No substance developed primarily for uses involving exposure to man should be allowed for widespread human intake without having been properly tested for carcinogenicity and found negative.

b. Any substance developed for use not primarily involving exposure in man but nevertheless resulting in such exposure, if found to be carcinogenic, should be either prevented from entering the environment or, if it already exists in the environment, progressively eliminated.

9. A system should be established for ensuring that bioassay operations providing data upon which regulatory decisions are made be monitored so that their results are obtained in accordance with scientifically acceptable standards.

10. A unified approach to the assessment and prevention of carcinogenesis risks should be developed in the federal legislation; it

should deal with all sources of human exposure to carcinogenic hazards.

11. Clear channels should be identified for the regulatory function of different government departments and agencies in the field of cancer prevention. Establishment of a surveillance and information program would alert all concerned government agencies to the extent and development of information on formation on carcinogenic hazards.

12. An ad hoc committee of experts should be charged with the task of recommending methods for extrapolating dose-response bioassay data to the low response region (1/10000% to 1/10000000%). The low doses corresponding to the responses in this range are the ones which have direct relevance to the human situation.

II. Background

Knowledge of cancer causation by chemicals originates from clinical observations, going back as far as 1775 with Pott's discovery of soot as the causative agent in chimney sweeps' cancer. Several major classes of carcinogenic agents were first discovered by their effects on man. Experimental animal models for the determination of the potential carcinogenic activity of chemicals were only developed in the last 50 years, and most of them have been studied only in the last 20 years.

The effects of carcinogens on tissues appear irreversible. Exposure to small doses of a carcinogen over a period of time results in a summation or potentiation of effects. The fundamental characteristic which distinguishes the carcinogenic effect from other toxic effects is that the tissues affected do not seem to return to their normal condition. This summation of effects in time and the long interval (latent period) which passes after tumor induction before the tumor becomes clinically manifest demonstrate that cancer can develop in man and in animals long after the causative agent has been in contact and disappeared.

It is, therefore, important to realize that incidences of cancer in man today reflect exposure of 15 or more years ago; similarly, any increase of carcinogenic contaminants in man's environment

today will reveal its carcinogenic effect some 15 or more years from now. For this reason it is urgent that every effort be made to detect and control sources of carcinogenic contamination of the environment well before damaging effects become evident in man. Similar concepts may apply to the needs for evaluation of other chronic toxicity hazards. Environmental cancer remains one of the major disease problems of modern man.

An agent which is causally related to the occurrence of cancer in man or animals is defined as a carcinogen or oncogen. The number of known carcinogenic agents includes several groups of viruses, various physical factors, and hundreds of chemicals.

Viruses of different types are known to induce cancer in animals; none has yet been proven to evoke cancer in man. If specific viruses are proven to be causally related to cancer induction in man, the frequency of certain human tumors might be reduced in the future by immunization procedures.

Physical factors are known to cause cancers in man and animals. For example, ultraviolet radiation causes skin cancer, and ionizing radiation cancer of various organs (e.g., leukaemias, lung cancer, bone sarcomas, skin cancer). Exposure to a "background level" has been widely considered as unavoidable and, in the case of ultraviolet light, even necessary as an integral part of our natural environment. Strong epidemiologic and experimental evidence indicates the existence of a direct dose-response relationship between exposure to radiation and carcinogenic effects. Tolerance levels have been suggested for various forms of radiation and health benefits have been realized from their application. Evaluation of radiation hazards has been approached through measurement of the total cumulative dose of radiation exposure. Some carcinogenic radiation hazards, such as certain occupational exposures (e.g., radiation in uranium mines), are still not effectively controlled.

Chemicals of many classes produce cancer in a large number of organ sites in animals. Cancers in man are known to be caused by several individual chemicals and by materials composed of mixtures of chemicals. Chemical carcinogens have been shown to act by surface contact with skin or mucosae, by inhalation, by ingestion, and occasionally by injection or implantation (medical or accidental). Chemicals may induce cancer at the site of initial

contact (e.g., skin cancer from polynuclear hydrocarbons), the site of selective localization (e.g., bone cancer radionuclides), the site of metabolism and detoxification (e.g., liver or kidney cancer from aflatoxin or nitrosamines), or the site of excretion (e.g., urinary bladder cancer from aromatic amines). A complex and often uneven approach to the problem of preventing exposure to chemical carcinogens has developed over the years. It has become increasingly obvious that the hazard from a single chemical carcinogen cannot be evaluated out of context of the total environmental exposure.¹ Estimation of the "cumulative carcinogenic dose" resulting from all possible chemical carcinogens or even from all sources of a single type or class of chemical carcinogens is presently impossible.

