REPORT TO THE CONGRESS

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

Federal Efforts To Protect The Public From Cancer-Causing Chemicals Are Not Very Effective

Federal efforts to protect the public from cancer-causing chemicals have not been too successful. Although Federal agencies, including the Departments of Labor and Health, Education, and Welfare; the Environmental Protection Agency; and the Consumer Product Safety Commission generally have enough authority to regulate the chemicals, they have encountered scientific problems in relating the results of animal safety tests to humans.

The Director of the National Cancer Institute is responsible for the overall direction of Federal efforts. He should establish a Federal policy on carcinogens with the cooperation, advice, and support of other Federal agencies. The policy should address the scientific issues that have hampered effective public protection from carcinogens.

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Contents

ABBREVIATIONS

CPSC	Consumer Product Safety Commission
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
GAO	General Accounting Office
HEW	Department of Health, Education, and Welfare
NCI	National Cancer Institute
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
OSHA	Occupational Safety and Health Administration

COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

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To the President of the Senate and the
Speaker of the House of Representatives

This report describes the problems Federal agencies face in trying to protect the public from cancer-causing chemicals and recommends certain actions to improve that protection. The Government's expanding efforts to conquer cancer prompted our review.

We made our review pursuant to the Budget and Accounting Act, 1921 (31 U.S.C. 53), and the Accounting and Auditing Act of 1950 (31 U.S.C. 67).

We are sending copies of this report to the Director, Office of Management and Budget; the Secretaries of Labor and Health, Education, and Welfare; the Administrator, Environmental Protection Agency; and the Chairman, Consumer Product Safety Commission.

Comptroller General
of the United States

COMPTROLLER GENERAL'S REPORT TO THE CONGRESS

FEDERAL EFFORTS TO PROTECT THE PUBLIC FROM CANCER-CAUSING CHEMICALS ARE NOT VERY EFFECTIVE

D I G E S T

Although up to 90 percent of human cancer, according to some scientists, is environmentally caused and controllable, Federal efforts to protect the public from cancer-causing chemicals have not been very effective.

Many chemicals cause cancer in animals, but Federal agencies have trouble determining which also pose a cancer threat for humans because

--there are no generally accepted principles concerning environmental causes of cancer (see p. 17),

--there are no uniform minimum guidelines for testing (see p. 17),

--test data are not always complete or appropriate (see p. 19), and

--scientists cannot accurately predict human response to chemicals on the basis of animal test results (see p. 20).

The Director of the National Cancer Institute is responsible for directing Federal efforts and should, with the cooperation of other involved Federal agencies, develop a uniform Federal policy for identifying and regulating cancer-causing chemicals.

The policy should at least cover

--the information needed to regulate cancer-causing chemicals,

--which chemicals should be tested in animals,

--how tests should be conducted,

--how results should be evaluated,

--how human risk can be assessed from animal studies, and

--what factors other than public health should agencies consider. (See p. 38.)

Although the Department of Health, Education, and Welfare agrees that a Federal policy is needed, it does not agree that a formal effort, headed by the Director of the Institute, is necessary. GAO believes a Federal policy can only be developed with the active support of every involved Federal agency, and the Institute Director, as head of the National Cancer Program, should coordinate these efforts. (See p. 35.)

GAO is also recommending that the Food and Drug Administration have all approved and proposed food additives tested for their cancer-causing potential because it had not been requiring data from such tests when the additives were unintentionally added to the food in amounts less than 1 or 2 parts per million. The Department disagrees, saying the risk of cancer is remote and the costs for testing would be substantial. (See pp. 12 and 37.)

EXTEND FEDERAL AUTHORITY TO CIGARETTES

Tobacco and tobacco products are on the Institute's list of known human carcinogens; since 1964 the Surgeon General has reported to the Congress on the relationship between smoking and cancer.

For the past 2 years the Secretary of Health, Education, and Welfare has recommended that the Congress give the executive branch the authority to control hazardous ingredients--such as tar and nicotine--in cigarettes.

GAO is suggesting that the Congress

--request the Department to prepare a study showing the available options for regulating tobacco and tobacco products and the impact each option would have on the rising U.S. lung cancer rate and then

--consider giving the Department or some other appropriate agency the specific authority to regulate tobacco and tobacco products. (See p. 38.)

BURDEN OF PROOF

The Government can control cancer-causing chemicals, but an important factor in achieving public protection is whether action is taken before or after the chemical gets into commercial use and the environment.

The Government requires only the manufacturers of pesticides, drugs, and food and color additives to prove their products' safety before marketing them. The Government must prove the health hazards of other products, air and water pollutants, and occupational hazards before initiating action.

The proposed toxic substances legislation would make manufacturers prove a chemical's safety before it is marketed rather than having the Government prove that it poses a hazard after it is marketed. GAO believes this legislation would improve Federal efforts to protect the public from cancer-causing chemicals. (See p. 38.)

CHAPTER 1

INTRODUCTION

Cancer is the uncontrolled growth of cells. 1/ About 1,000 Americans die every day with the 100 or more diseases called cancer. Cancer causes over 16 percent of all U.S. deaths, making it the second largest killer (after cardiovascular diseases). Estimates of cancer's annual cost to the Nation run as high as $15 billion, of which some $3 to $5 billion represents direct care and treatment costs; the balance is loss of earning power and productivity.

Cancer mortality in the United States ranks somewhere in the middle of the worldwide range, but the rank of mortality from specific types of cancer varies markedly. Compared with other nations, the U.S. white population has the lowest mortality from stomach cancer and close to the highest from cancers of the colon and female breast. As shown in the table on page 3, the incidence rates of various cancers in the United States are expected to fluctuate between 1970 and 2000, including an 84-percent decrease in the incidence of stomach cancer and a 179-percent increase in lung cancer. The table also suggests some of the possible causes and means of preventing various cancers.

