National Institutes of Health

National Cancer Institute

NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
October 4-6, 1982
Building 31
Conference Room 6
National Institutes of Health
Bethesda, Maryland

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

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October 4-6, 1982

The National Cancer Advisory Board (NCAB) convened its 43rd regular meeting at 8:30 a.m., October 4, 1982, in Conference Room 6, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, Maryland. Dr. Tim Lee Carter, Chairman, presided.

Board Members Present

Mrs. Angel Bradley
Dr. Victor Braren
Dr. Ed L. Calhoon
Dr. Tim Lee Carter
Dr. Maureen M. Henderson
Dr. Robert C. Hickey
Dr. Geza Jako
Dr. Joseph G. Katterhagen
Mrs. Rose Kushner
Ann Landers
Dr. LaSalle D. Leffall
Dr. William E. Powers
Dr. Janet D. Rowley
Mr. Sheldon W. Samuels
Mr. Morris M. Schrier
Dr. Irving J. Selikoff

President's Cancer Panel

Dr. Harold Amos
Dr. William P. Longmire, Jr.

Ex Officio Members

Dr. Robert Brandt, Labor
Dr. Ken Bridbord, NIOSH
Dr. Hollis Boren, VA
Dr. William Farland, EPA
Dr. Allen Heim, FDA
Dr. F. Kash Mostofi, DOD
Dr. Denis J. Prager, OSTP
Dr. Peter Preuss, CPSC
Dr. David P. Rall, NIEHS

Absent

Mr. Richard A. Bloch, National Cancer Advisory Board
Dr. Gerald N. Wogan, National Cancer Advisory Board
Dr. Armand Hammer, Chairman, President's Cancer Panel

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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.

Liaison Representatives

Dr. John S. Cook, Program Director, Cell Biology, National Science Foundation, Washington, D.C., representing the National Science Foundation.

Mr. Alan C. Davis, Vice President for Governmental Relations, American Cancer Society, New York, New York, representing the American Cancer Society.

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.

Dr. Paul Sherlock, Chairman, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York, representing the American Gastroenterological Association.

Dr. J. W. Thiessen, Acting Deputy Associate Director, Office of Health and Environmental Research, Office of Energy Research, Department of Energy, representing the Department of Energy (for Dr. Charles W. Edington).

Dr. Hugh R. K. Barber, Director, Department of Obstetrics and Gynecology, Lenox Hill Hospital, New York, New York, representing the Society of Gynecologic Oncologists.

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

Dr. John R. Nelson, Past President, Association of Community Cancer Centers, Jacksonville, Florida, representing the Association of Community Cancer Centers.

Members, Executive Committee, National Cancer Institute

Dr. Vincent T. DeVita, Jr., Director, National Cancer Institute
Dr. Richard H. Adamson, Director, Division of Cancer Cause and Prevention
Mr. Philip Amoruso, Executive Officer, National Cancer Institute
Mrs. Barbara S. Bynum, Director, Division of Extramural Activities
Dr. Bruce Chabner, Director, Division of Cancer Treatment
Dr. Peter J. Fischinger, Associate Director, National Cancer Institute
Dr. Peter Greenwald, Director, Division of Resources, Centers, and Community Activities
Dr. Jane Henney, Deputy Director, National Cancer Institute
Dr. Alan S. Rabson, Director, Division of Cancer Biology and Diagnosis

In addition to NCI staff members, meeting participants, and guests, 24 registered members of the public attended the meeting.

I. Call to Order and Opening Remarks--Dr. Tim Lee Carter

Dr. Carter called the meeting to order and welcomed members of the Board, the President's Cancer Panel, liaison representatives, and guests. He thanked Dr. DeVita and his staff for their support in organizing the meeting and thanked members of the Panel for an equally fruitful association. Dr. Carter cited the following oncologists for special commendation for their work: Dr. Gerald Murphy of the Roswell Park Memorial Institute, Buffalo, New York; Dr. Gerald Bodey; Dr. Emil Freireich; Dr. Emil Frei; Dr. James Holland; and Dr. Vincent DeVita. He then introduced the liaison representatives.

Members of the public were welcomed and invited to submit their comments in writing on items discussed by the Board to the Executive Secretary within 10 days after the meeting. Dr. Carter stated that any comments would be accorded careful consideration. He then reviewed procedures for conducting Board meetings and confirmed future meeting dates with the Board. The meeting that was tentatively scheduled for February 7-9, 1983, has been confirmed for January 31-February 2, 1983. Other confirmed meeting dates are November 29-December 1, 1982, May 16-18, 1983, October 3-5, 1983, and November 28-30, 1983. Mrs. Barbara Bynum will send Board members a list of future meeting dates.

