Yearly Report on Carcinogens Could Be a Potent Weapon in the War on Cancer

Regulatory performance will be evaluated

Mobilization of the science of environmental carcinogenesis to support and accelerate federal regulatory efforts in the "war on cancer" is receiving a major new push from two significant but little-noticed actions taken last fall by Congress and Secretary Joseph A. Califano, Jr., of the Department of Health, Education, and Welfare (HEW).

The first occurred in October when the 95th Congress, shortly before final adjournment, amended the National Cancer Act by requiring that HEW issue a report each year on carcinogens. This new mandate, if carried out to the letter, could turn out to be a sleeper worthy, perhaps, of comparison to the National Environmental Policy Act (NEPA) of 1969, a measure whose importance at first went unrecognized by both the public and most members of Congress despite the NEPA requirement for environmental impact statements.

Besides containing a list of subtances known or suspected to be carcinogenic, the new report is to include information on the nature and extent of human exposure to those substances. The report is also to show which carcinogens are being regulated and which are not and to evaluate the effectiveness of regulation in terms of the extent to which exposures have been reduced.

The other action, very much in keeping with the congressional requirement for a yearly report on carcinogens but coming independently of it, took place in November when Secretary Califano announced the establishment of a National Toxicology Program (NTP). This program represents an effort to improve and step up the pace of research, detection, and control activities with respect to toxic substances of all kinds, carcinogenic and noncarcinogenic; it involves pooling resources from the four relevant HEW agencies—the National Cancer Institute (NCI), the National Institute of Environmental Health Sciences (NIEHS), the National Institute of Occupational Safety and Health (NIOSH), and the Food and Drug Administration (FDA). These agencies are putting $41 million in resources into the NTP the first year; NCI is contributing more than half that amount, or $21.8 million, all of it representing money which had already been budgeted for testing carcinogens.

The initial plan of operation for the NTP is being prepared by the program director, David P. Rall, head of the NIEHS. The plan is to take effect in March, subject to the review by the NTP executive committee and the approval of HEW's assistant secretary for health, Julius B. Richmond. It will contain test schedules for specific compounds, identify the appropriate testing methods, and set forth projects for test development and validation.

The plan for the first full year, which is due in September, will be especially significant in that it will recommend what additional resources are called for in light of scientific and regulatory needs. Identifying these needs is the job of the executive committee which is chaired by the FDA commissioner, Donald Kennedy, and includes representatives of three major regulatory agencies outside of HEW, namely the Environmental Protection Agency (EPA), the Occupational Health and Safety Administration (OSHA), and the Consumer Product Safety Commission (CPSC). The NTP's Board of Scientific Counselors, to be made up of nongovernment scientists appointed by Secretary Califano, will aid the executive committee in this task.

Arthur C. Upton, director of NCI, is proposing, with the concurrence of Rall and Kennedy, that the NTP prepare the annual report on carcinogens which Congress has called upon HEW to produce. This yearly exercise could in turn have a major bearing on the NTP's own priorities. "This [the report] will constitute one of the drives that will make the NTP effective," Upton told *Science*.

The report could in fact generate powerful political pressures that would be felt by all of the parties caught up in the war on cancer, including the chemical and other companies that manufacture or use suspect substances, the regulatory agencies, the HEW scientific agencies, and Congress itself. Certainly Representative Andrew Maguire (D-N.J.), the principal sponsor of last year's cancer act amendments, means for the report to be a compelling document.

Speaking to NCI's National Cancer Advisory Board (NCAB) on 17 January at Upton's invitation, Maguire said that passage of the amendments—which mandate a generally increased emphasis on programs for preventing cancer from occupational or environmental causes—"reflected a feeling in Congress that [NCI] has tended to neglect the original concern of Congress with achieving, as rapidly as possible, some beneficial impact on public health." As Maguire later explained to *Science*, the annual report and the exercise of preparing it can serve as a device for enabling the scientific agencies such as NCI and NIEHS and the regulatory agencies such as EPA and OSHA "to knit their knowledge and efforts more closely."

