National Institutes of Health

National Cancer Institute

NATIONAL CANCER ADVISORY BOARD

Minutes of Meeting
October 5-7, 1981
Building 31
Conference Room 6
NIH Campus
Bethesda, Maryland

Department of Health and Human Services
Public Health Service
National Institutes of Health
National Cancer Advisory Board

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October 5-7, 1981

The National Cancer Advisory Board was convened for its 39th regular meeting at 8:30 a.m., October 5, 1981, in Conference Room 6, Building 31C, National Institutes of Health, Bethesda, Maryland. Dr. Henry C. Pitot, Chairman, presided.

Board Members Present

Dr. Amos
Dr. Henderson
Dr. Hickey
Dr. Katterhagen
Mrs. Kushner
Dr. Leffall
Dr. Pitot
Dr. Powers
Dr. Rowley
Mr. Samuels
Mr. Schrier
Dr. Seitz
Dr. Shubik
Dr. Wogan

Board Members Absent

Dr. Ames
Ann Landers
Mrs. Lombardi
Dr. Selikoff

Ex Officio Members

Dr. Victor Alexander, LABOR
Dr. Ken Bridbord, NIOSH
Dr. Allen Heim, FDA
Dr. F. Kash Mostofi, DOD
Dr. Denis J. Prager, OSTP
Dr. Peter Preuss, CPSC
Dr. John Todhunter, EPA
Dr. David P. Rall, NIEHS**

Representatives of the President's Cancer Panel

Dr. Amos
Dr. Fisher
Dr. Hammer

Liason Represetatives

Dr. Virgil Loeb, Jr., Professor of Clinical Medicine, Washington University, St. Louis, Missouri, representing the American Association for Cancer Research and the American Society of Clinical Oncology, Inc.

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* For the record, it is noted that members absented themselves from the meeting when discussing applications: (a) from their respective institutions, or (b) in which conflict of interest might occur. This procedure does not apply to "en bloc" actions.

** 2/3/82 -- Dr. Rall's name added to the attendance list. His name was not included originally.

Liaison Representatives (continued)

Dr. Martin Minthorn, representing Dr. Charles W. Edington, Acting Director, Office of Health and Environmental Research, Department of Energy, Washington, D.C.

Dr. Edwin A. Mirand, Associate Institute Director of Administration, Roswell Park Memorial Institute, Buffalo, New York, representing the American Association of Cancer Instititutes.

Dr. Stanley Order, Director of Radiation Oncology, Johns Hopkins University, Baltimore, Maryland, representing the American Society of Therapeutic Radiologists.

Dr. John F. Potter, Director, Lombardi Cancer Center, Georgetown University, Washington, D.C., representing the Society of Oncology, Inc., and the American College of Surgeons.

Members, Executive Committee, National Cancer Institute

Dr. Vincent T. DeVita, Director, National Cancer Institute
Dr. Richard Adamson, Acting Director, Division of Cancer Cause and Prevention
Mr. Philip D. Amoruso, Executive Officer, NCI
Mrs. Barbara Bynum, Director, Division of Extramural Activities
Mr. Louis Carrese, Associate Director for Program Planning and Analysis, OD
Dr. Bruce Chabner, Director, Division of Cancer Treatment
Dr. Jane Henney, Acting Director, Division of Resources, Centers, and Community Activities
Dr. Bayard Morrison III, Assistant Director, NCI
Dr. Gregory O'Conor, Associate Director, Office of International Affairs, OD
Dr. Alan S. Rabson, Director, Division of Cancer Biology and Diagnosis
Dr. Richard A. Tjalma, Assistant Director, NCI
Mr. Paul Van Nevel, Associate Director for Cancer Communications

In addition to staff, participants, and invited guests, 16 registered members of the public attended this meeting.

I. Call to Order and Opening Remarks - Dr. Henry C. Pitot

Dr. Pitot called the meeting to order and welcomed members of the Board and members of the President's Cancer Panel, liaison representatives, guests, and observers. He also introduced Dr. Ken Bridbord, Director of the Office of Extramural Coordination and Special Projects, NIOSH, who represents Dr. Donald Millar, Director of NIOSH.