Available evidence suggests that environmental agents and social practices are largely responsible for variations in the occurrence of cancer in different populations. Although the extent to which man-made environmental chemicals are responsible for U.S. cancer rates is not precisely known, some scientists claim that external factors cause as much as 90 percent of all human cancer. National Cancer Institute (NCI) officials pointed out that this high estimate includes voluntary exposures to such carcinogens as cigarette smoke, which appears to be responsible for about 40 percent of all cancer in white males. NCI officials added that cancer attributable to occupational exposure and exposure to natural carcinogens is included in the 90-percent value.

NCI, 1 of the 11 National Institutes of Health, aims at reducing the occurrence of the major types of cancer in the United States to the level of the lowest ranking country for

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1/More technically, cancer is a disease process characterized by the development of host-derived tissues which grow irreversibly in a manner uncoordinated with that of normal tissues and organs, which invade adjacent structures, which spread, and which persist after the stimuli are withdrawn.

that type. Such a reduction would cut U.S. deaths from cancer by one-third.

Seven Federal agencies have principal authority for identifying and/or regulating cancer-causing chemicals 1/ (carcinogens) or the products in which they appear.

--NCI.

--National Institute of Environmental Health Sciences (NIEHS).

--National Institute for Occupational Safety and Health (NIOSH).

--Food and Drug Administration (FDA).

--Environmental Protection Agency (EPA).

--Occupational Safety and Health Administration (OSHA).

--Consumer Product Safety Commission (CPSC).

Their roles and responsibilities are discussed in chapter 2. Despite this wide base, no single agency or official has assumed a leadership role, and as a result, many unresolved issues have hampered effective public protection from carcinogens. This report discusses the impact of several of those issues, including

--what chemicals are tested,

--how tests are designed,

--how results are communicated, and

--what agencies consider when deciding on regulatory action.

This report is concerned with Federal agencies' efforts to protect the public from carcinogens. Other GAO reports dealing with more general effects of chemicals and other environmental factors are listed in appendix IV.

1/Throughout this report, the term "chemicals" will be used to refer to individual chemicals, compounds, and mixtures, unless otherwise noted.

Cancer Incidence: Expected Number, 1970-2000

Change in Rates, 1970-2000; Deaths, 1970

Site	New cases (incidence) (note a) 1970	2000	Deaths 1970	Incidence year 2000 (percent change in rate) (note b)	Major causation	Means of prevention
Lung	81,000	295,000	62,000	179	Tobacco smoke. Air pollution (including on-the-job).	Stop smoking. Reduce pollution. Use less hazardous cigarette.
Large and small bowel	92,000	134,000	44,000	11	Intestinal flora? Heredity? Diet?	Viruses? Other insults. Identify susceptibles and eliminate their exposure.
Breast	82,000	111,000	30,000	4	Virus? Diet? Hormones? Genetic?	Vaccines. Identify susceptibles.
Pancreas	20,000	35,000	18,000	38	Diet? Virus? Other insults?	Identify etiology. Identify susceptibles.
Prostate	51,000	78,000	17,000	17	Hormones? Diet?	Identify etiology. Identify susceptibles.
Stomach	21,000	4,500	16,000	-84	Diet. Poor socio-economic conditions.	Diet modifications. Sociologic modifications?
Leukemias	20,000	32,000	15,000	26	Viruses. Radiation. Genetic.	Vaccines. Identify susceptibles and limit radiation.
Non-melanotic skin	376,000	585,000	5,000	20	Actinic rays. Genetic.	Limit radiation exposure. Identify susceptibles.
Miscellaneous	242,000	408,000	75,000	30	Multiple.	Identify extrinsic and intrinsic factors and modify them.

a/Based on data from Third National Cancer Survey, 1969-70. Cases in which the disease was confined to the site of origin without invading neighboring tissues (in situ) have been excluded.

b/Projected change in age-adjusted incidence rates (year 2000 compared to 1970), assuming the trend in rates noted from 1947 to 1969 continues to the year 2000.

Source: National Cancer Institute, Division of Cancer Cause and Prevention; Annual Program Review Document for Fiscal Year 1974.

CHAPTER 2

FEDERAL RESPONSIBILITY

The Federal Government attempts to protect the public from carcinogens through research and regulation. NCI sponsors most of the Government's research on cancer cause and prevention; NIEHS, NIOSH, and some of the regulatory agencies also conduct or sponsor such research. EPA is responsible for clean air and water and safe pesticides; OSHA sets and enforces standards to protect workers from safety and health hazards, including hazardous chemicals, in workplaces; FDA is responsible for the safety of foods, food and color additives, drugs, medical devices, and cosmetics; and CPSC has jurisdiction over every consumer product not covered by any other agency except those specifically excluded by the Consumer Product Safety Act.

Several other Federal agencies help to protect the public from carcinogens. Their activities, however, are generally initiated as a result of some other action taken by one of the principal organizations. Appendix V contains more information on these agencies.

RESEARCH AND REGULATORY AGENCIES

NCI--The National Institutes of Health attempt to improve the health of all Americans by sponsoring biomedical research activities. NCI is the largest institute, with appropriations for fiscal year 1976 of about $743 million. The National Cancer Act of 1971 (42 U.S.C. 282) was passed to strengthen NCI, mainly through increased authority and funding authorizations, to more effectively combat cancer. Among other things, the act authorized NCI's director to plan and develop an expanded, intensified, and coordinated cancer research program, encompassing programs of NCI, related programs of other research institutes, and other Federal and non-Federal programs. The National Cancer Program's ultimate goal is to develop the means for eliminating human cancer.

NCI established a research program on the causes of cancer in 1961, although it had previously supported such research. A more formal program dealing with chemical carcinogens (as opposed to other possible causes of cancer, such as viruses) was begun in 1968, and today NCI sponsors research to find out what causes cancer; who is likely to get cancer; how to study the causes of cancer; why, how, and where cells become cancerous; and what we can do to prevent cancer. In fiscal year 1974, NCI reported that it spent about $100 million researching environmental causes of cancer, of which

$9.5 million was spent on animal testing of suspected chemicals. The latter amount dropped to about $9.3 million in fiscal year 1975.