"The regulatory agencies are likely now to have the benefit of the first systematic evaluation of the universe of substances, and be better able to put their work in [an overall] context and not just act on a case by case basis," he said. "It should help them set priorities with the best scientific knowledge available as their baseline. What the NCI gets is a real world baseline to work back from."

> Few carcinogens have been regulated, and for those few, the reduction in exposure has often been patchy.

The first of the annual reports, due before the end of 1979, will necessarily show a large discrepancy in the number of substances known or suspected to be carcinogenic in animals and the number that have been regulated to eliminate or reduce human exposures. Federal agencies have issued regulations intended to stop or reduce exposure to about 26 carcinogenic substances. But

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some evidence of carcinogenicity has been found for about 400 chemicals, with about 30 to 35 (including asbestos, drugs such as DES, and chemicals in tobacco smoke) established as carcinogenic in humans. Actually, the number of carcinogens may be much larger than these figures suggest, for there are more than 30,000 chemicals already used commercially, with an additional 700 new ones being introduced every year.

Moreover, a thoroughgoing evaluation of those regulatory actions that have been taken will show that some of them have been quite limited or patchy in reducing exposure. For instance, while the manufacture and sale of polychlorinated biphenyls (PCB's) have now been banned, there is no comprehensive national program under way to recover the 750 million pounds currently in use.

Preparation of the annual report promises to be a big, if not daunting, job. The NTP executive committee has not yet decided how the various parts of the job should be distributed among the HEW agencies. But the task of making up the

Congress Seeks New Approach to Arms Control

A congressional report has recommended that the Arms Control and Disarmament Agency (ACDA) pay more attention to the problems posed by "aggregates" of developments in research and technology and to the dynamic, as well as the static, bean-counting aspects of the U.S.-Soviet arms race.

ACDA could make a more provocative contribution to future arms policy debates if it grouped certain R & D items and weapons programs together in evaluating their potential to upset the U.S.-Soviet balance, says the report. It assesses the agency's compliance with a 1975 law requiring that it submit annual arms control impact statements on weapons systems. The report was prepared by the Congressional Research Service for the subcommittee on international security and scientific affairs of the House International Relations Committee, headed by Representative Clement J. Zablocki (D-Wis.). The report also praised the impact statements ACDA submitted on fiscal 1979 weapons programs, contrasting them favorably with previous submissions by the Nixon and Ford Administrations.

Principally, the report offered its own provocative examples of aggregations of little-noted developments that could be destabilizing. These include developments in ballistic missile defense research, strategic air defense, and the growing accuracy of intercontinental ballistic missiles, each of which could adversely affect arms control. The idea was to show the arms control agency how such aggregate analyses might be done in complying with future requirements for impact statements.

But the most novel chapter in the report was a rare public look at the destabilizing impact of the United States' growing ability to detect Soviet submarines by antisubmarine warfare (ASW) methods.

The inability of either side to find, track, and simultaneously destroy the other side's force of ballistic missile-armed submarines, or SSBN's, has been a major contributor to stability. The report says the U.S. SSBN force remains secure because "today and in the near future the Soviets apparently have no effective capability for open ocean ASW."

But the Soviets can no longer be certain that the United States does not have the capability to find Soviet SSBN's. The $5 billion annual U.S. research effort in ASW computer technology, in improving sensors, and in signal processing could be "perceived" by the Soviets as giving the United States the ability to detect strategic submarines in the closed water areas and choke points where they must operate—near Greenland and Iceland for example. Several separate developments could add to this perception: the placement of the advanced Proteus data processor aboard the U.S. land-based PC-3 ASW aircraft, deployment of thousands of acoustically guided Captor mines moored to the ocean floor, retrofit of modern digital sonar processing equipment on older U.S. submarines, and improvements to the Navy's SOSUS network of underwater listening posts. SOSUS, in addition to protecting the U.S. coastline, can detect "every" submarine that leaves the Soviet port of Murmansk, north of Iceland, according to the report.

Finally, the Navy's program to build, by 1983, 32 of the quieter, faster, 688-class attack submarines, of which only a few are now at sea, could be perceived by the Soviets as a major escalation of the U.S. ASW threat.