Dr. Pitot welcomed members of the public and announced that anyone wishing to express views regarding items discussed during the open session could do so by submitting written statements to the Executive Secretary of the Board within ten days after the meeting. Any statement by members of the public will receive careful consideration.

After briefly reviewing the procedure for the conduct of Board meetings, Dr. Pitot asked Board members to review the minutes of the February meeting; the minutes were approved without changes. The Board also confirmed meeting dates of October 4-6, 1982, and November 29-December 1, 1982. Dr. Pitot then introduced the new chairman of the President's Cancer Panel, Dr. Armand Hammer. A physician who received his training at Columbia University, Dr. Hammer is Chairman of the Board of Occidental Petroleum Corporation and Chairman of the Salk Institute Executive Committee. Dr. Hammer is well known for his philanthropy in promoting research and education; he has endowed the Armand Hammer Cancer Center, the Salk Institute, and the Julia and Armand Hammer Health and Science Center at Columbia in addition to his support of the Eleanor Roosevelt Cancer Foundation.

II. Remarks by Dr. Armand Hammer, Chairman, President's Cancer Panel

Dr. Hammer thanked members of the Board for their warm welcome and indicated that he had long shared Board members' interest in finding a cure for cancer. He stated that his first duty as Chairman will be to enter into discussions with Board members to develop an action plan for the President's Cancer Panel. Dr. Hammer emphasized the need for improved communication between doctors and scientists, and stated that he plans to devote part of his time as President's Cancer Panel Chairman to soliciting cancer research funds from the private sector.

III. Report of the Director, National Cancer Institute - Dr. Vincent T. DeVita, Jr.

Staff Appointments. Dr. DeVita announced the appointment of several new staff members: Mrs. Barbara Bynum, Director, Division of Extramural Activities, who was formerly Chief of the Special Review Section, Division of Research Grants at NIH; Dr. Peter Greenwald, Director, Division of Resources, Centers, and Community Activities, and Editor-in-Chief of the Journal of the National Cancer Institute; Dr. Peter Fischinger, Associate Director, Office of the Director, who will direct the operation of the Frederick Cancer Research Center; and Dr. Bruce Chabner, Acting Director, Division of Cancer Treatment.

NCI is still under a hiring freeze; however, exceptions to the freeze were allowed for departments having patient-related duties and for senior appointments.

Dr. DeVita noted and expressed regret over the death of Dr. Herbert Rapp, Chief of the Immunology Branch of the Division of Cancer Biology and Diagnosis, on September 25, 1981.

Budget. Dr. DeVita gave a report on the status of both the 1981 and 1982 budgets. Approximately $989 million is obligated for 1981, and funds were purposely lapsed to cover disbursement of indirect costs for programs in previous years.

The President's 1982 budget was almost $1.026 billion; the Senate has allowed a budget of slightly over $1.034 billion while the House has allowed just over $1.030 billion. The National Cancer Institute's NCAB bypass budget called for $1.147 billion, excluding National Toxicology Program funds of $49.9 million. This program has been transferred to the National Institute of Environmental Health Sciences.

Dr. DeVita announced that grant funds available for FY 1981 were greater than had been expected. The R01 grant pool has received the recommended funding down to a priority score of 197, and program project grants were funded down to scores of 207. Although we started the year funding 7 percent more competing program project grants than in the previous year, we were able to end the year funding about double that or 14 percent above the previous year's number, but, in some cases, in amounts that were 50-70 percent of the recommended level. Thirty-four percent of approved applications in the research project pool (R01s and P01s) have been funded. NCI has been able to fund center grants fully down to priority scores of 198, with scores between 199 and 231 receiving varying amounts of money.

In the National Research Service Award Program (NRSA), funds were provided to pay for indirect costs as well as institutional allowances. NRSA funds for 1981 came mainly from two areas. Congress decided to restore amounts of money required to pay indirect costs and institutional allowances, and funds were redirected from other portions of the Institute into the grants program. Over the last two years, redirected funds have exceeded $40 million.

Congressional budget proposals will allow about a 4½ percent increase over the previous year's budget. Although this is not a tremendous amount, the added funds plus the flexibility to redirect funds from division to division should provide opportunities to proceed with new initiatives. However, since the President has proposed across-the-board cuts for all agencies, NCI is now preparing alternate budgets to reflect various levels of funding.