Dr. Carter welcomed the new member of the President's Cancer Panel, Dr. William Longmire, and invited Dr. Harold Amos to give the Panel report in the absence of the Chairman of the Panel, Dr. Armand Hammer.

II. Report of the President's Cancer Panel--Dr. Harold Amos

As a background to his report, Dr. Amos referred to the Panel's decision, under the leadership of Dr. Hammer, to hold hearings in different cities to get "grassroot" views on the National Cancer Institute's funding of research. He briefly reviewed the legislative mandate for the President's Cancer Panel and cited the serious problem of the shortage of funds and the need to exercise novel and imaginative approaches to gain maximum value from program resources as justification for these hearings. Dr. Amos mentioned recent meetings in Boston and Los Angeles and meetings to be held in Houston and Chicago next year.

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

Dr. DeVita welcomed the new Board members: Dr. Tim Lee Carter, Dr. Ed Calhoon, Dr. Victor Braren, Mrs. Angel Bradley, Mr. Richard Bloch (who was absent), and Dr. Geza Jako, as well as Dr. William Longmire, the new member of the President's Cancer Panel. He also introduced Dr. Tadeusz Koszarowski, Director of the Madame Curie Institute in Poland, now visiting the United States under a Polish-American agreement.

Staff Announcements

(1) Dr. Bruce Chabner has been named Director of the Division of Cancer Treatment, completing Division Director appointments.

(2) Members of the NCI Executive Committee were introduced, as well as other NCI/OD staff in attendance.

(3) Other appointments announced were: Dr. Samuel Broder, Associate Director for Clinical Oncology Programs; Dr. Joseph Cullen, Deputy Director, Division of Resources, Centers, and Community Activities (DRCCA); Dr. William De Wys, Assistant Director for Cancer Prevention, DRCCA; and Dr. Robert Esterhay, Special Assistant for the new Protocol Data Query (PDQ) system.

(4) Dr. DeVita cited Dr. Michael Potter of NCI on his election to the National Academy of Sciences for his work on multiple myeloma lines.

Board Followup Items

(1) The contract for an epidemiological study in Utah was awarded on June 1, 1982. The contract covers a 5-year period and amounts to approximately $6 million. In accordance with an NCAB resolution, NCI has obtained additional funding from the Department of Energy ($250,000 a year) and the Department of Defense ($200,000 a year).

(2) There is no evidence of tampering or interference on the part of NCI in the preparation of the Monograph on Benzene, produced by the International Agency for Research on Cancer (IARC). Dr. DeVita expressed some concern regarding the language in a proposed markup of a House Subcommittee bill, which would transfer funds for the monograph series to the NIH Office of the Director and which suggested that NIH request the IARC to develop written protocols for studies and for the selection of topics, working group members, and procedures to be followed in revising monographs. Dr. DeVita believes that this represents, for the first time, an attempt by the United States to interfere with the monograph series. This type of interference would be contrary to the terms of our agreement with the IARC and, he believes, would be resented by other member nations.

(3) Over 200 letters of intent have been received for the Community Clinical Oncology Program (CCOP). Some pediatric groups are included, and this issue, along with an update on the program, was addressed in a later report to the Board.

(4) The competition relating to the Frederick Cancer Research Facility (FRCF) has been completed. The contract was competed in five separate parts to allow maximum competition and include segments for small businesses. Funding for the program has been reduced by 20 percent, as directed by the Board.

(5) The review of NCI's intramural program conducted by the General Accounting Office (GAO) at the request of the subcommittee headed by Senator Paula Hawkins has been completed, and no written report will be issued by GAO. This is viewed as a good sign, and it was further mentioned that the verbal report from GAO was flattering to NCI. GAO praised the Institute for its tight management of the National Cancer Program, its external peer review system and its site-visit procedures for the review of intramural programs.

Budget

Dr. DeVita reviewed recent NCI budget history, noting in his presentation that adjustments had been made for the transfer of National Toxicology Program funds to NIEHS and the transfer of $4 million from the National Institute of General Medical Sciences to NCI for radiation research. In absolute dollars, the current NCI budget of $943 million represents a 1-1/2 percent decrease since 1980. Despite this decrease, however, overall funding for research projects has increased by 12-1/2 percent in the 2-year period, or by $40 million; the intramural research program has increased by 12 percent (10 percent, in actual NCI costs); and funding for the centers program has risen by 8.2 percent. To accommodate these increases, research support contracts have been decreased by 26 percent.

