National Cancer Plan: The Wheel and the Issues Go Round

The national cancer plan may soon be released; then again, it may not. The people at the National Cancer Institute (NCI) who are in charge of such things say that they would like to make the plan public as soon as possible. There are two problems.

The first seems to be that the people at NCI are not really in charge at all. People in the Office of Management and Budget (OMB) and in the White House are. Strictly speaking, the National Cancer Program Plan is a document the NCI submits to the President, who will then transmit it to Congress. The word is that certain OMB staff members are unhappy about parts of the first two volumes of the cancer plan and their unhappiness is forcing a delay. This is hard to prove one way or the other because OMB people will not talk about such things. However, it is certain that, without their approval, the NCI cannot make its plan public. When the OMB and the White House are ready, they will release it.

The second problem in getting the cancer plan into the open, so that the entire scientific community can see for itself what the cancer crusade is all about, is that the third volume is not exactly finished yet. This is the volume that NCI leaders say is the most important because it will tell how the cancer program is going to be run, not just this year, but for the next 5—a 5-year plan to be updated every year. Louis Carrese, associate director of NCI for program planning and analysis, describes the third volume as an "operating document, perhaps a manual." It will be completed soon, but that does not mean that it will be available to the public soon. It, like volumes 1 and 2, will have to wend its way through channels.

The cancer plan is a unique document in biomedical science, in that it is a tangible expression of this country's first attempt to wipe out a disease through a coordinated effort on a national scale. The sheer magnitude of the program for the conquest of cancer is unprecedented in biology.

The national crusade against cancer is grounded in the belief that cancer is susceptible to an organized attack. This presumption troubles many scientists today, as it has from the beginning. Their conviction that there is a lot of science that just cannot be targeted simply will not go away. The expectation that the cancer crusade would be backed by virtually unlimited money is also proving to be a troublesome presumption. Although it is perfectly true that there is more money for cancer research than for any other kind, it is apparently not true that the coffers of the NCI are overflowing.

As of this writing, the NCI is still operating with $378 million—its budget level for fiscal 1972. There is talk of a special presidential action to raise the level for 1973 to $432 million, as originally planned, but it has not happened yet. Meanwhile, of course, those anticipated extra funds are not available.

Thus, the situation is not an entirely happy one. The story of the cancer plan is, in ways, a reflection of the ups and downs within the national cancer program as a whole.

Plan Is for Everybody

In a recent interview with *Science*, Carrese talked about the plan. Whom is it for? For everybody. The plan, he says, is supposed to be "meaningful" to the lay public, the Congress, the scientific community, and the people in the OMB. At its heart is a single goal—"Develop the means to reduce the incidence, morbidity, and mortality of cancer in humans." To achieve it, the NCI has laid out seven objectives, which "reflect the aspects of the disease in man." The first is cancer prevention; the seventh is rehabilitation of the cancer patient. The others range from basic research to therapy. To achieve each objective, there is a series of "approaches"; for the approaches, a set of "approach elements," and, to refine the task further, a host of "project areas." It is at the level of a project area that actual research comes in.

Carrese emphasizes again and again that one of the most extraordinary features of the plan is its authorship. Out of a pool of 1000 scientists, the NCI asked about 250 to meet in small groups to decide what the cancer plan should say. From meetings held at Airlie House, a retreat in the Virginia countryside, they generated 40 reports, each of which talked about cancer from a different angle. From these, Carrese and his staff, with the advice of the chairmen of the various groups, put the plan together.

The first steps for the creation of a national cancer plan were taken in the fall of 1970 by Carrese and Carl Baker, who was then the director of NCI. Groups of scientists first began meeting in the late fall of 1971, so by the time the National Cancer Act of 1971 became law that December, the foundations of the master plan had already been laid. (The law required that there be a plan, as Carrese and Baker anticipated.)

Carrese is adamant about the flexibility of the cancer plan. "Its purpose is not to direct daily research; nor is it meant to exclude new ideas." Nevertheless, a lot of the people who have had access to the plan or who have heard a lot about it are pretty uneasy. Certainly one reason for this is that the plan, to a large extent, is written in the jargon of a systems analyst.