If the current congressional budget passes, funds will be provided in several areas. First, additional money would allow NIH to move closer to its goal of funding 5,000 competing research grants; NCI's share of these funds would be about $1.6 million. Cost-of-living factors for competing research projects will allow coverage of increases in cost due to inflation. The budget also provides for money for the Research Service Awards to allow for restoration of indirect costs and a portion of institutional allowances. Until Congress and the President reach an agreement and pass the budget, NIH is operating under a continuing resolution at the 1981 level of funding.

The bypass budget was submitted to OMB in September and reflected priorities identified by the Subcommittee on Planning and Budget. If the Institutes are asked to make further reductions in budgets for 1982, it may be necessary to ask members to participate in discussing various options at the November NCAB meeting.

Organization. Secretary Schweiker approved the transfer of the Bioassay Program from NCI to NIEHS as of October 1, 1981. This transfer resulted in a reduction in NCI's budget of approximately $50 million.

The Radiation Research Program developed in the Division of Cancer Treatment now has three components (a low-level radiation branch, a diagnostic imaging branch, and a radiotherapy development branch), all of which have been moved into the Office of the Director of DCT. NIGMS authorized a transfer of $4.3 million spread over 29 grants in the area of diagnostic imaging research.

Other organizational changes included the initiation of several new efforts to study chemical carcinogenesis: Dr. Curtis C. Harris is Chief of the Laboratory of Human Carcinogenesis; Dr. Jerry Rice is Chief of the Laboratory of Comparative Carcinogenesis; and Dr. Stuart Aaronson is Chief of the Laboratory of Cellular Carcinogenesis and Tumor Promotion. To increase the emphasis on and exploit interest in the field of molecular biology and recombinant DNA technology, the Laboratory of Molecular Oncology was created and is under the direction of Dr. George Vande Woude.

Legislative Issues. The Senate Investigations and General Oversight Subcommittee chaired by Senator Paula Hawkins met on May 21, 1981, to receive a progress report on the Institute. Dr. DeVita declined to elaborate since a discussion of the meeting was already on the agenda. He mentioned, however, that, at Senator Hawkins' request, an advisory committee headed by Dr. Charles Moertel had been organized to set up plans for a hospital oncology program to encourage communication between practicing physicians and clinical research teams.

Hearings before the Senate Committee on Labor and Human Resources, chaired by Senator Orrin Hatch, focused on contracting processes and monitoring of grantees. Intense press coverage of these hearings centered on allegations concerning a grantee, Dr. Mark Straus, and actions taken in the matter. Dr. DeVita said that details would be dealt with in the closed session, but volunteered his opinion that the Institute had made a mistake in its handling of the affair in 1978. He pointed out that since then, however, a different system for handling these cases has been developed.

The National Toxicology Program was evaluated in a meeting of the House Subcommittee on Investigations and Oversight, chaired by Representative Albert Gore. This meeting coincided with the Secretary's approval of the transfer of the program from NCI to NIEHS.

Dr. DeVita mentioned some bills pending in Congress that may influence the NCI budget. One is a bill establishing a small business set-aside for R&D funds. While the bill may have some advantages, it would be procedurally difficult to administer and may necessitate NIH setting up its own small business and contract

review function. If the present peer review system rejects small business contracts, the funds that are not spent on small business will revert to the Treasury. Another bill, H.R. 4022, introduced by Congressman Toby Moffett, relates to NCI contracting procedures. This bill is similar to the one introduced by Congressman Henry Waxman over a year ago that would have made the NCAB responsible for all contracts over an amount of $500,000. The current NCI policy, which requires review of all contract-proposed projects at the concept level by the Divisional Boards of Scientific Counselors, should have settled this issue, but apparently the wording in the proposed bill is causing some legal difficulties.

Frederick Cancer Research Facility. This contract expires in September 1982 and, after site visits by the Board and the Divisional Board, a decision was made to recompete the contract research portion with a 29 percent reduction in expenses. To ensure brisk competition, the contract has been separated into five parts: operation of the portion of the contract that supports the research; the research itself; animal production; computer services and library services, the latter two of which are small business set-asides. Since a number of companies have pointed out the lack of flexibility in continuing to operate a research program organized by NCI with no options for changes, the RFP was revised to allow bidders to make suggestions for alternatives.