In addition to research support contracts, programs that have borne the brunt of cutbacks are the Baltimore Cancer Research Facility (which was closed), the Frederick Cancer Research Facility, the Organ Systems Program, the Clinical Cancer Education Program, the Drug Development Program, some outreach programs of the cancer centers, the transfer of funds to EPA and NIOSH, the Centralized Cancer Patient Data System, and programs in pediatric oncology. In accordance with the wishes of the NCAB, funding for research grants (the P01 and R01 grants) has received first priority.

Despite tightened resources, analysis of dollars spent for research grants since 1978 indicates the emphasis that NCI has placed on funding investigator-initiated research. The number of total grant projects funded has remained between 2,300 and 2,600 in the 4-year period since 1978, although the percentage of competing grants funded declined from 46 percent in 1978 to 31 percent in 1982. The funding plan for 1983 is geared to maintaining the 1982 level of 31 percent. Even though resources are more limited, NCI is actually funding more research project grants in 1982 than it did in 1978.

The history of the 1982 budget was reviewed. The final budget figure represented a 4 percent reduction in the budget amended by President Carter ($1.025 billion). Procedures undertaken by NCI to accommodate this reduction included a 4 percent reduction in noncompeting grants and in the recommended level of funding for new grants. As a result of these actions, NCI was able to fund an additional 100 grants in 1982, amounting to $11.2 million.

Funding options for 1983 are based on a projected increase of 1.3 percent over the 1982 President's budget. The general guidelines considered by NCI were that research projects would increase by 4 percent over the 1982 congressional estimate, that an additional 5 percent reduction would be made in research and support contracts, and that intramural research would be held to the same 4 percent level of increase as research projects. Following are the 1983 operating policies selected for presentation to the Board: All grants will be funded at 20 percent below recommended levels, no grant will receive less than its current level, grant dollars will be allocated by program area, Program Directors may approve a 10 percent variance in funding for individual grants with the concurrence of Division Directors, an additional 5 percent reduction will be made in contract support, intramural research will be limited to a 4 percent growth

over 1982, and the review of P01 grants will be modified to alleviate any concern over the size of projects and the amount of money commanded by some because of size. Under this plan, NCI would be able to fund approximately 750 grants, including 20 transferred from the Organ Systems Program, or about 30 percent of the number approved. The priority score cutoff for grants would probably be lower than previously.

NCI is currently operating at the 1982 budget level ($943 million) under a continuing resolution that expires December 15. The 1983 budget submitted by the President is $955 million. The Senate has not yet acted on an appropriations bill for NIH; however, legislation in the House includes a $25 million increase for NCI, representing only 2.7 percent of the total NIH increase over the President's budget. Appreciation was expressed for the generous congressional support for health research in past years, but it is believed that NCI is not getting its "fair share" in the present House budget. Concern was voiced over maintaining current programs intact through 1984 if NCI increases are held to this level. NCI submitted its bypass budget for 1984 to the Office of Management and Budget in September. The budget calls for a 12.5 percent increase over the 1983 level, which would allow for the funding of 912 grants, or about 32 percent of those approved. The bypass budget and other budgetary matters will be discussed more fully at the NCAB Subcommittee on Planning and Budget.

New Items

(1) The name of the Division of Resources, Centers, and Community Activities will be changed to the Division of Prevention and Control, thus more accurately reflecting the Division's mission. Programs in breast cancer and preventive oncology have been transferred to DRCCA.

(2) Dr. Charles Heidelberger, Director for Basic Research and Distinguished Professor of Biochemistry and Pathology at the University of Southern California, received the Athayde Award of the International Cancer Congress for his work in basic research. The next meeting of the International Cancer Congress will be held in Budapest, Hungary, in 1986.

(3) A Freedom of Information request from the Washington Post that might require "conflict of interest" statements from members relating to their institutional affiliations has been received. The request has been denied and the denial upheld in court, but the decision is being appealed.

(4) A total of $200,000 from the Director's gift fund has been given to the Patient Welfare Fund at the Clinical Center; some funds are also being used to establish an NCI summer traineeship program for medical and predoctoral students.

(5) NCI's new PDQ system, a data file for the International Cancer Research Data Bank program, is operational. This new system will be discussed more fully at the November meeting.

(6) New procedures were discussed for the review of P01 grants to ensure the quality of individual projects included in these grants. A letter

of intent will be required before grant submission to assure linkages in individual projects and to allow NCI staff time to help an investigator develop the application. NCI will insist that review committees score every project in a PO1 application so that the overall priority score will reflect the scientific merit of all projects. The new scoring system will put the burden on the investigator to include only high quality projects. Dr. Henderson will chair a committee to look into the development of a weighted scoring system for these grants. NCI hopes to implement this review system by the May 1983 Board meeting and apply it to grant applications submitted after June 1983.