Carrese is a systems analyst who has made a career of trying to adapt the traditional concepts of systems analysis to the process of biomedical research. He and Baker shared the view that systems analysis could be appropriately modified, and, in the April 1967 issue of *Management Science* they described their approach in a paper entitled, "The Convergence Technique: A Method for the Planning and Programming of Research Efforts." "Planning," Carrese says, "is not strange to science. Some of the most detailed plans are called experimental designs. I don't know a single scientist who arrives at his lab not knowing what he is doing."

According to Carrese, the cancer plan not only lays out the scientific and medical problems to be solved but does so in a way that allows administrators to know at a glance what is going on. He points out that the plan is designed to have "something for everybody" and that what you see in it depends upon how you look at it. In that regard, he says that he can look at it and tell in dollars and square feet of space how

much effort is being committed to research on cancer prevention, causation, or rehabilitation.

To make the whole thing graphically clear, the plan has been drawn up in the form of a wheel that sets out the objectives and approaches of the cancer program. It hangs on the wall in dozens of laboratories and offices throughout the National Institutes of Health (NIH) and, depending upon the wall, is meant to be taken quite seriously, or, alternatively, as pop art.

The systems analysis approach, so foreign to most scientists, bothers many of them, and there is growing concern that the emphasis on supporting only those things that fit into the cancer *program* will lead to unhealthy rigidity. NCI officials, of course, insist such fears are foolish.

One "official" reaction to the first two volumes of the cancer plan comes from a committee of the Institute of Medicine, a part of the National Academy of Sciences. (The NCI asked the institute to review the plan last summer.)

Under the chairmanship of Lewis Thomas, who has recently resigned as dean of medicine at Yale to become president of the Memorial Sloan-Kettering Cancer Center in New York, a committee of nine* spent most of their fall weekends conducting the review in order to meet a crash deadline of 1 December. They read and reread the plan, admitting that the systems analysis jargon made the going rough in spots. (Carrese says most of that jargon was deleted from the final draft.) They interviewed many of the principals involved in the creation and execution of the plan. And they looked at the 40 reports from which the plan was synthesized. Then they summed up their feelings about it all in a succinct, 23-page report, which, like the cancer plan itself, remains officially a confidential document, although numerous copies are in existence.

By prior agreement with the NCI, the institute will not release its critique until the plan itself is unveiled. Many members of the review committee concede that they are not particularly happy about the necessity for such confidentiality this long after the review's completion.

On first reading, the institute's review sounds rather innocuous. It is written in language that is neither abrasive nor laudatory, and it sounds in places as if its authors are merely politely asking questions that they are sure can be answered. A second or third look can leave one with the impression that the reviewers' opinion of the plan, and of what it represents, is scarcely as neutral as it first seemed.

In their introduction they say, "We are impressed by the skill with which the plan has succeeded in organizing, conceptually, a stupendous mass of biomedical scientific material, even though we have reservations concerning the framework within which the study was conducted and the material organized." The framework, of course, is one which assumes that research can be effectively programmed on a massive scale. Throughout their review, the authors explicitly or implicitly question this.

They find the plan "reasonably sound" as an inventory of the problems of cancer, an "assurance that nothing falls between the cracks." Carrese points out, in this regard, that the identification of rehabilitation of cancer patients as a primary objective emerged as a result of the comprehensive planning. Rehabilitation has not received much attention in the past.

On the other hand, some of the members of the review committee worried that the systems analysis approach might "represent the underlying philosophy of the whole program." Carrese wants to know why that prospect should worry anyone.

The reviewers addressed themselves to the issue of centralization of planning of research and felt uncomfortable with their impression that there is going to be too much of it.

> It seems to us a defect of the NCPP [cancer plan] that the enormity of our ignorance about cancer receives less emphasis than it merits. Much is said about the lines of research that appear most promising today—virology, cellular immunology, and genetics, for example—but too little acknowledgment is made of the genuine possibility that any or all of today's leads, including all of those proposed by the 250 scientists in the Airlie House Conference, could turn out to be the wrong leads.

