DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH

NATIONAL CANCER INSTITUTE

NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
May 15-16, 1989

Building 31, Conference Room 6
National Institutes of Health
Bethesda, Maryland

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

Summary of Meeting*
May 15-16, 1989

The National Cancer Advisory Board (NCAB) reconvened for its 70th regular meeting at 8:30 a.m., May 15, 1989, 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
Dr. Gertrude B. Elion
Dr. Bernard Fisher
Dr. Phillip Frost
Dr. David Korn
Dr. Walter Lawrence, Jr.
Dr. Enrico Mihich
Mrs. Irene S. Pollin
Dr. Louise C. Strong
Dr. Howard M. Temin
Dr. Samuel A. Wells

President's Cancer Panel

Dr. Armand Hammer
Dr. William P. Longmire
Dr. John A. Montgomery (Absent)

***Ex Officio* Members**

Dr. Dorothy Canter, NIEHS
Dr. William Farland, EPA
Captain Bimal Ghosh, DOD
Dr. Richard Greene, VA
Dr. John Johnson, FDA
Mr. Richard Lemen, NIOSH
Mr. John Maddox, DOE
Dr. Lakshmi C. Mishra, CPSC
Dr. William F. Raub, NIH
Dr. Ralph Yodaiken, DOL

Members, Executive Committee, National Cancer Institute, NIH

Dr. Samuel Broder, 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. Alan S. Rabson, Director, Division of Cancer Biology and Diagnosis
Executive Secretary, Ms. Iris Schneider, Assistant Director for Program Operations and Planning

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

Liaison Representatives

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

Dr. Clarence Ehrlich, President, Society of Gynecologic Oncologists, representing the Society of Gynecologic Oncologists.

Dr. Walter Faggett, Speaker of the House, National Medical Association, representing the National Medical Association.

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. John Laszlo, Senior Vice President for Research, American Cancer Society, Washington, D.C.

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

Ms. Mary McCabe, Clinical Trial Specialist, 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. Warren Pearse, Executive Director of the American College of Obstetricians and Gynecologists, Washington, D.C., representing the American College of Obstetricians and Gynecologists.

Ms. Yvonne Soghomonian, Associate Director, the Candlelighter's Childhood Cancer Foundation, Washington, D.C., representing the Candlelighter's Childhood Cancer Foundation.

In addition to NCI staff members, meeting participants, and guests, a total of 34 registered members of the public attended the meeting.

I. CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF FEBRUARY 6-7, 1989, NCAB MEETING MINUTES--DR. DAVID KORN

Dr. Korn, Chairman, called the 70th meeting of the National Cancer Advisory Board (NCAB) 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 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.

Approval of the February minutes was postponed until the following day's session.

Dr. Korn noted that each member had received a proof copy of the book *Horizons in Cancer Research* for review. He recalled that the Board had planned to sponsor the publication of this book as part of the 50th anniversary celebration of the National Cancer Program as a follow-up to one published a decade earlier celebrating accomplishments of the Cancer Program and pointing out opportunities and challenges.

II. FUTURE MEETING DATES

Dr. Korn called Board members' attention to the following confirmed meeting dates: September 18-19, 1989; December 4-5, 1989; January 29-31, 1990; May 14-16, 1990; October 1-3, 1990; and December 3-5, 1990. Dates for 1991 to be reviewed and confirmed were February 4-6, May 13-15, September 23-25, and November 25-27. Dr. Korn pointed out that although some meetings continue to be listed as 3-day meetings, the intent was to continue the 2-day meeting format unless it was necessary to do otherwise.

III. REPORT OF THE PRESIDENT'S CANCER PANEL--DR. ARMAND HAMMER

Dr. Hammer reported that since the previous NCAB meeting, the President's Cancer Panel held meetings devoted to the subject of cancer diagnosis, treatment, and prevention in minority populations at the Howard University Cancer Center in Washington, D.C. (March 6), and Meharry Medical College in Nashville, Tennessee (April 26). Dr. Samuel Broder, Director of NCI, spoke at both meetings. Dr. Hammer said the meeting at Howard University was especially relevant because the District of Columbia leads the nation in the rate of deaths from cancer among blacks. He noted that many factors responsible for these statistics were identified in the discussions, some of which it may be possible to affect through the various programs (e.g., outreach and education) of the NCI, and others, such as the lack of health insurance and access to primary health care and screening, that will require a much broader effort by all segments of society. Dr. Hammer said the Panel was encouraged by the determination shown by Howard University scientists to improve the situation and by the work of segments of the local community, especially the churches.