Retirements. Dr. Bernard Fisher, a member of the President's Cancer Panel, is completing his term of office. The terms of six members of the NCAB will expire in March 1982. Nominations for new members can be submitted to the Office of the Director, directly to the President, or to Secretary Schweiker. Two of the positions being vacated must be filled by "laypersons." Of the four scientists leaving the Board, three are specialists in environmental carcinogenesis.

Intramural Program. The Department has introduced a review of the Intramural Program, including reviews of its funding, position, and orientation. A position review to examine every position in the Institute and reallocate ceilings across divisions to meet pressing requirements has been introduced. Positions must be filled in new programs in the DEA; staffing is required for the Radiation Research Program, the Biologic Program, the Chemoprevention Program, and the Hospital Oncology Program, and others.

Cooperative Agreements. Board members received a draft cooperative agreement chronology. DCT is in the process of converting its clinical trials program to a cooperative agreement arrangement. Several points were emphasized: first, cooperative agreements are grants, not contracts, and thus require the review and approval of the NCAB; and second, there is no intention of using the cooperative agreement for any other grant that now exists. The history of the cooperative agreement was briefly reviewed and Board members were reminded that this mechanism is basically a grant that requires substantial involvement on the part of the government.

In May 1981, the Board approved a cooperative agreement package that required the conversion to grants of clinical cooperative groups then under contract. In June 1981, the Assistant Secretary for Health approved use of the cooperative agreement mechanism for research trials. Although members of cooperative groups are still debating the language of the cooperative agreement document, most have already signed the document.

Dr. Pitot urged that pertinent members of the cooperative groups receive a copy of the draft chronology. All group members have been asked to sign the agreement by November 1; those concerned with the language of the document have been assured that the required changes will be made. The groups can wait until the current funding year ends before converting to the cooperative agreement arrangement, and at that point R10 grants will cease to exist and groups will have to sign for U01 cooperative agreements. The cooperative agreement will provide two essential features: it will spell out NCI staff obligations and cover NCI in terms of ongoing investigations by FDA and other agencies. In addition, groups will have access to funds to support protocols up to 100 patients per study without having NCI approval of the protocol. Beyond that, NCI will have the option of disapproving protocols that are duplicates of existing protocols.

An objection was voiced that members of cooperative groups had not been given an opportunity to express their viewpoints before the Board. Cooperative groups may be more concerned about NCI control of their groups rather than the abolishment of cooperative groups.

It was explained that no single NCI staff member could possibly direct some 600 different protocols. The whole process has been drawn out over three years, every step debated publicly, and everyone had an opportunity to express their viewpoints in the appropriate places. Dr. DeVita admitted that some cooperative groups had initially expressed concern over the cooperative agreements. However, the majority of people consulted agreed that under the circumstances this mechanism was appropriate. It would be a waste of staff time and effort to go back and renegotiate because some groups are having second thoughts. At any rate, some of the people who had expressed concern have now changed their minds, and anxiety over the whole matter has died down with no further difficulty expected.

Dr. William Powers asked whether an investigator refusing to sign the cooperative agreement would be funded. The answer was that a decision would have to be made, depending on circumstances, at the time the investigator's funding ran out. It is possible that a few investigators would not be funded, but it was felt that objections raised by two or three individuals should not offset something that has been discussed and agreed to by hundreds of individuals.

Dr. Powers had heard the opinion that the majority were forced into agreement by threat of cancelling funding. Dr. Amos agreed that the matter had been discussed repeatedly and that it was necessary to take the approach most beneficial to the majority. Dr. DeVita offered to take responsibility for the fact that there was no formal way for people to present opposing viewpoints to the Board; and that this was not required, since it does not involve converting grants into contracts. Many people who objected to converting grants to cooperative agreements were very enthusiastic about converting contracts to cooperative agreements.

The cooperative agreement could have an impact on NIH. There is concern that almost all NIH clinical trials, which are now conducted by contract, will be forced to convert to cooperative agreements. Dr. Fisher feels that clinical trials should be conducted by contract; however, he believes that cooperative agreements will overcome a number of difficulties and there is no real reason for not going ahead with them.

