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PRESENT FEDERAL PROGRAMS ADDRESSED TO ENVIRONMENTAL CARCINOGENS

In recent years, the General Accounting Office has placed increased emphasis on evaluating the effectiveness of Federal programs and suggesting ways in which these programs can be made more cost-effective. This does not mean that we have lost our interest in the financial aspects of these programs nor in the economy and efficiency with which these programs are managed. It simply means that we are attempting to carry out the intent of the Congress in legislation enacted in 1970 and expanded upon in 1974 that we analyze the costs and benefits of Federal programs.

In order for GAO to better perform analyses of Federal programs with technical content, we have had a policy for several years of adding to our staff persons with specialized training in various technical disciplines. Disciplines represented include engineering, economics, medicine, biochemistry, chemistry, psychology and automatic data processing. These staff members help us analyze complex technical issues such as those I will be discussing with you today.

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We in GAO also have a unique opportunity--because of our central location in the legislative branch--to examine programs for which responsibility is vested in several Federal agencies. Federal health care and health research programs are excellent examples. Our discussion today centers upon a GAO report of June 16, 1976, entitled "Federal Efforts to Protect the Public from Cancer Causing Chemicals Are Not Very Effective."

The basic reason for the conclusion stated in this report was that some chemicals which are known to produce cancer are not regulated at all and that the Federal Government, through the seven agencies charged with some phase of regulation, does not have uniform policies.

Chemicals found in our environment--the air and water, our food, our workplaces, cigarettes, and other tobacco products--are evidently responsible for a considerable portion of the cancer cases reported in this country. There have been estimates that up to 90 percent of cancer is caused by environmental factors.

We, as individuals, can exert very little control over our exposure to environmental contaminants. We have little choice but to breathe our city's air or drink the water piped into our homes. Some exposures such as drinking alcoholic beverages and smoking are largely voluntary at their outset, although I should note that the voluntary initial exposure is often conditioned by social pressures. When and if addiction occurs, it would be difficult to call further exposure "voluntary."

Most exposures seem to be a mixture of voluntary and involuntary, although the involuntary aspects of the exposure seem to clearly predominate. For instance, there has been discussion recently of possible links between cancer and diet, particularly high-fat diet. Certainly you can exercise control over your diet, even to the extent, as some have, of becoming a vegetarian. But in a society seemingly dedicated to consuming large quantities of red meat, control is difficult.

Since we can exert only limited control over the environmental contaminants in our daily lives, it is important that the Federal agencies empowered to protect us from exposure to harmful chemicals have rational and efficient programs for research and regulation. The topic of my talk this morning is basically the substance of the the recent GAO report which dealt broadly with this problem.

In our report, we concentrated on involuntary exposure of humans to environmental factors, making only passing reference to the role of social and individual habits in cancer causation. This morning, I will discuss Federal cancer research and regulatory policy, highlighting the findings from our report on these subjects.

The principal authority for identifying and/or regulating cancer-causing chemicals or the products in which they appear is centered in seven Federal agencies.

The National Cancer Institute sponsors most of the Government's research on cancer's cause and prevention; the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, and some regulatory agencies also conduct or sponsor such research.

The Environmental Protection Agency is responsible for regulating air and water pollutants (many of these pollutants are chemicals) and is also responsible for regulating pesticides. The Occupational Safety and Health Administration sets and enforces standards to protect workers from safety and health hazards, including hazardous chemicals, in workplaces. The Food and Drug Administration is responsible for the safety of foods, food and color additives, drugs, medical devices, and cosmetics. The Consumer Product Safety Commission has jurisdiction over every consumer product not covered by any other agency, except those products specifically excluded by the Consumer Product Safety Act.

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 there is no Federal authority requiring that they be proven safe before significant human exposure occurs through use or marketing.

For the Government, ease of regulation of chemical carcinogens depends on where the burden of proof as to the safety of chemicals lies. That is, must the manufacturer prove that a chemical is safe before the chemical can be used or marketed, or must the Government prove lack of safety after the chemical is already in use?

The recently enacted Toxic Substances Control Act gives the Environmental Protection Agency the authority to require that chemical manufacturers test products that may pose an unreasonable risk to human health or the environment. Companies planning to produce a new chemical or to market an existing substance for a new purpose now have to notify EPA 90 days in advance, giving the agency a chance to hold up marketing while more testing is being done or even to ban a chemical in an extreme case.

The act does not apply to food additives, including food colors, drugs, or pesticides, all of which are already covered by statutes which require premarket clearance by the Government.