In addition to Dr. Broder's presentation, the Panel heard Dr. Reed Tuckson, Commissioner of Public Health for the District of Columbia, discuss the problems addressed by his office and his efforts to deal with a myriad of difficult circumstances. The Panel also heard Mrs. Bynum report on possible solutions to the shortage of minority personnel in the health science manpower pool. Dr. Hammer noted that Mrs. Bynum's suggestions would likely be considered by the NCI's National Black Leadership Initiative on Cancer and by the NCAB's Subcommittee on Manpower Development. He singled out the audience/participant exchanges stimulated by the presentations as probably the most useful part of the meeting, particularly Dr. Broder's response to the many

questions concerning ways in which the community can play a more effective role in reducing the excessive rate of cancer fatalities among blacks and minorities. He said Dr. Broder made it clear that while the NCI will take part in this effort, much would be required on the local, community, and state levels as well.

Turning next to the Meharry Medical College meeting, Dr. Hammer noted many of the problems discussed were similar to those in the District of Columbia, but Tennessee's difficulties are compounded by the isolation of many of its rural communities. He said the Panel was pleased to hear presentations on the work of the new Drew-Meharry-Morehouse Consortium, and he reminded the Board that the idea for a consortium grew out of an earlier Panel meeting held in Los Angeles on the role of cancer centers in the National Cancer Program. At that meeting, the special problems of the minority populations with regard to cancer were highlighted, and the concept of a consortium of black medical institutions was suggested as a means to deal with them. The Drew-Meharry-Morehouse consortium was eventually brought into being with the help of the NCI and then-Director, Dr. Vincent DeVita. Dr. Hammer stated that impressive work is being accomplished by each segment of the consortium and that the combined program is beginning to make a significant impact in dealing with the problems of cancer control in minority populations.

Dr Hammer said the Panel also heard Dr. Linda Clayton report that less than 2 percent of the patients entered on NCI-supported clinical trials are blacks or minorities and that no clinical trials have published results as they affect minorities. He expressed the hope that as the clinical trials program develops, a way can be found to increase the rate of minority accrual to the trials.

In reviewing the activities of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS (Dr. Louis Lasagna, Chairman), Dr. Hammer reported that the first two meetings of the four held to date were devoted to discussions with representatives of the Food and Drug Administration (FDA) and the NCI, with a special focus on the problems the two institutions had in establishing mutually acceptable clinical endpoints for determining the effectiveness of drugs to treat cancer. At the March 15 meeting, Dr. Lasagna reported that as a result of Committee suggestions at the previous meeting, the FDA and NCI have established regular monthly meetings to review both broad policy questions and specific implementation details at the staff level. Dr. Hammer extended the Committee's and Panel's commendations to Dr. Carl Peck (FDA) and Dr. Broder for taking the initiative in this matter. He said the Committee was satisfied that a reasonable approach to the consideration and resolution of questions relating to appropriate endpoints for clinical trials on cancer drugs had been identified as a result of good interaction between the Division of Cancer Treatment's (DCT) Board of Scientific Counselors and the FDA's Oncologic Drugs Advisory Committee. In his summary, Dr. Lasagna reported that the Committee believed most of the important technical questions raised about appropriate design and interpretation of clinical trials for new anticancer drugs raised at its first two meetings were being resolved or their solution sought by the FDA and NCI. Committee plans are to monitor progress in these matters in the coming months.

Dr. Hammer said subsequent meetings of the Committee have focused on the problem of who should be responsible for financing patient costs associated with experimental therapies. Presentations at these meetings were made by representatives of the insurance and pharmaceutical companies as well as by advocates for cancer and AIDS patients. On behalf of the Panel, Dr. Hammer expressed appreciation for the dedication and hard work of Committee members and for their accomplishments to date. He announced that he would provide periodic updates.

Finally, Dr. Hammer reported that his "Stop Cancer" project was progressing and that he would be meeting with Congressman William Natcher, Chairperson of the Subcommittee on Labor, Health, and Human Resources and the House Committee on Appropriations, to discuss providing the matching funds to those already generated by the project. He said he hoped to make the first disposition of these funds (approximately $25 million total) to NCI in the near future for the funding of high quality research that cannot be funded because of current budgetary restraints. He stressed the serious consequences of every year's delay in finding a cure for cancer, the enormous possibilities presented by the newly emerging immunological approach to cancer treatment, and the need for funds to further such research. In closing, Dr. Hammer asked that all join him in the crusade to raise $500 million from the private sector and matching funds from the Government over the next 4 years, to be used to attain the goal of a cancer-free world for future generations.