The plan fails, they said, because:

> It leaves the impression that all shots can be called from a central headquarters; that all, or nearly all, of the really important ideas are already in hand, and that given the right kind of administration and organization, the hard problems can be solved. It fails to allow for the surprises which must surely lie ahead if we are really going to gain an understanding of cancer.

They went so far as to propose that certain areas of basic research are, per se, relevant to cancer and should, therefore, be funded by the NCI whether the investigators doing the work consider themselves cancer researchers or not. Their choices: DNA replication, the cell cycle, regulation of transcription, regulation of membrane assembly and function, cell differentiation, regulation of protein synthesis, and all aspects of cellular immunity. They indicated they would be perfectly happy to see them changed as cancer biology progresses.

The institute review committee then tried to soften its criticism by saying these defects in the plan may be merely a matter of language, not one of intent on the part of the cancer planners. But they are not very convincing. Their concern with targeted research is pervasive and it is significant because, whether the planners intend centralization and rigidity or not, vast numbers of scientists—young and not so young—*believe* that this is the effect the plan will have. That in itself is stifling.

One of the primary sources of discontent among "cancer" scientists in both clinical and fundamental research is the feeling that they have surrendered control of the direction of science to the administrators of the NCI. The verbal protestations of those administrators notwithstanding, many members of the scientific community share the impression that the important decisions about what to fund and at what level are being made almost exclusively by content among "cancer" scientists in NCI officials whose interpretation of what is suitably part of the cancer program and what is not does not square with their own.

The authors of the Institute of Medicine's review based their concern about an excess of planning on their reading of the cancer plan. To some extent, their concerns were validated recently at a meeting of the advisory committee of the NCI's "molecular control" program, which could be one of the principal channels for funding basic research in the cancer crusade. Issues raised at that meeting are likely to come up again and again as the cancer program takes shape. The molecular control program, new to the NCI table of organization, is headed by Timothy

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* Lewis Thomas, Yale; David Baltimore, Massachusetts Institute of Technology; Harry Eagle, Albert Einstein College of Medicine; Herman Eisen, Washington University; Judah Folkman, Harvard; Paul Marks, Columbia University; Rufus Miles, Washington, D.C.; George Palade, Rockefeller University; Helen Ranney, State University of New York at Buffalo; Alvin Weinberg, Oak Ridge National Laboratories.

O'Connor, a virologist by training, who is respected as one of the most scientifically sophisticated administrators in the institute. O'Connor, visibly enthusiastic about his program, is particularly anxious that it foster interdisciplinary research. The advisory committee includes a couple other NCI staff members and several university scientists. Their job is to define the goals of the molecular control program, take a hand in implementing them, and to offer an opinion on whether specific contracts (or possibly grants) should be approved. Such recommendations then go to the NCI brass for final action.

From the outset, it was apparent that some of the university scientists did not fully understand how the NCI operates; nor did they fully agree with some of the premises of the NCI program once they got them straight.

When the meeting opened, O'Connor informed the group of four contracts that had won final clearance. The conversation quickly turned to policy when Christian B. Anfinsen, who shared the 1973 Nobel prize in chemistry, asked about how contracts originate. Do they just come from the "stratosphere" for approval, or can the committee initiate things, he queried.

O'Connor said that the ideas for contracts are often generated by investigators themselves at the annual NCI meeting for contractors. Saul Schepartz added to the answer, saying, "Every once in a while you might get a really good proposal that is unsolicited [by NCI], but then you have to ask whether it fits our program." Anfinsen found the answer "disappointing."

Briefing

Two Academies at Parting of Ways?

The strained relationship between the National Academy of Sciences (NAS) and the National Academy of Engineering (NAE) is apparently at the breaking point. At its 16 March meeting the NAE's governing council reportedly decided that differences between the two academies could not be reconciled and separation was in order. Unless a last minute reversal occurs, the matter is expected to be put to the membership of NAE at the organization's annual meeting in early May.