NIEHS--NIEHS is also part of the National Institutes of Health. Its mission is to (1) identify the chemical, physical, and biological factors in the environment that can adversely affect people, (2) contribute to an understanding of the mechanisms and manifestations of human diseases produced by these agents, and (3) provide the scientific basis for developing control measures by other agencies. NIEHS is particularly concerned with the effects of low levels of chemicals over long periods of time.

NIEHS officials said they generally avoided cancer research because of NCI's established role. Although NIEHS does not routinely test chemicals to determine their cancer-causing ability, it funded over 40 studies during fiscal year 1974 that dealt in some way with the carcinogenic effects of certain chemicals. For example, one study involved the effect of various environmental chemicals on lung cancer in hamsters.

NIOSH--Under the Occupational Safety and Health Act of 1970 (29 U.S.C. 651), NIOSH conducts and sponsors research and reviews literature to develop criteria for protecting workers from occupational safety and health hazards. A major NIOSH responsibility is to provide OSHA with proposals and supporting data (criteria documents) for new or improved occupational safety and health standards. In fiscal year 1974 NIOSH funded about 225 research projects (contracts, grants, and interagency agreements) at a cost of about $16.3 million; of these only 4 dealt specifically with occupational carcinogenesis. According to the Department of Health, Education, and Welfare (HEW), NIOSH has increased its efforts in occupational carcinogenesis research and in fiscal year 1976 will spend about $7 million.

FDA--The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301) gives FDA authority to protect Americans from foods that are not pure, wholesome, and safe to eat; from drugs and therapeutic devices that are not safe and effective when used as intended; and from cosmetics that are not safe or made from appropriate ingredients.

The law is designed to protect consumers by requiring manufacturers to prove the safety of drugs, food additives, and color additives before they can be marketed. Food additives must be "generally recognized as safe" or manufacturers must scientifically prove their safety for their intended use

to FDA's satisfaction before marketing them. FDA checks to see that residues of pesticide chemicals in foods do not exceed tolerance levels 1/ set by EPA.

Cancer is a specific health effect for FDA to consider only when judging the safety of food or color additives. The Delaney Clause, a 1958 amendment to the Federal Food, Drug, and Cosmetic Act, requires FDA to ban the use of a food additive when:

> "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 the safety of food additives, to induce cancer in man or animal."

A 1960 amendment applied the language of the Delaney Clause to color additives used in foods, drugs, or cosmetics. Further amendments in 1962 allow carcinogenic chemicals to be used in animal feeds but only if no residue of the chemical can be found by an approved method in food products taken from the animal and if the additive does not adversely affect the animal.

FDA and EPA jointly sponsor the National Center for Toxicological Research to study the biological effects of potentially toxic environmental chemicals. The Center's principal mission is to develop better methods to evaluate the degree of toxicity of chemicals.

EPA--EPA was established in 1970 to centralize Federal activities for, among other things, controlling pesticides, air and water pollution, and drinking water quality.

The Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 135) requires pesticide manufacturers to prove the safety of their products to EPA before selling them. If a pesticide remains in or on a food product, EPA has to set a tolerance for the pesticide. If the pesticide is a carcinogen, EPA must set a tolerance or exempt the pesticide from the tolerance requirement.

The Federal Water Pollution Control Act (33 U.S.C. 1251) requires EPA to publish a list of toxic water pollutants and set limits for their discharge into waterways. The act also requires EPA to publish water quality criteria which would

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1/Tolerance levels are the maximum levels of pesticides that may legally remain in food.

provide the basis for State water quality standards. The recently enacted Safe Drinking Water Act (Public Law 93-523) requires EPA to set drinking water standards to protect the public health and provide an esthetic water supply. In setting the standards, EPA must consider recommendations from the National Academy of Sciences on the maximum level of contaminants that EPA should allow in drinking water.

The Clean Air Act (42 U.S.C. 1857) authorizes EPA to develop air pollutant standards in seven categories, including primary ambient air quality (to protect the public health), secondary ambient air quality (to protect the public welfare), and hazardous air pollutants (to prevent increased death or illness). EPA can require manufacturers of fuels or fuel additives to conduct tests to assess the chemical's carcinogenic potential.

EPA also has the authority to set standards for protecting the general environment from radioactive materials. The Nuclear Regulatory Commission and the Energy Research and Development Administration are primarily responsible for developing, implementing, and enforcing radiation standards for individual nuclear facilities.

EPA research is conducted through grants, contracts, and agreements with several sources as well as through its own laboratories. In fiscal year 1975 it spent $170 million for research and development of pollution processes, effects, and control technology. The research is not usually concerned specifically with carcinogenesis but with the whole range of possible adverse health effects from the environment.

CPSC--In 1972 the Consumer Product Safety Act (15 U.S.C. 2051) created CPSC as an independent regulatory agency to reduce the unreasonable risk of injury associated with consumer products. CPSC became operational in May 1973.

In addition to the new responsibility under the 1972 act, CPSC assumed responsibility for several existing consumer protection statutes, including the Federal Hazardous Substances Act (15 U.S.C. 1261). Under its general authority, CPSC can perform research necessary to regulate carcinogens in consumer products. CPSC also has the authority to ban or regulate the marketing of consumer products which can cause personal injury or illness.

Specifically excluded from CPSC's authority under the Consumer Product Safety Act are (1) articles not normally considered consumer products, (2) tobacco and tobacco products, and (3) certain products, such as drugs, pesticides, and motor vehicles, regulated under other Federal laws.

In fiscal year 1975 CPSC awarded 104 contracts for about $6 million. An official of CPSC's Bureau of Biomedical Sciences said that five of the contracts, costing about $1.1 million, related in some way to carcinogens and consumer products. Although CPSC emphasizes hazards and injuries rather than illness, one of the agency's objectives is to develop methods for testing carcinogens in consumer products.

