THE CANCER LETTER

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OPPOSITION TO LEDERBERG MAY HAVE CAUSED DELAY IN PANEL APPOINTMENTS; FY 1980 FUNDS HELD UP

Opposition to the reported appointment of Joshua Lederberg as chairman of the President's Cancer Panel may have been responsible for the continuing delay in filling the two vacancies on the Panel. Although President Carter ignored the Panel's recommendations when it was chaired by Nixon/Ford appointee Benno Schmidt and has shown little interest in restoring it to the role mandated by Congress, the White House reportedly developed concern when some Cancer Program advocates denounced the selection of Lederberg.

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In Brief

FORGET HEW—IT'S NOW HHS; CANCER CONTROL ADVISORY COMMITTEE MEETING SET FOR OCT. 22

IT'S NOW the "Dept. of Health & Human Services"—HHS instead of the familiar HEW (Health, Education & Welfare) with the final approval by Congress of legislation removing the education agencies from HEW and creating a separate Dept. of Education for them. . . . **NCI'S CANCER CONTROL** & Rehabilitation Advisory Committee scheduled a meeting for Oct. 22 too late to get into last week's listings of October meetings. The committee will review planning for projects funded with FY 1980 money. Meeting will be in NIH Bldg 31 Rm 4, starting at 9 a.m., and is open. . . . **KRESGE FOUNDATION** has awarded a $600,000 grant to Sidney Farber Cancer Institute for renovation of the institute's Jimmy Fund Research Laboratories. Total cost of the renovation is $5.4 million; NCI is helping with a $2.8 million construction grant. . . . **ABRAHAM CANTAROW**, former chief of NCI's Program Analysis & Formulation Branch who retired last April, died of cancer last month in Philadelphia. . . . **MARVIN SCHNEIDERMAN**, NCI associate director for science policy, has been elected vice president and president elect of the Washington Statistical Society. . . . **AMERICAN COLLEGE** of Toxicology has scheduled its first national meeting for Dec. 5-7 at the Sheraton Park Hotel in Washington. Sessions will be held on critical issues in toxicology and environmental health; aquatic toxicology; intervention epidemiology and epidemiological potential for active modification of occupational and environmental cancer risk; chemical carcinogenesis and the urinary bladder; scientific aspects of risk assessments; and social and legal aspects of regulation and benefit assessment. Session chairmen will be Congressman Andrew Maguire (D.-N.J.); John Cairns Jr., VPI; Irving Selikoff, Mt. Sinai School of Medicine; E. Cuyler Hammond, American Cancer Society; Bernard Wagner, Columbia Univ.; Gerald Wogan, MIT and a member of the National Cancer Advisory Board; and Norton Nelson, NYU Institute of Environmental Medicine. Contact M.A. Mehlman, Director of Toxicology, Mobil Oil Corp., P.O. Box 1026, Princeton, N.J. 08540.

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CALIFANO'S PANEL RECOMMENDATIONS RETURNED TO HEW SECRETARY HARRIS

(Continued from page 1)

A Nobel Prize winner and now the president of Rockefeller Univ., Lederberg has not been considered one of the Cancer Program's more ardent supporters. He was a member of the Yarborough Panel of Consultants for the Conquest of Cancer which developed recommendations that resulted in the National Cancer Act of 1971. Certain other members of that group recalled, after the report that then HEW Secretary Joseph Califano had recommended him as Schmidt's replacement, that Lederberg had not been very active on the Yarborough Panel.

However, Schmidt, who also was chairman of the Yarborough Panel, was not one of the Lederberg critics. He commented at the meeting last May of the National Cancer Advisory Board, "If the two individuals I have been told would be the new members of the Panel are in fact appointed by the President, I couldn't be more pleased. They are excellent choices."

Neither Schmidt nor anyone else in an official capacity would confirm for the record that Lederberg was the choice as Panel chairman, but privately it was accepted as fact by NCI executives. The identity of the other appointee, to fill the position left vacant when the term of Paul Marks expired, was not as clear. The most reliable information was that it would be William Shingleton, director of the Duke Univ. Comprehensive Cancer Center.

Despite the flap over Lederberg, it appeared two weeks ago that President Carter was ready to make the appointments, at least three months after Califano had submitted his recommendations and 20 months after Schmidt's term had expired. But then someone reportedly pointed out that these were the recommendations of Califano, now deposed and the object of considerable bitterness on the part of the White House aides. It was decided that new Secretary Patricia Harris should have something to say about it, so back they went to HEW.