Prevention of exposure to known carcinogenic chemicals depends largely on man's ability to control their entry into the environment. Certain chemical carcinogens are natural products (e.g., metabolites of the amino acid tryptophan) or naturally occurring contaminants (e.g., mycotoxins). Others are formed in the processing of natural products. Many, such as polynuclear hydrocarbons (e.g., benzo[a]pyrene), occur almost ubiquitously in our modern industrialized environment. They derive from most sources of organic combustion. A class of very potent carcinogens discovered only in recent years, the N-nitrosamines, include compounds that may be formed in the environment from nitrites and secondary amines. Many other known chemical carcinogens have been introduced as synthetic materials or by-products into man's present environment through a wide range of newly developed industrial processes. Some of these, such as food additives, medicinal products, cosmetics, and certain household products or pesticides, were developed for human use. Several carcinogens derive from products such as tobacco smoke, developed exclusively for human use. In other cases chemical carcinogens not intended primarily for human exposure are introduced into the general environment and eventually come in contact with its inhabitants; many substances (certain polynuclear hydrocarbons, pesticides, metals, dusts, and fumes, etc.) gain widespread environmental distribution, thereby becoming pollutants of the air, soil, water, and food. Prevention of exposure to this broad spectrum of chemical carcinogens must take a variety of forms.

The production of chemicals recognized as carcinogens for uses involving intentional human exposure can be identified and effectively eliminated. Exceptions to this approach should be made for substances that involve a well-defined health benefit (e.g., certain chemotherapeutic drugs). Use of such substances should be accepted on the basis of extraordinary evidence that their health benefit outweighs their risk.

The production of specific carcinogenic chemicals for uses that do not primarily involve an intentional exposure of man, but which result in such environmental contamination that extensive human exposure becomes inevitable, must also be controlled. The most effective prevention of exposure in man is the elimination of carcinogen production, or control of entry into the environment.

A large group of chemical carcinogens (e.g., combustion products, mycotoxins, and other natural products) is widely disseminated in the environment from sources that can only be partly controlled. For these contaminants, as well as for products which have been wisely spread in the environment before their carcinogenicity was recognized, the only possible approach to exposure reduction is to monitor their environmental distribution and subsequently minimize their contact with humans.

Modifying factors are known to condition the development of neoplasia in man and animals. They can act intrinsically or extrinsically (e.g., hormonal imbalances, metabolic characteristics or abnormalities, caloric intake, dietary factors). Understanding of their specific effects in man, however, is still not adequate to serve as a reliable basis for preventative action.

Interactions among multiple factors have received limited attention to date. There are well-documented instances in animal studies of strong synergistic effects produced by chemicals in combination with radiation, viruses, or other chemicals. The epidemiological patterns of certain human cancers implicate combined effects of multiple agents (e.g., inhalation of radon and radon daughters in uranium mines and cigarette smoking).

The types of cancer in man that are due, directly or indirectly, to extrinsic factors are thought to account for a large percentage of the total cancer incidence.² These include tumors of the skin, the respiratory, gastrointestinal and urinary tracts, hormone-dependent organs (such as the breast, thyroid, and uterus), and

the hemopoietic system. During the past decade considerable progress has been made in the detection of carcinogenic agents and the analysis of their biological effects. New approaches to the interpretation of quantitative relationships between exposures and carcinogenic effects in man and animals are being developed. It is estimated, therefore, that the majority of human cancers are potentially preventable.²

III. Animal Bioassay Results and Evaluation of Risks in Man

In order to evaluate the hazard of a chemical for man, one must extrapolate from the animal evidence. It is essential to recognize that no level of exposure to a carcinogenic substance, however low it may be, can be established to be a "safe level" for man. This concept, put forward in the 1950s, remains true in 1970. The current legislation in the field of food additives, with its "anticancer clause," is based on this principle (Federal Food, Drug and Cosmetic Act, as amended, Sect. 409 (c) (3) (A)).

The reasons for retaining this "anticancer clause" were effectively summarized in 1960 by Secretary of Health, Education and Welfare Arthur S. Flemming in testimony to Congress³ on the subject of extending the clause to cover the use of food colors, with the following statement.

"The rallying point against the anticancer provision is the catch phrase that it takes away the scientist's right to exercise judgment. The issue thus made is a false one, because the clause allows the exercise of all the judgment that can safely be exercised on the basis of our present knowledge. The clause is grounded on the scientific fact of life that no one, at this time, can tell us how to establish for man a safe tolerance for a cancer-producing agent.

"Until cancer research makes a breakthrough at this point, there simply is no specific basis on which judgment or discretion could be exercised in tolerating a small amount of a known carcinogenic color or food additive.

"As I pointed out in my original testimony, the opposition to inclusion of an anticancer clause arises largely out of a misunderstanding of how this provision works. It allows the Department

and its scientific people full discretion and judgment in deciding whether a substance has been shown to produce cancer when added to the diet of test animals. But once this decision is made, the limits of judgment have been reached and there is no reliable basis on which discretion could be exercised in determining a safe threshold dose for the established carcinogen.

"So long as the outstanding experts in the National Cancer Institute and the Food and Drug Administration tell us that they do not know how to establish with any assurance at all a safe dose in man's food for a cancer-producing substance, the principle in the anticancer clause is sound.

"I want to emphasize the statement I made on January 26 that the Food, Drug, and Cosmetic Act, as it now stands, will be enforced to prohibit the addition of cancer-producing substances to food unless a law should be passed directing us to follow another course of action.

"Even though we have this authority in the law, we urge the Congress to join with the executive branch to give added assurance to the consuming public by directing the anticancer clause in the proposed additives amendment.