OSHA--OSHA sets and enforces occupational safety and health standards, which pertain to a wide range of areas, such as farm vehicles and a chemical worker's exposure to a carcinogen. OSHA cannot ban production or use of hazardous chemicals but can protect a worker from exposure to them. The Secretary of Labor can, through order of the U.S. district courts, restrain employers from exposing employees to imminent dangers.

BURDEN OF PROOF

Several sources indicate that almost 2 million chemical compounds exist today and that about 250,000 new compounds are created annually. About 300 to 500 new compounds, some of which may be carcinogenic, get into the environment and into commercial use each year, and for most of them no Federal authority requires that they be proved safe before they are used.

Protecting the public from carcinogens depends greatly on (1) where the burden of proving safety rests and (2) whether the proof must be established before the public can be exposed. Before manufacturers can begin marketing drugs, pesticides, and food and color additives, they must prove such products are safe. The burden of proof remains with the manufacturers even after they receive initial Federal approval. For example, FDA needs only to gather information indicating an association between a marketed drug and an adverse reaction; the manufacturer retains the burden of proving the drug's safety in light of the new information.

In contrast, the burden of proving the health hazards of chemicals in other products rests with the Government. Because manufacturers can market these products without proving their safety, the public can be exposed to such chemicals before the Government can prove their harm. EPA must prove which chemicals already in the air and water are health hazards; FDA must prove that chemicals in cosmetics are injurious to health; OSHA must prove what levels of chemical exposure in workplaces threaten workers' health; and CPSC must prove the health hazard of chemicals used in consumer products.

An exception to the general burden of proof rule may be when an agency is petitioned to regulate carcinogenic chemicals, in which case the burden of proof rests with the petitioners. For example, in December 1975 CPSC was petitioned to regulate certain fluorocarbons in consumer products because of a potential increased risk of skin cancer. CPSC denied the petition because the petitioners had not proved the health hazard of the fluorocarbons.

As a result, the public may be exposed to certain chemicals for a long time before the Government regulates them because of their carcinogenicity. For example, workers had been exposed to beta-naphthylamine for more than 50 years by February 1974, when OSHA regulated it because of its carcinogenicity.

PENDING AND SUGGESTED LEGISLATION

The proposed Toxic Substances Control Act (S. 3149), passed by the Senate on March 26, 1976, states that adequate data should be developed with respect to chemical substances and mixtures concerning their effect on human health and the environment and that such data development should be the responsibility of those who manufacture or process such substances. The Senate version would require manufacturers of new chemicals to notify EPA of the existing data concerning environmental or health effects of the new chemical at least 90 days before first manufacturing it. Additionally, if EPA determines that new or existing chemicals may present an unreasonable risk to health or the environment, or if EPA lacks sufficient data to judge their environmental or health effects, it may require the manufacturer to make safety tests. Such tests may be made to detect the chemical's cancer-causing potential, at EPA's discretion. The act would not apply to pesticides, drugs, or food and color additives which now receive premarket safety testing. As of May 27, 1976, the House Interstate and Foreign Commerce Committee had not passed this bill.

The Surgeon General's report on the health consequences of smoking identifies cigarette smoking as the major cause of lung cancer. About 72,000 people died of lung cancer in the United States in 1973. On June 27, 1974, the Secretary of HEW recommended that the Congress consider legislation to set maximum permissible levels for hazardous ingredients--such as tar and nicotine--in cigarettes. HEW officials told us, however, that as of April 1, 1976, HEW had not introduced such legislation but that two bills dealing with this subject had been introduced--S. 2248, which would require the Federal Trade Commission to establish acceptable levels of tar and

nicotine in cigarettes; and S. 2902, which would tax cigarettes based on their tar and nicotine content and use these tax revenues for increased support of biomedical research.

CONCLUSIONS

The Congress has given NCI, NIOSH, and NIEHS broad authority to conduct or sponsor research to identify carcinogens. NCI has done most of the research. The regulatory agencies do little research on their own to identify carcinogens, but manufacturers of drugs, pesticides, and food and color additives must do research to prove their products' safety before these products can be marketed.

For chemicals that reach the public through other products and through the environment, however, the Government must initiate a regulatory action to remove them from the market. Cancer-causing chemicals can be controlled--either by safety testing before the chemical is marketed or by Government testing and regulation after it is marketed.

The Congress is considering toxic substances legislation to require premarket safety testing of chemicals which may present an unreasonable risk to health or the environment. Enactment of the Toxic Substances Control Act could shift the burden of proving a new chemical's safety to the manufacturer by requiring such proof before the chemical could be marketed. Enactment, we believe, would improve public protection from carcinogens.

Because tobacco and tobacco smoke are known human carcinogens (see app. VI), the Congress should request HEW to prepare a study showing the available options to regulate tobacco and tobacco products and the impact each option would have on the rising U.S. lung cancer rate. The Congress should then consider, as the Surgeon General has recommended, giving HEW or some other appropriate agency the specific authority to regulate tobacco and tobacco products.

CHAPTER 3

NEED FOR A FEDERAL POLICY CONCERNING CARCINOGENS

Federal agencies have problems accepting and applying the results of animal tests to people because (1) NCI has only recently developed minimum testing guidelines for determining a chemical's carcinogenicity and other agencies have not officially adopted them as a basis for carcinogenicity testing and (2) there are no scientific principles to help Federal agencies apply animal test results to humans. As a result, some carcinogens are not regulated at all while others are regulated differently by the different regulatory agencies. All agencies responsible for protecting the public from carcinogens should, we believe, cooperate to develop a uniform policy for identifying and regulating carcinogenic chemicals and the products in which they appear. The policy should also deal with such issues as under what conditions regulatory agencies will allow public exposure to carcinogens.

EFFECTIVENESS OF PREMARKET AND POSTMARKET TESTING

Premarket testing

Although some legislation discussed in chapter 2 is intended to assure the safety of all pesticides, drugs, and food and color additives before they appear in commercial use, not all chemicals used in these products have received the kind of long-term tests that experts agree are needed to detect any cancer-causing potential.