In our June 16 report we recommended a coordinated and uniform Federal policy to deal with the unresolved scientific issues, which, in our opinion, have hampered more effective regulation and research efforts. Among these unresolved issues are the following:

--Which chemicals should be tested?

--How should tests be conducted?

--How should test results be evaluated?

--What do animal tests mean for humans?

Although the Federal agencies, in their comments on our report, agreed that a uniform Federal policy was needed, they did not agree on which agency should develop it. We recommended that the Director of the Cancer Institute be given that responsibility because of the authority vested in him by the National Cancer Act of 1971. Section 407 of the act requires that the Cancer Institute Director develop a cancer research program that would be coordinated with related programs of other research institutes and other Federal and non-Federal programs.

We did not intend that NCI unilaterally set regulatory policies or policies for other research agencies. However, we did intend that NCI be the focal point for seeing that a uniform policy is established and that NCI more actively coordinate all Federal policies dealing with carcinogens so that these policies reflect the latest scientific advances and afford maximum protection to the public.

We believe that the matters I will touch on this morning--the question of what is tested, how the tests are performed, and how the results are evaluated--must be addressed and agreed upon by all agencies. Regulation of carcinogens would proceed more smoothly and rationally if Federal agencies had uniform test guidelines and procedures for determining

whether a tested chemical is a carcinogen. We believe that these issues are among the most important that must be resolved by a coordinated Federal policy on chemical carcinogens.

SELECTION OF CHEMICALS FOR TESTING

Because the Government has the burden of proving whether or not many of the chemicals in our environment are carcinogenic, it must use its limited testing resources wisely. This means that strict criteria must be used in selecting chemicals for testing. The Cancer Institute is now considering production and public exposure data, in addition to chemical structure, when selecting chemicals for its testing program.

The Cancer Institute is the only Federal agency that routinely tests large numbers of chemicals for their cancer-causing potential. These tests have short-term impact on regulatory decisionmaking by such agencies as FDA and EPA. However, the principal function of the Cancer Institute is to determine why certain chemicals cause cancer, and how we can intervene in the process of carcinogenesis.

It thus becomes necessary to segregate for policy purposes and for our discussion today the testing of chemicals for regulatory purposes from the study of chemicals as part of a basic research program on the mechanisms of chemical carcinogenesis.

ANIMAL TESTING

Because testing suspected chemicals on humans is neither ethical nor practical, scientists use animals. Animal testing

takes from 3 to 4 years from start to finish and now costs from $150,000 to $205,000 for each chemical. Experience indicates that chemicals that are carcinogenic in animals can be expected to be carcinogenic in people, and vice versa. The way a test is designed--the number of animals used, dose levels, the length of the test, and other laboratory conditions--can directly affect the validity of the results and their value to regulatory agencies.

The Cancer Institute has developed standard testing guidelines which commercial labs under its contract follow when conducting animal tests. Institute officials hope that these guidelines, issued in January 1975, will (1) make research results more easily comparable and more applicable to humans, (2) increase the tests' sensitivity, and (3) provide better data for regulatory agency decisionmaking. Unfortunately, however, the regulatory agencies have not agreed on a set of standards, or minimum guidelines, for testing suspected carcinogenic chemicals. Cancer Institute officials believe that tests conducted according to their guidelines will provide an adequate scientific base for regulatory actions, but apparently regulatory agencies are not as confident as the Cancer Institute.

DATA EVALUATION

The Cancer Institute guidelines cover the conduct of tests, but they do not cover analysis of the data the tests produce. Evaluation of test results presents serious problems for regulatory

agencies. These problems include determining whether a test animal has cancer or some other tumorous growth, deciding whether or not a chemical should be classified as a carcinogen, and extrapolating data from animals to man.

Pathology is the science involved in study of gross or microscopic samples of animal tissues in order to determine whether cells, tissues or organs are affected by a disease. Human tumor pathology is, I understand, fairly well defined at this point, although pathologists will still disagree at times on the evaluation of biopsy material. Animal tumor pathology is evidently not as well developed as human tumor pathology at this time. Rodent pathology is especially important, since many of the bioassays are conducted using rodent populations. We would expect the continued development of animal pathology to resolve the problems mentioned above.

There are disagreements as whether a chemical which causes nonmalignant (benign) tumors should be classified as a carcinogen. These disagreements have resulted in several law suits and much debate in the scientific community.