In discussion, the following points were made:

- Scientists engaged in research frequently have multiple grants; therefore, the number of approved grants not presently funded plus the number funded is not equal to the total number of research scientists.

- The "Stop Cancer" project is seeking medical solutions to the cancer problem; it then becomes a public health and cancer control problem to see that the solutions are effectively used.

IV. NCI DIRECTOR'S REPORT--DR. SAMUEL BRODER

Dr. Broder began by announcing that two vacancies exist on the NCAB as a result of Mr. Louis Gerstner's resignation and Dr. Louis Sullivan's appointment as Secretary of Health and Human Services. He congratulated Mrs. Nancy Brinker on the upcoming publication of a book about her sister, Susan Komen.

Dr. Broder noted with regret the death of Dr. John Heller, who had served as Director of NCI from 1948 to 1960, a period in which the budget increased from $1.8 million to $91 million. During Dr. Heller's directorship, areas of investigation included the role of viruses in cancer, vaccines against cancer, screening tests for cancer, carcinogens, and the potential of chemotherapy versus radiation or surgery as a treatment modality. Dr. Broder praised Dr. Heller's many wise decisions that have proved to have lasting influence.

In discussing staff changes, Dr. Broder announced the following appointments: Dr. Michael Grever as the DCT Deputy Director, Dr. Michael Hawkins as Chief of the DCT Investigational Drug Branch, and Dr. Gregory Curt as DCT Associate Director for the Clinical Oncology Program. Among staff leaving the Institute are Dr. Joseph Cullen, Deputy Director of the Division of Cancer Prevention and Control (DCPC), to become Director of the American Medical Center's Cancer Center in Denver; Dr. Dan Nixon, Associate Director for Cancer Prevention Research Programs in DCPC, to join the American Cancer Society in Atlanta as Vice President for Professional Education; Dr. Flossie Wong-Staal, Laboratory of Tumor Cell Biology (LTCB) to the University of Southern California; Drs. Mika Popovic and Susan Gartner, from the LTCB, to join the Primate Research Institute at New Mexico State University; Dr. Mary Knipmeyer, legislative liaison, to become the Director of the Division of Legislation and Policy Implementation at the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA); and Ms. Rose Mary Romano, formerly Chief of the Information Projects Branch, Office of Cancer Communications, to become Chief of the Public Information Branch in the Office of Smoking

and Health, CDC. Dr. Broder congratulated departing staff members on their career advancements. He also welcomed Dr. Maryann Roper back from maternity leave.

Dr. Broder next acknowledged awards and recognition received by NCI staff: Public Health Service (PHS) Superior Service Award to Mr. John P. Hartinger; PHS Special Recognition Award to Dr. Roper; PHS Special Recognition for Productivity to Ms. Marianne Wagner; PHS Distinguished Service Medals to Drs. Stuart Aaronson and Alan Rabson; 1989 Paul Ehrlich and Ludwig Darmstaedter Award to Dr. Aaronson; Milliken Family Medical Foundation Awards to Drs. Charles Meyers, Steven Rosenberg, and Lance Liotta; Society of Toxicology Arnold J. Lehman Award to Dr. Richard Adamson; and election of Dr. Thomas Waldmann as a Fellow of the American Academy of Arts and Sciences.

Turning to discussion of testimony that he gave before a House committee on March 22 and before a Senate committee on May 1, Dr. Broder stated that his message relayed both good news and bad news. While the committee members seemed to be satisfied with his statement of priorities--(1) basic research, (2) clinical trials, both for treatment and prevention, and (3) cancer centers--Dr. Broder said he detected a sense of impatience in both the House and the Senate. Congress wants to know what results have been achieved with the billions of dollars allocated to the National Cancer Program.

To respond, Dr. Broder said he tried to convey several themes, the first being that the study of rare cancers can lead to important scientific advances and that there is an interplay between clinical investigation and basic science in both directions. He cited as an example retinoblastoma, a disease that afflicts only about 1,000 children per year in the United States. As a result of the identification of the retinoblastoma gene on chromosome 13, new categories of genes--known as anti-oncogenes, recessive oncogenes, or suppressor genes--were found. The retinoblastoma gene, when mutated or deleted (13 q 14 deletion) or functioning abnormally, has an important role in the development of cancer, especially small cell lung cancer and certain kinds of breast cancer.

Dr. Broder also focused on the issue of adjuvant therapy in pointing out to Congress that the administration of adjuvant chemotherapy to node negative breast cancer patients can have a significant impact on disease-free survival at 3 years. He underscored the need to expand clinical trials that involve adjuvant therapy for other kinds of cancer.