A meeting of the Panel was scheduled for Oct. 15, when it seemed the new members would be on board. If the appointments have not been made by then, it will be rescheduled to November.

Meanwhile, NCI and the rest of HEW are faced with operating for a few days and even weeks into the 1980 fiscal year without any money.

Congress failed to provide interim appropriations for agencies still without regular appropriations legislation when the House recessed until Oct. 9 without resolving differences with the Senate over congressional, senior executive and federal judge pay increases. Those differences have stymied the continuing resolution that would have funded HEW and the others until the deadlock over abortion funding in the regular bill is broken.

If interim funding is not agreed upon promptly when the House returns, HEW and NCI employees could find themselves with reduced paychecks on the next payday, Oct. 16. This week's payday was not affected, since it covered a pay period entirely within the 1979 fiscal year.

NCI obligations for grants and contracts funded with 1979 money also will not be affected, and payments can be made on schedule. However, projects to be funded with FY 1980 appropriations will not receive any money until Congress acts. This probably will not create any hardship, since payments from new fiscal year funds normally are not required until at least two or three months into the year.

One immediate effect is that travel by NCI employees will be strictly limited until 1980 money is available. All travel requests must be approved by Executive Officer Calvin Baldwin.

Another immediate effect of the impasse is that federal senior executives, members of Congress, Cabinet members and federal judges received a 12.9% pay increase. For those executives who had bumped up against the $47,500 pay celing, the increase will put them up to $53,627. The raise came about because the law provides for automatic increases based on the cost of living, unless Congress specifically decides otherwise. The House and Senate had agreed that the raise should be held to 5.5%, but the Senate, piqued by the House' obstinance over the abortion issue, voted that the raise for House members could not go into effect until after the 1980 election. The House recessed in a rage without further action.

The raise most likely will be trimmed back, except that for the judges. The Constitution prohibits Congress from reducing the pay of a federal duge during his term, and they are appointed for life.

Others who received the big increase probably will collect it in full for the period from Oct. 1 until it is rescinded.

FOX CHASE, U. WASHINGTON, UCLA LAND NCI NEUTRON RADIOTHERAPY CONTRACTS

With a commitment of more than $40 million over 10 years, NCI has awarded contracts for development of clinically dedicated fast neutron radiotherapy facilities to Fox Chase Cancer Center, Univ. of Washington and UCLA.

The awards were made last week, just prior to the end of the 1979 fiscal year, permitting the projects to be started with 1979 funds. The projects are supported by the Div. of Cancer Treatment.

The Cancer Letter's previous information (Sept. 21) on identity of the successful competitors for one of the most sought after contracts in NCI's history was not entirely correct:

• One award was to the Univ. of Washington (not the Fred Hutchinson Cancer Research Center, as re-

ported), for $13,182,176 for 10 years.

• Another award was to the Fox Chase Cancer Center in Philadelphia (not the Univ. of Pennsylvania as reported), for $11,771,982 for 10 years. Fox Chase will make use of the DT generator developed by the Univ. of Pennsylvania with a grant from NCI.

UCLA received the biggest award, $15,348,891 for 10 years. UCLA and Washington will develop cyclotron facilities.

The awards include support for clinical trials, which probably will not start for at least five years.

Other contracts awarded last week included:

–Biospherics Inc., $3.3 million for three years to perform technical writing, publication distribution and telephone answering services for the Office of Cancer Communication. The firm will respond to written inquiries NCI receives from cancer patients, their families, physicians, and the public (NCI received 280,000 last year); handle the distribution of publications produced by OCC (from 150,000 in the 1975 fiscal year, the total grew to 15 million in 1979. This includes smoking literature, to the general public, and cancer site pamphlets, distributed through 50,000 physicians); and operate the toll free phones backing up the Cancer Information Service, going to all 50 states.

–Johns Hopkins Univ., $996,270 for three years to develop, field test and evaluate three health education protocols–smoking cessation education in urban family planning clinics; occupational health education in urban vocational education technical schools; and breast self examination for college women in urban settings.

NEW GOVERNMENT-WIDE POLICY FOR ACTION AGAINST CARCINOGENS SET BY COUNCIL

The White House Regulatory Council revealed last week what it called the "first government wide policy for controlling hazardous substances that may cause cancer." The policy's main points are:

• Animal tests are a valid method for determining whether a substance will cause cancer in people.