Classifying chemicals as carcinogens has occupied much time and energy in regulatory agencies and the scientific community in the past decade. I am not going to go into the details of this problem at this time, but I do wish to stress that GAO recognizes the importance of this problem and its implications for both research and regulatory agencies.

EXTRAPOLATING RESULTS

One of the most critical problems in regulating carcinogens is trying to predict the human risk of relatively low exposures to chemicals solely on the basis of the results of animal tests.

Historically, 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. Application of safety factors has been predicated on a disease meeting the following three conditions:

--The disease process is reversible;

--A safety threshold exists; and

--The chemical is acutely toxic.

Unfortunately, these conditions do not hold for cancer. The cancer process seems to be irreversible, no safety threshold for a carcinogen can be measured, and cancer is a disease which can occur after exposure to low levels of a chemical, with disease becoming apparent many years after exposure to the chemical occurred.

The application of "safety factors" to carcinogens is, therefore, not consistent with the scientific understanding of the carcinogenic process.

Most scientists agree that a chemical that causes cancer in animals is a potential cancer hazard for humans. Most scientists also agree with the former Director of the National Cancer Institute that "there is no practical scientific method

to prove experimentally the safety of any level of exposure to a carcinogen." Thus, any chemical that causes cancer in animals is presumed to be a potential cause of cancer in humans, regardless of the level of human exposure.

FACTORS OTHER THAN PUBLIC HEALTH

In some cases, laws require that regulatory agencies take into account factors other than the carcinogenic risks of a chemical when deciding whether or how to regulate the chemical.

If regulatory agencies took only scientific factors into account when deciding how or whether to control human exposure to carcinogens, given current scientific knowledge, demonstration that a chemical causes cancer in animals would be sufficient for the agencies to set a zero exposure level to the chemical for humans; this would effectively ban many widely-used chemicals and would also pose problems for marketing of foodstuffs which have become inadvertantly contaminated with persistent pesticides such as Dieldrin or natural carcinogenic substances such as aflatoxins.

There are rare pieces of legislation, such as the Delaney Clause of the Food, Drug, and Cosmetic Act, which require that a chemical which can be detected in food be banned for human use once the chemical has been shown, by "appropriate" tests, to cause cancer in animals. More commonly, however, laws require regulatory agencies to weigh health risks against the social, economic, and other possible benefits of a chemical

for which regulation is being considered. Therefore, decision-making by regulatory agencies on carcinogens usually involves both scientific and non-scientific data.

For instance, the Federal Environmental Pesticide Control Act of 1972 defines a pesticide's "unreasonable adverse effects on the environment" 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." This legislative language calls for balancing the risk of cancer against such factors as crop yield and quality, and the cost of producing a crop without resorting to the pesticide in question.

In early 1975, the Office of Management and Budget required executive branch agencies--including FDA and OSHA--to prepare inflationary impact statements for any proposed regulatory action.

When Federal agencies take into account factors other than scientific data when regulating carcinogens, such non-scientific factors should be clearly identified in the public records of the regulation, and should not be confused with scientific data. Further, it is necessary to avoid attributing a regulatory decision to scientific data when the decision is really based on non-scientific data. It is important that risk-benefit balancing show the impact on public health of regulating--or not regulating--a chemical, as well as the impact of the regulation on the balance sheets of an industry or the pay envelopes of a group of workers or costs to the consumer.

REPORT CONCLUSIONS

Our report concluded that the public has been exposed to carcinogenic chemicals such as asbestos and benzidine. In addition, new chemicals which may be carcinogenic are entering the environment because in some cases premarket testing is insufficient or lacking. For example, indirect food additives, such as packaging materials, which migrate to the food in amounts of less than one or two parts per million, are not always subjected to the long-term testing which cancer experts agree are necessary to determine a chemical's carcinogenicity.

Even if all chemicals are subjected to long-term testing, Federal agencies have problems accepting the results of those tests and applying them to people because the agencies do not have minimum test guidelines for determining a chemical's carcinogenicity or scientific principles to help the agencies apply animal test results to humans.

As a result of these problems, some carcinogenic chemicals are not regulated at all, while others receive inconsistent regulation. A uniform Federal policy on how to identify and regulate chemical carcinogens is needed. Some of the issues which we believe should be included in such a policy are the

--chemicals that should be tested,

--test guidelines that should be followed,

--procedures that should be used for evaluating test results, and

--factors other than public health which should be considered.

CRITICISM OF THE DELANEY CLAUSE

Most of the criticism of the Delaney Clause relates to the rigid standard it imposes on FDA, requiring the agency to prohibit or ban any food additive which, when properly tested, causes cancer in animals or humans. These critics usually call for repeal of the legislation to allow FDA to exercise greater scientific discretion.