(7) NCI proposes an "Outstanding Investigator Award," which would be directed to the support of researchers rather than projects. This would not be a lifetime award, but would be recompeted and stringently reviewed at reasonable intervals. It would allow for the support of "risky" research in times of tight money. Dr. Hammer will form an ad hoc committee to consider specific questions relating to this award, such as NCI review procedures, the duration of the award, requirements relating to time commitments, funding mechanisms, and a recipient's eligibility for other NCI/NIH grants. Dr. Amos has agreed to chair the committee. If approved, the award will be implemented by the end of FY 1983.

Legislation--Dr. Mary Knipmeyer

A law (P.L. 97-219, "Small Business Innovation Development Act of 1982") requiring small business set-asides for innovative research programs at NIH and other Government agencies has been passed. In testimony before the House Subcommittee on Oversight Investigations on September 20, Department of Health and Human Services Secretary Richard Schweiker testified that NCI had exerted no undue influence with regard to the IARC Monograph on Benzene. Several bills relating to the use of animals in scientific research have been introduced in the House during the past year. One bill currently being considered may be passed in the lame-duck session of the next Congress. This is H.R. 6928, the "Humane Care and Development of Substitutes for Animals in Research Act." This bill has 17 bipartisan supporters. Among provisions of the bill are a requirement for accreditation committees within research centers and Government agencies to monitor overall procedures and care of research animals, a requirement for the development by the Secretary of DHHS of nonanimal methods of research, and a requirement for special justification for researchers to employ conscious animals in research projects. The Congressional Budget Office estimates that implementation of the accreditation portion of the bill would cost $500 million, that $65 million would be required by research facilities for manpower, and that 1,300 additional personnel would be needed to fulfill reporting requirements of the bill. No separate funds for these activities are provided in the legislation. A similar version was recently introduced in the Senate by Senator Robert Dole. Other legislation currently under consideration in the Congress includes a bill relating to the development of orphan drugs that would provide grants or tax credits to pharmaceutical firms for the development of these agents. The current status of this legislation was not clear.

The House Reauthorization (Waxman) Bill was passed on September 30. One amendment to this bill would prohibit research on fetuses. Specific provisions of this bill relating to NCI include an 11 percent increase in total NIH funding, an appropriation of $63 million for Cancer Control Programs, an authorization of $83 million for Cancer Research and Demonstration Centers, requirements for information and education centers, and a funding limit of $35,000 on grants not requiring approval by the NCAB. The bill also eliminates separate reporting requirements for NIH Advisory Boards and creates a new Arthritis Institute at NIH. The legislation is not supported by DHHS.

The Senate Reauthorization Bill, which is in committee, calls for a 6 percent increase in NIH funding and sets a $50,000 limit on grants not requiring NCAB approval. The Senate version establishes cancer control programs at a $58 million level and contains no separate authorization for cancer centers, clinical education programs, or the Organ Systems Program. It includes requirements for programs on the continuing care of cancer patients and their families, continued support for the ICRDB program, and requirements for NIH to establish procedures for the appeal of grant peer review determinations. Possible Senate amendments to this legislation include the Goldwater Amendment to establish an Arthritis Institute, an amendment relating to clinical cancer education programs, an amendment concerning the significance of cancer centers and overall NCI funding, and an amended version of the Moynihan Amendment relating to the Organ Systems Program. NCI, along with DHHS and NIH, is opposed to the Moynihan Amendment, which would maintain separate administrative centers for Organ Systems Program components and special review procedures for project funding. It carries the Program as a line item in the budget at a level of $20 million beginning in FY 1983. NCI believes that this proposed legislation disregards NCAB's recommendations concerning the Organ Systems Program and interferes with the Board's processes. The Moynihan Amendment is expected to be considered in the lame-duck session of Congress after the November elections. Other versions of the amendment were described. At this time it is impossible to state which version of the amendment will be proposed.

Discussion

Dr. Amos' comment that the animal welfare legislation would paralyze scientific research and that the estimate of $500 million was too low was seconded by several members of the Board. Dr. Amos expressed interest in testifying against the bill. Ann Landers warned that the animal research issue is a highly emotional one and that the Board must be prepared for a storm of public protest. It was pointed out that the tendency away from the use of animals in research is striking because of improvements in technology. In response to a question from the Board, the Director, NCI, said that the percentage of approved grants funded by NCI (31 percent) is comparable to that of other NIH Institutes. In response to a question from Dr. Selikoff regarding the decrease in constant dollars since 1975, it was stated that NCI is supporting four times the number of new grantees with only half the amount of resources in terms of constant dollars. He also reiterated that criteria for the proposed Outstanding Investigator Award will be determined by a committee.

