Department of Health and Human Services

Public Health Service

National Institutes of Health

National Cancer Institute

National Cancer Advisory Board

Summary of Meeting
September 26-28, 1988
Building 31, Conference Room 6
National Institutes of Health
Bethesda, Maryland

Department of Health and Human Services
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September 26-28, 1988

The National Cancer Advisory Board (NCAB) reconvened for its 67th regular meeting at 8:30 a.m., September 26, 1988, in Building 31, 6th Floor, Conference Room 6, National Institutes of Health (NIH). Dr. David Korn, Chairman, presided.

NCAB Members

Dr. Erwin P. Bettinghaus
Dr. Roswell K. Boutwell
Dr. David G. Bragg
Mrs. Nancy G. Brinker
Mrs. Helene G. Brown
Dr. John R. Durant (absent)
Dr. Gertrude B. Elion
Dr. Bernard Fisher
Dr. Phillip Frost
Mr. Louis V. Gerstner, Jr.
Dr. David Korn
Dr. Walter Lawrence, Jr.
Dr. Enrico Mihich
Mrs. Irene S. Pollin
Dr. Louise C. Strong
Dr. Louis W. Sullivan
Dr. Howard M. Temin
Dr. Samuel A. Wells

President's Cancer Panel

Dr. Armand Hammer
Dr. William P. Longmire
Dr. John A. Montgomery

Ex Officio Members

Dr. David Rall, NIEHS
Dr. Ralph Yodaiken, DOL
Dr. Richard Greene, VA
Mr. John Whalen, NIOSH
Dr. Lakshmi Mishra, CPSC
Dr. James B. Wyngaarden, NIH
Captain Bimal Ghosh, DOD
Dr. John Johnson, FDA

Members, Executive Committee, National Cancer Institute, NIH

Dr. Alan S. Rabson, Acting Director, National Cancer Institute
Dr. Maryann Roper, Acting Deputy Director, National Cancer Institute
Dr. Richard H. Adamson, Director, Division of Cancer Etiology
Mr. Philip D. Amoruso, Associate Director for Administrative Management
Mrs. Barbara S. Bynum, Director, Division of Extramural Activities
Dr. Bruce A. Chabner, Director, Division of Cancer Treatment
Dr. Peter Greenwald, Director, Division of Cancer Prevention and Control
Dr. Werner Kirsten, Associate Director, Frederick Cancer Research Facility
Dr. Ihor Masnyk, Acting Director, Division of Cancer Biology and Diagnosis
Executive Secretary, Ms. Iris Schneider, Assistant Director for Program Operations and Planning

*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. The procedure does not apply to *en bloc* actions.

Liaison Representatives

Mr. Alan C. Davis, Vice President for Public Relations, American Cancer Society, Washington, D.C., representing the American Cancer Society.

Dr. Clarence Ehrlich, Professor and Chairman, Department of Obstetrics and Gynecology, University of Indiana, Indianapolis, Indiana, representing the American College of Obstetricians and Gynecologists for Dr. Warren H. Pearse.

Ms. Margaret Foti, Executive Director, American Association for Cancer Research, Philadelphia, Pennsylvania, representing the American Association for Cancer Research.

Dr. Robert N. Frelick, Past President, Association of Community Cancer Centers, Wilmington, Delaware, representing the Association of Community Cancer Centers.

Dr. George Langford, Program Director for Cell Biology, National Science Foundation, Washington, D.C., representing the National Science Foundation.

Dr. Raymond E. Lenhard, Jr., Professor of Oncology and Medicine, the Johns Hopkins Hospital, Baltimore, Maryland, representing the American Society of Clinical Oncology, Inc.

Ms. Deborah K. Mayer, President, Oncology Nursing Society, Cambridge, Massachusetts, representing the Oncology Nursing Society.

Dr. Edwin A. Mirand, Associate Institute Director and Dean of the Roswell Park Memorial Institute Graduate Division, Buffalo, New York, representing the Association of American Cancer Institutes.

Dr. John F. Potter, Professor of Surgery, Vincent T. Lombardi Cancer Research Center, Georgetown University, Washington, D.C., representing the Society of Surgical Oncology and American College of Surgeons.

Dr. James Robertson, Director, Human Health and Assessment Division, U.S. Department of Energy, Washington, D.C., representing the U.S. Department of Energy.

Mr. William Tipping, Executive Vice President and Chief Executive Officer, American Cancer Society, Atlanta, Georgia.

Dr. Sidney J. Winawer, Chief, Gastroenterology Service, Memorial Sloan-Kettering Cancer Center, New York, New York, representing the American Gastroenterological Association.

In addition to NCI staff members, meeting participants, and guests, a total of 16 registered members of the public attended the meeting.

I. Call to Order, Opening Remarks, and Consideration of May 9-11, 1988, NCAB Meeting Minutes--Dr. David Korn

Dr. Korn, Chairman, called the 67th meeting of the National Cancer Advisory Board to order and welcomed Board members, the President's Cancer Panel, liaison representatives, guests, staff of the National Cancer Institute (NCI), and members of the public. He greeted new members Drs. David Bragg and Erwin Bettinghaus, who were unable to attend the May meeting. He then invited members of the public who wished to express their views on any part of the meeting to do so by writing to Mrs. Barbara Bynum, Director, Division of Extramural Activities (DEA), within 10 days of the meeting.

For those present who did not already know, Dr. Korn announced the death of Mrs. Marlene Durant, wife of NCAB member Dr. John Durant, on Friday, September 15. He stated that a contribution had been sent on behalf of the NCAB to the Marlene Durant Memorial Comprehensive Cancer Center at the University of Alabama and that Board members were invited to attend a memorial service at the Fox Chase Cancer Center on Friday, September 30. A moment of silence in memory of Mrs. Durant was observed.

Approval of the May meeting minutes was postponed until the Wednesday morning session.

In concluding his opening remarks, Dr. Korn welcomed Dr. Vincent DeVita back as a guest; the former Director of the National Cancer Institute is now Physician-in-Chief of the Memorial Sloan-Kettering Cancer Center. He noted that Dr. DeVita had recently been awarded the Pezcoller Foundation Award in recognition of his innovative work on the chemotherapy of lymphoma and for his general leadership to the field of oncology. Dr. Korn introduced the following resolution (dated September 26, 1988) for consideration by the Board:

> Whereas Vincent T. DeVita has served the National Cancer Institute with uncommon dedication and vision, challenging his staff and his colleagues, but never more than he challenged himself; and
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> Whereas Vincent T. DeVita has been a keen and effective advocate for cancer research, a champion of basic research, and tireless in urging transfer of new scientific advances into medical practice, as well as promoting adoption of the best prevention strategies across the country; and
>
> Whereas his deep concern as a physician for patients has intensified and warmed his scientific interests; and
>
> Whereas Vincent DeVita fostered an unrivaled atmosphere of excellence, which created a time of high achievement, as well as laid the essential groundwork for future accomplishments: Be it therefore
>
> *Resolved*, That the National Cancer Advisory Board wishes to acknowledge the extraordinary character and devotion of Vincent T. DeVita's service at the National Cancer Institute, dating from 1963, as a member of the staff, as Director of the Division of Cancer Treatment, as Clinical Director and, since 1980, as Director, and on behalf of the nation, congratulate him on his distinguished scientific achievement and honor him for service to the country.

Dr. Bernard Fisher moved for endorsement of the resolution. The motion was seconded by Dr. Gertrude Elion and passed by acclamation.

Dr. DeVita thanked the Board for the gesture and stressed that he would continue to work with NCI and the board toward the goals of the National Cancer Program, especially in the area of technology transfer. In conclusion, he commended the staff and noted that they were the secret to the operation of the National Cancer Institute.

II. Future Meeting Dates

Dr. Korn called the Board members' attention to the following confirmed meeting dates: December 5-7, 1988; February 6-8, 1989; May 15-17, 1989; September 18-20, 1989; December 4-6, 1989; and January 29-31, 1990.

III. Report of the President's Cancer Panel--Dr. Armand Hammer

Dr. Armand Hammer, Chairman, stated that he would discuss the Stop Cancer Project and the proposed agreement with the National Cancer Institute following his report of Panel activities since May. These included a meeting at the University of Arizona Cancer Center, where the Panel heard presentations on the Center's research into hyperthermia as a treatment modality, the Arizona cancer prevention program, and multidrug resistance. Dr. Hammer said the final meeting of the year would probably be held on the NIH campus so that the Panel could receive an update from NCI division directors on program activities.

Next, Dr. Hammer reported that the Panel prepared a resolution, similar to that of the NCAB, urging the President, Congress, and state and local governments to enact legislation that would not curtail the necessary use of animals in cancer research. He said the Panel further urged that those who act illegally to disrupt such research be vigorously prosecuted.

Dr. Hammer expressed the Panel's best wishes to Dr. DeVita as he undertakes his new position. He said the Panel is pleased to work with Dr. Alan Rabson as Acting Director, and he assured continued cooperation and assistance in the months ahead.

Turning next to the Stop Cancer Project, Dr. Hammer noted that the discussion had been scheduled so that Board members could review the proposed memorandum of agreement between NCI and "Stop Cancer" that had been distributed. He briefly reviewed the status of the project and plans for the future. He reminded the Board that the goal of the project is to raise $500 millon from private sources to be matched by an equal amount in Federal funds. These funds will be provided to the NCI for allocation based on and subject to the statutes, regulations, and guidelines governing NCI. In addition, the funds would be accounted for in accordance with standards established for nonprofit charitable organizations and would be subject to annual audit. Dr. Hammer said the memorandum had been developed with the assistance of Dr. DeVita and has been reviewed by NCI legal counsel and by Mr. Philip Amoruso, Associate Director for Administrative Management. He said $8 million in individual donations had already been raised although the campaign would not officially kick off until the October 12 gala at the new Wintergarden at the World Financial Center in New York. The gala, featuring performances by the Philadelphia Orchestra (Mstislav Rostropovich conducting and in solo), Isaac Stern, and Sherrill Milnes, is expected to raise an additional $2 million, and

fundraising efforts will continue until October 12, 1992, the five hundredth anniversary of the discovery of America.