• Except in restricted circumstances, every proposal by an agency to control a carcinogen will be accompanied by some form of risk assessment including a determination of how many people are exposed to the cancer agent.

• In deciding which suspect compounds to tackle first, agencies should consider such things as the level of risk, whether populations of "special concern," such as children, are exposed, and whether regulatory action would reduce not only cancer threats but also other human or environmental hazards.

• Agencies should consider "zero risk" from carcinogens an appropriate goal where the economic and social costs would be slight, but that in other situations, zero risk may not be "routinely achievable."

• In planning cancer controls, agencies should identify and consider the least costly and least disruptive course of action.

The Regulatory Council, which is composed of representatives of 16 executive departments and agencies and 19 independent regulatory agencies, agreed at least in part with recommendations of the Toxic Substances Strategy Committee of the Council on Environmental Quality (***The Cancer Letter,*** Sept. 28). The Regulatory Council's policy, and the TSSC recommendations, are not final. Douglas Costle, administrator of the Environmental Protection Agency and chairman of the Regulatory Council, told reporters that comments and suggestions from the public would be accepted through the end of October. "We look forward to receiving comments and suggestions," Costle said, "although we do not expect to change the policy substantially."

The Regulatory Council thus declined to take the advice of one of its consultants, John Elliott, who wrote a report which challenged the assumption that cancer incidence can be decreased by improving regulatory action against chemical carcinogens (***The Cancer Letter,*** June 8). Elliott suggested that before the Council undertakes efforts to strengthen regulations against carcinogens, it should ask the National Academy of Sciences to undertake a study to determine the total incidence of cancer reasonably attributed to industrial chemicals.

The policy, which Costle said provides "a consistent, intellectual strand through all the regulatory agencies," is intended to be a "general framework" around which the individual agencies can develop their own specific detailed policies relating to carcinogens.

The policy is based to a large extent on a report by the Interagency Regulatory Liaison Group Working Group on Risk Assessment. The report is titled, "Scientific Bases for Identification of Potential Carcinogens and Estimation of Risks," published in the July 6, 1979, *Federal Register.* NCI's representatives on that group were Umberto Saffiotti, chief of the Laboratory of Experimental Pathology, and Marvin Schneiderman, associate director for science policy.

Costle said the policy "breaks some new ground in prescribing factors to be considered by regulatory agencies in deciding how best to control carcinogens." Although noting that environmental causes of cancer include tobacco, diet, alcohol, radiation and toxic chemicals, Costle said the policy is concerned only with chemicals.

"It ensures that agencies such as EPA, Dept. of Agriculture, Occupational Safety & Health Administration, Consumer Product Safety Commission and others will operate from the same scientific base in determining whether a compound is carcinogenic," Costle said. "It also ensures that, to the extent their respective laws allow, they will consider the same criteria in selecting a regulatory course of action."

The policy addressed four major areas of activity

related to the regulation of chemical carcinogens—determining whether a chemical may cause cancer; assessing the risk of cancer to humans; establishing regulatory priorities; and undertaking regulatory activities.

Excerpts from the policy statement on each of those four areas follow:

Determining whether a chemical substance may cause cancer

The first step in regulating a substance as a carcinogen is to examine and evaluate the evidence that it may cause or contribute to the occurrence of human cancer. The two principal sources of such evidence are epidemiological studies involving people exposed to the substance, and testing in laboratory animals.

It is important that the regulatory agencies make such evaluations in accordance with current scientific thinking and in a consistent manner. The IRLG document "Scientific Bases for Identification of Potential Carcinogens and Estimation of Risks" is a significant step in this direction. One portion of this document describes the basis for making qualitative evaluations of whether a particular substance presents a carcinogenic hazard, and how the results of epidemiological studies and animal testing, along with other types of information, are used in making these evaluations.

Regulatory agencies will base their determinations of whether a substance is likely to be carcinogenic upon a rigorous evaluation of all relevant, available scientific evidence. Epidemiological studies or animal tests provide the best evidence of carcinogenicity, but other types of information can also be important. Although they cannot be adequately summarized in a few sentences it is important that there be a general understanding of several basic concepts involved in these evaluations.

Epidemiological Studies

Properly designed and conducted epidemiological studies showing a significant statistical relationship between human exposure to a substance and an increased occurrence of cancer in the exposed population are considered to provide good evidence that the substance is carcinogenic.