IV. Announcement--Mr. Sheldon Samuels

The Board unanimously applauded Dr. Irving Selikoff in response to Mr. Samuels' announcement that in approximately two weeks Dr. Selikoff will receive the Italian Government's highest civilian award for his work in environmental cancer.

V. Staff Reponses to Nutrition Subcommittee Report--Dr. Maureen Henderson and Dr. Peter Greenwald

Dr. Henderson reiterated the recommendations of the NCAB Ad Hoc Subcommittee on Nutrition to the NCI Director and Executive Committee. These recommendations centered on the subcommittee's beliefs that there should be an emphasis on research in nutrition and cancer and improvements in the quality and quantity of this research. An effort should be made to develop interdisciplinary planning in nutrition and cancer research and an outline of an appropriate research agenda. The subcommittee felt that a mechanism to initiate this research should be developed which would fit into existing peer review and funding mechanisms and bring new scientists into the field. The subcommittee asked the Director, NCI, and Executive Committee to plan a way to implement the program. Dr. Greenwald's report represents NCI's response to these recommendations.

Dr. Greenwald's presentation included a brief review of diet and nutrition research related to cancer, including epidemiological and laboratory studies, NCI's role in nutrition research, and future directions in nutrition and cancer research as viewed by NCI. The report highlighted studies in the new area of chemoprevention, which he defined as a method of intervening in the cancer process by adding a nutrient or synthetic compound to lower cancer risk. The Board members were reminded of the National Academy of Sciences review of diet and cancer research, which was performed under contract with NCI, and the Academy's interim and final recommendations, which are expected in June 1983.

Dietary factors thought to increase cancer risk include high levels of dietary fat, alcohol, and nitrosamines; factors thought to lessen cancer risks include fiber, vegetables, selenium, and vitamins A, C, and E. Much recent research in diet and nutrition has focused on micronutrients and synthetic analogs as protective factors in cancer. The consumption of vitamins by Americans increased tremendously between 1968 and 1980, and now 40 percent of adults take vitamins, according to a National Center for Health Statistics (NCHS) survey. Although there have been reports of side effects from the excessive use of some vitamins, further studies are needed to ascertain the safety of using megadoses of vitamins. NCI and NCHS are conducting a followup study of people surveyed in the early 1970's on their dietary habits to assess the protective effects, if any, of dietary constituents and megavitamin use. Findings from several studies in this country and abroad that examined the protective effects of vitamin A or its synthetic analog, retinoic acid, were summarized. All of these studies, both animal and epidemiological, showed a consistent pattern that suggested a protective effect from vitamin A or retinoic acid. Several of these studies included lung cancer patients, and the same inverse relationship between vitamin A intake and lung

cancer was noted. Studies to date indicate the effects from synthetic analogs of vitamin A appear to be stronger than those from the vitamin itself and that different types of retinoids have varying effects. NCI's aim is to identify compounds with the strongest antitumor effects. There is a need for further human intervention and prospective studies to determine whether retinoids or other promising agents can lower cancer risks and a need to develop standard laboratory procedures pertaining to the maintenance and analysis of frozen blood samples used in long-term prospective studies. Chemoprevention scientists are interested primarily in agents that work in the latter stages of cancer promotion (to benefit people in their fifties and sixties) and that are not toxic in humans.

NCI has stimulated new interest in nutrition and cancer research through RFA's and is currently reviewing 49 applications; half of these are human studies. Planning for chemoprevention and diet and cancer research will include participation of all NCI Divisions, as well as NCAB and other relevant Government agencies. Looking ahead, NCI hopes to have results from studies of the benefits and risks of vitamin use by the second year of the program. The Institute also hopes to have some early results from ongoing intervention studies dealing with the use of chemopreventive agents (i.e., beta-carotene) as cancer inhibitors. Dr. William De Wys, the newly appointed Assistant Director for Cancer Prevention, will be assuming responsibility within DRCCA for diet and cancer research, including chemoprevention studies.