Dr. Hammer stated he had assured Mr. William Tipping and other officials of the American Cancer Society that the project would not be in competition with ACS and noted that he had received a letter of congratulations for setting a goal to strengthen NCI's research program, signed by the ACS President and Chairman of the Board. He expressed confidence in the support of the American people and reported that he had received assurances from Congressional leaders that matching Federal appropriations would be forthcoming as the private funds are raised.

Dr. Hammer called attention to the statement in the memorandum of agreement that the funds would be used primarily to support cancer biology and immunological research, over and above the regular NCI appropriations. He cited Dr. Steven Rosenberg's new protocol combining IL-2, TILs, alpha interferon, and cytoxan as an example of research that could be advanced by the availability of additional funds. He stressed the need to take advantage of the opportunities presented by the advent of such combined modality therapies and said the sums of money raised by "Stop Cancer" and matched by Congress would make it possible for NCI to fund more than the present one-third of approved grants.

In response to the question as to how an increase of a relatively small magnitude--approximately $250 million per year--could produce the expected results in four years, Dr. Hammer pointed out that present appropriations permit funding of only one-third of approved grants. With more funds, additional qualified scientists could be put to work on projects that have been approved.

In the discussion, the following points were raised:

- The effect of the additional funding would be to move the payline up.
- Because of present budget restrictions and the tough priorities, there are excellent approved grants that cannot be funded.
- There are many causes of cancer, and the new era of biologic therapies, represented by the work of Dr. Rosenberg and others, provides an opportunity to stop cancer.
- An issue to be considered is the precedent created by the provision in the memorandum of agreement that makes NCI an exclusive recipient of the funds and, by inference, an exclusive partner in raising funds.

In response to a concern expressed that the advisory panel alluded to in the proposal might interfere with the NCI peer review process and lead to some conflict, Dr. Hammer pointed out that the memorandum prescribes that recommendation of projects will have to be in accordance with the statutes and policies of NCI, which include peer review.

Further discussion was postponed until later in the morning's agenda.

IV. Remarks by the Director, NIH--Dr. James B. Wyngaarden

In beginning his presentation, Dr. James Wyngaarden recognized Dr. DeVita's enormous contribution, and thanked Dr. Alan S. Rabson for agreeing to serve as Acting Director of NCI during the transition period and the Board and Panel for their pledges of support.

Turning next to the search for Dr. DeVita's successor, Dr. Wyngaarden announced that the White House had appointed a Search Committee, comprised of Mr. Don Newman, Undersecretary of Health and Human Services (HHS); Dr. Robert Windom, Assistant Secretary for Health; Ms. Helen Stafford; and himself, as well as several advisors. He said he had been asked to chair the committee and had agreed. He reported that the committee had already held two planning meetings and, with the help of NCI, drafted a solicitation letter which, after approval, was sent to about 1,000 individuals including all deans of medical schools and schools of public health, presidents of all the cancer societies, and members of cancer centers. Dr. Wyngaarden solicited additional suggestions from the Board and Panel. He said the committee would review the credentials of all suggested nominees and the Board would arrange interviews with the outstanding candidates. A final slate is to be submitted to the President on or before November 10.

For the Board's information, Dr. Wyngaarden reported that Dr. Charles Putman had submitted, on behalf of the Coalition of Diagnostic Radiology Societies, a proposal that NIH mount an intramural program in diagnostic radiology research. He noted the existence at NIH of the Interinstitute Coordinating Committee on Diagnostic Radiology (led largely by NCI), although the effort of that body is directed predominantly toward extramural funding. In response to the proposal and an offer of resources, Dr. Wyngaarden said he has appointed a committee, headed by Dr. Ronald Neumann, to inventory those activities on the NIH campus that might fit such a program. The Board will be kept informed of any developments.

With regard to the FY 1989 NIH budget, which had been signed into law by the President the previous week, Dr. Wyngaarden noted that it presents a substantial increase for AIDS research and essentially a cost-of-living increase for the non-AIDS component, and it does not dictate a precise number of new and competing awards. He added, however, that because of the increased number of new and competing awards in recent years NIH has a substantial commitment in noncompeting renewals. He said the cancer budget of $1.575 billion represents a $103 million increase over FY 1988 and will permit funding of 726 new and competing awards, 250 fewer than in FY 1988.

Noting that the reduction in new and competing awards experienced by NCI is greater than for other Institutes, Dr. Wyngaarden stated that the increase requested by NIH for NCI during the FY 1990 budget process would be at least the average of NIH as a whole--that the plan is to request funds for more than 800 new and competing awards. He stressed that the NIH administration supports an end to the decrease experienced by the NCI budget this year.

In concluding his presentation, Dr. Wyngaarden announced the appointment of Dr. James Watson as Associate Director for the Human Genome Project, an effort that will initially focus on information handling, developing improved methodology, and mapping. He said the responsibilities of the new office will include liaison and collaboration and coordination with other agencies of the U.S. Government, the private sector, industry, and organizations from other countries.

In response to a question as to what can be done to bring NCI's rate of budget increase in line with those of other Institutes, Dr. Wyngaarden explained that some of the disparity of budgets comes from the complex process of reconciling the Administration's requests for the non-AIDS part of the budget (an average increase over the past 6 years of about 1.7 percent over each previous year's budget) with the actual budget voted by Congress (usually in the 8 to 9 percent range). He added that the amount of increment generally available for NIH distribution is quite small and, because it is often subject to priorities established by the Department and by the Congress, cannot be distributed by formula across the Institutes.

Dr. Wyngaarden pointed out that the number of NCI new and competing grants was high the previous year, and his office considers the average of the past three years in making budget decisions because of the cyclical response to fluctuations in numbers of grants funded. He added that the creation of two Institutes in the past few years had also diverted resources.

In response to another question, Dr. Wyngaarden stated that a sum of approximately $28 million has been specially earmarked in the FY 1989 budget for the human genome project and that these funds will be tracked separately. He stressed that NIH did not intend to siphon funds from other programs for that project.

V. Remarks by the Executive Vice President, American Cancer Society (ACS)-- Mr. William Tipping

Mr. Tipping greeted members of the NCAB and President's Cancer Panel, NCI staff, and guests and noted that the occasion signaled a new era of cooperation between NCAB and the ACS. He described ACS as the world's largest voluntary health organization with a membership of 2,500,000 persons (in 3,300 units spread across 57 geographical divisions) united to fight cancer through balanced programs in research, education, patient service, and rehabilitation. The ACS raises and spends $300 million annually to support those programs.

Mr. Tipping reported that discussions between Dr. DeVita and key ACS officials at the annual National Science Writers' Seminar earlier in the year explored areas where cooperation and coordination of effort between NCI and the ACS could be effected. How the Cancer Society could help promote and publicize NCI-sponsored clinical trials was a focus of the discussions.

As a result, according to Mr. Tipping, ACS has planned programs in public and professional education to help medical practitioners, cancer patients, and the general public to greater awareness and acceptance of clinical trials. The first program is a series of eight hearings focusing on cancer in the socioeconomically disadvantaged, to culminate in a major hearing in Washington, D.C. The hearings will provide opportunities to study access to adequate cancer treatment, incidence rates, and access to care and rehabilitation by those who have contracted the disease.

Secondly, Mr. Tipping stated that the ACS will work closely with NCI on the National Tobacco Use Reduction Demonstration Project, which will take place in about 25 metropolitan and statistical areas when all approvals have been granted. The third program described by Mr. Tipping was the second phase of a cancer prevention study (CPS2) in which ACS is gathering epidemiological data on the lifestyles of 1.5 million families. He added that the results of the first 5-year study would soon be available.

Finally, Mr. Tipping expressed ongoing support on behalf of the ACS for NCI reauthorization and appropriations. He pointed out that ACS, through its dedicated staff and volunteers, can provide energy and support for NCI programs at the local level, and he emphasized the need for continued coordination between the two organizations.

In discussion, the following points were raised:

- ACS has indicated publicly at the appropriations hearing that it supports the National Cancer Program goals for the year 2000 and has worked to achieve the same objectives through its education (e.g., the tobacco use reduction demonstration project), research ($85 million for peer-reviewed grants), and service programs.

- It would be beneficial to public perception and understanding of the programs and goals of both organizations if ACS and NCI were to coordinate similar activities such as public information (the 800 numbers) and public hearings.

- ACS would like to continue discussions begun with Dr. DeVita on ways to enhance cooperation between the two organizations.

- ACS has moved its headquarters to Atlanta and the 800 number has been moved into the communication sector of the American Cancer Society, away from the medical side.

- The hearings on cancer treatment for the socioeconomically disadvantaged will complement and reinforce issues covered in the hearings of NCAB's National Black Leadership Initiative on Cancer.

- The ACS has played a continuing and valuable role in training young people through its financial support of fellows and junior faculty members.

- NCAB, through its black leadership and public hearing initiatives, has adopted a more active stance and is moving in a path convergent with longstanding activities of the ACS; therefore, continued coordination of activities will help avoid redundant and reiterative efforts.

VI. Discussion of the Stop Cancer Project--Dr. David Korn and Dr. Armand Hammer

To provide a focus for this discussion, Dr. Korn suggested that it was the business of the Board to consider in some detail the specifics of the formal relationship, if any, between NCI and the Stop Cancer Project and the degree to which that relationship should or should not be memorialized in some form of written agreement. If a written agreement were deemed advisable, Dr. Korn said, the Board could choose to accept the draft document, revise it, or replace it.