"Again, we say, however, that we believe the issue is so important that the elected Representatives of the people should have the opportunity of examining the evidence and determining whether or not the authority should be granted."

The scientific basis on which the government's position was established in 1960 remains valid. The progress of knowledge in carcinogenesis in the last decades has only strengthened the points made in Secretary Flemming's testimony.

IV. Detection of Low Levels of Carcinogens in the Environment

To establish the presence of "low levels of carcinogen in the environment" requires that (1) the presence of the material in question be recognized in the environment and (2) the material be recognized as carcinogenic. To evaluate the impact of a chemical in the human environment, it is useful to prepare an "environmental profile" to reflect the distribution of this material in time

and space. Failure to detect the presence of a compound implies only that the compound is present, if at all, in concentrations below the detectable limit of the analytical method used. These "sub-detection levels" cannot be differentiated from "zero." From the distribution profile and additional information on the conditions of uptake in man the approximate level and extent of exposure for population segments can be estimated.

In recognizing a chemical as a carcinogen, the limiting factor is the sensitivity and specificity of the bioassay system used. A bioassay system designed to detect tumor induction only at or above a given level under the conditions of the test (e.g., a 25 percent incidence of a specific tumor type) will fail to reveal carcinogenicity below that level. Compounds whose carcinogenic effects fall below specific bioassay detection limits must not be considered innocuous. Such materials must be characterized as presenting a carcinogenic risk no greater than that defined by this lower limit.

Methodology for the determination of chemical contamination in the environment and of biological activity of carcinogens are discussed in the following sections.

A. Chemical Detection Methods

Methods for detection of low levels of carcinogens in the environment have increased in accuracy and reliability over the past several years. The lower limits of detection for different types of known carcinogenic substances are extremely variable, extending over several orders of magnitude from very sensitive methods (e.g., 1 part per billion of benzo[a]pyrene or aflatoxin) to rather insensitive ones (e.g., for aromatic amines). In principle, analytical methods should be capable of detecting carcinogenic materials at any level or in any condition which has relevance to human exposure. For this reason, increasingly sensitive analytical techniques are needed, and indeed many have been developed over the last 10 years. Much of the improvement in methodology is attributable to the application of gas-liquid chromatographic techniques. Within the next few years sizable additional improvements in the sensitivity of analytical methods are likely to be achieved.

It is important to consider how widely the new analytical methods can be applied for the detection of a given carcinogenic

contaminant in different materials. While highly sensitive analytical methods can be devised to detect a chemical in specific materials, these same methods might be powerless in the analysis of the same chemical from other source materials (e.g., dimethylnitrosamine can be detected in the alcoholic beverages at 1 ppb, but in foods only at 10–100 ppb). An uneven evaluation of the sources of environmental contamination may result. Development of widely applicable procedures will provide a more balanced evaluation of environmental contamination.

B. Biological Detection Methods

The carcinogenic activity of materials can only be detected by long-term biological tests. At the present time the chemical structure or physico-chemical properties of a compound do not provide a reliable basis for prediction of freedom from carcinogenic activity. Several structure, activity correlations are valuable indicators of the possible carcinogenicity of a compound, but none can be used to classify the compound as non-carcinogenic. Short-term bioassays that determine the effect of certain chemicals on selected biologic targets have not been reliable for prediction of carcinogenic activity.

The present state of the art requires long-term bioassays in mammalian species for the experimental identification of carcinogenic activity. United States law requires that food additives and various other materials be tested in animals by the intended route of human exposure. Similar tests have not been required for some materials to which humans are exposed by other than the oral route. The expanding production and use of chemicals in household products results in extensive human exposure (via the skin and respiratory tract) to dusts and aerosols; little information is available on the chronic toxicity of these materials by these routes of administration. It would not be wise to wait for the results of these "experiments in man" before instituting animal experimentation.

Bioassays are always performed on a number of animals which is extremely small when compared with the millions of humans exposed to most environmental carcinogens. Such studies can only detect carcinogenic effects resulting in fairly high incidences. For

example, an observed outcome of no tumors in a test group of 100 animals, as well as in 100 negative controls, only provides assurance, at the 99 percent probability level, that the true tumor risk is under 4.5 percent. The maximum probable risk is 0.46 percent if groups of 1,000 animals are used. It would require tumor-free results in 450 animals to establish with like probability that the risk is under 1 percent.⁴

The assessment of the carcinogenic activity of a chemical depends on a variety of parameters. These include not only the total number of tumors induced but also their multiplicity, latent period, morphologic type, and degree of malignancy. The induction of tumors diagnosed as benign as a result of treatments has been interpreted by certain groups in the past as not sufficient to demonstrate a "carcinogenic" effect. This is a dangerous position since few, if any, substances are known to have produced only benign tumors and no malignant ones when properly and repeatedly tested. This has been pointed out in the Report of the Subcommittee on Carcinogenesis of the FDA Committee on Protocols for Safety Evaluation.⁵

The important scientific problem of defining the sensitivity of a bioassay system used for testing materials of unknown activity has received insufficient attention. The interpretation of both positive and negative findings is strictly dependent on such definition as well as on the results obtained in negative, vehicle, positive and colony control animals. A bioassay result is meaningful only when accompanied by a statement of the sensitivity and specificity of the bioassay design used. An observed incidence of a given tumor type in a test group has no meaning without adequate information on the appropriate controls. Far too little work has been done using adequate positive controls. Lack of tumor response in a given experimental system cannot be interpreted as negative evidence if positive controls also yield negative results or if no positive controls have been included to show that the experimental system used is appropriate.