In the past many people argued that such studies should be considered a prerequisite to undertaking any significant regulatory action. There are, however, limitations on the usefulness of epidemiology. Everyone is exposed to many chemicals in his or her lifetime. And cancer may not occur until 30 years or more after exposure to a carcinogen. Thus, there may be a substantial delay, allowing many additional people to be exposed, before any epidemiological evidence can be obtained. Even then, it may be very difficult to associate the occurrence of cancer with exposure to specific chemicals many years previously. Epidemiological studies often cannot detect even large increases (which could involve thousands of people) in the occurrence of cancer resulting from exposure to chemicals. For these reasons:

- The failure of an epidemiological study to detect an association between the occurrence of cancer and exposure to a specific substance should not be taken to indicate necessarily that the substance is not carcinogenic.
- Because it is unacceptable to allow exposure to potential carcinogens to continue until human cancer actually occurs, regulatory agencies should not wait for epidemiological evidence before taking action to limit human exposure to chemicals considered to be carcinogenic.

Testing in Animals

Properly designed and conducted tests in laboratory animals also provide good evidence of a substance's potential human carcinogenicity. From a biological standpoint the development of cancer is similar in humans and animals, even though different species and different strains of a species may demonstrate different sensitivities to specific substances. Because we cannot test substances in humans or wait for demonstrations of carcinogenicity from epidemiological studies, federal agencies must continue to use animal tests to identify chemical substances that may cause human cancer. In interpreting and applying the results of these tests they should use the following precepts unless there is substantial scientific or legal reason not to:

- A substance that causes cancer in animals, when tested under appropriate conditions, will be considered a potential human carcinogen.
- Animal tests provide valid information even though the dosage administered to the animals may be higher than humans are likely to experience. Animals are given relatively high doses both to increase the sensitivity of the test by maximizing the likelihood that a cancer-causing substance will actually produce cancer, and to compensate for the relatively small numbers of animals typically used in the tests. Although the likelihood of detecting a carcinogenic effect and the time between exposure to the carcinogen and the occurrence of cancer may be related to the dose level tested, the intrinsic ability of a substance to induce cancer is independent of dosage. A noncarcinogen can be toxic when administered in high doses, but it will not directly cause cancer at any dose level. In fact, the majority of chemicals tested in animals, even at high doses, has not been found to be carcinogenic.
- Evaluation of the results of animal testing is simplied when the animals are exposed by the same route by which people are or will be exposed, but the results are also relevant to human risks where exposure is by a different route. For instance, if a substance causes cancer when tested by ingestion, there is good reason to expect it to be able to cause cancer when inhaled.
- In evaluating results of animal tests, the occurrence of benign tumors in the treated animals is an indication that the substance being tested may produce malignant tumors as well. Benign tumors often are a precursor stage of malignant growths. Furthermore, virtually all extensively tested chemicals that have produced benign tumors have also produced malignant tumors.
- If a substance has been shown to be carcinogenic under the conditions of a single properly designed and conducted test, it should be considered as posing a risk of cancer to humans. Although the agencies should attempt to obtain additional data, they should not take the risk involved in waiting the two to four years required to complete an additional animal bioassay before initiating regulatory action.
- Evidence that a chemical is a carcinogen is strengthened by test results indicating carcinogenicity under two or more tests or test conditions (for example, at two or more dose levels, in both sexes, or in two or more animal strains or species). Similarly, evidence that a substance is not a carcinogen is strengthened if there is a lack of carcinogenic response in two or more properly designed and conducted tests.
- In cases where there are conflicting results from more than one properly designed and conducted test, results failing to demonstrate a carcinogenic response do not detract from the validity of results showing such a response if different

species of animals were tested, and they do not ordinarily detract from such results if the same species were tested. Even known carcinogens would be expected to show no response in some tests, particularly, for instance, when relatively few animals are involved, dose levels are low, or an insensitive animal strain is used.

Other Types of Evidence

In recent years there has been encouraging progress in developing certain short term screening tests (involving animals, mammalian cells, or microorganisms) and in using chemical structure to predict carcinogenic potential. Such approaches may provide a substantially faster and less expensive way of obtaining evidence on a substance's potential carcinogenicity. Such evidence, although currently only considered suggestive, can properly be used for the following purposes:

–To help identify chemicals that should be more thoroughly tested.

–To help in planning priorities for regulatory actions.

–To buttresss evaluations of the results of long term testing in animals.