In responding to concerns expressed by a Board member, Dr. Hammer gave his assurance that NCI would not be expected to help with the fundraising in any way, and he suggested deleting the phrase in the draft that could be wrongly construed. As for the matching funds, Dr. Hammer said his conversations with Congressional leaders have indicated that they would be flexible in providing funds to coincide with the programs and needs of NCI.

In response to a concern about how to develop a plan for the most efficient use of the funds, Dr. Hammer replied that the draft agreement had been developed with Dr. DeVita's help, and use of the funds would have been subject to his review. As the situation has changed, he suggested that he, Dr. Rabson, Dr. Korn, and Project staff meet to work out all potential problem areas. He stressed that this is a voluntary gift, and all funds raised by the Project will go directly to NCI whose responsibility it will be to distribute the funds in accordance with established procedures.

In concluding the discussion, the Board expressed thanks to Dr. Hammer and appreciation of the project and agreed that a representative committee could meet to work out the specific language of the agreement.

VII. NCI Director's Report--Dr. Alan S. Rabson

Dr. Rabson stated that it was a privilege and an honor for him to serve as Acting Director of the Institute. He recognized the outstanding staff in the Office of the Director (OD) and joined Dr. Korn in welcoming the new Board members.

Dr. Rabson summarized staff changes as follows: Dr. Federico Welsch joining the OD staff as Associate Director, Office of International Affairs; Dr. Ihor Masnyk serving as Acting Director of the Division of Cancer Biology and Diagnosis (DCBD); Dr. Edward Tabor becoming Associate Director of the Biological Carcinogenesis Program in the Division of Cancer Etiology (DCE); Ms. Susan Hubbard becoming Associate Director of the International Cancer Information Center in the Office of the Director; Dr. Charles Myers serving as Chief of the Medicine Branch, Division of Cancer Treatment (DCT); Dr. Robert Young assuming responsibility for the Cancer Centers Program; Dr. Vincent Cairoli becoming Chief of the Cancer Training Branch in the Division of Cancer Prevention and Control (DCPC); Dr. Gregory Curt leaving as Deputy Director of DCT to become Director of Medical Education and Chief of Clinical Pharmacology at Brown University Medical School; Dr. Robert Wittes leaving as the Director of the Cancer Therapy Evaluation Program (CTEP) and Acting Deputy Director of DCT to become Senior Vice President for Cancer Research at Bristol Myers; and Dr. Marc Lippman leaving as Head of the Breast Cancer Section in the Medicine Branch to become Director of the Vincent Lombardi Cancer Center at Georgetown University.

Dr. Rabson next identified several of NCI's leading researchers and clinicians and noted their major fields of activity. He concluded by describing the Board's opportunity to build and support the NCI and noting Dr. DeVita's contribution as a physician offering hope to cancer patients, as well as directing the NCI.

Budget Update

Mr. Philip D. Amoruso presented highlights of the FY 1989 budget. He stated that having the budget in advance of the fiscal year would greatly facilitate planning. He pointed out that the appropriations bill includes support for the Human Genome Program and the establishment of a Deafness Institute, and planning money for a consolidated office building.

Mr. Amoruso said that all of NCI's FY 1988 budget of $1.468 billion would be obligated. Although the President's budget for FY 1989 for NCI represented an increase of $125 million, a deficit control agreement necessitated a $19 million reduction down to $1.574 billion. An additional reduction was made based on potential savings from procurement reform. Further reductions could occur on October 15 following Gramm-

Rudman review. Mr. Amoruso said the budget of $1.571 billion represented a 7 percent increase overall, with the cancer portion receiving a 5 percent increase and the AIDS portion a 37.6 percent increase. Certain Programs, Projects and Activities (PPAs) are specifically designated by Congress, and money cannot be moved among these activities without Congressional review. The two new, separately identified PPAs for NCI are construction and cancer prevention and control, making a total of five.

With respect to competing and noncompeting awards, Mr. Amoruso said that NCI would receive an increase of $69 million and would be able to fund a total of 63 more grants than last year. However, the number of competing grants that can be funded will decrease by 249, meaning that about 25 percent will be funded. The cutoff priority score is expected to be about 160, or the 23rd to 24th percentile. In concluding his presentation, Mr. Amoruso noted that NCI has received about $2.7 million in gifts, with a current Gift Fund balance of $580,000. Of the $1.9 million NIH received from patents in 1987, NCI received $1.7 million. Some of these funds are used for the administration of patents and licensing by the Department of Commerce. Investigators can receive up to $100,000 a year, although most receive much smaller amounts. NCI received approximately $981,000 from patents in 1987 and these funds go back to the laboratory where the discovery was made.

The following points were raised in discussion:

- The expected funding of only 25 percent of approved grants is an all-time low.
- In the past, cash gifts generally have been used to fund intramural activities.
- NCI cannot accept conditional gifts; such gifts would have to be approved by the Director of NIH.
- Because of the designated funds for PPAs, NCI has limited flexibility in allocating funds.

Information Items

Dr. Maryann Roper called to the Board's attention the summary of the Cancer Centers Subcommittee's Workshop on Comprehensiveness. Based on the Workshop discussions, Dr. Durant will compile a definition of comprehensiveness and suggest alternative grant support mechanisms for such centers.

Dr. Roper said that as instructed by the Senate, the Institute of Medicine (IOM) will conduct a study of the Centers Program. The study will consider the organizational location of the Centers Program within the NCI and the type and amount of funding needed to enable the program to fulfill its mission. NIH has asked NCI for help in defining the work scope of the study, which is expected to be completed around February 1989.

In discussing full-time equivalents (FTEs), Dr. Roper compared AIDS and non-AIDS FTEs for all of NIH from 1984 through 1989. Although the NIH budget increased during that time, the number of FTEs decreased by 5.6 percent. However, the number of AIDS FTEs increased from 160 to 580 and the number of non-AIDS FTEs decreased by about 1,700. In 1984, NCI had 2,400 FTEs, but for 1989 will have a ceiling of 2,094 FTEs. Of these, 143 are involved in AIDS work, but only 53 are officially designated as AIDS FTEs. Dr. Roper summarized the issue as follows: NCI's total number of FTEs has decreased by 13 percent over the 5-year period, compared to loss of 5.5 percent for NIH

overall, and NCI's programs require people. While there is a hiring freeze at NIH, Congress has appropriated funds for 350 new slots for NIH during FY 1989; however, the Office of Management and Budget (OMB) has not yet released these positions. Two hundred of the new slots have been designated for AIDS, and when needs were identified, it was pointed out that NCI has the largest intramural AIDS program on campus. Dr. Roper suggested that NCI's contributions to both AIDS and cancer research should enable the Institute to compete effectively for the new positions.

In response to a question about the imbalance in NCI's assignment of FTEs, Dr. Chabner stated that AIDS is considered a higher priority than cancer. NCI has only 10 percent of the NIH AIDS positions, but has conducted the majority of intramural research on AIDS. NCI uses cancer slots for AIDS work.

Legislative Update

Dr. Mary Knipmeyer defined and discussed authorization and appropriation processes and reported on the status of reauthorization of the National Cancer Act. Authorization is the mission or statement of work for a particular program, usually for a particular time period. The Appropriations Committee uses authorized ceilings as guideposts for funding, which is usually below the ceiling. Appropriations are for one year. Dr. Knipmeyer said NCI's current authorization expires on September 30, 1988, and the appropriation for fiscal 1989 is already in place. The authorizing committees are the House Subcommittee on Health and Environment, chaired by Rep. Henry Waxman, and the Senate Labor and Human Resources Committee, chaired by Senator Edward Kennedy. If authorization lapses, NCI would continue normal operations under the general research authority in Section 301 of the Public Health Service Act and under authorities provided by current appropriation law.

Dr. Knipmeyer pointed out some unique features of NCI's authorization. NCI's special authorities include increased access to the President through the Presidential appointment of the Director, the President's Cancer Panel, and the NCAB, and the annual By-Pass budget. Also, the National Cancer Act facilitates an expedited cancer program through construction authority, special peer review authorities, and authorities to appoint special advisory committees. Dr. Knipmeyer noted that the NCI has a line item authorization for cancer prevention and control. Dr. Knipmeyer said many of the National Cancer Act authorities have been extended to other NIH Institutes, because they work so well.

Dr. Knipmeyer noted that the Senate has passed a reauthorization bill that maintains the special authorities of the National Cancer Act and clarifies some of the changes that occurred in 1985 with the last reauthorization. The Senate bill includes a new ex officio member to the NCAB from the Department of Energy. The House passed a separate bill to establish a Deafness Institute at the NIH, and Dr. Knipmeyer said the question is whether the House will introduce its own NIH reauthorization bill or go to conference with its Deafness Institute measure and the Senate-passed NIH reauthorization. If Congress is unable to reauthorize NIH by the time they adjourn, the process will begin again in the 101st Congress, which convenes in January 1989.

The following points were raised in discussion:

- NCI must officially support the President's budget. Members of the NCAB, professional groups, and constituency groups are free to speak on behalf of the By-Pass budget as a realistic document based on professional judgment.

- Issues that may be affecting House reauthorization include fetal research and scientific fraud and misconduct issues.