A body of knowledge has developed over the years on the response of experimental animals to chemical carcinogens. Several committees of experts in the field of carcinogenesis convened by national and international bodies over the past 15 years have formulated general principles for performance and evaluation of

carcinogenesis studies in animals. The recommendations put forth by these committees have shown remarkable unanimity^{2,5-10} and are widely accepted in principle by the scientific community.¹¹⁻¹⁵ General requirements for testing procedures, which have been outlined by these groups, include specification of criteria for the following.

1. Selection of materials to be tested
2. Chemical and physical characterization of the test materials
3. Selection of appropriate animal species and group size
4. Choice of appropriate routes and levels of administration

In addition, recommendations concerning the lifetime maintenance and pathological examination of experimental animals have been outlined.

Two principles are recognized as fundamental to the evaluation of carcinogenesis bioassays.

1. The minimum requirements for carcinogenesis bioassay should include adequate numbers of animals of at least two species and both sexes with adequate positive and negative controls, subjected for their lifetime to the administration by appropriate routes of a suitable dose range of the test material, including doses considerably higher than those anticipated for human exposure.
2. Any substance which is shown conclusively to produce tumors in animals, when tested under these conditions, should be considered potentially carcinogenic for man.

V. Quantitative Relationships

The major new argument presented today against the "anticancer clause" is that the marked increase in sensitivity of many analytical methods makes it possible to detect low levels of carcinogens in a broader segment of the environment and that, therefore, the immediate enforcement of regulations requiring a zero tolerance becomes more difficult, in some instances impossible.

New and very potent classes of chemical carcinogens, such as aflatoxin and nitrosamines, have been detected in the environ-

ment. Striking examples of potentiation in cancer induction have been reported in experimental animal tests and in epidemiologic observations. Bioassays have revealed the carcinogenicity of such widespread environmental chemicals as DDT and cyclamate, to which a large majority of the American population has been exposed.

In contrast to the analytical methods, bioassay methods have remained tools of low sensitivity, capable only of detecting the highest peaks of carcinogenic activity. The factor which limits bioassay sensitivity is usually the small number of test animals used. If the bioassay design has a low probability of detecting carcinogenic effects produced by hazards at levels comparable to those present in environmental samples, then tests at such levels are wastes of time, effort and money. The need to test levels higher than those found in the environment is thus founded. Some substances, on the other hand, are potent carcinogens in animal test systems at levels not currently detectable in the environment. An example is provided by the recent evidence on aflatoxin. Its lowest analytically detectable level is 1 ppb. One hundred percent tumor incidence was produced in rats by a dose as low as 15 ppb. in the diet. Experiments now under way suggest that aflatoxin, when fed to rats at the lowest detectable level (1 ppb), is still carcinogenic.¹⁶ It has already been demonstrated to be carcinogenic at 1 ppb in the trout. These data indicate that aflatoxin may be present in food at undetectable levels and still be capable of producing cancer incidences so high as to be detectable in tests involving relatively small numbers of experimental animals.

It is impossible to establish any absolutely safe level of exposure to a carcinogen for man. The concept of "toxicologically insignificant" levels (as advanced by the Food Protection Committee of the NAS/NRC in 1969), of dubious merit in any life science, has absolutely no validity in the field of carcinogenesis. Society must be willing to accept some finite risk as the price of using any carcinogenic material in whatever quantity. The best that science can do is to estimate the upper probable limit of that risk. For this reason, the concept of "safe level for man," as applied to carcinogenic agents, should be replaced by that of a "socially acceptable level of risk."

While science can provide quantitative information regarding

maximum risk levels, the task of ultimately selecting socially acceptable levels of human risk rests with society and its political leaders. The evaluation of the balance of benefits and risks, required for such a decision by society, should not be the result of uninformed guesswork but should be reached on the basis of complete and pertinent data, social as well as scientific. It is necessary, therefore, to define the extent in the processes of interpreting animal response data and subsequently extrapolating them to man. The principle of zero tolerance should be applied in all but the most extraordinary of cases.

VI. Conclusion

Modern society has been extremely fortunate—given the technical limits on detection of carcinogenic effects—that at least some environmental carcinogens have been identified. So-called negative data, obtained in bioassays often incapable of detecting effects below the 10 percent level, are grossly inadequate to give assurance of safety for man. Information on about 2,500 compounds tested for carcinogenic activity up through 1960 has been compiled and published.¹⁷ Most of these materials, however, are of no environmental significance. Data on tests reported since 1960 will be published shortly. It is estimated that data on 3,500 previously unevaluated chemicals will be included in the forthcoming volume. It is seen, then, that about 6,000 chemicals are documented as having undergone carcinogenesis bioassay to date. Many of the referenced tests, however, were inadequate according to presently recommended standards.