–To support regulatory actions dealing with groups of substances having similar chemical or biological properties.

Testing Policy

Because long term testing in animals is so important in evaluating the cancer causing potential of chemical substances, and because such testing is time consuming and expensive and requires scientific expertise and specialized facilities, it is essential that it be performed as efficiently as possible. The current government policy on such testing is that:

• The primary responsibility for much of this testing, as specified in several federal laws, lies with the firms involved in manufacturing chemical substances. Agencies having the authority to do so should ensure that any required testing is carried out properly and as expeditiously as possible.

• The federal regulatory agencies specify the chemicals to be tested and the testing procedures to be used by industry, and ensure industry compliance with testing requirements. They also cooperate with the federal research agencies responsible for basic research on cancer causes and treatment, to support the development and validation of new testing procedures, and to perform testing (as well as epidemiological studies) in certain circumstances, for instance, where it is not practical to rely on industry to do so or where an agency is not authorized to impose such requirements on industry.

• Although a substance may sometimes need to be tested more than once to assess its potential carcinogenicity under differing conditions, regulatory agencies will avoid, whenever possible, imposing duplicative or conflicting testing requirements. The IRLG agencies are already preparing testing guidelines to accomplish this goal.

Assessing the risk of cancer to humans

After it has been determined that a chemical substance is likely to be carcinogenic, the next step in regulatory decision-making is to assess the risk that people face of developing cancer from their exposure to the substance.

Contents of Risk Assessments

All risk assessments contain two basic components. The first is an analysis of the evidence of the carcinogenicity of the substance, and the second is an analysis of the human exposure to the substance in order to assess the health risk it may pose.

The analysis of the carcinogenicity involves a determination of whether a substance is likely to cause cancer in humans, accompanied by a characterization of the extent and quality of the evidence supporting this determination. It may also include an analysis of the relationship between the observed carcinogenic effects and the dose levels used in animal tests or the apparent levels of exposure in epidemiological studies.

The analysis of human exposure involves at least an estimate of the size of the exposed population, and may also include such factors as exposure sources, routes, and conditions, the duration, frequency, and intensity of exposure, and the relevant characteristics (e.g., age, sex, health) of the exposed population. The agencies will use exposure measurements when they are available and reliable; otherwise, they should estimate exposure based upon reasonable assumptions and interpretations of the best data available, which may be limited to information on the manufacture, use, or environmental discharge/disposal of the chemical substance in question.

Although all risk assessments include these two basic components (analyzing the evidence of carcinogenicity and likely human exposure) the form, methodology, and elaborateness of the assessment may vary substantially. Depending upon the characteristics and extent of the available information and on the regulatory agency's specific needs, the range of approaches varies from quantitative estimates of the increased human risk of developing cancer to nonquantitative assessments of relevant epidemiological and/or testing data and evidence that people are likely to be exposed to the substance.

Risk Assessment Precepts:

When undertaking risk assessments, the regulatory agencies will follow the following precepts:

• Except where a statute, as in the case with the Clean Water Act, explicitly indicates which substances are to be controlled and how, every regulatory proposal will be accompanied by some form of risk assessment which includes, at a minimum, an analysis of the evidence of the substance's carcinogenicity and a determination that people are likely to be exposed to the substance.

• The particular form and type of risk assessment undertaken will depend upon the suitability of the available information to support different types of analyses, and upon the amount of information the agency needs to support proposed regulatory actions.

• Because there is no currently recognized method for determining a no-effect level for a carcinogen in an exposed population, substances identified as carcinogens will be considered capable of causing or contributing to the development of cancer even at the lowest doses of exposure.

Where the available data are scientifically adequate to support them, quantitative risk estimates can provide useful information for proposed regulatory decisions. When they make such estimates in initiating regulatory actions, the agencies will use the procedures described in the IRLG document "Scientific Bases for the Identification of Potential Carcinogens and Estimation of Risks."

However, quantitative risk estimates are not yet sufficiently developed to be regarded as more than rough indicators of the level of human risk. The sources of uncertainty include, for instance, the difficulties of extrapolating from one population group to another, from high doses to low doses, and from animals to man, and the impossibility of identifying or considering all the factors that affect the response of people to exposure from specific carcinogenic substances.

In certain instances, it is impractical or unnecessary to make quantitative exposure or risk estimates. This may be true when it is impossible to predict what exposure may

occur, in dealing with complex chemical mixtures of unknown or varying composition where it is not feasible to regulate each of the constituents independently, or when regulatory action is concerned with substances to which the population is exposed through a multitude of sources or products at different levels and in different ways.