Dr. Knipmeyer went on to update Board members on legislation of interest. Both the House and Senate have passed AIDS bills, and of particular interest to NCI, is whether outpatient AIDS research or inpatient beds for AIDS research will be expanded at the Clinical Center. The Pet Theft Act, passed by the Senate, would ban USDA-Class B animal dealers from purchasing animals at auctions for animal research and would require an animal to be held in a pound or shelter for seven days before it could be released to an animal dealer. The USDA draft regulations to implement the amendments of the 1985 Animal Welfare Act are under review by OMB. Dr. Knipmeyer said USDA has estimated that it will cost $1.07 billion to implement the regulations. In conclusion, she stated that the President has signed the Medicare Catastrophic Coverage Act, which allows $50 reimbursement for screening mammographies. NCI will be asked to consult on the frequency and quality of mammography.

In response to a question about radon, Dr. Richard Adamson said the Environmental Protection Agency (EPA) estimates that between 5,000 to 20,000 cases of lung cancer per year may be caused by radon. Cigarette smoking probably multiplicatively increases the risk. Studies are in progress in Missouri, New Jersey, and two foreign countries to attempt to clarify the degree of risk from radon exposure.

VIII. The Role of Retinoblastoma and Other Chromosomal Deletion Genes in Lung Cancer --Dr. John D. Minna

In describing the magnitude of the problem, Dr. Minna stated that 150,000 patients in the United States are diagnosed each year with lung cancer and 90 percent of them die within one year of diagnosis. Worldwide, a very large number of deaths is projected from lung cancer over the next 20 to 25 years. In China, because of the high incidence of smoking, more people will die from lung cancer than were killed during World War II on a yearly basis. Dr. Minna said research is in progress--clinical trials and cell and molecular biology studies--to develop new ways to diagnose, treat, and prevent lung cancer.

The working model used by Dr. Minna involves taking cells from primary or metastatic lesions in patients, and then putting them in culture to establish continuously growing lung cancer cell lines, or alternatively, xenografting tumor cells into nude mice, transplanting them, and then putting them into culture. Dr. Minna said this model enables a series of genetic, cytogenetic, biochemical, and morphologic studies, as well as drug sensitivity testing. He said the cytology of cell lines is exactly as it appears in the patient, and it is thought that the cell lines, to a great degree, maintain in tissue culture the expression of a series of markers and the behavior of the cells in patients. Approximately 150 cell lines are actively growing, including 90 small cell lung cancers, 40 non-small cell lung cancers, and other types such as bronchioalveolar cancers, mesotheliomas, and carcinoid tumors. Dr. Minna stated that the current epidemic of bronchioalveolar cancer in the United States raises the question of whether there is some new toxin or virus as the cause.

Dr. Minna attributed to molecular genetics the simplifying concept that cancer is a result of several genetic changes occurring in specific genes in cancer cells. Other factors in the person and in the environment influence these changes. Some oncogenes act in a dominant fashion and in the presence of a gene product, requiring changes in only one chromosome, to cause a malignancy. For recessive oncogenes, which require

changes in both maternal and paternal chromosomes, it is thought that it is the absence of the gene product that causes the malignancy. In explaining the genetic basis of cancer, Dr. Minna said that in a person with no genetic lesions, a mutation could occur in some oncogene, causing a tumor to arise, and then all progeny tumor cells would inherit the genetic change as a somatic event. Another possibility is that parents pass on to their children genes with genetic changes in one of the oncogenes. Dr. Minna suggested that a mixture of the two possibilities occurs in several types of human cancer.

Molecular genetic studies have been performed to identify the sites of action of some of the oncogenes, especially dominant-acting oncogenes. Dr. Minna said oncogenes can act like membrane receptors transducing signals to the nucleus or they can act like proteins that either bind to the DNA of the nucleus or to one another and turn genes on or off. He said his discussion would focus on two oncogenes in which lesions affect their transcription and expression of RNA. The myc family of oncogenes has putative protein factors that sit on the gene, either turning it on or blocking its expression. This is studied by a nuclear run-off assay. Dr. Minna used slides to show that in some small cell lung cancer lines the myc gene is turned on. One of the lesions that turns this on is greatly increased copy amplification of the gene. In some cases, when the transcription of the gene is turned on, the mechanism to block its expression is also present. The recently described c-jun oncogene, discovered in a bird retrovirus, works in the nucleus, and its normal function seems to be to turn on the transcription of genes. The jun oncogene codes for 39 kilodalton protein and forms a complex with another oncogene protein C-fos, which is identical or closely related to a transcription factor AP-1 shown to turn on the expression of a set of genes. The genes turned on all have a very specific DNA sequence in their 5' region. The biochemical activity of the oncogenes is stimulated by tumor promoters, serum, and some growth factors. Dr. Minna said many lung cancer cells, as well as normal lung cells, have been found to have high levels of expression of this gene. However, no genetic abnormalities have been identified in a variety of lung cancers; therefore, study has been undertaken on whether normal genes, if expressed to levels as high as in lung cancer, will cause malignancy.

Dr. Minna then turned to discussion of recessive oncogenes or tumor suppressor genes. In studying childhood retinoblastoma, Dr. Al Knudson hypothesized that in familial cases, one lesion on chromosome 13 was inherited from a parent and a second lesion was acquired early in life, and in sporadic cases, both lesions were acquired early in life. The questions of what gene was involved and whether the same gene was involved in both types of tumor was addressed through chromosomal analysis and restriction fragment length polymorphism (RFLP) analysis. The RFLP analysis showed that a gene had been lost in tumor DNA. Dr. Minna said that the similarity of cytogenetic abnormalities in retinoblastomas and small cell lung cancers led to the finding that in nearly every case of small cell lung cancer there has been a deletion or translocation or change in band 13q14, which was also noted in retinoblastoma. In about 20 percent of retinoblastomas and small cell lung cancer, homozygous deletion has been found in the DNA. When deletion is not found, Dr. Minna stated that there is often complete absence, greatly reduced amounts, or truncated size of the retinoblastoma message. Those small cell lung cancers that do express the message are being studied to determine whether they are making normal protein. A 3p deletion has also been found in many small cell lung cancers and some carcinoids, non-small cell lung cancers, and mesotheliomas.

Dr. Minna pointed out the similarity of these cytogenetic abnormalities to those described by Dr. Strong in renal cancer. Using RFLP analysis, in all 59 pairs of informative (heterozygous polymorphism in normal tissue) small cell lung cancer, the tumor cells lost a DNA band in the 3p region. He said that more tumors are being found

to have abnormalities in this region, and he suggested that this deletion may have implications for finding a recessive oncogene. Dr. Minna also noted that changes and translocations have been found on other chromosomes, and by cloning deletion genes from lung cancer cells it may be possible to develop a panel of deletion genes. The next step in ascertaining whether this is a recessive gene is to isolate the gene on chromosome 3. An additional piece of useful information is the finding that the enzyme aminoacylase, which is in the chromosome 3p area, is inactivated in small cell lung cancer. In studies of lung cancer patients who were cured and developed second tumors, the 3p deletion was found. Although Dr. Minna said lung cancer is not usually thought of as an inherited disease, there are enough clues to indicate that a person might inherit some predisposition or metabolic phenotype, which combined with smoking, radon exposure, and other factors, would result in lung cancer.

Dr. Minna suggested that clarification of the significance of these genetic changes could be useful for the early diagnosis or prevention of lung cancer. A therapeutic approach might involve replacing the genes that are deleted and using drugs or other factors to block the function of oncogenes.

In discussion, the following points were raised:

- The best prevention of lung cancer is to stop smoking.
- Advances have occurred in recent years to enable the culture of normal lung epithelial and lung cancer cells.
- The technology is available to induce lung cancer in vitro, but appropriate studies need to be developed.
- There is general agreement that the 3p deletion is found in all small cell lung cancer, but the question remains as to how often it is found in non-small cell lung cancer (at least in 40 percent of cases).
- Multiple deletions may be needed to knock out multiple tumor suppressor genes, just as multiple oncogenes are needed in tumor cells.
- Extrapulmonary small cell lung cancers have the retinoblastoma, but not the 3p deletion.
- It will be possible to perform genetic analyses to predict who would be susceptible to certain cancers.
- Blood relatives of persons with lung cancer have a significantly increased risk of getting even non-smoking related lung cancer.

IX. Early Diagnosis of Lung Cancer Using Monoclonal Antibodies--Dr. James Mulshine and Dr. John Ruckdeschel

Dr. Mulshine said he would report on research conducted in collaboration with Johns Hopkins University on a new technique for early detection. Dr. Ruckdeschel, from the University of Albany Medical Center and the Lung Cancer Study Group (LCSG) would then describe a proposed clinical trial to confirm the utility of this approach. In beginning his presentation, Dr. Mulshine reiterated the magnitude of the lung cancer problem and the importance of addressing that problem. Even if all smoking were to

stop, lung cancer deaths would continue into the next century. Although efforts are in progress to address systemic lung cancer, no treatment now appears likely to have a significant impact on mortality.

The NCI-sponsored Early Lung Cancer Detection Study involved the evaluation of screening chest x-rays and sputum cytology as means to improve the early detection of lung cancer. The study involved 30,000 patients screened over 10 years. The study demonstrated that dual screening enabled patients to be diagnosed at early stages of disease, but there was no change in lung cancer mortality as a result of lead-time bias or length bias.

Dr. Mulshine said that because the carcinogenic process from initiation through promotion to the development of frank neoplasia occurs over many years, it should be possible to detect early changes in cells that would identify those who would develop lung cancer. In working in Dr. Minna's laboratory to develop monoclonal antibodies (MoAbs) to lung cancer, Dr. Mulshine said they and others found classes of differentiation antigens that were slightly expressed in normal tissues, expressed somewhat more over time, and densely expressed in malignancy. Dr. Mulshine suggested that using selected differentiation markers may permit identification of those bronchial cells in the process of carcinogenesis but before the development of frank cancer to detect patients at very high risk of developing cancer. The collaborative study with the NCI and Johns Hopkins involves investigators previously involved in the Early Detection Study. The study uses triple-antibody, double-bridge technique. The antibody is conjugated to an enzyme that produces a characteristic immunohistochemical reaction. Dr. Mulshine said that this technique, developed by Dr. Gupta, clearly enhances the signal in tumor tissue.