Neither NAS president Philip B. Handler nor NAE president Clarence H. Linder would comment on the current state of negotiations. On 12 March, however, the NAS announced the first major steps toward reorganization of the National Research Council (NRC), the operating arm through which the two academies provide advice to government. The action was taken unilaterally by NAS and this was taken as at least an indirect sign that the NAS-NAE talks were foundering.

The long-running negotiations between the two academies had focused on governance. The NAE, which was created in 1964 under the NAS charter as a "parallel" organization, has felt that it has never achieved parity. Control of the National Research Council has been regarded by the NAE as a main issue in the dispute.

NAS officials note that the NRC reorganization was designed "in the hope" that the reshaped NRC could eventually be guided by a joint governing board of the two academies but the hope now seems very slim.

The aim of the announced reorganization of NRC is to replace the NRC's traditional divisions, organized along disciplinary lines, with a structure better suited to dealing with problems that require multidisciplinary action. The reorganization will begin with the establishment of an Assembly of Behavioral and Social Sciences and a Commission on Natural Resources. The new assembly and commission are prototypes of the main components of the new structure given general approval at the NAS meeting last year.

In effect, the activities of the NRC's existing divisions will be distributed between assemblies and commissions which will also take on additional functions. According to a description issued by the NAS:

"The principal concerns of each Assembly will be the welfare of its component disciplines and their contribution to national life; the Assemblies will also serve as sources of both manpower and ideas for the Commissions. Additional Assemblies in the Life Sciences and in the Physical Sciences and Mathematics will deal with programs and studies within those scholarly fields. The Executive Committee of each Assembly will be drawn largely from among the membership of the Academy.

"Activities in broad national problem areas—which by their nature will involve disciplines in both the natural and social sciences, as well as engineering—will be the concern of the Commissions. Those yet to be established will deal with human resources, peace and national security, international scientific affairs, and technologies in large, complex social systems—for example, in the areas of transportation, communication, and urban development. The membership of each Commission, then, will be multidisciplinary in character and again will be drawn largely from the membership of NAS and NRC."

Academy officials expect the basic reorganization to be completed by the end of the year.

A lot of details remain to be worked out. The assemblies are not only expected to provide the commissions with names of members, but also to review reports of projects. Assemblies will not be tied to particular commissions, and the commissions are not subordinate to the assemblies. Most of the contract work now done by the divisions will be taken on by the commissions, but assemblies will also take on projects which fall within their disciplinary boundaries and interests. The commissions will be expected to go considerably further than did the divisions in planning their own programs and in undertaking projects they feel they ought to do as well as those they are requested to do.

In designating the first assembly and commission, the academy seems to have picked two of the more manageable and logical components. The new assembly closely matches the Behavioral Sciences Division it supplants, and the Commission on Natural Resources comfortably accommodates NRC's work on the environment. Other decisions on fitting functions into new forms are expected to be a lot more difficult.

As for the NAS-NAE relationship, if the divorce goes through, there is little uncertainty about who gets custody of NRC.—J.W.

The meeting moved on. The committee set about defining the goals of the molecular control program and, after some discussion, agreed on four, roughly as follows: (i) membrane processes, including structure and membrane interactions with various agents; (ii) replication, integration, and transcription of genetic material; (iii) mechanisms by which messenger RNA is processed and by which it translates the information coded in DNA; and (iv) integration of biophysics into research on all of the above.

The goals won general acceptance as being broad enough to encompass a considerable variety of research, but they were not accepted without reservation. Anfinsen asked, somewhat rhetorically, "Our four goals essentially all say the same thing—control of protein synthesis [is important]. Might we be missing something?" The question passed, but other knotty questions arose as the discussion progressed to the ways of implementing research on the goals.

It seems safe to draw the conclusion that the non-NCI scientists present shared O'Connor's conviction that the program must be interdisciplinary. Britton Chance of the University of Pennsylvania pressed the cause of biophysics and had no trouble winning his colleagues to his view. William Joklik of Duke University was firm in his belief that the fields of protein synthesis and membrane biology and related areas could probably benefit from the help of some good organic chemists. He mentioned the problems that nucleic acid workers are having in getting an iodine tag on the RNA molecule without breaking it and postulated that an organic chemist might have the solution. That sounded sensible. (Years ago, it was an organic chemist who helped James Watson and Francis Crick work out the structure of DNA.) There was a suggestion that one thing to do would be to let the entire scientific community in on the idea of soliciting organic chemists by publishing, in some conspicuous place, the fact that the cancer program was open to the contributions that organic chemists might make.