Before requiring manufacturers to conduct long-term animal tests for drugs, FDA considers the type of exposure people will get (one-time dose or prolonged use) and the number of people expected to be exposed.

The Federal Fungicide, Insecticide, and Rodenticide Act requires manufacturers to test and prove to EPA that their pesticides are not harmful to human health. Since 1963, when the Department of Agriculture administered the act, manufacturers of pesticides which leave residues on foods have been required by the administering agency to conduct long-term tests to detect carcinogenic potential. In safety evaluations for 30 randomly selected pesticides with tolerances for residues on foods, we found that, of the 36 chemicals used in those pesticides, 7 did not receive

the appropriate long-term testing. 1/ EPA officials said required safety data may not be available because (1) the pesticide was approved before 1963, (2) later EPA reviews were inadequate, or (3) the data could have been submitted but later lost during moves or reorganization.

Unintentional food additives

As discussed on page 6, the Federal Food, Drug, and Cosmetic Act requires that manufacturers of food additives prove their products' safety to FDA and that FDA disapprove any food additive that, when properly tested, is shown to cause cancer in animals or humans. The act covers both intentional and unintentional food additives. According to the legislative history of the act, examples of these additives are "substances intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food."

In discussing the concept of safety in regulating food additives, a Senate report on 1958 amendments to the act (S. Rept. 2422, 85th Congress) stated:

> "Since the scientific investigation and the other relevant data to be taken into consideration by the Secretary [of HEW] include information with respect to possible cancer causing characteristics of a proposed additive, the public will be protected from possible harm on this count."

Although FDA's Deputy Chief Counsel advised us that the Federal Food, Drug, and Cosmetic Act requires manufacturers of food additives to test for carcinogenicity, FDA's Associate Chief Counsel for Foods advised us that the act only requires that safety be assured before FDA approval.

According to officials in FDA's Division of Food and Color Additives, all intentional food additives must receive long-term tests to detect carcinogenicity before FDA will approve them. Intentional additives are to (1) improve nutritional value, (2) maintain freshness, (3) improve esthetic appeal, or (4) aid in processing.

1/See the GAO report to the Congress: "Federal Pesticide Registration Program: Is It Protecting the Public and the Environment Adequately from Pesticide Hazards?" (RED-76-42, Dec. 4, 1975), p. 7.

Unintentional additives are used mainly in packaging foods and, according to the FDA officials, receive long-term testing only when the consumer would be exposed to more than 1 or 2 parts per million of the additive in the food unless FDA had valid reasons to suspect that the additive might be carcinogenic. FDA officials explained that the long-term tests were very expensive, and because virtually none of the unintentional additives migrate from the packaging material to the food, the amount of the additive which may be ingested is virtually nil. FDA's principle in this regard is the higher the anticipated human exposure, the greater the amount of toxicological data required to assure human safety.

One official said that FDA had approved about 10,000 unintentional food additives, but he could not readily determine how many of the 10,000 had not received long-term testing. We noted that FDA has approved a few suspected carcinogens for adhesives that are used for packaging, transporting, and holding food.

In commenting on our report (see app. I), HEW stated that, although extending carcinogenicity testing to indirect food additives that have only remote possibilities of risk might be reassuring, it does not foresee any benefit to the public great enough to justify the substantial costs of such a policy.

We noted, however, that an April 1970 report to the Surgeon General by the Ad Hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens recommended that:

--No level of exposure of a chemical carcinogen should be considered toxicologically insignificant for humans.

--No chemical substance should be assumed safe for human consumption without proper negative lifetime biological assays of adequate size.

Under this view, FDA would be unable to assure the safety of food additives that do not receive long-term testing.

Postmarketing testing

Scientists believe that most cancer is caused by chemicals already in the environment. As discussed on page 8, the Government must initiate regulatory action to control potentially carcinogenic chemicals that appear as air or water pollutants, as occupational health hazards, or in consumer products.

Although several Federal agencies conduct and sponsor some long-term chemical testing, except for NCI they do not routinely test large numbers of existing chemicals for carcinogenicity. NCI's tests take about 3 years from initial chemical selection to final reporting. NCI spends from $150,000 to $205,000 to test each chemical, and at its fiscal year 1975 funding level it can add about 50 to 60 chemicals to its testing program each year.

IDENTIFICATION OF CARCINOGENS

Many chemicals have been tested for their carcinogenicity in animals, but Federal agencies and non-Federal organizations have trouble identifying which chemicals cause cancer in humans.

NCI

NCI sponsors research to detemine whether chemicals cause cancer. At January 1, 1975, NCI had 550 chemicals in its test program. NCI also reviews the scientific literature to identify carcinogens. It has compiled a list of 36 chemicals or chemical compounds (see app. VI) which definitely cause cancer in humans. NCI said that the scientific community generally accepted these chemicals as definitely being human carcinogens, yet the public can be exposed to at least 32 of the 36 substances. At our request, an NCI staff member classified the exposure hazard of the 36 substances into the following 6 categories. (See app. VII.)

Controlled or restricted use; protection requires technical surveillance	15
Voluntary; personal choice by the user	3
Poorly controlled	14
Prescribed by physician	1
Used in laboratory only	2
No longer produced in significant quantities	1
	36

Although the NCI staff member stated that the use of 15 of the known human carcinogens is controlled or restricted by regulatory agencies, the public is not, we believe, adequately protected from some of these chemicals because Federal regulations neither ban their use nor cover all means of public exposure. Many cancer experts--including the 1970 ad hoc committee of the Surgeon General--agree that a safe level of a carcinogen cannot be established and that any exposure may cause cancer. Two human carcinogens which the NCI staff member classifies as being controlled or restricted--asbestos and benzidine--are discussed in more detail on pages 23 to 25.