Press Coverage. NCI was to be covered on ABC's "20-20" in October, which was not expected to be a favorable review of the cancer program. The Washington Post also was carrying a negative series dealing with the chemotherapy program. It is believed that this was based on people's beliefs that the program increases the risks of the subjects. Concern was expressed over the series, since it was not believed it would be balanced by a report of the advances being made in the program.

National Toxicology Program. Since $50 million had been transferred and lost along with the National Toxicology Program (NTP), one committee member was concerned as to why no effort was being made to regain at least a portion of these funds and was told that some effort probably will be made. The history of the NTP, including the decision to transfer it out of NCI, was reviewed. In light of the current budget difficulties, there was some discussion of whether the NCAB would have voted to transfer the program if it were being done now. Since NCI has provided such a large portion of the Program's funding, the Chairman requested that the Board be kept up to date on the NTP's actions and progress. A suggestion was made that a report might be given at the November review.

IV. Report on the DCT Toxicology Studies - Dr. Bruce Chabner

Dr. Chabner reviewed the role of the NCI in the discovery and development of new anticancer drugs. He pointed out that developing antitumor drugs is not financially rewarding; the NCI has been the major force in this process for the last 25-30 years.

Animal toxicology, which involves studying the effects of potentially active antitumor agents in animals prior to testing them in man, is an important step in the development of drugs and has two primary objectives. The first, and most important, objective is the establishment of a safe starting dose in man; the second is the study of the pattern of specific tissue toxicity.

Dr. Michael Loeb, Acting Chief of the Toxicology Branch, discussed the development of toxicology protocols at NCI over the past 10 years and addressed the issue of changes now being proposed in toxicologic testing of new drugs.

Dr. Loeb reviewed the role of toxicology in the drug development process, explaining that when the program acquires a new compound, it is evaluated for its antitumor efficacy. If the compound proves to have experimental anticancer activity, it is tested toxicologically. Finally, an investigational new drug application (called an INDA) is filed with the FDA. When the FDA approves the drug, human trials may be initiated.

Toxicology studies are intended to provide information on safe starting doses and to identify major toxicities and organ systems at risk. However, since these drugs are chosen for their antitumor effects, an attempt is made to enter them into clinical trials as rapidly as possible. Specific toxicity tests are described in a "toxicology protocol." This protocol stipulates what animals should be used and how the tests should be performed.

Lethality studies, which are conducted to determine lethal doses of new drugs, are useful in quantitatively predicting clinical starting doses. In contrast, toxicity studies are conducted to determine drug-induced changes in hematologic, chemical, clinical, or histological parameters. They are used to qualitatively predict the major organs at risk with the new drug.

Dr. Loeb then discussed changes in the toxicology protocol from 1972 to 1980. For example, the 1972 protocol required studies in three species: dogs, monkeys, and mice. However, it was concluded that the use of monkeys was not justified because monkeys rarely exhibit toxicities not predicted by dogs. This, as well as the fact that monkeys were becoming scarce, led to the decision to drop the requirement for monkey studies.

Based upon the lack of usable information from monkeys and upon analyses that indicated the quantitative usefulness of mice, it was decided to develop a new toxicology protocol. It was believed that studies performed under the new protocol would be equally predictive of human toxicities, could be conducted more rapidly, and would be less expensive.

In late 1979, the FDA accepted new guidelines for toxicological testing of cytotoxic antitumor drugs. Based on the new FDA guidelines, NCI drafted a new protocol which consists of lethality studies in mice and toxicity studies in dogs. The mouse studies are designed to predict safe starting doses, while the dog studies will be used to confirm the safety of the starting doses determined in mice as well as to detect toxicities. NCI is conducting additional toxicity studies in mice to determine the qualitative predictiveness of the mouse for human toxicities. Initial experiences with the draft protocol led to a revised 1980 toxicology protocol.

Dr. Loeb added that each new drug study conducted under the 1972 protocol would cost $351,000 today. Under the 1980 protocol, it costs approximately $256,000 when the extra mouse toxicity study is included. However, if FDA guidelines were followed, each study would cost only $161,000.