If this nation wishes to identify a large segment of existing and potential carcinogenic hazards, it must institute a comprehensive program involving a concert of activities. Scientific and technical plans for the development of methodological standards should be provided by experienced agencies in collaboration with qualified advisors. It is essential that the objectivity of these advisors not be damaged by any conflicting interests.

Resources needed for the extensive bioassay screening of environmental chemicals will be considerable. In addition to the myriad of substances presently in the environment, several thousand

new compounds are introduced each year. Up to 20,000 materials should be tested for carcinogenicity as a first screening of the environment. Testing 20,000 compounds by bioassay would cost about \$1 billion. This estimate would increase accordingly for the more extensive testing required in less superficial evaluation. Yet even were such funds available today, they could not nearly be spent effectively. Bioassay laboratory and professional resources are just not available in quantities capable of supporting a huge testing program. A great deal of "tooling up" is prerequisite to any such expanded level of effort.

Because the latent period in human carcinogenesis is so long, epidemiologic evidence develops only over periods of 15 to 20 years. Timely decisions to exclude materials from uses involving exposure to man, therefore, must be based solely on adequately conducted animal bioassays. Retrospective human evidence of risk must not be allowed to show itself before controlling action is taken. Chemicals should be subjected to scientific scrutiny rather than given individual "rights"; they must be considered potentially guilty unless and until proven innocent. Valid evidence must come from biological assays; every bioassay report should include a statement of its limits of sensitivity. Experimental design should provide for reproducibility of test results. Since the bioassay plays such a key role in a total carcinogen control scheme, more effort must be devoted to setting standards for both the performance of tests and the interpretation of results. Only given good bioassay data can science possibly provide sound information to those who are charged with making social decisions regarding the acceptability of carcinogenesis risk levels.

An effective program to protect man from the mass of environmental cancer hazards is within reach. No more time should be allowed to pass before the recommendations set forth in this report are applied to reality.

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Appendix III

Substances Regulated as Recognized Carcinogens

1. Workplace Standards under §6, Occupational Safety and Health Act

SUBSTANCE	DATE OF FINAL ACTION
Asbestos	June 7, 1972 (37 Fed. Reg. 11318)
14 Carcinogens	Jan. 29, 1974
2-Acetylaminofluorene	(39 Fed. Reg. 3756)
Alpha-naphthylamine	
4-Aminobiphenyl	
Benzidine	
Beta-naphthylamine	
Beta-propiolactone	
Bischloromethylether	
3,3'-Dichlorobenzidine	
4-Dimethylaminoazobenzene	
Ethyleneimine	
Chloromethylmethylether	
4,4'-Methylene bis(2-chloroaniline) (MOCA) (deleted)	
4-Nitrobiphenyl	
N-Nitrosodimethylamine	
Vinyl chloride	Oct. 4, 1974 (39 Fed. Reg. 35890)
Coke oven emissions	Oct. 22, 1976 (41 Fed. Reg. 46741)

**2. Hazardous Air Pollutants under §12,
Clean Air Act**

SUBSTANCE	DATE OF FINAL ACTION
Asbestos	April 6, 1973 (38 Fed. Reg. 8820) May 3, 1974 (39 Fed. Reg. 15396) Oct. 14, 1975 (40 Fed. Reg. 48302)
Vinyl chloride	Oct. 21, 1976 (41 Fed. Reg. 46559)

**3. Toxic Pollutants Effluent Standards Under
§307, Federal Water Pollution Control Act**

SUBSTANCE	DATE OF FINAL ACTION
DDT (and DDE, DDD)	Jan. 12, 1977 (42 Fed. Reg. 2587)
Aldrin/dieldrin	Jan. 12, 1977 (42 Fed. Reg. 2587)
Benzidine	Jan. 12, 1977 (42 Fed. Reg. 2587)
PCBs	Feb. 2, 1977

**4. Food, Color, and Cosmetic Products Banned Under
Federal Food, Drug, and Cosmetic Act**

SUBSTANCE	DATE OF FINAL ACTION
Dulcin, P-400	15 Fed. Reg. 321 (1950)
Coumarin	19 Fed. Reg. 1239 (1954)
Safrole, oil of sassafras, dihydrosafrole, iso-safrole	25 Fed. Reg. 12412 (1960)
DES (for use in poultry)	21 CFR 510.120 (1960)
Flectol H (1-2, Dihydro-2,2,4-trimethquinoline, polymerized)	32 Fed. Reg. 5675 (1967)
Oil of calamus	33 Fed. Reg. 6967 (1968)
Cyclamates	34 Fed. Reg. 17063 (1969)
MOCA (4,4'-methylenebis- (2-chloroaniline))	34 Fed. Reg. 19073 (1969)
DEPC (diethylpyrocarbonate)	37 Fed. Reg. 15426 (1972)
Mercaptoimidazoline	38 Fed. Reg. 33072 (1973)
FD&C Violet #1	38 Fed. Reg. 9077 (1973)
Vinyl chloride	39 Fed. Reg. 26842 (1976)
FD&C Red #2	41 Fed. Reg. 5823 (1976)