The negative arms control impact of these incremental improvements is worsened, the report says, by "ambiguities" in U.S. ASW policy and by technical limitations on the ability of commanders to communicate with their forces. Since U.S. policy is to keep the deterrent secure, the United States does not officially want to aquire the ability to find, track, and destroy Soviet SSBN's. On the other hand, the Navy actively seeks the ability to find, track, and destroy Soviet conventional submarines. Since, from a technological point of view, the two capabilities are quite similar, the Soviet Union might well perceive the advancing U.S. "tactical" ASW capability as an improved capability against its SSBN's and hence a threat to the strategic balance.

As dangerous as the policy implications of improved U.S. ASW are the operational mistakes that could take place. The report quotes a former director of Navy ASW, Dan Murphy, as saying that the United States "would not be in a position of differentiating their attack submarines from their SSBN's" in a conventional warfare situation. Thus, U.S. commanders under orders to attack ordinary Soviet submarines could attack a Soviet SSBN in a battle "about which higher authorities could not be quickly informed."

"The United States has acquired a considerable ASW capability involving a threat to Soviet SSBN's (even if the capability is a by-product of other missions) without benefit of official public awareness of the fact or its implications," the report concludes. Arms control measures to constrain this threat to stability "are not comprehensively evaluated in the open literature," and are not being discussed in the current strategic arms limitation talks. Thus, the report tries to drive home to the Executive Branch that in anticipating future arms control problems, something more than weapon-by-weapon analysis is required.

—DEBORAH SHAPLEY

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list of known and suspected carcinogens will inevitably fall to NCI, whereas FDA, NIOSH, and NIEHS will play the head roles with respect to assembling the exposure information and evaluating the effectiveness of regulation.

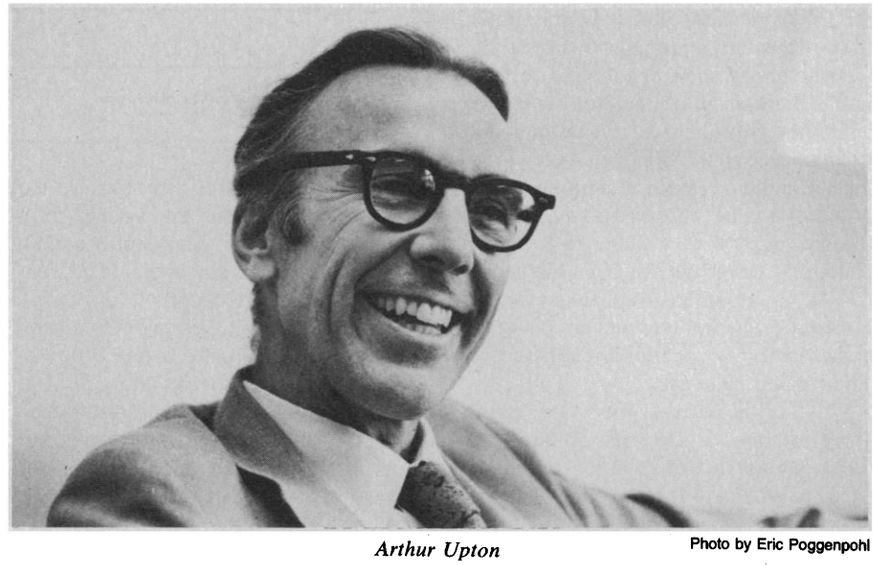
In preparing a complete list of carcinogens relevant for regulatory purposes, NCI will, as the NCAB is uncomfortably aware, be stepping beyond its customary role. Bioassays done by NCI on selected chemicals have been critically important to the regulatory agencies all along, but now NCI will be deciding, as an agency, which chemicals are carcinogenic and which (to cite the language of the act) "may reasonably be anticipated to be carcinogens." As Maguire frankly told the NCAB, NCI's judgments will provoke criticism and controversy, but this cannot be helped if the agency is to give the regulators effective support.

There is even potential for sharp disagreement within the NCAB itself over the list-making, especially now that the regulatory agencies are (as a result of last year's Maguire amendments) represented on the board. While attending the recent NCAB meeting, Maguire witnessed just the kind of interaction between scientist and regulator that his amendments were intended to foster.