Dr. Loeb reminded the Board members that it is the NTP's intention to expose no patient to undue risks. However, the degree of risk acceptable is based on two factors: first, these drugs are selected on the basis of their ability to kill cells, a common property of antitumor drugs; and second, these drugs offer hope for patients who have no other therapeutic alternatives.

The protocol was presented to NTP's Board of Scientific Counselors earlier in the year, and Dr. J. Richard Crout, Director of the Bureau of Drugs of FDA, has expressed general agreement. There has been some opposition to this protocol at lower levels of FDA. The major reservations are that (1) one less large species (the monkey) is being used in the trials; some feel that this would offer a bit of additional safety, though this is hard to prove; and (2) fewer schedules of administration are being tested; in general this would offer additional information of value only in unusual or exceptional circumstances. Agreement has been reached with the commissioner of drugs in the oncology area that histopathology would be supplied within 90 days of application to FDA for IND approval.

NTP was awaiting a decision from the Commissioner; however, the protocol has now been approved. The three INDAs under that protocol are now released.

The cost or the time involved is irrelevant, and the safety of the patient should always be taken into account. The general public does not understand that the studies that were thrown out did not provide needed information. One compound in 5,000 screened makes it to clinical trial, and one compound in 50,000 screened makes it to marketing.

V. Pros and Cons of Animal Models--Alternate Methods - Dr. William F. Raub

Dr. Raub's presentation brought to the attention of the Board a number of issues concerning the use of laboratory animals in biomedical research and testing. The two major foci of interest, particularly in the last year, have been concerns related to animal welfare and alternatives to the use of animals.

With respect to the concern for animal welfare, various legislative proposals call for increased regulatory oversight, either by strengthening the responsibilities and enforcement powers of the Department of Agriculture or by providing for local review by animal care committees.

Few people agree on the definition of "alternatives" to animals. NIH has chosen a narrow definition and has been looking at areas where replacement of animals by non-animal systems might be appropriate. A broader definition of "alternatives" to animals includes seeking refinements of existing research methods that would lessen the difficulties to which animals are subjected or would decrease the number of animals used.

Last winter NIH presented a symposium concerned with bioassay methods, which discussed prospects of lesser dependency on animal systems. A report of this conference is now available in summary form. As a result of the symposium, consideration was given to the establishment of a government-wide forum that would identify opportunities for improved test method development on a regular basis.

NIH is working to ensure that distinctions are made in terminology to prevent the introduction of arguments which would conflict with the nature of research itself. A general hearing later this month (House Subcommittee on Science and Technology) will identify bills relating to this issue and invite commentary from both the public and the scientific community.

Two bills were identified that will receive the bulk of attention: the Research Modernization Act (H.R. 556) and the Amendments to the Animal Welfare Act (H.R. 4406). The first bill focuses on the definition of the subject of alternatives to animals, to promote greater interest in the scientific community to searching for such alternatives. The second bill seeks to assure that every reasonable step is taken for adequate housing, handling, and appropriate uses for animals.

Dr. Raub saw no explicit proposal for funding for building new quarters or updating existing ones. NIH has provided some facility development grants through the Division of Research Resources for improving conditions. However, there is generally not enough funding made available to build facilities that meet the approval of local animal care organizations.

FDA and other regulatory agencies would like to see more animals used to improve reliability of test results. This runs counter to the arguments that fewer animals be used. There should be more dialogue between the regulatory agencies and the research agencies. Board members were encouraged to provide comments on these issues to the general hearing. It was pointed out that stringent regulations on animal facilities and handling might cut off important research projects that lacked funding to improve their facilities.

VI. Review of Joint Studies with Formaldehyde Institute - Dr. Aaron Blair

The Environmental Epidemiology Branch of the NCI conducts a program of occupational studies on determinants of cancer associated with the workplace. The studies, which are often collaborative with labor unions, companies, professional organizations, and Federal and state agencies, are used to identify and clarify occupational hazards. Occupations now under study include petrochemical workers, dry cleaners, jewelry manufacturers, pesticide applicators, farmers, shipyard workers, and persons having contact with formaldehyde. The latter occupation is the focus of this presentation.

Formaldehyde. Formaldehyde is a one-carbon chemical that reacts readily with DNA, RNA, and proteins. It can enter the body through inhalation, ingestion, or dermal absorption, and is rapidly converted to formate in many tissues.