In our work, we have accepted the public policy judgment embodied in the Delaney Clause. Let me briefly review two of the considerations that led us to that position.

First, the congressional intent. When the food additive amendments were added to FDA's legislative authority in 1958, the Delaney Clause was included to draw special attention to the problems of cancer. The Congress was aware that the amendments would read and mean the same with or without the Delaney Clause. Nevertheless, it included the Clause to emphasize its intent that no substance that might cause cancer in humans be sanctioned for use in food.

Second, the uniqueness of the cancer risk to human health. As I stated earlier, cancer differs from other diseases caused by environmental contaminants in that the

cancer process seems to be irreversible, no safety threshold for a carcinogen can be measured, and clinical symptoms of the disease usually become apparent only after long latent periods. Also, scientific consensus seems to be that any exposure to a carcinogen involves some risk, and that the risk cannot be quantified.

Now that the Delaney Clause is to be invoked against an additive that very many people, for whatever reason, consider essential to their food supply, the Congress is being called upon to reevaluate the need for such a strict requirement. Consider for a moment what could happen if the Congress were to repeal the Delaney Clause. FDA would be left with its basic responsibility to insure the safety of food additives. It would be allowed to consider such factors as the probable consumption of the additive, cumulative effects of the additive in the human diet, and appropriate safety factors--if such "appropriate" factors exist--for interpreting animal test results.

So we would have FDA making the same risk-benefit decisions on food additives which currently plague so many of the Federal regulatory agencies. We at GAO are concerned with such general questions as

--How valuable are risk-benefit comparisons in decisionmaking?

--How accurate can risk-benefit analyses become?

--What are legitimate costs and benefits of regulatory option and how can they be quantified?

We are contributing to the public discussion of regulatory options. For example, we reported to Senator Tunney on December 4, 1975, about the expected costs to industry from the Toxic Substances Control Act. Our efforts, I would like to think, balanced the estimates which the industry and the EPA had given to the Committee.

RELATED GAO REPORTS

By this time, some of you may be asking yourselves what the General Accounting Office is doing in such a technical area. Let me respond to this unasked question in two ways: by first discussing our legislated responsibility and then some of our related work in the area.

Our responsibility, in short, is to evaluate and recommend improvements in Federal programs wherever we can. We try to show what is and is not being accomplished and compare that to the intent of the Congress, as best we can interpret it; and some of you who have tried to interpret the laws know this is not always an easy thing.

Our experience in the general area of environmental health and safety has produced a number of reports over the past few years dealing with specific products such as maleic hydrazide and saccharin, and specific problems such as delays in developing occupational health standards for toxic chemicals.

I would like to comment on some of these efforts, beginning with three recent reports to Senator Gaylord Nelson on FDA's performance in determining the safety of three additives--FD&C Red No. 2, saccharin, and aspartame.

RED NO. 2 - On October 20, 1975, GAO reported that FDA had allowed the use of the food color additive for 15 years without making a final determination of its safety. During that time scientific studies questioned its safety, including its ability to cause cancer. One of the problems FDA faced in evaluating those studies was the test protocols. Eventually, FDA banned Red No. 2 because new evidence showed that it caused a statistically significant increase in the number of malignant tumors in test animals. I am sure the issues in FDA's regulation of Red No. 2 will be fully explored by this morning's panel.

SACCHARIN - Although this artificial sweetener had been "generally recognized as safe" for years, by February 1972 questions about its potential to cause cancer became prevalent enough for FDA to reconsider its safety. FDA issued an interim regulation to allow the continued use of saccharin in food for a limited time while the cancer questions were resolved. That limited time had been expected to extend to mid-1978. GAO reviewed the chronology of the saccharin issue and in an August 16, 1976, report concluded that the extended use of any food additive whose safety has not been established and for which questions of carcinogenicity have been raised could expose the public to unnecessary risk.

The key issue which caused the scientific debate was again the test protocols; in this case the route of administration, the dose levels, the tissue processing, and the number of animals that survived the test period.

On March 9, 1977, FDA announced its intention to ban the use of saccharin in foods and beverages. The decision was based on the results of a Canadian study which showed that some rats fed saccharin developed cancer and was essentially required by the Delaney Clause.