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Chloroform	41 Fed. Reg. 26842 (1976)
FD&C Red #4	41 Fed. Reg. 41852 (1976)
Carbon black	41 Fed. Reg. 41857 (1976)
Acrylonitrile	42 Fed. Reg. 13546 (1977)
Nitrofurans	42 Fed. Reg. 17526, 18611, 18619, 18660 (1977)
Graphite	42 Fed. Reg. 60734 (1977)
D&C Red #10-13	42 Fed. Reg. 62475 (1977)
D&C Yellow #1	42 Fed. Reg. 62482 (1977)

5. Consumer Products Under Consumer Product Safety Act/Federal Hazardous Substances Act

SUBSTANCE	DATE OF FINAL ACTION
Vinyl chloride	39 Fed. Reg. 30114 (1974)
Tris	42 Fed. Reg. 18856, 61621, (1977)
Asbestos products	42 Fed. Reg. 63354 (1977)

**6. Pesticides Under Federal Insecticide,
Fungicide, and Rodenticide Act**

SUBSTANCE	DATE OF FINAL ACTION
DDT	37 Fed. Reg. 13369 (1972)
Vinyl chloride	39 Fed. Reg. 14753 (1974)
Aldrin/dieldrin	39 Fed. Reg. 37265 (1974)
Heptachlor/chlordane	41 Fed. Reg. 7552 (1976)
Kepone	41 Fed. Reg. 24624 (1976)
Mirex	41 Fed. Reg. 56694 (1976)
DBCP (dibromochloropropane)	42 Fed. Reg. 57543 (1977)

Source: Marion F. Suter and Warren R. Muir. "Federal Programs in Cancer Research," unpublished report.

Appendix IV

*Labor Publications on Occupational Health**

ACTWU Labor Unity

Amalgamated Clothing and Textile Workers Union (AFL-CIO)
15 Union Square
New York, N.Y. 10003

Aluminum Light

Aluminum Workers International Union (AFL-CIO)
818 Olive St., Suite 338
St. Louis, Mo. 63101

American Flint

Glass Workers Union of North America (AFL-CIO)
1440 S. Byrne Rd.
Toledo, Ohio 73614

Butcher Workman

Amalgamated Meat Cutters and Butcher Workmen of North America
2800 N. Sheridan Road
Chicago, Ill. 60657

Carpenter

United Brotherhood of Carpenters and Joiners of America
101 Constitution Ave., N.W.
Washington, D.C. 20001

* All are published monthly unless noted otherwise.

Chemical Worker

International Chemical Workers Union (AFL-CIO)
1655 W. Market St.
Akron, Ohio 44313

Facts and Analysis

Industrial Union Department (AFL-CIO)
815 16th St., N.W.
Washington, D.C. 20006

Glass Workers News

United Glass and Ceramic Workers of North America
(AFL-CIO)
556 E. Town St.
Columbus, Ohio 43215

Health and Safety Bulletin (6 issues annually)

International Union of Electrical, Radio and Machine
Workers (AFL-CIO)
AFL-CIO/CLC
1126 16th St., N.W.
Washington, D.C. 20036

International Firefighter

International Association of Firefighters (AFL-CIO)
1750 New York Ave., N.W.
Washington, D.C. 20006

International Teamster

International Brotherhood of Teamsters, Chauffeurs,
Warehousemen, and Helpers of America
25 Louisiana Ave., N.W.
Washington, D.C. 20001

IUE News

International Union of Electrical Radio and Machine Workers
(AFL-CIO)
1126 16th St., N.W.
Washington, D.C. 20036

Labeletter

Union Label and Service Trades Department (AFL-CIO)
815 16th St., N.W.
Washington, D.C. 20006

Lifelines

Oil, Chemical, and Atomic Workers Union (AFL-CIO)
Health and Safety Department
P.O. Box 2812
1636 Champa St.
Denver, Colo. 80201

Light

Utility Workers Union of America
815 16th St., N.W., Suite 605
Washington, D.C. 20006

The Machinist

International Association of Machinists and Aerospace Workers
(AFL-CIO)
1300 Connecticut Ave., N.W.
Washington, D.C. 20036

Metaletter

Metal Trades Department (AFL-CIO)
815 16th St., N.W.
Washington, D.C. 20006

Monitor (8 issues annually)

Labor Occupational Health Program
Institute of Industrial Relations
Center for Labor Research
2521 Channing Way
Berkeley, Calif. 94720

NABET News (bimonthly)

National Association of Broadcast Employees and Technicians
(AFL-CIO)
1601 Connecticut Ave., N.W.
Washington, D.C. 20009

Occupational Health and Safety (6 issues annually)
International Union of Auto, Aerospace, and Agricultural
Implement Workers of America
8000 E. Jefferson Ave.
Detroit, Mich. 48214

Painters and Allied Trades Journal
International Brotherhood of Painters and Allied Trades of U.S.
and Canada (AFL-CIO)
United Unions Building
1750 New York Ave., N.W.
Washington, D.C. 20006

Paper Worker
United Paperworkers International Union (AFL-CIO)
163-03 Horace Harding Expressway
Flushing, N.Y. 11365

Pennsylvania AFL-CIO News
Pennsylvania AFL-CIO
101 Pine St.
Harrisburg, Pa. 17101