The EPA representative present observed that his agency had decided at least tentatively that "promoters" (substances that are cancer enhancing agents rather than causative agents) should, for regulatory purposes, be treated as carcinogens. At this, Philippe Shubik, director of the Eppley Institute for Research in Cancer at the University of Nebraska and one of the board members most troubled by what he terms "the plunge into list making," spoke up. "It is a terrible idea," he said, for, in his view, as he later told *Science*, the distinction between carcinogens and promoters should be preserved even for regulatory purposes because the establishment of tolerances for promoters may be possible.

(In Upton's view, as expressed last April at a regulatory hearing, knowledge of cancer causation is so incomplete that distinctions between "causative agents" and "enhancing agents," cannot be considered relevant in ascertaining cancer hazards.)

The NCI will be affected in still another way by the requirement for the annual report on carcinogens and the creation of the NTP. Some part of the effort devoted to basic cellular research on cancer will probably have to be given up so that a greater effort can go into reducing the bioassay program's formidable backlog of suspect but untested or inadequately tested compounds. Maguire thinks that such a refocusing of priorities is necessary, and so does Upton, who says that it is already under way, as indicated by the fact that the funding for the NCI's big program in viral ontology is not being increased despite inflation.



Arthur Upton Photo by Eric Poggenpohl

Of all the information required for the annual report on carcinogens, data that will have to do with the nature and extent of exposures is expected to be far and away the most difficult to get. Maguire talks of it as largely a matter of assembling, from various regulatory agencies and other sources, information already available. In fact, however, such information is often simply not available, and what there is of it often consists of model studies built on uncertain data.

Take, for instance, the problem of estimating the extent of human exposure to the ethylene dibromide (EDB)—a known carcinogen in animals—used in leaded gasoline. With the current popularity of self-service pumps at gasoline stations, exposure to this chemical is presumed to have been increasing, but by how much? There are questions about how much EDB is actually used; the effectiveness of vapor recovery devices and the extent to which they are used; how much people actually use self-service pumps; and on and on. A recent study for EPA concluded that some 30 million people are exposed to gasoline vapors containing EDB at self-service pumps, but it was conceded that this estimate might be grossly in error.

In a political and bureaucratic sense the most delicate—and, in the view of some at NCI, the least desirable—task involved in preparing the carcinogen report is that of evaluating the effectiveness of regulations. Originally, Maguire proposed that NCI be responsible for the entire report, but in deference to Upton's wishes, the Secretary of HEW was given this overall responsibility.

Representative Andrew Maguire

What had bothered Upton was the posibility that NCI's role as a provider of objective scientific information to the regulatory agencies might be badly compromised if the institute also had to act as their evaluator and overseer. The job of evaluator will in all likelihood go to either NIEHS or to NIOSH, for if NCI is not an appropriate choice, neither is FDA because of its own major regulatory responsibilities.

Maguire says that he does not expect the report to contain a lot of "second guessing" or criticism of regulatory actions already taken. In his view, as in Upton's, the evaluation of regulatory performance will have to do principally with carcinogens not yet regulated.

But Joseph Highland, a scientist with

the Environmental Defense Fund, hopes to see close attention paid to substances already under some regulation, lest the public not recognize half measures for what they are. The lack of a national program to recover PCB's from the environment Highland regards as a prime case in point. Also, he observes that, whereas the use of Tris as a flame retardant in children's sleepwear has been banned by CPSC, no action has been taken by OSHA to see whether workers are being put at hazard by occupational exposures to Tris-treated materials.

Whether the annual report turns out to be a spur to more effective regulatory action and much better scientific support of such action may depend on how much effort HEW and its scientific agencies put into preparing it. Officials such as Upton, Rall, and Kennedy seem clearly in sympathy with Maguire's aims. The NTP was, after all, in the works for many months before the cancer act amendments became law; it came about, in fact, as the result of a proposal made to Secretary Califano by Upton soon after he took over as NCI director in mid-1977. Now Upton wants the data-gathering for the report to be supported generously, with perhaps $500,000 or more spent even in this first year's effort—which, for lack of time, will have to consist mainly of assembling bioassay data and other information that is already close to hand.