Analyses were performed on sputum specimens from 626 of the originally randomized 5,000 patients who had moderate to severe atypia. Two monoclonal antibodies were applied to the most recent atypical sputum specimens. The correlation between positive staining and the development of lung cancer was highly significant. Detection was better in those who developed lung cancer within two years of the sputum sample than in those who developed lung cancer six years after the sputum sample. The technique was 90 percent accurate in detecting lung cancer two years before diagnosis. Dr. Mulshine stated that the study is limited by the fact that it represented only 40 percent of all those who got lung cancer and only those with moderate to severe abnormalities in sputum cytology.

Dr. Mulshine suggested that there may be antibody markers that are differentiation markers and could be used to detect early cell surface changes associated with carcinogenesis. He said it would be useful to determine if the predictive accuracy achieved retrospectively could be confirmed in a prospective study. Improvements in the diagnostic approach might result from the use of additional antibodies, optimization of staining technique, and use of image analysis technique to eliminate variations in observer interpretation.

Dr. Mulshine next discussed his group's research on the autocrine lung cancer growth factors and how these might be used in early diagnosis. Again using the carcinogenesis model, Dr. Mulshine said that the growth factors are thought to be important in the early stages of tumor promotion. Levels of neuropeptide or bombesin-like immunoreactivity have been found by Miller and co-workers to increase in the bronchial lavage fluids of persons who smoke but do not have cancer. Dr. Mulshine suggested that this may be similar to the role of estrogens in breast cancer. A Phase I trial is in progress to determine whether a monoclonal antibody to this neuropeptide can

be used to treat patients with advanced small cell lung cancer by blocking the autocrine loop. In two different small cell lung cancer cells, a transferrin-like moiety has been found to have all the features of an autocrine growth factor. His group also recently published data indicating that insulin-like growth factor (IGF) can function as an autocrine growth factor in small cell lung cancer, and they have preliminary data for a similar activity in non-small cell lung cancer. Therefore, Dr. Mulshine said, as part of the proposed collaboration with the Lung Cancer Study Group, studies will be done to determine if growth factor levels in the lavage fluid correlate with clinical outcome and can improve the accuracy of early detection. Growth factors and cell surface changes are thought to be two aspects of lung cancer biology that offer potential for detecting early changes. Dr. Mulshine stated that the critical question is whether the detection of early changes can affect outcome, i.e., the prevention or treatment of lung cancer. Therapeutic options that might be combined with early detection might include conservative surgery, hematoporphyrins and argon lasers, pre-neoadjuvant therapy, anti-growth factor approaches, and anti-metastatic therapies.

Dr. Ruckdeschel described the Lung Cancer Study Group as a multi-institutional cooperative group, funded by NCI, with a primarily surgical focus on studies in early lung cancer and local regional disease. He said the proposed trial is to use sputum cytology immunostaining for early detection of second primary lung cancers. The Group has an appropriate data base from earlier trials with nearly 1,000 patients in active, regular followup. He said the annual incidence of second primary lung cancers varies between 2 and 5 percent; therefore, over three years, approximately 70 to 100 second primary lung cancers could be expected in the group of patients being followed. Because that incidence is significantly higher than the incidence in any high-risk population, this group offers a unique opportunity for evaluating methodologies for early detection and diagnosis.

Dr. Ruckdeschel stated that the proposed trial would involve annual induced sputum cytology on previously resected Stage 1 patients. If a positive cytology is found, the patients will undergo fiberoptic bronchoscopy, bronchial lavage, or whatever diagnostic tests their physicians recommend. If the cytology is negative, but on subsequent review of the immunostaining the results are found to be positive, those patients will also undergo further diagnostic tests at the recommendation of the physician. Annual followup will be continued on those patients with negative cytology and immunostaining. The immunostaining studies will be done at Johns Hopkins University and aliquots of fluid from further diagnostic tests will be examined in Dr. Minna's and Dr. Mulshine's laboratories and in Dr. Steven Rosen's laboratory in Chicago. Dr. Ruckdeschel said one objective of the trial is to determine whether immunostaining of induced sputum can add to the sensitivity and specificity of routine morphologic atypia to detect those individuals at greatest risk of developing a second primary lung cancer. In those patients with severe atypia, immunostaining should be positive three to five years before cytologies turn positive. In those with moderate atypia, it has not been possible in the past to detect cancer early. Dr. Ruckdeschel identified as a primary focus of the trial, the early identification of adenocarcinomas and small cell lung cancers. However, he expressed uncertainty about the results in the 60 percent of patients who develop lung cancer but do not demonstrate atypia. As another objective, Dr. Ruckdeschel said the archive of preserved specimens and bronchial washings would be made available for further analysis of new antibodies and techniques.

The following points were raised in discussion:

- Further studies will be done on all patients with positive immunostaining.

- In the study, second primary tumors must have different histologies from the first primary tumor.

- If the confirmatory trial is positive, consideration should be given to what therapeutic options might be pursued in those patients with positive cytology or immunostaining. It is hoped that physicians would repeat bronchoscopy with lavage, as well as chest x-rays and CAT scans to look for the occult primary tumor.

- The antibodies used are 703D4, a non-small cell antibody that binds to an intracellular protein antigen, and 624H12, thought to bind to a glycolipid.

X. Reimbursement and Clinical Trials--Dr. Robert Wittes

Dr. Wittes outlined issues related to third-party reimbursement for patient care costs associated with clinical trials. He stated that most health care insurance contracts exclude coverage for investigational therapy (i.e., therapy with drugs or biologics not yet approved by the FDA for any indication). He noted that this exclusion has not been rigorously enforced uniformly across the United States. In some cases, however, the entire cost of a hospitalization has been disallowed by insurance carriers when an investigational agent has been given during the course of hospitalization. In particular, many insurance carriers balk at reimbursing for high-cost investigational therapy, such as LAK/IL-2, which may be the best systemic therapy for certain types of refractory metastatic neoplasms and which was the basis for the group C designation given in 1987. Another problem has been disallowing reimbursement for hospitalization costs when the hospitalization resulted from outpatient therapy that included an investigational agent.

Dr. Wittes explained that a second dimension to reimbursement problems has been coverage for therapy with agents for indications not approved by the FDA. For example, the FDA has approved alpha-interferon for use only in the treatment of hairy cell leukemia, and third-party carriers are refusing payment for "non-label use" of alpha-interferon. Dr. Wittes noted that this problem will become increasingly pressing as more relatively expensive biologics become available and are approved initially for narrow indications. He expressed concern that there was evidence that such reimbursement policies were already slowing the LAK/IL-2 trials significantly.

In an effort to address these issues, NCI organized a meeting that included representatives from various organizations, such as the cooperative groups, cancer centers, IOM, FDA, and AMA, and lawyers experienced in reimbursement policies. Dr. Wittes stated that there was a fair consensus that insurance carriers should be asked to provide reimbursement for all medical care given in the context of approved clinical trials. There was also a consensus that it was not reasonable to ask insurance companies to pay for investigational therapies for which they had no proof of the validity of the research. Some representatives also thought it was unreasonable to ask insurance companies to pay for high-cost, resource-intensive, very early clinical trials.

Dr. Wittes stated that this meeting had also addressed whether the issue of reimbursement for investigational anticancer therapy should be considered separately from that in other fields of medicine. He pointed out that most of the meeting organizers believed that the cancer field should probably be considered separately because the cancer community has a well-developed clinical trials mechanism and the PDQ database which can function as a national repository of clinical trials of scientific stature, whereas other medical communities may not be as organized. The question of whether

reimbursement policies should be dealt with independent of developing a Federal policy toward the fostering of clinical research also was raised. As a result of the meeting, a consensus document is being drafted to express the views of the participating organizations. Another meeting will be held in October 1988 to complete the consensus document and to continue plans to meet with the insurance industry. Dr. Wittes noted that in fact NCI staff had recently met with the Blue Cross Association staff in Chicago, who had expressed concerns over reimbursement issues, particularly reimbursement for therapy for which there is no evidence of efficacy. The Blue Cross staff has expressed interest in conducting a pilot study on the costs of clinical trials. An IOM committee on the clinical research enterprise, chaired by Dr. Paul Marks, will also consider reimbursement issues.

Dr. Wittes stated that the Health Care and Financing Agency (HCFA) and Medicare policy excludes reimbursement for all investigational therapy, except for group C drugs. Because HCFA is currently rewriting some of its regulations, NCI staff will meet with HCFA to persuade them that medical therapy on clinical trials should be construed as "reasonable and necessary treatment," which is the legislative language with which the Congress directs HCFA to pay for medical care. Dr. Wittes closed by stating that if the HCFA does not agree to this, NCI will probably request a supplemental appropriation within the NCI budget to pay for investigational therapy within the Medicare population.

Points raised in discussion included the following:

- To address reimbursement issues related to investigational therapy in California, for example, questions about validity of therapies were referred to the California Medical Association. The Blue Cross-Blue Shield carriers accepted judgments made by the Medical Association.

- In some instances when an investigational agent has been added to a regimen of several standard approved drugs, the entire cost of hospitalization has been disallowed.

- An alarming example of further reimbursement issues has arisen in the area of postmyocardial infarction care where HCFA does not want to provide coverage for tissue plasminogen activator (TPA), which has been approved by FDA for use in inducing recanalization of occluded arteries, because there are no data from randomized trials yet suggesting a survival advantage to TPA therapy over streptokinase, a much less expensive agent.