Plasterer and Cement Mason
Plasterers' and Cement Masons' International Association of the
United States and Canada (AFL-CIO)
1125 17th St., N.W.
Washington, D.C. 20002

Service Employee
Service Employees International Union (AFL-CIO)
2020 K St., N.W.
Washington, D.C. 20006

Solidarity
International Union of Auto, Aerospace and Agricultural
Implement Workers of America
8000 E. Jefferson Ave.
Detroit, Michigan 48214

Spotlight on Health and Safety (quarterly)
Industrial Union Department (AFL-CIO)
815 16th St., N.W.
Washington, D.C. 20006

Steel Labor
United Steelworkers of America (AFL-CIO)
Five Gateway Center
Pittsburgh, Pa. 15222

UE News (biweekly)
United Electrical, Radio, and Machine Workers of America
11 E. 51st St.
New York, N.Y. 10022

United Rubber Worker
United Rubber, Cork, Linoleum, and Plastic Workers of America
(AFL-CIO)
URWA Building
South High St.
Akron, Ohio 44308

Union Tabloid (10 issues annually)
Graphic Arts International Union (AFL-CIO)
1900 L St., N.W.
Washington, D.C. 20036

United Mine Worker Journal (bimonthly)
United Mine Workers of America
900 15th St., N.W.
Washington, D.C. 20005

Voice of the Cement, Lime, Gypsum, and Allied Workers
United Cement, Lime, Gypsum, and Allied Workers (AFL-CIO)
7830 W. Lawrence Ave.
Chicago, Ill. 60656

Appendix V

Public Interest Groups Concerned with Cancer Prevention

Action on Smoking and Health

A national organization concerned with problems of smoking; also represents the rights of non-smokers through legal action.
2000 H St., N.W., Washington, D.C. 20006
Tel: 202-659-4310

Center for Science in the Public Interest

Concerned with energy conservation, nuclear energy, nutrition, and toxic chemicals, particularly in food, and the performance of voluntary health agencies. Publishes *Nutrition Action*, reports and books.

1757 S St., N.W., Washington, D.C. 20009
Tel: 202-322-4250

Commission for the Advancement of Public Interest Organizations

A public interest group supported by the Monsour Medical Foundation. Concerns include increasing contacts between the professional, governmental, and public interest communities, and with creating loose, ad hoc coalitions of public interest and labor groups around critical issues such as control of environmental and occupational carcinogens.

1875 Connecticut Ave., N.W., Washington, D.C. 20009
Tel: 202-462-0505

Consumer Federation of America

The leading national federation of consumer, cooperative, and labor groups, which lobbies for consumer protection legislation and publishes *Monthly News* and pamphlets.

1012 14th St., N.W., Washington, D.C. 20005

Tel: 202-737-3732

Consumers Union (CU)

The largest consumer group in the country, with a membership of approximately 190,000; primarily devoted to advancing the well-being of the consumer and to testing consumer products for their effectiveness and safety, as well as such concerns as contamination of water with organic pollutants and carcinogens. Publishes *Consumer Reports* (monthly) and a *Consumers Union News Digest* (bimonthly). Regional offices in Washington, D.C., and San Francisco, files suits and petitions on consumers' rights.

265 Washington St., Mount Vernon, N.Y. 10550

Tel: 914-664-6400

Environmental Action

Founded in 1970, when it convened the first "Earth Day" in the U. S. Researches and lobbies on environmental issues, including toxic and carcinogenic substances.

1346 Connecticut Ave., N.W., Washington, D.C. 20036

Tel: 202-833-1845

Environmental Defense Fund

A public interest law firm with a highly effective track record in the banning of toxic and carcinogenic chemicals, including DDT, aldrin/dieldrin, chlordane/heptachlor, and Tris. Has also played a major role in passage of the Safe Drinking Water Act.

1525 18th St., N.W., Washington, D.C. 20036

Tel: 202-833-1484

Environmental Improvement Associates

A recently formed group dedicated to workers' rights to air unpolluted by tobacco smoke in the workplace.

109 Chestnut St., Salem, N.Y. 08079

Tel: 606-935-4200

Federation of American Scientists

A nationwide lobbying group of natural and social scientists and engineers concerned with problems of science and society, including environmental carcinogens.

203 C St., N.E., Washington, D.C. 20002

Tel: 202-546-3300

Federation of American Homemakers

A public interest group representing interests of consumers and housewives with particular interests in problems of food and consumer product safety.

P.O. Box 5571, Arlington, Va. 22205

Health Policy Advisory Center

(HEALTH/PAC)

Concerned with monitoring and interpreting the health system to change-oriented groups of health workers, consumers, professionals, and students. Publishes a bimonthly journal, the *Health-Pac Bulletin*, on important developments in the health system, including occupational and environmental health.

17 Murray St., New York, N.Y. 10007

Tel: 212-287-8890

*Health Research Group of
Public Citizens, Inc.*

A highly effective medico-legal group with concerns that include the quality of medical care, carcinogenic drugs, food and feed additives, and occupational health and safety. Has published a series of hard-hitting reports and is active in petitions and congressional testimony.