If they undertake quantitative estimates of risk, agencies will attempt to identify the range of risk that could, on the basis of available information, reasonably be associated with possible exposure to the substance. Because underestimating cancer risks could have serious public health consequences, the agencies will in particular attempt to estimate the maximum risk that could reasonably be expected.

Because all risk assessments, whether quantitative or not, necessarily involve substantial degrees of uncertainty, they will be accompanied by statements discussing these uncertainties.

Setting priorities for regulating carcinogens

A substantial number of cancer causing chemicals has already been identified. As other chemicals are tested, some of them also are likely to be found capable of producing cancer. In deciding which ones to regulate first, federal agencies will generally assign higher priorities to substances for which:

- There is substantial evidence that the substance is likely to present a risk of human cancer. Epidemiological studies and/or animal testing are sources of such evidence.
- There is reason to believe that the level of human exposure and/or risk is high. Either quantitative or nonquantitative risk assessments may provide a basis for such belief.
- The exposed population is large or is of special concern, such as children.
- Regulatory action could significantly reduce the extent of intensity of human exposure.
- Regulatory action could reduce not only cancer risk but also other human health and environmental hazards.
- Substitute is, or could be, available that would pose a lower risk of cancer or other serious human health problems, or available evidence otherwise suggests that the social and economic costs of regulation would be small.

The relative importance of these priority setting criteria will necessarily vary from case to case, and in establishing their final priorities the agencies also consider:

—The requirements of applicable laws or court orders which may limit their flexibility to establish their own priorities.

—Their responsibilities for dealing with other health and environmental hazards.

—The regulatory actions being taken or planned by other agencies.

Although the agencies will continue to coordinate their regulatory actions, each agency will establish its own regulatory priorities. Specific substances usually are not equally important from the standpoint of every agency's statutory mission. As an example, one substance may provide a serious risk to workers, but very little in consumer products. Another, however, might provide a serious risk in consumer products, but present little risk to workers. The most effective public health protection would occur if the agency concerned with protecting workers gives the former a higher priority and the agency concerned with protecting consumers gives the latter a higher priority.

In general, the regulatory programs will provide the most public health protection if each agency dealing with a specific area of exposure places the highest priority on the substance which provides the greatest health risk in its area of concern. Otherwise, agencies might be regulating substances which are of relatively little importance in their area of concern, creating unnecessary regulations and costs, with little public health benefit, and putting off actions which would provide much more benefit. For these reasons, it is neither necessary nor desirable that all agencies assign the same priority to each substance.

Considering regulatory action

Federal laws governing the regulatory programs often prescribe the factors to be considered in choosing among regulatory options and deciding how extensive and stringent regulatory action should be. In many instances, however, regulatory agencies have latitude to interpret and apply the statutory language.

Bases for Regulatory Action

In brief, regulatory decisions generally are based upon one or some combination of the following approaches:

Risk: A few statutes require agencies, when making a regulatory decision, to consider solely or primarily the risk a substance poses. If a statute requires the elimination of risk, this can be accomplished only by eliminating human exposure, because there is no known way to identify levels below which exposure to cancer causing substances presents no risk.

Technical and Economic Feasibility: Various federal laws require that regulatory decisions be based solely or primarily upon the technical and/or economic feasibility of controlling the release of or human exposure to cancer causing substances. The stringency sought in such feasibility based standards is stated in the applicable law—for example, "best available technology." The statute's language determines how an agency chooses among technologies capable of reducing environmental releases of (or human exposure to) chemical substances, and whether and how it considers associated economic and other impacts in making this choice. In some instances the technological standard is also determined by requirements to achieve certain ambient exposure levels.

Comparing Costs and Benefits: Various statutes permit or sometimes require regulatory agencies to ensure that the economic and social costs of regulatory action are taken into account along with the expected risk reduction. Such statutes may refer to consideration of either the costs and benefits of regulatory action or the risks a substance poses and the benefits it provides.

In some statutes, Congress, after considering the advantages and disadvantages of these different approaches, has specified that one of them be used. For instance, Congress enacted a section of the Food, Drug & Cosmetic Act that requires the Food & Drug Administration to prohibit the use of any food additive found to be carcinogenic which presumably reflected a judgment that, among other considerations, the seriousness of the risk posed by carcinogenic food additives would exceed the benefits they provide and the costs associated with not using them; while a statute enacted to regulate pesticides indicates that the agency must take into account "the economic, social, and environmental costs and benefits" associated with the pesticides' use.