XI. Update on Cooperative Group Clinical Trials Accrual--Dr. Michael Friedman

Dr. Friedman began his presentation by noting that each year approximately 27,000 new patients are entered on cooperative therapeutic trials. There were about 428 active studies by 18 clinical cooperative groups supported by DCT at a cost of $56 million in 1988.

Dr. Friedman presented accrual data on 123 active Phase III studies from April 1 through July 31, 1988. He pointed out that compared to the previous quarter the number of Phase III studies was reduced by 5 percent (13 studies closed and 5 opened) and that the overall annual accrual rate had increased by 8 percent (i.e., from 14,268 to 15,344 patients per year). He emphasized that overall there was a 13 percent decrease in the number of studies and an increase of 20 percent in accrual to Phase III studies since January 1988, illustrating that study questions were being addressed in a more efficient

and timely fashion. He showed that most of the groups were fairly accurate in predicting accrual rates to studies, although some groups (e.g., the Brain Tumor Study Group and the Lung Cancer Study Group) were accruing patients more slowly than predicted while others (e.g., the Pediatric Oncology Group and the National Surgical Adjuvant Breast and Bowel Project) were accruing patients in excess of original estimates. He also compared the accrual rate (in thousands of patients per year) to Phase III studies from July 1987 through June 1988 to the annualized rate for April 1988 through June 1988, illustrating a trend toward an increased accrual rate for most groups. He showed that the average study duration based on the current rate of accrual to a total of 123 active Phase III trials was, however, slightly more than 6 years, with some studies requiring more than 10 years to complete the accrual phase.

Turning to a discussion of the Cancer Therapy Evaluation Program's efforts to reduce such lengthy study durations, Dr. Friedman stated that in reevaluating the terms of award for the cooperative agreements, limits for the accrual phase of Phase III studies of between three and five years were being proposed. He briefly described the high-priority trials previously presented to the Board and outlined the process by which these trials were identified. He summarized the status of the high-priority trials as follows:

- One study was closed after it completed enough accrual to allow for interim analysis, which revealed an important clinical difference between the treated and control groups.
- Five Phase III studies were in the active accrual phase.
- Three trials were progressing at or above the projected accrual rate.
- The annual accrual rate had increased 23 percent (i.e., from 1,008 to 1,244 patients per year).

In conclusion, Dr. Friedman emphasized that no monies had yet been applied to the high-priority trials program and that ongoing efforts would likely be affected by constraints on the cooperative group clinical trials budget.

Points raised in discussion included the following:

- Designation of the high-priority trials was made after an interchange of ideas between the NCI and extramural investigators, with an emphasis on promising clinical situations, worthwhile scientific hypotheses, and high-incidence cancers (e.g., colon cancer).
- The importance of adequate, continued funding for a broad range of clinical trials initiatives was emphasized.
- Funding for participation in the high-priority trials is on a per case basis.

XII. Fast Neutron Beam Clinical Trials--Dr. John E. Antoine and Dr. Thomas Griffin

Dr. Antoine stated that the Radiation Research Program, DCT, develops, funds, administers, and evaluates research in the diagnosis, staging, treatment, and post-treatment evaluation of the cancer patient in whom radiation or related forms of energy are used. A high priority of the Radiotherapy Development Branch is the Neutron Program. The Fast Neutron Program began in the 1970s, and Phase III trials are

currently in progress. Dr. Antoine introduced Dr. Thomas Griffin, Professor and Chairman of the Department of Radiation Oncology at the University of Washington in Seattle, and a participant in the extramural radiation research group.

Dr. Griffin began by reviewing the history of the use of neutrons in the treatment of cancer beginning in the 1930s. He showed a slide of a patient with head and neck cancer being treated with neutrons from a cyclotron at the Berkeley Laboratory of Dr. Stone in the late 1930s. These early studies demonstrated that fast neutron therapy was effective in eradicating tumors but the side effects on normal tissues were too great. Dr. Griffin said the therapy was essentially abandoned until the 1960s when techniques improved.

In describing the various types of radiation therapy, Dr. Griffin said that the effects of standard radiation therapy are based on knocking electrons out of their orbits and causing the ionization of tissue around the atoms. Fast neutron and other particulate radiation works through a nuclear reaction in which the recoil proton damages tissue. This results in an increased deposition of energy in the area of interaction and leads to more efficient cell killing. The benefits of neutron therapy compared with standard radiation are better killing of hypoxic cells, lessened ability of cells to repair radiation damage, and less variation in radiosensitivity across cell cycles. Dr. Griffin said that based on the expectation that neutrons would be effective in tumors with low growth fractions, NCI funded the first neutron radiotherapy program in 1971. Cyclotrons in physics laboratories were modified to produce neutron beams for cancer treatment, resulting in rather primitive treatment situations. Nonetheless, approximately 9,000 patients were treated with the old machines, yielding an extensive data base.

Dr. Griffin summarized several of the early studies, beginning with an NCI-supported study of patients with inoperable, unresectable, or recurrent salivary gland carcinomas, randomized to receive either photon radiation therapy or neutron radiation therapy. The study was planned to accrue 40 patients but was stopped early when a statistically significant difference in response rates was found. The complete response rate for photon therapy was 33 percent and for neutrons, 85 percent. Tumor control was maintained for 2 years in 67 percent of the neutron-treated patients versus 17 percent of the photon-treated patients. Two patients failed in each treatment arm. Survival at 24 months was 62 percent for neutron-treated and 25 percent for photon-treated patients. The acute complications were more severe in patients treated with neutrons, but there was no difference between the groups in the incidence of serious complications. Dr. Griffin pointed out that results from studies around the world are strikingly consistent and indicate that use of fast neutrons to treat salivary gland tumors represents a significant advance.

Other studies were done in prostate cancer patients with advanced local disease treated with either photons or a mixture of neutrons and photons. Dr. Griffin said that a mixture was used because of the poor depth dose characteristics of neutrons. The 5-year results for local tumor control were 80 percent for photon therapy and 92 percent for mixed beam. Survival with photon therapy was 55 percent and 70 percent for mixed therapy. Stepwise analysis to determine the most important factors in survival revealed the mode of treatment to be the most important factor in the difference.

A third study noted by Dr. Griffin involved treatment of squamous cell carcinomas of the head and neck. More than 300 patients were randomized to receive photon or mixed beam radiation therapy. After 6 years, no significant difference was seen in primary tumor control. However, there was a dramatic and statistically significant

improvement in nodal tumor control in patients who received mixed beam therapy. No difference in survival was observed.

Summarizing other published data, Dr. Griffin stated that neutrons have been shown to offer an advantage in treatment of salivary gland tumors, prostate cancer, and sarcomas of bone and soft tissue. Equivocal results have been obtained in treatment of squamous cell carcinomas of the head and neck, lung cancers, bladder cancers, and cancer of the cervix. Tumors in which neutrons showed no potential advantage included brain cancers and carcinomas of the esophagus and pancreas. Based on these results, NCI funded a program, starting in 1979, to develop hospital-based neutron generators. The three different approaches were a deuteron (DT) generator, a negative ion cyclotron, and positive ion cyclotron. Dr. Griffin said that although the DT generator had many theoretical advantages, it did not work. The two negative ion cyclotrons had significant problems and their installation was greatly delayed. The positive ion cyclotron at the University of Washington has been very reliable and used to treat patients since 1984. The neutron beam is shaped by a multileaf collimator that can be conformed to the shape of the tumor and changed as the machine rotates around the patient. The machine is completely computer controlled.

Dr. Griffin stated that after the cyclotron became operational at the University of Washington, efforts were directed at determining the optimum dose of neutrons in each area of the body where treatment is given. Once these studies were completed, Phase III trials were begun and four are currently open: squamous cell carcinomas of the head and neck, prostate cancer, non-small cell lung cancer, and radioresistant histotypes, such as soft tissue sarcoma. These studies randomized patients to be treated with neutrons, delivered in 12 fractions over 4 weeks.

Next, Dr. Griffin discussed neutron capture therapy, which is based on the concept of depositing treatment solely in the cancer cell, excluding all normal tissue. A neutron is put into an element to create an isotope that breaks down and deposits energy close to the site of capture of the fast neutron. Dr. Griffin said that neutron capture therapy was first theoretically proposed in 1936, and clinical trials were begun in the United States and Japan in the 1950s. As with all cancer treatment modalities, the objective was to increase the difference between normal tissue damage and tumor control, thereby increasing the therapeutic ratio. Dr. Griffin said problems with early trials using boron to treat brain cancer included intense capillary damage, which led to brain necrosis, and poor penetration of the thermal neutron beam, which resulted in skin and scalp necrosis.

Dr. Griffin suggested that technologies have improved enough to make neutron capture therapy a feasible modality. Factors needed for effective boron capture therapy are a source of neutron capture agent, a delivery vehicle, and a high flux neutron source. The only cancer studied to date is brain tumors, but Dr. Griffin speculated that fast neutron therapy could be expected to enhance local tumor control in head and neck cancers, cancer of the cervix, and sarcomas. Another possible use is regional tumor control in cancers of the ovary, stomach, colon, and pancreas, and melanoma. Dr. Griffin said studies proposed at the University of Washington would use neutron capture therapy for bone marrow purging for solid tumor patients treated with autologous bone marrow transplantation.

The following points were raised in discussion:

- One objective of the neutron therapy trials initiated in 1979 was to determine what would be the best machine for clinical use. The positive ion cyclotron

was found to be the best machine and its use is being implemented throughout the world.

- Reimbursement for neutron therapy is in the best interest of commercial carriers because although the cost per treatment is higher than for standard radiation therapy, fewer treatments over a shorter time are required for neutron therapy.

- Cyclotrons produce isotopes, which can also be used for metabolic studies.