Formaldehyde is a relatively inexpensive chemical used in the production of phenol, urea, and melamine resins. These resins are used to make plywood and particle board, protective coatings, electronic equipment, insulation, decorative laminates, textiles, foundry shovels, plastic dinnerware, and paper. Formaldehyde is also used in leather tanning, photographic film production, pesticides, pharmaceuticals, cosmetics, embalming fluids, biologic specimen preservation, and various sorts of filters.

The current OSHA standard for formaldehyde is a time-weighted average of 3 ppm, although in 1976 NIOSH recommended that the limit be lowered to 1 ppm. Primary complaints arising from formaldehyde exposure are odor, skin reactions, sensitivity and irritation of the conjunctiva and nasopharyngeal mucosa, coughing, and headaches. NIOSH estimates that 1.6 million workers have been exposed to formaldehyde; workers from over 200 occupations may come into contact with the chemical.

Since formaldehyde is such a widespread and highly reactive substance, there is much concern over findings from recent tests. The chemical has given positive (though weak) mutagenic responses in many laboratory animals. Several laboratory studies have indicated formaldehyde carcinogenicity at high exposure levels.

It is reasonably clear that formaldehyde is a mutagen and a carcinogen under laboratory conditions. Although few epidemiologic studies have been completed, dermatitis and respiratory problems from formaldehyde exposure have been reported. Preliminary epidemiologic findings raise the possibility that humans occupationally exposed to formaldehyde may experience elevated risk to certain cancers. However, findings are based on small numbers and uncertain exposures.

The Environmental Epidemiology Branch has several epidemiologic studies under way to evaluate cancer experience in persons having contact with formaldehyde. Studies of embalmers and histologic technicians were initiated before the laboratory reports of nasal tumors in rats were available. A case-control study on nasal cancer is now under way in North Carolina and Virginia. More recently, a mortality study of anatomists was initiated.

The Formaldehyde Institute has been enlisted to help identify companies that could be studied. An NCI-funded feasibility study was initiated to determine if a scientifically sound investigation of industrially exposed workers could be mounted. An advisory panel reviewed the results and recommended the implementation of a full-scale study, which should be completed within three years.

After some discussion of the pros and cons of having industries fund all or part of such studies, there was a suggestion that the Subcommittee on Environmental Carcinogenesis might take up this question.

VII. Report of the Subcommittee on Planning and Budget - Dr. Frederick Seitz

NCI formulates and presents two budgets to the government: one, the bypass budget, goes directly to Congress and represents the Institute's estimate of the ideal budget for cancer work; the other budget is worked out jointly with OMB. Under ideal conditions, the two budgets would be identical. However, the bypass budget and the budget worked out with OMB have been growing wider apart.

This Subcommittee was asked to consider which techniques should be used to handle the bypass budget to bring it closer to the budget prepared with OMB. Various fields in the bypass budget have been prioritized so that if cutbacks become necessary, they can be taken in accordance with the list of priorities. The list ranks research-related projects first, followed by cancer centers and National Research Service Awards.

Using this list, a bypass budget for 1983 (amounting to $1.197 billion) was agreed on. The base budget, with a cost-of-living adjustment of 7.2 percent, would be $1.1 billion, a difference of about $100 million.

In the case of NCI, a 12 percent cut in current budget levels would involve about $120 million. It was agreed that the entire Board should be consulted to help in the plan to be submitted. However, final decisions may have to be made before the Subcommittee's next meeting.

The Subcommittee has agreed that it would be unwise to simply cut everything by 12 percent. Decisions must be made on which areas can be cut. One suggestion was that indirect costs be cut back; another was that new grants be delayed.

Several Board members suggested that cuts be made across-the-board in every program, giving program directors the control to make cuts within their programs as they see fit. Others insisted that the Board should protest the continued cuts in NCI programs.

A decision was reached to vote on the motion presented by the report of the Subcommittee: that any budget reductions should be made on a selective basis and not on a fixed percent across-the-board and that, in addition to the Subcommittee members, the full voting members of the NCAB should participate in the priority-setting process. If budget cuts prove necessary, it was proposed that Board members and members of the Boards of Scientific Counselors would be asked to offer their suggestions as to which programs would be affected and how. These suggestions would serve as a guide to NCI staff in making the actual decisions. The Subcommittee report with its recommendations was accepted by a vote of 7 to 2 with 2 abstentions.