Discussion

Several Board members stressed the need to pay careful attention to the potential toxicity of agents used in human intervention studies. Dr. Greenwald agreed, mentioning that an additional step--review by a safety/protocol committee--had been added to the review process for human intervention trials. The Board entered into a discussion of dietary fat as a causative agent in cancer. In reference to studies of Finnish and Mormon populations, both of whom have low incidences of cancer yet consume high to moderate amounts of dietary fat along with high quantitites of fiber, it was noted that the emphasis in dietary research is not necessarily on what foods to take out of the diet, but rather on what can be added to moderate cancer risk. The need for long-term prospective studies--in terms of decades--to ascertain the effects from vitamins or other dietary constituents was reaffirmed. Data from a long-term prospective study of 1 million people begun in 1960 will be published shortly. The study, which included questions on dietary habits and vitamin intake, shows no difference in rates of lung cancer or other cancers among vitamin takers. The need was suggested for long-term studies to determine the effect of smoking cessation augmented by chemo-preventive agents in reducing risks of smoking-related cancer and/or in reducing time/risk factors in the development of these cancers. Dr. Amos commented that the importance of chemoprevention research is obvious. It should focus on interventions aimed at specific objectives and NCI should encourage other kinds of fundamental research in this area.

VI. Frederick Cancer Research Facility Recompetition--Dr. Peter Fischinger

The report on the Frederick Cancer Research Facility will be covered in two consecutive sessions of the NCAB. This presentation described the recent recompetition of the FCRF contract, the facilities and history of FCRF, the various activities conducted at the research center, the costs, and the rationale for the facility's existence. The next session's report will include a detailed look at the contractor-initiated portion of research at the facility, particularly in relation to other scientific activities of NCI. FCRF comprises 60 buildings on 70 acres and has a staff of over 1,000, representing a mixture of contractor and NIH/NCI employees. Of the over 800 people employed under contract, 190 are engaged in pure research. Because of its location 40 miles from the NIH campus, all facilities and services must be concentrated in Frederick. Activities conducted at the facility include research in biological and chemical carcinogenesis, cancer biology (including genetic engineering), and metastasis and treatment. Support services include management and facility maintenance and construction, a fermentation program, environmental control and research, occupational health care, computer and library services, animal holding and production, and various research support elements. In November 1981, Dr. Fischinger was appointed NCI Manager of the Frederick Program, reporting directly to Dr. DeVita. Dr. Berge Hampar is Resident Manager of the facility. A number of NCI intramural laboratories are housed at FCRF along with laboratories of NIAID and NINCDS.

Cancer research activities at FCRF began in 1971, when the facility was transferred to DHHS. Litton Bionetics, Inc., was the first contractor. Litton continued to operate the facility as sole contractor until this year, when the FCRF contract was recompeted as five separate contracts. The decision to split the FCRF operation was made by NCI staff in consultation with the NCAB and following the suggestion of a House investigation subcommittee, which recommended that the contract be broken into several parts to allow smaller organizations with special expertise to compete. Separate contracts were designated for the following components: Animal Production, Computer Services, Library Services, Operations and Technical Support, and Research. Following recompetition and review, contracts were awarded to the firms of Harlan Sprague Dawley for animal production ($1,655,097); Information Management Services, Inc., for computer services ($774,066); Data Management Services, Inc., for library services ($557,206); Program Resources, Inc., for operations and technical support ($30,107,840); and Litton Bionetics, Inc., for research ($7,268,810). Contract amounts cover the first year of support, and the contracts have been awarded for 5-year periods.

Dr. Fischinger discussed several issues critical to the development of Frederick and relating to the justification for this contract-supported facility. FCRF provides space for intramural research laboratories displaced by NIH building and renovation activities and has allowed NCI to move off-site laboratories into either the Frederick or NIH Bethesda complexes, saving costs and centralizing intramural research activities. The net effect of moving intramural programs to FCRF lowers the cost of such research to NCI by shifting costs of materials and supplies and some management and administrative costs to the contract. A savings

of 25 percent is achieved when intramural programs previously performed off-site are moved to Frederick. Moreover, FCRF provides a unique capability for adjusting to shifting program needs by allowing for the rapid deployment of resources and staff if necessary. In addition to centralized management of the facility, scientific activities at FCRF are monitored regularly by advisory committees and review committees composed of representatives from the NCI Division Boards of Scientific Counselors and by NCAB members. Dr. Fischinger stressed that the quality of scientific research performed at Frederick is as good as that performed within NCI. Total expenditures for FCRF represent a 20 percent reduction in overall contract costs, as proposed by NCI and endorsed by NCAB. Support costs for the facility are estimated to rise by $7.5 million in calendar year 1983, which reflects such items as construction of two new buildings, costs involved in shifting two NCI laboratories to FCRF, a new computer system, updating equipment, inflation, and award fees. Savings to NCI are estimated at a minimum of $3 million, primarily because of the shifting of intramural laboratory activities to Frederick.