The chief of NCI's carcinogen bioassay and program resources branch stated that, of all chemicals tested by NCI contractors between 1962 and 1973, 214 were carcinogenic in animals. The public is exposed to some of these chemicals.

An NCI official said that the traditional method of releasing test results is through publication in scientific journals and through symposia but that this method has worked poorly. NCI is initiating a technical reporting series that would contain certain information on each chemical's exposure, use, and production, as well as a detailed explanation of test procedures and results. Chapter 4 contains a detailed discussion of NCI's role in identifying carcinogens.

Public Health Service

The Public Health Service--a part of HEW which includes the National Institutes of Health, FDA, NIOSH, and several other operating agencies--publishes general information on any animal carcinogenicity experiments of which it is aware. An NCI official said that the publications contained 6,000 chemicals. Although the Public Health Service does not indicate whether a chemical is a carcinogen but merely recaps information provided in published studies, NCI officials advised us that about 1,000 of the 6,000 have been reported in the literature to cause cancer in animals; many of these reports, according to NCI, appear to be based on inadequate data.

NIOSH

NIOSH conducts and sponsors research and reviews existing research literature to develop criteria for OSHA standards. NIOSH has developed and published a list of all known toxic substances. In its 1975 edition, NIOSH reported that information was included on the carcinogenicity of 1,500 chemicals.

World Health Organization

The International Agency for Research on Cancer, a part of the World Health Organization, publishes monographs on its evaluation of the carcinogenic risk of chemicals but makes no recommendations for preventive measures.

In March 1975 the agency reported that, of 196 compounds evaluated, 151 (77 percent) were carcinogenic. Of the 151, 17 were associated with human cancer, 93 were definitely carcinogenic in animals, and 41 had a limited carcinogenic effect on animals.

The type of exposure to the 17 human carcinogens was occupational for 14, medicinal for 2, and dietary for 1. In addition, some of the 93 chemicals found to be definitely carcinogenic in animals are produced in very large quantities.

Regulatory agencies

At the time of our review, the regulatory agencies--FDA, EPA, OSHA, and CPSC--did not maintain lists of carcinogens but had from time to time regulated chemicals because of their carcinogenicity. For example, from 1950 to 1974 FDA banned 14 food and color additives because of a finding or suspicion of carcinogenicity. In 1973 EPA published a list of toxic water pollutants and included benzidine because it was a carcinogen. When EPA proposed drinking water guidelines in 1974, it listed toxic chemicals, including arsenic and chromium, which it acknowledged as suspected carcinogens. In 1974 OSHA regulated the use of 14 chemicals 1/ in the workplace and CPSC banned the use of vinyl chloride in self-pressurized containers because the chemicals were carcinogenic. The regulatory agencies have taken or proposed action on several other carcinogens as well.

By November 1975 OSHA had developed a priority list of 220 chemicals to be used in its standard development activities; of the 220, OSHA indicated that 50 were suspected carcinogens. An OSHA official stated that OSHA wanted NIOSH to use this list in developing criteria documents.

PROBLEMS IN IDENTIFYING HUMAN CARCINOGENS

As previously stated, NCI considers that at least 1,000 chemicals have been reported to cause cancer in animals. Federal agencies have trouble determining which chemicals also pose carcinogenic threats for people. Some of the problems are that:

--Federal agencies have not been able to adopt a set of general principles concerning environmental carcinogenesis.

1/On December 17, 1974, the U.S. Court of Appeals for the Third Circuit vacated the standard for 1 of the 14 chemicals (4, 4'-methylene bis(2-chloroaniline)) because OSHA made a procedural error in formulating the standard. The court also vacated the standards of the other 13 chemicals as they applied to research laboratories.

--NCI has only recently developed minimum testing guidelines which other agencies have not yet officially adopted as a basis for carcinogenicity testing.

--When experimental data are available, they may not be as complete or appropriate as the agencies would like.

--The limited state of the art does not allow scientists to accurately predict human response to chemicals on the basis of animal test results.

In addition, even though Federal agencies believe a chemical to be carcinogenic, legislation and court decisions may require them to consider factors other than public health when deciding whether and how to regulate carcinogenic chemicals.

Principles of carcinogenesis

The April 1970 report to the Surgeon General by the Ad Hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens discussed the problems of environmental exposures to chemicals and the scientific criteria for evaluating carcinogenic hazards. The report, which is not HEW policy, deals with evaluating animal test results, problems in establishing a safe level of exposure, need for proper lifetime tests, and the principle of a zero tolerance for all exposures to chemical carcinogens. Several cancer experts restated some of these principles during administrative hearings on EPA's efforts to ban two carcinogenic pesticides--aldrin and dieldrin.

Representatives from six agencies met in August 1974 to discuss several areas concerning environmental carcinogenesis. According to the EPA representative, Federal agencies had a growing need to agree on a national policy, particularly in terms of risk-benefit considerations. As of April 1, 1976, however, no such policy had been developed. (See p. 32.)

Most recently, a subcommittee of the National Cancer Advisory Board is considering the general criteria for assessing the evidence for carcinogenicity of chemical substances, and NCI has chartered a new committee to review, evaluate, and interpret carcinogenicity data generated by the NCI testing program.

Minimum test guidelines

Because testing suspected carcinogenic chemicals on humans is neither ethical nor practical, scientists use animals. Experience with laboratory animals has shown that nearly all

chemicals that are carcinogenic in people are also carcinogenic in animals. The way a test is designed--the number of animals and dose levels used, the length of the test, and other laboratory conditions--can directly affect the validity of the results and their value to regulatory agencies.

The more animals tested, the more statistically sensitive are the results. Similarly, the more species used, the greater is the assurance that the chemical, and not some other factor, caused the cancer. Also, the more test dose levels administered, the better a scientist can estimate the relationship between the dose and the animal response. Finally, the tests should be conducted over the animal's lifetime to better approximate human exposure.