The fact that cancer causing substances enter the environment and come into contact with people by various routes means that no single regulatory approach is equally suitable for dealing with cancer causing substances in media as different as foods, drugs, household products, workplaces, air, and drinking water. Accordingly, it is, and will continue to be, necessary for federal regulatory agencies to make appropriate

use of different regulatory approaches when making regulatory decisions.

Regulatory Principles

The agencies nevertheless will follow several common regulatory principles. These principles will ordinarily guide the agencies in initiating regulatory actions, but they will not be rigidly and uniformly applied in all cases.

- In some cases, zero risk will be an appropriate regulatory goal. It is established as such in a few national policies and statutes. It is also an appropriate goal where (e.g,, in controlling specific commercial products or specific types of discharges) the economic and social costs of regulation are so slight that almost any risk would be unreasonable. This might be the case, for instance, when there are several available substitutes for the substance being regulated which are no more costly than that substance and which create no known health risks.
- Zero risk will not routinely be considered achievable. For carcinogens, existing scientific knowledge indicates that zero risk requires zero exposure. But cancer causing substances often occur in so many different consumer products, industrial raw materials, and commercial and industrial wastes that completely eliminating exposure, even if possible to do so, could, in many cases, have unacceptable economic, social and even health impacts.
- When planning a major regulatory action, in keeping with Executive Order 12044 and other Administration regulatory reform initiatives, agencies will analyze the economic consequences of proposed regulations, will identify and consider alternatives that would achieve their health protection goals, and, to the extent consistent with applicable laws, will choose the alternative that achieves their goals with the least economic and social costs.
- In limiting a substance's use, it is sometimes appropriate to consider other products or processes which might be adopted as a substitute for the substance being regulated. In these cases, one of the factors the agencies will consider, to the extent practicable, in making their regulatory decision is the health hazards associated with such substitutes.
- To avoid conflict and duplication, if several agencies are planning to adopt regulations controlling a specific substance or problem, they will coordinate the development of their regulations. The IRLG and the Regulatory Council have already adopted mechanisms to promote such coodination.

Further Actions

Agencies responsible for regulating carcinogens have and will continue to identify and evaluate ways of improving their regulatory programs. Among other possibilities, they have considered or will consider, when appropriate, adopting generic policies for regulating carcinogens. Some are also evaluating the advantages and disadvantages of taking interim regulatory action to reduce high exposures to cancer causing chemicals before they undertake the usually time-consuming task of establishing permanent standards and regulations.

In general, the agencies should continue their efforts to develop carcinogen regulatory programs which will effectively protect public health without imposing unnecessary or unreasonable burdens upon the economy. In this process they should ensure that their actions are consistent and coordinated, and that the public has substantial opportunity to contribute.

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COUNCIL'S PROPOSAL "NOT SCIENTIFICALLY BASED POLICY," INDUSTRY GROUP SAYS

The response of industry to the Regulatory Council's proposals was one of skepticism. The American Industrial Health Council, an industry supported organization, said that the Council's cancer policy "is a recitation of what government agencies have been doing and is not the scientifically based national cancer policy the nation needs."

Ronald Lang, AIHC executive director, said, "We're disappointed. . . . We've been calling for a comprehensive, scientifically sound national cancer policy since 1977. But this isn't it."

A statement released by AIHC said:

"AIHC scientists have pointed out that cancer prevention policies based on magnified risks inevitably generate magnified expenditures for dealing with such risks. Too often this draws down resources that should be applied against major causes of cancer.

"Internationally renowned scientists have supported this view. Philip Handler, president of the National Academy of Sciences, recently put it this way: 'We should lay to rest the idea that it is these man-made compounds, abroad in the land, that are responsible for the fact that 25% of Americans die of cancer. They are not. The possible effects of all known man-made chemicals, when totalled, could contribute only a miniscule fraction of the total of all carcinogenesis in our population.'

"AIHC finds these aspects of the Regulatory Council's cancer policy to be scientifically questionable:

"Failure to endorse scientific risk assessment to its full extent, and the acceptance of the now outmoded concept of zero risk.

"Excessive reliance on animal tests and inadequate weight for human experience and epidemiological studies.

"Misapplication of important toxicological principles such as dose-response relationships and overload of metabolic pathways.