That did not go over as well. One of the NCI administrators warned that the result of such a general announcement would merely be a flood of grant applications, many of them from "nuts," and that the NCI is swamped with applications as it is. Furthermore, there is the matter of limited funds. A proposal to organize small conferences to which a few investigators from fields not traditionally connected with cancer would be invited won greater acceptance from the NCI people. Some of the committee members just could not shake the feeling that NCI wants to call the shots, relying less on the advice of outside people than ever.

Relevant Research Only

The other issue that pervaded the discussion was the matter of relevant versus irrelevant research. Is there such a thing as good membrane research that is relevant to the cancer program and good membrane research that is not? Such a question seemed to some to be marginally out of place at a meeting devoted almost entirely to very fundamental research problems, but the question was very much there nevertheless. O'Connor mentioned several times that the overriding aim of the molecular control program is to use appropriate research findings to develop new, rational approaches to the design of drugs for eventual use at the bedside. O'Connor expressed it simply: "Good science for its own sake, no matter how beautiful it is, will not get funded. Good research that may lead to cancer control will." (After the meeting, O'Connor reiterated his position. The idea is to translate—through deliberate effort—basic discoveries into something practical—namely, a drug. To this end, he hopes scientists can learn to see how their work can be used in ways they might not otherwise have considered. "The end of a good experiment has to be more than just the publication of a paper that sits on a shelf," he said.)

Again Anfinsen, who by his own admission was not happy with the framework he felt he'd been forced into, spoke up. "The nub is that we can tell good science that is relevant from good science that is not. I don't think I can."

In a sense, there are two issues here and, in one regard, less discord than appears on the surface. Certainly, one is the issue of relevant research and the extent to which anybody can be sure what that is. Underneath that is the issue of money and the ways the NCI as a whole chooses to allocate it. Anfinsen is talking about principles. O'Connor is trying to get the most sophisticated science he can for a comparatively meager amount of money. The molecular control program, which, no matter what its limitations, is considered by many cancer workers to be one of the more promising of the NCI programs, has an indefinite budget. So far, it has allocated about $1 million.

If one puts that beside the budget for the traditional NCI drug screening program—as both clinicians and basic researchers do—one raises a question that has come up before but which many people still think needs answering. Under the category of cancer treatment, the drug sceening program has $23,900,000 or 46 percent of that category's total budget. Anfinsen, who was not buying much of anything the day of the molecular control program meeting, spoke to the issue with regard to a contract the molecular control program itself has given out.

The program, with the approval of its advisory board, has awarded Litton Industries a $301,000 contract to screen anticancer drugs and antiviral agents. Anfinsen suggested that, if the "silver bullet" approach to curing cancer is to be pursued under the heading of molecular control, it might be wise to award the same contract to two groups to see if competition would lead to a better idea. "Screening has been going on at NCI for a long time and not much has come of it," he said. "It is like trying to get to Mars by building a more powerful moon rocket. It's not very imaginative." O'Connor defends this drug screen as being different from the rest. It will only look at compounds carefully selected as potential anticancer drugs on the basis of their molecular structure. It will not be a random screen and will limit itself to about 800 compounds a year. (The existing screen-program, which uses an animal system to identify promising agents, tests almost 40,000 compounds a year.)

The advocates of the existing drug screening program, can, of course, point to the present arsenal of anticancer drugs as vindication of their efforts—and they have a case. But the questions being raised address themselves to matters of proportion—priorities, if you will—and in this there is still no resolution. The NCI administrators have the upper hand, or, at least, the scientific community thinks they do. And it has no tangible evidence that it is misreading the situation. It may just be a matter of approach—the two "sides" may not really be hopelessly far apart—but it is hard to believe much significant progress will be made until these issues are set straight.—BARBARA J. CULLITON