The positive official climate in which the requirement for the annual report on carcinogens has been received is one that Congressman Maguire is in a good position to foster and reinforce. Coming from a heavily industrialized area in northern New Jersey that figures prominently on NCI's cancer map, Maguire has made cancer prevention and research a major focus of his activities during his first two terms in the House. Although not trained in science, he holds a Ph.D. in government from Harvard and discusses issues of science policy with a sophistication that has impressed the members of the NCAB.

Moreover, as an influential member of the House Health and Environment Subcommittee, Maguire can either reward or chastise the HEW agencies, as in supporting or taking issue with the balance struck by NCI between cancer prevention programs and basic cellular research (which, incidentally, Maguire says deserves continued support). If the report on carcinogens should fall short of expectations, he has the resourcefulness to express his disappointment in a way the people who run those agencies will understand.—LUTHER J. CARTER

Laetrile's Day in Court

The Laetrile furor has reached the Supreme Court at last, framed as a contest between personal freedom and government authority. On 22 January the Court accepted a petition from the Justice Department to rule on whether or not the Food and Drug Administration (FDA) has the power to ban the interstate sale and distribution of Laetrile, the apricot pit extract used as a cancer cure and regarded by most of the medical establishment as a fraud (*Science*, 13 October 1978).

This case grows out of a suit filed by Glen Rutherford, a cancer patient in Oklahoma, who charged that the FDA was interfering with his personal rights in banning the interstate shipment of a drug which could do him no harm and which he wanted to use. He won a partial victory in a local district court in Oklahoma in 1977 and a second victory last July in a federal appeals court in Denver, where the case landed after the government tried to have the earlier decision reversed. The judges in the appeals court found that the FDA had virtually no authority to control drugs sought by terminally ill cancer patients. If this interpretation is allowed to stand, the FDA believes, it would create a large loophole. As the government put it in the Supreme Court petition, the decision "would make it difficult if not impossible for the [FDA] Commissioner to discharge his statutory responsibility to keep unproven drugs out of the marketplace."

The appeals court arrived at its decision by playing with definitions, as follows. The judges reasoned that the FDA by law must base its policies on a drug's safety and effectiveness. By definition, a terminal cancer patient is someone for whom there are no effective drugs. "Therefore, we hold as a matter of law," the court ruled, "that the 'safety' and 'effectiveness' requirements of the statute as now written have no application to terminally ill cancer patients who desire to take the drug." The judges thought it would be easy to resolve the absurd situation they created. A physician would simply certify the patient to be "terminally ill with cancer," putting him in a special legal category for which the FDA law does not apply. The physician would then be allowed to administer Laetrile intravenously. The court did not approve of Laetrile tablets.

There is no scientific evidence that Laetrile helps cancer patients, and there is some thin evidence that it may do harm, especially when taken orally. Doctors at the Massachusetts General Hospital, for example, recently testified that a child named Chad Green showed signs of cyanide poisoning as a result of oral Laetrile treatments given him by his parents. (In January a local court in Massachusetts ordered the parents to stop using the drug; the parents took their child and left the country.) It is also argued that Laetrile, if widely available, could act as a dangerous placebo, causing people to postpone seeking other therapies that are known to be efficacious.

Despite its bad press, Laetrile has many devotees. Between 50,000 and 75,000 people are said to have used it in the United States. A Harris poll taken in 1977 found that about two-thirds of those surveyed favored the enactment of pro-Laetrile laws in their state. The Supreme Court can hardly ignore the political passions in this controversy. Americans are stubborn about rights, including the right to induce cancer with cigarettes and the right to treat it with the extract of apricot pits.

Meteorites and Nuclear Power

The Nuclear Regulatory Commission (NRC) created a dilemma on 19 January when it endorsed a critique of a study of the hazards posed by nuclear reactors, a study whose findings were accepted by the commission in 1975. Although it accepted the critique, the NRC did not flatly repudiate the earlier study.

The first study, headed by Norman Rasmussen, a nuclear engineer at the Massachusetts Institute of Technology, concluded that the likelihood of a major nuclear accident occurring in the United States was roughly equal to the likelihood that a disaster might be caused by a meteorite falling to the earth. It might happen once every million years. The second report, written by University of California physicist Harold Lewis and six others,

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