Discussion

The possibility of outside scientists using laboratory and other facilities at Frederick and the resources being made available to researchers with innovative or promising research approaches was raised. Also, NCI should develop resource pools such as Frederick or the SEER program that would be made available to individual investigators under appropriate offices and control. In response to a question from a Board member relating to the displacement of scientists as a result of the recompetition, Dr. Fischinger noted that all but 1 or 2 scientists out of a staff of 832 were retained by the new contractors. In a discussion about the laboratory animals produced and maintained at the facility, he pointed out that the production of laboratory animals was in effect a self-supporting operation in that animals were supplied to other grantees and contractors through the program. The high quality of the animal production program at Frederick was stressed. There has been no real rise in the costs of FCRF because of the increase in the number of NCI laboratories being moved to the facility.

VII. Preliminary Report of Environmental Carcinogenesis Subcommittee on Quantitative Risk Assessment--Mr. Sheldon Samuels

A review of events leading to the current effort to quantify human risks from environmental and toxic exposures was presented by Mr. Samuels, beginning with a report in 1966 that introduced the concept of "no safe level of exposure." This concept eventually led to the need for scientific input into methods of determining "significant risk" to humans from toxic exposures in order to develop social policy. Mr. Samuels reiterated the specific charge to the subcommittee, which was to draft a policy decision on the adequacy, limitations, and use of quantitative risk assessment methodologies in humans for possible adoption by the Board. The subcommittee has had two meetings thus far. The first meeting in New York City was attended by Dr. Philippe Shubik and Dr. Gerald Wogan and by representatives from the National Academy of Sciences, NIEHS, NCI, EPA, FDA, and OSHA. At the second meeting, the subcommittee examined specific attempts at quantitative risk

assessments (saccharin and arsenic) and heard a presentation by Dr. Stephen Lamb, representing the Chemical Manufacturers Association, on alternative quantitative risk assessment. A number of issues raised by Mr. Samuels also were discussed at this meeting. Mr. Samuels cited the participation of Dr. Arnold Brown, a former NCAB member, in this second meeting. The subcommittee will prepare a final report for presentation to the Board at the subcommittee's third, and final, meeting on November 15. Dr. Charles Brown of the NCI's Biometry Branch and Dr. William Nicholson of Mt. Sinai School of Medicine have consented to act as consultants in this effort.

Discussion

Several Board members commented on the possibility of additional input from other experts in this area. Dr. Amos expressed some concern over the advisability of NCAB taking a position on quantitative risk assessment. He advised a cautious approach.

VIII. Status of CCOP RFA--Dr. Jerome Yates

NCI has received 232 letters of intent from the CCOP RFA issued in July. The letters are from a variety of institutions and individuals, representing approximately 600 hospitals and 1,000 individuals. Several consortiums--the largest consisting of 28 hospitals--are among the respondents. All States except Nebraska, Idaho, Wyoming, and Alaska are represented. Many letters were received from potential applicants in the metropolitan areas of New York, Los Angeles, Chicago, and Miami. Applications are due on November 9, and NCI has sent return letters to all those responding to the RFA. Dr. Yates asked Board members to inform him of the anyone they know who has not received a return letter. NCI will hold a conference on procedural matters for business representatives of applicant organizations and plans to develop a suggested format for applications to assist reviewers and applicants who are unfamiliar with the review process and application techniques. A session for members of the three proposed review committees will be held before the applications are reviewed, and Dr. Yates expects that about 200 responsive applications will be received.

Discussion

Questions relating to the inclusion of pediatric patients in the CCOP program were discussed by the Board. Some members expressed particular concern over groups proposing to include pediatric and adult patients in the same program. Several Board members expressed the view that NCAB should not revise the RFA at this date and that in taking a hard and fast position with regard to pediatric patients, the Board might be exluding high quality integrated programs. The Board could ensure good integration of pediatric and adult patients in its review of these applications. In response to a question relating to the possible impact of the CCOP on the Cooperative Group and cancer centers programs, Dr. Yates expressed the opinion that the CCOP would strengthen these programs by bringing in a new population of patients and stimulating the centers to be more responsive to the public. In response to Dr. Janet Rowley's question about the composition of review committees, Mrs. Bynum explained that the committees will be carefully constructed to avoid conflict of

interests with regard to institutional associations and will attempt to achieve a balance of participation in areas addressed by the RFA.

IX. Announcement of Subcommittee Assignments--Dr. Tim Lee Carter

The Chairman referred members to subcommittee assignments given in their resource books. He announced the disbanding of two subcommittees that had fulfilled their purposes--the Subcommittee on Centers and Construction and the Ad Hoc Subcommittee on Nutrition--and the formation of a new Ad Hoc Subcommittee on Program Project Grants to plan a forum for the resolution of the critical question of merit evaluation of program project grants. Dr. Henderson will chair this subcommittee and Dr. Carter will serve as ex officio member. Other members will be selected from NCI's program project review committees and from the Division Boards of Scientific Counselors. Dr. William A. Walter is the Executive Secretary. The charge to this subcommittee is "to report to this Board at its May meeting their recommendations as to the most equitable mechanism for achieving an accurate representation, via priority scores of the intrinsic quality and substantive scientific merit of P01 applications."