XIII. Closed Session

The second day of the meeting was closed to the public because it was devoted to the Board's review of grant applications. A total of 1,200 applications were reviewed, requesting support in the amount of $178,530,902. Of these, 1,070 were recommended for funding at a total cost of $147,757,526.

XIV. Report of the Subcommittee on AIDS--Dr. Gertrude Elion for Dr. Howard Temin

Dr. Elion reported that the Subcommittee on AIDS had heard a summary from Dr. William Blattner, Chief, Family Studies Section of the Environmental Epidemiology Branch, DCE, on the diagnostic and follow-up studies performed on a laboratory worker accidentally infected with the AIDS virus. The worker was a prevalent seropositive, i.e., the first specimen obtained in the study was positive. Although it is not known how the infection occurred and standard risk factors were negative, the worker had handled large quantities of concentrated virus. The virus infecting the worker was found to be similar to the virus used in the worker's laboratory. Approximately 2.5 years ago, the worker's antibody response to HIV was type-specific but has recently become group-specific with a shift in viral epitopes also noted. Dr. Temin requested that additional information on NIH's HIV safety program be provided to the Subcommittee, and the Subcommittee had recommended that any information developed by NIH about HIV safety precautions be disseminated to all NIH grantees working with HIV.

Dr. Elion said the Subcommittee had also heard a report from Dr. Chabner on the current status of the AIDS drug screen and the drug development program. He said that the program can fully develop four compounds a year, and a number of promising compounds have already been identified. Dr. Elion expressed the view that four compounds per year is probably an adequate number if preference is given to compounds with novel structures and different mechanisms of activity. Dr. Chabner also noted the serious problem of obtaining adequate numbers of FTEs to staff the AIDS drug development program, a problem he will present to the PHS AIDS Task Force. In the interim, the Subcommittee recommended that the NCAB inform Dr. Anthony Fauci, NIH Associate Director for AIDS research, of NCI's need for FTEs and urge that NCI be given adequate FTEs from the new AIDS FTE allotment. A memorandum was drafted from Dr. Temin to Dr. Fauci asking that FTEs taken from the cancer program to work on AIDS be replaced. Although NCI devotes 143 FTEs to AIDS research, only 53 have been officially designated by NIH as AIDS FTEs.

The Subcommittee received a report from Dr. Werner Kirsten, Associate Director of the Frederick Cancer Research Facility, on the NCI AIDS Vaccine Task Force. Dr. Kirsten stated that as a liaison member of the NCI Task Force and member of the

NIH AIDS Vaccine Committee and Co-chairman of the PHS AIDS Vaccine Committee, he had the opportunity to share in information exchange and scientific coordination.

The report of the Subcommittee on AIDS was unanimously accepted as presented. The memorandum from Dr. Temin on behalf of the NCAB will go forth to Dr. Fauci.

XV. Report of the Subcommittee on Information and Cancer Control for the Year 2000--Mrs. Helene Brown

Mrs. Brown stated that the Subcommittee heard a report from Ms. Shelagh Smith, Office of Cancer Communications, on the evaluation of the NCAB Public Participation Hearings. Most of the hearings' objectives were met, these being to learn more about existing cancer prevention and screening programs, identify gaps in current programs, publicize the year 2000 goals, and involve organized sectors of the community in turning their attention to cancer control and the year 2000 goals. It is too early to measure whether another objective--to enlist private sector and community organizations in working toward the year 2000 goals--has been achieved. Those who were interviewed for the evaluation, including those who participated and testified, were satisfied with the hearings and excited about the participation of Dr. DeVita, Dr. Korn, and other members of the NCAB. The cost of the hearings was about $360,000, which Mrs. Brown suggested was a worthy expenditure of funds. Mrs. Brown said the Subcommittee would reserve judgment on future hearings until the report to the President and Congress has been submitted and reactions to that report studied. The Subcommittee will provide comments on the draft report to Mr. J. Paul Van Nevel (Associate Director, Office of Cancer Communications) by October 10, and a final draft will then be prepared and sent to the NCAB for their review. Mrs. Brown said it was hoped that the Board would give approval of the report at the next meeting so that it can be released.

Dr. Louis Sullivan reported to the Subcommittee on the National Black Leadership Initiative on Cancer. The last of the six regional meetings will be held in Houston on September 29-30, and the organizers in the six cities will meet with NCI senior staff in October to develop a follow-up plan of activities. Dr. Sullivan added that the participation in and enthusiasm for the Initiative had been much greater than envisioned. He underscored the interest in furthering cancer education efforts in local communities. Dr. Sullivan also noted the contributions of several celebrities (Diahann Carroll, Dionne Warwick, Phylicia Rashad, Marla Gibbs) who made videotapes and public service announcements to help spread the message about cancer in blacks. To reinforce one of the concerns that had engendered the Initiative, Dr. Sullivan said that during the Congressional Black Caucus he conveyed to Representative Louis Stokes the concern about black organizations, including the Black Caucus, accepting money for activities from tobacco companies.

Dr. Edward Sondik met with the Subcommittee to suggest several tools for assessing progress in reaching the year 2000 goals. The annual statistics report is expected to be available by the February 1989 Subcommittee meeting and will be the major topic of that meeting.

Mrs. Brown said the Subcommittee had also discussed the possibility of an award for extraordinary achievements in cancer prevention and control. Dr. Strong pointed out that one of the General Motors awards is in cancer prevention research.

The following points were raised in discussion:

- Because of the linkage of the year 2000 goals with resource commitments as described in the By-Pass budgets, an assessment of progress towards those goals should indicate how much progress towards these goals may have been compromised by funding levels below those projected in the By-Pass budget.

- The American Cancer Society's hearings will address underserved areas of the community, and efforts are in progress to coordinate NCI and ACS activities, especially at the staff level.

- Women's organizations are also under pressure to accept funds from tobacco companies for support of their activities.

- The planning committee for the Washington meeting of the National Black Leadership Initiative includes the public health commissioners of Richmond, Baltimore, Philadelphia, and Washington, DC. The National Medical Association has also expressed interest in helping to involve black physicians in the treatment aspects of the Initiative.

The report of the Subcommittee on Information and Cancer Control for the Year 2000 was unanimously accepted as presented.

XVI. Report of the Subcommittee on the Organ Systems Program--Dr. Roswell Boutwell for Dr. Bernard Fisher

Dr. Boutwell recalled that at the February 1988 meeting the Board agreed to several changes in the Organ Systems Program (OSP): the portfolios of the various research grants would be distributed to the appropriate intramural divisions; the cooperative agreement for supporting the current extramural coordinating office would not be recompeted and will expire in July 1989; and the working groups will be maintained. He noted that lung is not one of the seven working groups. Following the Board's February 1988 decision, Dr. DeVita appointed an Organ Systems Program Committee, chaired by Dr. Brian Kimes. Dr. Boutwell summarized that committee's recommendations as follows: (1) maintain the current complement of seven working groups; (2) explore the opportunities for using the working group concept for other organ systems as long as these do not reduce the effectiveness of the existing working groups; and (3) evaluate the effectiveness of the OSP again in three years. The recommendations were unanimously endorsed by the Subcommittee on the Organ Systems Program.

The Board unanimously accepted the recommendations.

Dr. Boutwell also asked for endorsement of other aspects of the Organ Systems Program Committee report, particularly with respect to criteria for initiation/termination of working groups, including consideration of personnel and budget resources available to the Committee, total dollar resources allocated to basic and applied research, the magnitude or impact of each cancer, extremely low survival rates for cancer of high or moderate incidence, and performance of working groups in helping the NCI evaluate existing activities. Implementation of the criteria would involve the Subcommittee on Organ Systems and a vote by the NCAB.

The Board unanimously accepted the initiation/termination criteria.

Dr. Boutwell stated that tasks remaining to be accomplished included the development of a complete operational statement, the definition of the relationship of the working groups to the overall NCI structure, and the selection of working group members. He also reported that the Subcommittee had approved a concept for a task order logistics contract to support a maximum of 14 meetings of the working groups per year, a maximum of 12 working group subcommittee meetings, and a maximum of 7 workshops per year. Dr. Kimes noted that about half of the $940,000 per year contract would pay for travel expenses.

The following points were raised in discussion:

- The working groups represent opportunities for research that has scientific merit. Both RFAs and investigator-initiated grant applications are driven by scientific opportunities.

- The Organ System Program was originally started to stimulate research on frequently occurring neoplasms with low survival.

XVII. Subcommittee on Planning and Budget--Dr. Louise C. Strong

Dr. Strong briefly reviewed details of the NCI's FY 1989 budget and then called attention to the following issues of concern to the Subcommittee on Planning and Budget.

- Funds for AIDS, training, construction, and cancer prevention and control are specifically designated by Congress and are not subject to reallocation at the NIH level.

- The level funding for training means fewer trainees in FY 1989 because of the significant increase in stipend and the cap on the total pool of dollars.

- The FY 1989 budget allocation for centers could mean eliminating several centers or negotiating competing center grants significantly below recommended levels.

- While the research grant pool increased, fewer new and competing grants will be funded due to continuing commitments (noncompeting renewals).

- The intramural research program, with a 2.4 percent increase exclusive of AIDS funds, did not receive a fair share of the budget increase.

The 1990 By-Pass budget was also discussed. Dr. Strong reported that the Committee discussed ways to make the By-Pass document more effective in making the Administration and Congress recognize the needs of the Cancer Program. One suggestion was to prepare, along with the "professional judgment" budget, a no-growth budget that outlines minimum requirements to maintain the cancer program at a current-services level.

In discussion, it was noted that the actual amount NCI devotes to minority biomedical research support is considerably more than the $3 million line item in the budget.

The report of the Subcommittee on Planning and Budget was unanimously accepted as presented.