NCI has developed standard testing guidelines to be used by commercial labs under NCI contracts to test environmental chemicals. NCI officials hope that these guidelines, issued in January 1975, will (1) make research results more comparable and more applicable to humans, (2) increase the tests' sensitivity, and (3) provide better data on which regulatory agencies can act. In addition to prescribing animal care standards, the guidelines call for at least 2 doses to be given to 50 animals of each sex and each of 2 species.

NCI has shared these guidelines with other Federal agencies and at least two of them--EPA and NIOSH--have provided for consideration of these guidelines in some of their test procedures. None of the agencies, however, has officially adopted the guidelines as a basis for carcinogenicity testing. Some agency officials even question the need for such guidelines, stating that each test should be designed individually. NCI believes that the guidelines describe many features which are common to all well-designed and properly conducted long-term animal studies and which need to be considered whenever a carcinogen test is planned or undertaken. Chapter 4 discusses some of NCI's problems in designing tests for use by regulatory agencies.

Before the NCI guidelines were developed, Federal agencies had no common guidelines for testing chemicals for their carcinogenicity. EPA had proposed guidelines for testing pesticides which called for 2 species, 3 dose levels, and between 25 to 50 animals of each sex and species per dose level. The National Academy of Sciences, under contract to EPA, recommended 2 rodent species, tested at several dose levels, with 40 to 50 animals of each sex surviving the highest dose. An international cancer group recommended at least two species (one of which should be a nonrodent mammal), one

dose level 1/ (the highest dose tolerated by the animals), and enough animals to yield reasonably significant results. An FDA advisory committee suggested two rodent species tested at several dose levels, including one which would yield the most tumors, but did not say how many animals should be used.

Past regulatory actions have been based on results of research conducted under a wide variety of protocols. For example, the animal studies which conclusively linked vinyl chloride to a rare form of liver cancer included three species and seven dose levels. EPA on the other hand, proposing to limit the amount of benzidine in water, cited several studies to establish the carcinogenicity in animals and humans, but relied on an animal study which included only one species and one dose level through a route of administration (injection) not normally experienced by the public. 2/

Incomplete and inappropriate data

In some cases, the experimental data available to the regulatory agency is not as complete or appropriate as necessary. For example, the first link between vinyl chloride and cancer came in 1970 when a scientist reported tumors in rats exposed to extremely high doses of the chemical. Although these results were statistically valid, they were not viewed with alarm because the concentration of vinyl chloride was near the explosive limit and was not likely to be found in industrial situations. Similarly, a U.S. court of appeals denied EPA's proposed ban on dumping asbestos into the drinking water of Lake Superior because EPA could not prove that asbestos causes cancer when ingested. The carcinogenicity of inhaled asbestos has been documented for about 40 years.

Many chemicals have been reported to cause tumors in test animals, but regulatory agencies are hesitant to base any action on a single test. The 1970 report to the Surgeon General recommended that the test designs provide for reproducibility of results.

1/The international group considered it advisable to test more than one dose level.

2/As of May 27, 1976, this proposal was still pending. See page 24 for more information on EPA's proposed benzidine standard.

Predicting human response from animal tests

A critical problem in regulating carcinogens is trying to predict the human risk of exposure to small levels of chemicals solely on the basis of results of animal tests. The limited state of the art restricts scientifically sound regulation.

Conventionally, toxicologists have applied "safety factors" to animal test results and have assumed that an animal's reaction would not differ from a person's reaction by more than that factor. NCI's associate director for carcinogenesis has questioned whether this safety procedure can be applied to cancer risks because of the differences between cancer and other diseases.

The validity of tests on laboratory animals is most easily accepted when people are exposed to the chemical in the same way the test animals were. However, people are exposed to practically all chemicals at such low levels and for such long periods that an impractically large number of animals is needed to produce statistically valid results under those conditions. To further complicate the matter, a person's reaction to a chemical may be different than an animal's in terms of absorption, distribution and storage, metabolism, excretion and reabsorption, arrival at the site of action, and reaction with the biological receptor. One analysis of the state of the art for extrapolating results of animal tests to people concludes that there is a basis for comparing the median mouse to the median rat to the median dog to the median person. But the report warns of the greater difficulties in comparing the median animal to the not-so-average person.

At congressional hearings held in 1971 on "Chemicals and the Future of Man," concern was expressed about unduly frightening the public about adverse health effects from chemicals which had been commonplace. A House Appropriations Committee report gave some examples of how much of a banned substance a human would have to consume to receive amounts comparable to those given to experimental animals. The purpose of the examples, all of which dealt with carcinogenic food additives banned by FDA, was to translate abstract scientific studies into their real-life equivalents. According to the Committee's report:

--An adult would have to drink from 138 to 552 bottles of soft drink each day to get a comparable amount of cyclamate that caused cancer in mice and rats.

--A person would have to drink 250 quarts of vermouth each day to get a comparable amount of oil of calamus that caused cancer in rats.

--A person would have to drink 613 bottles of root-beer-flavored soda or eat 220 pounds of hard candy each day to get an amount of safrole comparable to that which caused cancer in rats.

Factors other than public health

The 1970 report to the Surgeon General stated:

"Any substance which is shown conclusively to cause tumors in animals should be considered carcinogenic and therefore a potential cancer hazard for man * * * [and] 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."

Strictly applying this criteria, any chemical that causes cancer in animals would be presumed to cause cancer in people, regardless of level of exposure. But in some cases, laws require regulatory agencies to consider more than the carcinogenic risks of a chemical. When considering whether to approve a drug for marketing, FDA weighs its benefits against any safety risks. For example, some drugs used to treat cancer have also been shown experimentally to cause cancer. Certain drugs used to treat severe heart conditions are also carcinogenic. But FDA has determined that the immediate benefits from those drugs outweigh the potential risks.

Likewise, EPA considers the benefits and dangers to the public health and welfare from the use of pesticides. The Federal Environmental Pesticide Control Act of 1972 (7 U.S.C. 136) defines the "unreasonable adverse effects on the environment" of a pesticide as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."