ASPARTAME - This is another artificial sweetener which was developed in 1965 but has not yet been marketed. Our April 8, 1976, report on FDA's regulation of aspartame pointed out a problem in evaluating animal tests. A by-product of aspartame was fed to rats for 115 weeks and resulted in a significant incidence of uterine polyps in two test groups. Although three groups of pathologists, including one group from FDA, reviewed the data and concluded that the polyps were not "cancerous, precancerous, or potentially cancerous." FDA agreed to consider the carcinogenic potential of the polyps at a planned public hearing on aspartame's safety. I understand that these scientific issues have yet to be resolved.

I might add that GAO is now looking at FDA's entire program for regulating food and color additives, including its criteria for reviewing safety and its ability to protect the public from unsafe additives.

Pesticides - GAO reported to Congresswoman Julia Hansen in October 1974 that questions regarding the safety of a particular pesticide used on potatoes and other crops had not been answered. We pointed out that researchers had raised the possibility that the pesticide, maleic hydrazide, may cause cancer or mutations or may affect reproduction. EPA commented that the data it relied on to approve the use of the pesticide were valid and that the studies GAO cited had various scientific weaknesses, such as improper routes of administration. We recognized that the evidence was not compelling and recommended that the EPA further evaluate its risk to human health and the environment.

In December 1975 we reported to the Congress that EPA's pesticide registration program was not adequately protecting the public and the environment from pesticide hazards. Some of the conditions we found that led to that conclusion were:

--safety data, including information on cancer, genetic changes, birth defects, and reproduction, had not been submitted to support marketing many pesticides;

--safety and efficacy data were not required for the pesticides as marketed, only for the individual active ingredients; and

--inert ingredients (such as vinyl chloride) were not subjected to the full range of safety testing.

EPA is currently engaged in a massive reregistration program to evaluate existing safety data on all approved pesticides. Although originally scheduled to be completed in October 1976,

EPA now estimates that its review will not be completed for another 5 to 7 years.

Occupational Health - In May 1973, OSHA issued an emergency temporary standard to regulate employee exposure to 14 chemicals considered to be carcinogenic. In September of that year, eight members of the House of Representatives asked GAO to review OSHA's basis for that standard.

We reported that OSHA's decision was based on the scientific evidence available at the time, the criteria established by a committee of the Surgeon General, a petition from a public interest group and a union, and public comments on that petition. We concluded that OSHA's decision to issue the standard was reasonable.

This past October, GAO criticized the EPA for not monitoring the health of its laboratory personnel even though many of them were being exposed on a continuing daily basis to highly toxic chemicals, including carcinogens.

Drugs - In a 1973 report to the chairman of a subcommittee of the Senate Government Operations Committee, GAO discussed FDA's supervision over the investigational use of selected drugs. One topic of that report was the human testing of drugs with major safety questions. We examined situations where data from animal tests indicated possibilities of major drug-related adverse effects in humans and FDA permitted clinical testing. Because some of the animal test

results raised the possibility of the drug being a carcinogen, we recommended that FDA at least document the benefit/risk determinations that were being made before allowing human testing.

The Chairman of the House Commerce Committee's Oversight Subcommittee was interested in the use of cancer-causing drugs in food-producing animals. We reported to him in February 1976 that nitrofurans--one class of animal drugs--had been considered suspected carcinogens since at least 1967 but that at the time of our report FDA had not taken effective action to remedy the public health hazard.

I am not trying to be a Monday morning quarterback and say that we should have known then what we know now. I know that improvements and refinements in test methods that take place almost every day. What I am trying to suggest, however, is that a uniform policy, at least in the Federal Government, might prevent public exposure to cancer-causing chemicals by selecting proper chemicals for testing, applying some minimum standards to those tests, evaluating the test results against some agreed-upon criteria, and balancing the results against the socio-economic factors which have been deemed proper by the Congress.

In conclusion, I leave with you the question as to what should be the proper role of the Federal Government in this important area. This has been a subject of debate for many

years and it is a far from settled matter at this point. In my opinion, the issue can be best described as a scientific-socio-political-economic choice which should be resolved by the Congress as a matter of high priority. The form of this decision and the timing of actions which flow from it will be based primarily on the best scientific evidence that our research scientists and physicians can bring to bear upon it. Despite this, it is possible that the incontrovertible evidence needed to make such a decision may not be obtainable--at least in the minds of those who would place greater emphasis upon the political and economic issues involved. But the stakes are high and scientists should not hesitate to develop to the best of their ability the data on the precise relationship between chemical use and disease--for without this scientific effort our political leaders are faced with a much more difficult decision as to what should be a rational national policy.