2000 P St., N.W., Washington, D.C. 20036

Tel: 202-872-0320

National Clean Air Coalition

A national coalition of environmental and other groups concerned with air pollution and lobbying for improvements in the Clean Air Act.

620 C St., S.E., Washington, D.C. 20003

Tel: 202-543-0305

National Public Interest Research Group

Provides technical resources to nationwide PIRGs.

1346 Connecticut Ave., N.W., Washington, D.C. 20036

Tel: 202-833-3934

Natural Resources Defense Council

A public interest law firm with a good track record in petitions on carcinogenic food contaminants, air and water pollutants, and radiation, and is currently developing major emphasis on international environmental problems.

15 West 44th St., New York, N.Y. 10036

Tel: 212-869-0150

*Rachel Carson Trust for
the Living Environment*

A resource group devoted to increasing public awareness of hazardous pesticides and other toxic chemicals.

8940 Jones Mill Rd., Washington, D.C. 20015

Tel: 301-652-1877

Sierra Club

Apart from its primary conservation interests, has played an important role in lobbying for toxic substances legislation and monitoring its implementation.

530 Bush St., San Francisco, Calif. 94108

Tel: 415-981-8634

Urban Environment Conference

An organization founded by the late Senator Philip A. Hart which convenes representatives of environmental, labor, and minority groups for training, information exchange, and developing joint positions on environmental issues of common interest.

1302 18th St., N.W., Washington, D.C. 20036

Tel: 202-466-6040

Appendix VI

Human Cancers Following Drug Treatment

DRUGS	RELATED CANCER
Radioisotopes	
Phosphorus (P^{32})	Acute leukaemia
Radium, mesothorium	Osteosarcoma and cancer of nasal sinuses
Thorotrast	Liver angiosarcoma
Immunosuppressive drugs (for renal transplantation)	
Antilymphocyte serum	Reticulum cell sarcoma
Antimetabolites	Soft tissue sarcoma, other cancers (skin, liver)
Cytotoxic drugs	
Chlornaphazine	Bladder cancer
Melphalan, cyclophosphamide	Acute leukaemia
<i>Hormones</i>	
Synthetic estrogens	
Prenatal	Cancer of the vagina and cervix
Postnatal	Cancer of the uterus
Androgenic-anabolic steroids (for treatment of aplastic anemia)	Liver cancer

Others

Arsenic	Skin cancer
Phenacetin-containing drugs	Kidney cancer
Coal tar ointments	Skin cancer
Diphenylhydantoin?	Lymphoma
Chloramphenicol?	Leukaemia
Amphetamines?	Hodgkin's disease
Reserpine?	Breast cancer

Source: Based on R. Hoover and J. F. Fraumeni, Jr., "Drugs," ch. 12, in J. F. Fraumeni, Jr., ed., *Persons at High Risk of Cancer* (New York: Academic Press, 1975).

Appendix VII

Some Specialized Cancer Treatment Centers

CANCER SITE	RECOMMENDED CENTER
Lung	Roswell Park Memorial Institute, Buffalo Mayo Clinic, Rochester, Minnesota Johns Hopkins Medical Institution, Baltimore
Breast	M.D. Anderson Hospital, Houston Massachusetts General Hospital, Boston Cleveland Clinic
Uterus	Fred Hutchinson Cancer Center, University of Washington, Seattle
Prostate and genito-urinary	Roswell Park Memorial Institute, Buffalo, New York
Lymphomas and leukaemias	Memorial Sloan-Kettering, New York Stanford University Medical Center, Palo Alto, California
Sarcomas	Moffett Hospital, University of California, San Francisco University of Arizona, Tucson Sidney Farber Cancer Center, Boston
Melanoma	Tufts-New England Medical Center, Boston
Thyroid	Rush-Presbyterian-St. Luke's, Chicago

Pancreas	Ohio State University Hospital, Columbus
Brain	Moffett Hospital, University of California, San Francisco

Abbreviations

Agencies

CDC	Center for Disease Control
CEQ	Council on Environmental Quality
CPSC	Consumer Product Safety Commission
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FTC	Federal Trade Commission
GAO	Government Accounting Office
HEW	Health, Education and Welfare
NCI	National Cancer Institute
NCTR	National Center for Toxicological Research
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
OSHA	Occupational Safety and Health Administration (in Department of Labor)
PHS	Public Health Service
USDA	United States Department of Agriculture

Chemicals

A/D	aldrin/dieldrin
AN	acrylonitrile
BCME	bischloromethylether
C/H	chlordan/heptachlor
CMME	chloromethylmethylether
DES	diethylstilbestrol
DMN	dimethylnitrosamine

NO _x	nitrogen oxides
PCBs	polychlorinated biphenyls
PVC	polyvinyl chloride
VC	vinyl chloride

Units

kg	kilogram (2.2 pounds)
g	gram (1/1000 kilogram)
mg	milligram (1/1000 gram)
μg	microgram (1/1000 milligram)
ppm	parts per million (1 ppm=one ten-thousandth of one percent)
ppb	parts per billion (1 ppb=one ten-millionth of one percent)
ppt	parts per trillion (1 ppt=one thousandth of a ppb)

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CHAPTER 6

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CHAPTER 9

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CHAPTER 11

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