Since January 28, 1975, the Office of Management and Budget has required that agencies of the executive branch consider the inflationary impact of major legislative and regulatory proposals.

In revising its permanent standard for vinyl chloride, OSHA decided that no detectable level should be allowed in the workplace. After receiving industry views on the costs of compliance and a consultant's report of the economic

impact of the proposed standard, OSHA raised the permissible level to 1 part per million. OSHA did not claim, however, that 1 part per million was a safe level of exposure to vinyl chloride.

Regulatory agencies also consider the practicality of their proposed actions, including the state of the art of analytical and detection equipment. When EPA developed a standard for asbestos in the air, an important consideration was the lack of satisfactory methods of measuring asbestos emissions. As a result, the asbestos standard was not written in terms of numerical values; instead, it limited visible emissions and required certain manufacturing techniques to reduce those emissions.

Federal agencies should consider these factors, when properly authorized and documented, in deciding on regulatory action against carcinogens. It is important for the public record that the documentation show the impact of the regulation on the public health, as well as on the other factors considered.

DIFFERENCES IN PUBLIC EXPOSURE TO CARCINOGENS

If a carcinogenic chemical is not banned, people may be exposed to it. Despite differences in the degree of such exposure, scientists have not proved that any exposure is harmless. Therefore, the public faces some risk of getting cancer when carcinogenic chemicals are not banned.

In its comments on this report (see app. I), HEW stated that, although it may be true that any exposure to a chemical carcinogen will cause cancer within the exposed population, the risk or probability that cancer will occur may very well be related to exposure levels. HEW said that, when exposure cannot be completely eliminated or the benefit is deemed to outweigh the risk from exposure, efforts must be made to estimate the upper limits of risk from specific levels of exposure using the best evidence obtainable by applying current research tools. HEW also recognized that current animal test procedures do not provide a quantitative assessment of the hazard to exposed human populations which would be required to resolve certain regulatory needs and questions.

We selected two chemicals that NCI has concluded to be known human carcinogens--asbestos and benzidine--to determine how the public is being protected from them. We found varying degrees of regulation over the two chemicals for various reasons.

Asbestos

Asbestos refers to a family of hydrated silicates that, when crushed or processed, separate into flexible fibers. Only six of the many asbestos minerals are of commercial importance.

Asbestos is used in over 3,000 products, and in 1972 over 800,000 tons were used in the United States. The regulatory agencies we reviewed all consider asbestos to be carcinogenic, but they regulate it differently.

On June 7, 1972, OSHA specified a numerical standard allowing some asbestos in the workplace. When NIOSH recommended the standard to OSHA, it conceded that the standard was based on the health hazards of asbestosis--a type of lung impairment--and not cancer, because there was insufficient information to set a standard to prevent lung cancer unless the standard was zero. This is consistent with NCI's belief that no level of exposure to a carcinogen should be considered safe for humans. However, on January 29, 1974, OSHA required that workers' exposure to 14 other chemicals it considered to be carcinogens be reduced to the maximum extent practical.

In October 1975 OSHA proposed lowering the permissible level of asbestos in most workplaces by 90 percent, recognizing the cancer risk of asbestos in the workplace and the technological and economic factors which, OSHA reasoned, had prevented such a regulation. If enacted, the new regulation would allow up to 0.5 fibers of asbestos per cubic centimeter of air in the workplace, averaged over an 8-hour work period.

On April 6, 1973, EPA developed a standard for asbestos in the air. The asbestos standard was not written in terms of numerical values, as is the OSHA standard for asbestos, but instead it limited visible emissions and required certain manufacturing techniques to reduce those emissions. An important consideration in the EPA standard was the lack of satisfactory methods of measuring asbestos emissions. Therefore, the standard was not based on a "safe" level of emission.

In January 1972 EPA tried to ban the dumping of asbestos into the drinking water of Lake Superior because asbestos was a carcinogen. A U.S. court of appeals denied this ban, however, because EPA could not prove asbestos causes cancer when ingested, although the carcinogenicity of inhaled asbestos has been documented for 40 years.

On September 28, 1973, FDA proposed several regulations to restrict the use of asbestos filters for drug manufacturing and to prohibit the use of asbestos-containing talc as a

food, as a food or drug ingredient, or in food and drug packaging materials because of asbestos's carcinogenicity. On March 14, 1975, however, FDA decided to delay any final regulations because it stated that it could not prove that asbestos was present in those substances or that ingested asbestos caused cancer. FDA did, however, regulate the use of asbestos filters for manufacturing drugs used for injection in humans.

CPSC stated that asbestos is in a number of consumer products it is responsible for regulating, but it has not identified specific products. CPSC does not plan to regulate the use of asbestos in consumer products until considerable research is completed in the area.

The Government is studying whether ingested asbestos can cause cancer. Representatives from several Federal agencies developed a test protocol, and on June 30, 1975, NIEHS awarded two contracts for lifetime ingestion studies in rats and hamsters. The studies are to run for 4 years at an estimated total cost of about $2.9 million.

Benzidine

Benzidine occurs as white or slightly reddish crystals or leaflets or as a crystalline powder. Its domestic marketable production in 1972 was 1.5 million pounds. One source lists 361 dyes derived from benzidine and its salts. In addition, it appeared as a contaminant in workplaces before 1974 and as a toxic water pollutant. The suspicion that benzidine induced bladder cancer in workers was reported before 1940.

OSHA recognized both the animal and human carcinogenicity of benzidine and included it as 1 of the 14 chemicals it regulated in January 1974. Under these regulations, workers can only handle benzidine in a closed system--one where benzidine is not released into the work environment.

EPA recognized the potential for increased water pollution from benzidine and listed it as a toxic water pollutant in July 1973. In December of that year, it proposed an effluent standard to limit the discharge of benzidine into navigable waters.

EPA's proposed standard would have allowed each user of benzidine to dump up to 1 pound a day into the water. The amount each user could dump would depend on the char-