"Overstatement of the case for animal carcinogens being human carcinogens."

Lang said that "the Regulatory Council has also apparently ignored AIHC's often stated suggestion that a substance's carcinogenicity and risk should be determined by a panel of independent scientists chosen by a prestigious scientific organization such as the National Academy of Sciences. However, we are encouraged that the Council is recommending that regulations include some risk assessment and the consideration of economic and social effects of banning or restricting a substance. That's progress."

NCI CONTRACT AWARDS

Title: Breast Cancer Detection Demonstration Project, extensions

Contractors: Vanderbilt Univ., 18-month extension, $278,413; Univ. of Louisville, six-month phaseout, $78,286; and Rhode Island Hospital, one year renewal, $233,876.

Title: Clinical Oncology Program, continuations
Contractors: Methodist Hospital of Indiana, $286,000; and Butterworth Hospital, Grand Rapids, Mich., $264,977.

Title: Prototype comprehensive network demonstration project in head and neck cancer, 11-month renewal
Contractor: Roswell Park, $133,514.

Title: Eight additional alteration/renovation/maintenance/upgrading projects at Frederick Cancer Research Center
Contractor: Litton Bionetics, $730,692.

Title: Model system for screening agents against spontaneous murine mammary cancer, modification
Contractor: Catholic Medical Center of Brooklyn and Queens, $224,999.

Title: Antigens of human lymphoid organs: Immunodiagnosis of leukemias and lymphomas, continuation
Contractor: Univ. of Minnesota (Minneapolis), $66,022.

Title: Case control study of carcinoma of endometrium, continuation
Contractor: Boston Univ. Medical Center, $31,335.

Title: Studies on the molecular biology of oncornaviral proteins, continuation
Contractor: Johns Hopkins Univ., $495,140.

Title: EPA/NCI special skin cancer epidemiological study, continuation
Contractor: Westat Inc., Rockville, $48,851.

Title: Special projects in hereditary cutaneous melanoma
Contractor: Univ. of Pennsylvania, $98,000.

Title: Rescue of human "src" genes and identification of related tumor antigens, continuation
Contractor: Univ. of Southern California, $167,757.

Title: Wild mouse studies, continuation
Contractor: Univ. of Southern California, $447,236.

Title: Facility to provide and maintain non-human primates for cancer research, continuation
Contractor: Litton Bionetics, $28,476.

Title: Computer support services for the national nonmelanoma skin cancer study
Contractor: Triton Corp., Washington D.C., $79,997.

Title: Induction and control of MuMTV expression in mouse mammary preneoplastic tissues
Contractor: Baylor College of Medicine, $499,474.

Title: Develop effective methods for modifying smoking behavior in special at-risk groups
Contractors: Univ. of Houston, $670,776; and Johns Hopkins Univ., $984,717.

Title: Evaluation of the effectiveness of cancer education
Contractor: American Assn. for Cancer Education, Rochester, N.Y. $199,996.

Title: National Cancer Program management information system support services
Contractor: System Sciences Inc., $499,679.

Title: Approaches to cancer patient management: A synopsis of the network program experiences (breast cancer)
Contractor: Rand Corp., $362,851.

Title: Identification of effective cancer control promotion approaches directed to the general public
Contractor: Univ. of Denver, $104,588.

Title: Comprehensive cancer centers communications network
Contractor: Univ. of Alabama, $517,142.

Title: Data management and analysis center for Breast Cancer Detection Demonstration Project followup
Contractor: University City Science Center, Philadelphia, $3,036,776.

Title: Prototype comprehensive network demonstration project in head and neck cancer, 11-month renewal
Contractor: Illinois Cancer Council, $413,947.

Title: Immunodiagnostic markers for breast carcinoma, continuation
Contractor: Emory Univ., $160,134.

Title: Preparation of antisera to oncogenic or potentially oncogenic viruses, continuation
Contractor: Huntingdon Research Center, Brooklandville, Md., $48,000.

Title: Cytogenetic evaluation of high risk cancer, continuation
Contractor: Biotech Research Laboratories, $84,339.

Title: Definition of epidemiologic characteristics of pre- and post-menopausal breast cancer, continuation
Contractor: Duke Univ., $110,000.

Title: Cytotoxic activity of syngeneic complement, continuation
Contractor: Stanford Univ., $90,000.

The Cancer Letter _Editor Jerry D. Boyd
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