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

A primary role of this subcommittee is to develop appropriate agenda subjects for NCAB activities. Dr. Amos asked Board members to submit any potential subjects for Board consideration to Mrs. Bynum, to Dr. Mary Fink, or to the subcommittee. He announced that Dr. Henderson will succeed him as Chairman.

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

Dr. Henderson reported that the subcommittee had concluded its report at Monday's session and had nothing further to add.

XII. Report of the Subcommittee on the Organ Systems Program--Dr. William Powers

Dr. Andrew Chiarodo reported on the implementation of NCAB's recommendations concerning the Organ Site Program. One of the recommendations, to change the name of the program to Organ Systems Program, has been implemented.

Discussion

Several issues relating to the review of R01 grants emanating from the program were raised by the Board. Dr. Powers expressed concern for the multidisciplinary competence of peer review groups considering these grants and urged the establishment of an appropriate review process for projects that involve several disciplines. Other questions related to interruptions in the review process for current applications. Mrs. Bynum believed that these concerns could be resolved with the Division of Research Grants and raised the possibility of initiating special review procedures. The Board then discussed the impact of the proposed Moynihan Amendment on the Organ Systems Program, characterizing the amendment as a step backward and counter to the efforts of the NCAB to reshape the program

to better meet current research needs. NCI and the Board are on record as opposing the Moynihan Amendment.

XIII. Report of the Subcommittee on Planning and Budget--Mr. Lou Carrese and Dr. LaSalle Leffall

Dr. Leffall summarized highlights of the 1974 bypass budget and the 1983 budget and its implications for NCI. Dr. DeVita's report to the subcommittee included a review of the NCAB's role in developing the bypass budget, reviews of the FY 1982 and FY 1983 budgets (as marked up by the House Appropriations Committee), problems concerned with the bypass budget, and review and consideration of funding plan options for 1983. Under the National Cancer Act, NCI submits a budget directly to the President for transmittal to Congress. This budget represents the professional judgment of the NCAB, the President's Cancer Panel, and NCI's Executive Committee of the resources needed to maintain the program's momentum and take full advange of existing opportunities and leads. The bypass budget ($1.087 billion) presented to OMB for FY 1984 represents a 12.5 percent increase over the current 1983 level and would allow for the funding of 900 research project grants. Details of the bypass budget were discussed by the subcommittee along with review processes for Organ Systems Program grants. The report was accepted unanimously by the Board.

Discussion

Dr. Longmire noted the $20 million item for construction included in the 1984 bypass budget and suggested that the Board retain a subcommittee on construction. Dr. DeVita concurred that a subcommittee on construction should be retained as a separate function of the Board. There was some discussion as to what constituted "construction" and whether the use of this term would act to NCI's disadvantage at OMB. NCI explained the difference between "construction" and "renovation," and Dr. DeVita pointed out that construction funds included money for renovation activities, primarily to upgrade laboratory facilities. Any changes in terms used in budget requests would require OMB approval. He suggested that costs for renovation might be built into other activities of grant programs and limits set.

XIV. Report of the Subcommittee on Cancer Control and the Community--Dr. Joseph Katterhagen

Dr. Katterhagan presented an overview of areas of subcommittee activity. The subcommittee will monitor the CCOP program and will work closely with staff in the Office of the Director on the new Protocol Data Query System. Other areas of interest include working with the Office of Cancer Communications in its professional, patient, and public outreach education efforts; interrelating and communicating with other Federal agencies in areas relevant to cancer control, such as reimbursement through Medicare and Medicaid programs for cancer detection tests; and examining NCI's role in such areas as rehabilitation, pain and symptom control, terminal care, bereavement, and the fast-growing specialty of oncology nursing.

Discussion

In response to a question relating to NCI support for rehabilitation programs, Dr. Yates stated that NCI currently is reviewing its programs in rehabilitation and continuing care and will be developing plans for future activities in these areas.

XV. Request Regarding the Ad Hoc Subcommittee on Minorities

Dr. Leffall inquired about the current status of this subcommittee and asked that it be continued. There were no objections to this request, and the subcommittee was reinstated. Dr. Carter invited interested Board members to serve on the subcommittee.

XVI. Adjournment

The 43rd Meeting of the NCAB was adjourned at 10:30 a.m. on October 6.

Tim L. Carter, M.D.
Chairman
National Cancer Advisory Board