Dr. Shubik presented a short statement describing the NCAB's apprehension over the budget cuts. It read:

> This statement of the National Cancer Advisory Board greets with great apprehension the suggestion that it may be necessary to reduce the budget of the National Cancer Institute by 12 percent. The National Cancer Advisory Board notes that it has been necessary to reduce the proportion of meritorious projects supported during the past several years and that the national effort in cancer research is steadily declining. The present budget allocations are barely adequate to meet the present commitments, and any cuts would have serious effects now and jeopardize the future irreparably. The cancer problem is finally starting to yield to a farsighted attack mounted several decades ago. However, much of our problem still remains a major concern of the U.S. population. Recognizing needs for economic stringencies, the National Cancer Advisory Board still believes the attack on cancer merits a special priority and should be spared from any overall cuts.

A motion was made that the Chairman of the Board write a letter containing this statement; signing it as Chairman of the NCAB; sending it to the President, the Secretary, with a copy going to the Panel and to the leaders of the House and Senate who prepare the budget; including a statement that the members of the Board are aware of the contents and approve the letter. The Board members should then receive a copy of the letter as soon as possible so that they can act to reinforce the contention. The letter would also be made available to the press. The motion passed unanimously.

A suggestion was made and approved that this statement be sent as a telegram, since this would eliminate use of government stationery.

VIII. A Proposal for the NCAB Regional Meetings - Mr. Sheldon Samuels

This presentation was deferred until a later meeting.

IX. Report of the Subcommittee on Activities and Agenda- Dr. Harold Amos

This Subcommittee was to consider the question of the effectiveness of the present review process. Items of concern included: (1) the study section practice of selecting fundable parts for grant applications of RO1s and giving priorities on those parts; (2) grants of high program relevance that do poorly in review; and (3) the fate of interesting ideas that are not in the mainstream

and often fare less well than they merit. Consideration of these issues was postponed until a later date when both the Panel and the NCAB will participate in more formal discussions. A second major concern, which deals with clinical trials and changing sources of patients for those trials, will be part of the discussions of the November meeting.

Policy guidelines for inviting outside speakers to participate in NCAB meetings were discussed; the Subcommittee recommended that there not be a formalized policy, but that the Board deal as a whole with each of those requests on the basis of their merits.

It was added that accepting the report of this Subcommittee would create a new, ad hoc Subcommittee involved in control and related areas. The report of the Subcommittee was approved with three abstentions.

X. Report of the Subcommittee on Nutrition - Dr. Maureen Henderson

Dr. Henderson presented an interim report, alerting the Board and the Director to recommendations that will be included in the final report. The Subcommittee and a group of NCI staff reviewed NIH, NCI, National Academy of Science, and National Research Council research activities in nutrition and cancer, covering the substance, organization, and levels of funding of research in this area. The Subcommittee believes that research in nutrition related to cancer is important and timely and that it has to be given consideration when budget priorities are set and when Institute organization and staffing decisions are made.

Research is opening up to look at natural defenses and to explore both protective and repair mechanisms as well as the process of damage. The findings of this research are likely to provide insight into the function of normal cells as well as into cancer cause and prevention.

The Subcommittee explored and found that little has been done to look at the influence of the nutritional status on the outcome of treatment of malignancies and that there is widespread acceptance of suppositions that the effect of diets and nutrition on specific and general physiological factors will prove to be of major importance when finally studied in detail.

The NCI should define and focus a program to offer new approaches to nutrition and its physiological implications for human disease, which should be multidisciplinary and draw upon the expertise and experience of all divisions. Maximum use of existing resources should be exploited.

XI. Report of the Subcommittee on National Organ Site Programs - Dr. William Powers

The Subcommittee is working on a statement of the Organ Site Program rationale and objectives, which, still in draft form, was to be sent to Board members after the meeting. Discussion of the statement's contents will take place at a later date.

XII. Adjournment

The meeting was adjourned at 11:05 a.m. on October 7, 1981.

DATE / /

Henry C. Pitot, M.D., Ph.D. /
Chairman
National Cancer Advisory Board