XVIII. Subcommittee for Review of Contracts and Budget for the Office of the Director--Dr. Phillip Frost

Dr. Frost recalled that this committee deals with funds to support the Office of the Director with activities such as maintenance of contracts and grant records and communication vehicles. He presented the Subcommittee report that included the newly approved FY 1989 budget of approximately $43 million for the OD and pointed out the increases over FY 1988 of $915,000 for personal services and $2.5 million for resource contracts as well as the new associate directorship. He reported that Ms. Susan Hubbard, who was appointed Associate Director of the new International Cancer Information Center, gave an overview of this activity, which includes distribution of journals and publications such as the Cancergrams. He said the Committee had requested that Board members receive a list of these publications, which could then be made available to them on a regular basis.

The report of the Subcommittee for Review of Contracts and Budgets for the Office of the Director was accepted as presented.

XIX. New Business--Dr. David Korn

Stop Cancer Project Draft Agreement

Dr. Korn presented for the Board's review a memorandum of agreement drafted following the original discussion at the Monday session. He reported that Dr. Hammer had asked that he, Dr. Rabson, and Mrs. Brown meet with him and Mr. Denver Frederick, Executive Director of the Stop Cancer Project, fairly soon to complete the drafting process.

Dr. Korn stated that the issues to be discussed included whether there should be a written agreement between NCI and the Stop Cancer Project, and if so, what would be the most appropriate form of such an agreement. He called Board members' attention to the draft memorandum, noting that Dr. Hammer had not seen it. Dr. Korn said he hoped to have the full backing of the Board when he meets with Dr. Hammer.

The following points were raised in discussion:

- The Stop Cancer Project differs from other gifts to NCI in that it involves active fundraising.
- Provisions need to be made so that the initiative would not be viewed as replacing any part of NCI's budget, but rather as providing supplemental funding.
- Some type of endorsement of the Project by NCI might serve to differentiate it from disreputable activities.
- Information is needed on the organization that is running the Project.
- Consideration needs to be given to the impact of the Stop Cancer Project on fundraising activities by other cancer-related organizations, including the cancer centers.

- Legal staff have indicated that there is nothing illegal about the proposed initiative and arrangements between the Project and NCI; legal staff would review any type of agreement before it is signed.

- The National Cancer Act authorizes the Director of NCI to accept unconditional gifts, and there is a precedent for having a memorandum of understanding for large gifts.

- Caution needs to be exercised so that NCI, a public institution, is not perceived as raising funds in the private sector.

- It may be dangerous to imply that the simple availability of more money will be sufficient to stop cancer.

In summarizing the discussion, Dr. Korn said he would express the concerns raised by the Board at the meeting with Dr. Hammer and suggested that a letter be prepared from the Board indicating NCI's enthusiastic support of any efforts to raise more funds for cancer research. The letter would be worded to recognize the authority of the Director, NCI, to receive such funds.

Clinical Alerts

The Board received two handouts related to the Clinical Alert released by the Institute presenting data on the use of adjuvant therapy for early stage node-negative breast cancer: "Of Clinical Alerts and Peer Review," an editorial by Dr. Robert Wittes published in the Journal of the National Cancer Institute (JNCI), and "Clinical Alert Follow-up Study Report," prepared for the Office of Cancer Communications (OCC). Mrs. Brown initiated a discussion of the Alert by expressing concern about calls received by the UCLA Cancer Information Service (CIS) from women who were alarmed because they had received breast cancer therapy different from that summarized in the Clinical Alert. She directed the Board's attention to the four areas of controversy regarding the Clinical Alert, as summarized by Dr. Wittes in the JNCI editorial:

- Many physicians who should have received the Clinical Alert did not.

- The contents of the Alert were incomplete in that they referred to data not yet available.

- It should not be the role of the NCI to tell physicians how to practice medicine.

- Is a direct mailing that bypasses the normal processes of peer review an appropriate vehicle for disseminating medical and scientific information?

Dr. Wells emphasized that his most serious concern was the fact that the Clinical Alert bypassed the peer review process. Dr. Walter Lawrence also stated strong objections in this regard and noted that the Board's role in the development and actual approval of the Alert had been unclear to him at the May 1988 meeting. However, he stated that it seemed that the Alert also had positive impact in the medical community. For example, the American Cancer Society had decided to form a committee (to be chaired by Dr. Lawrence) to determine how the ACS could assist in expanding clinical trials, and the American College of Surgeons, under Dr. Wells' direction, was also initiating activities in this area.

To clarify the NCI's motivation for issuing the Clinical Alert, Dr. Chabner stated that the primary focus was to direct attention to the potential value of the therapy described in the Alert for women who developed node-negative breast cancer in the interval between completion of the protocols and publication of the study results. He emphasized that the Alert did not endorse the described treatment but simply stated that the information should be available for consideration. He supported the fact that the Alert should have had a wider circulation, particularly to surgeons. Dr. Lawrence agreed that the Alert presented the information clearly but noted that the perception of the information, especially by the press, was entirely different.

Dr. Chabner also emphasized that although the long-term survival benefits of the therapy remain unknown, the studies showed improvement in disease-free survival and that, at least in the tamoxifen study, the risk of therapy was very small.

Dr. Korn stated the importance of having available some type of rapid peer-review mechanism by which journals would be willing to publish results of this type. Dr. William Longmire also mentioned the possibility of calling emergency consensus conferences to review such results. Dr. Chabner noted that the authors had been encouraged to submit the articles to the JNCI, which has a rapid review mechanism, but had declined to do so. In response to a suggestion from Dr. Korn, Dr. Chabner agreed that it might be appropriate to discuss possible mechanisms for release of information on "high-priority" treatments with the Board of Scientific Counselors, DCT.

Dr. Roper stressed the role of the NCI, as an agency supported by public tax dollars, to inform the public of information that could provide potential benefit. She expressed the opinion that the NCI should address the problem of the often lengthy gap between completion of studies and publication of results. Dr. Wittes reemphasized that data related to treatment belongs in the public domain as quickly as possible. He stated that the JNCI can now publish accepted manuscripts within six to eight weeks of receipt of the final article.

Dr. Chabner closed the discussion by reiterating the points that information such as that in the Alert should receive wider extramural review prior to release and that such releases should only be considered when they will have significant public health impact. He emphasized that the studies described in the Alert were supported by public monies and that the protocols had been closed because the cooperative groups felt it was no longer ethical to randomize patients because of the positive nature of the trials. Dr. Chabner will ask the DCT Board of Scientific Counselors to consider the need to develop procedures for issuance of clinical alerts.

Minority Involvement in Institutional Training Programs--Mrs. Barbara Bynum and Dr. Vincent Cairoli

Mrs. Bynum reminded the Board that the problem of identifying, recruiting, and training minority candidates under the aegis of NIH training grants was discussed at the May meeting and noted that current NIH guidelines were not only to encourage greater compliance but also to identify, through the deliberations of the various BIDs and their advisory councils, ways of enforcing these guidelines. She introduced Dr. Vincent Cairoli, Chief of the Cancer Training Branch, DCPC, to present data on present minority involvement in training programs and some options for addressing the issue as requested by NCAB in May.

Dr. Cairoli referred to reports distributed to each member and pointed out that minority postdoctoral fellows and pre- and postdoctoral trainees on large institutional

training grants total between 6 and 8 percent. He said subcommittees were then formed at the NIH level to consider the state of compliance with the NIH guidelines requiring that plans to recruit minorities be incorporated in the institutional training grants. The results of a survey of all Institutes and analysis of the October round of grants revealed generally poor compliance. He reported that a committee comprised of Cancer Training Branch and Grant Review Branch personnel had met and developed the following list of recommendations to present to the Board for approval: (1) on the Board level--creation of a subcommittee to work with the NCI staff committee in implementation of this policy; (2) at the grant review level--require that a minority recruitment plan be included in all applications before they are accepted for review; (3) at the Program level--require that, to be considered complete, annual progress reports (Type 5's) include information from the principal investigator on development of a minority recruitment plan or progress of an ongoing plan.

Dr. Wells moved that an NCAB subcommittee be formed to review this matter, and Dr. Bragg seconded the motion. The motion was unanimously approved. Dr. Cairoli agreed to serve as Executive Secretary and Dr. Sullivan agreed to chair the committee. Board members interested in taking part were requested to so inform Mrs. Bynum.

After ascertaining that adequate notice is presently included in the NIH Guide notice and in the directions for 398 applications, Mrs. Brown moved that grant applications be considered incomplete without a minority recruitment plan report. The motion was seconded and unanimously approved.

In discussion of this motion, the following points were made:

- The next revision of Form 398 should include "minority recruitment plan" as an item in the table of contents and checklist.

- The NIH guidelines requirement of a minority recruitment report is not new. However, sufficient time should be allowed for those who have not complied in the past to do so after they receive a reminder of the requirement.

Because of the need for immediate clarification of this issue, it was agreed that the new subcommittee would meet in December and, as a first order of business, review plans under consideration by the NIH committee that may have some benefit and recommend a course of action. It was further agreed that the action of returning applications that do not include a minority recruitment plan be delayed until June or July 1989 and the interim period be used to disseminate information of the pending enforcement.

Other New Business

In other new business, Dr. Roper called attention to a handout provided for the Board's information entitled "Comments of the Department of Health and Human Services on the General Accounting Office's Draft Report, 'Cancer Treatment: The National Cancer Institute's Role in Encouraging Doctors to Use Breakthroughs.'"

It was requested that ample time be allocated in a future meeting for an update from DCT on the new in vitro screen and discussion by the Board.

XX. Adjournment

There being no further business, the 67th meeting of the National Cancer Advisory Board was adjourned at 10:56 a.m. on September 28, 1988.

November 23, 1988
Date

David Korn, M.D.