Dr. Broder suggested to Congress that progress can be measured by endpoints other than mortality. Limb-sparing surgery for osteogenic sarcoma, breast reconstruction, improved technologies for colorectal cancer and treatment for bladder cancer to retain bladder function represent advances that improve the quality of life and alleviate suffering of cancer patients.

In addressing the issue of the cancer death rate, Dr. Broder used slides to illustrate changes in the cancer death rate since 1973, about the time that the National Cancer Act took effect. Reductions in the number of annual deaths per 100,000 in persons under 65 have occurred in colorectal cancer (14 percent), ovarian cancer (24 percent), stomach cancer (25 percent), bladder cancer (30 percent), uterine cancer (30 percent), and cervical cancer (40 percent). Dr. Broder emphasized that Congress wanted to hear about progress against common tumors, although the progress against Hodgkin's disease (50 percent reduction in the death rate in persons under age 65) and testicular cancer (60 percent reduction) has been astonishing. He acknowledged that for some cancers, notably lung cancer in women under age 65, the death rate has increased, but that overall progress has been made in the under-age-65 group. In contrast, in individuals over age 65, death rates increased for a number of cancers, which Dr. Broder described as not a record that demonstrates progress. He noted the overriding importance of lung cancer in these statistics,

especially in the over-age-65 group, but pointed out that Utah has already achieved the year 2000 goals in terms of number of cases of lung cancer per 100,000.

Dr. Broder stated his disagreement with the view that cancer is an unavoidable and natural consequence of living. He contended that, with the help of all components of NCI and the cancer centers, much can be achieved in terms of prevention, early diagnosis, and treatment that will positively affect the cancer death rate in persons over age 65. Dr. Broder recalled the recent request to investigators that age limitations be eliminated from NCI-funded studies unless there is a scientifically defensible reason for excluding persons on the basis of age.

Other statistics, which Dr. Broder described as emblematic of both bad and good news, are those that relate to cancer in blacks and other minorities. The bad news is the differential death rate in blacks and the upward trends, leading to increased disparity between blacks and whites. The good news is that the technologies that have been engendered by NCI and the National Cancer Program can have an impact for those who can gain access to them. Dr. Broder commented that the disparity between blacks and whites reflects an unequal application of knowledge, which NCI must address as a major priority.

Turning to a discussion of AIDS, Dr. Broder termed AIDS an important, but secondary mission of NCI. He stated his view that progress is being made against AIDS, citing the increased probability that a person diagnosed with AIDS will survive for 18 months. This increase became dramatic in 1987, which coincides with the introduction of AZT in late 1986 and its subsequent widespread use. Dr. Broder suggested that NCI's commitment to devote efforts and resources to AIDS is having an impact on the disease. Large-scale testing of dideoxycytidine is expected in the near future to determine whether ddC has the beneficial virostatic effects of AZT, but less toxicity.

Dr. Broder next discussed issues associated with experimental cancer treatments. He remarked that experimental has connoted an inherently dangerous treatment, which brings more harm than benefit to the patient. In fact, experimental therapies may offer patients their only realistic chance for survival. Dr. Broder suggested that experimental may also be a codeword for denying therapy when insurance coverage is not available, thereby restricting access to a limited number of patients. The effect on reimbursement extends to clinical trials and ultimately would impede progress in cancer research and treatment.

A related issue is the increasing number of patients, not only cancer patients, who need care but cannot pay. When the health of hospitals is threatened by the loss of revenue, cancer centers and clinical trials are inevitably affected. Dr. Broder noted that NIH had asked the Institute of Medicine (IOM) to study the issue of reimbursement, and the report recommended that Medicare and state regulatory agencies cover patient costs for those enrolled in clinical trials. The report cites the issues of concern to NCI--suboptimal accrual rates to clinical trials and reluctance of some third-party payers to reimburse for care associated with investigational therapies. Dr. Broder reiterated NCI's position that investigational therapy is standard therapy for patients for whom there is no curative therapy. Further, cancer patients on clinical trials receive therapy that is at least equivalent to and often better than standard therapy. Dr. Broder reported that NCI continues to discuss with various organizations, including the Health Care Financing Administration and Blue Cross/Blue Shield, reimbursement for off-label use of approved drugs and biologics.

Dr. Broder next discussed the efforts of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS and expressed thanks to

Dr. Lasagna for his leadership. The Committee has addressed the issue of third-party payers and clinical investigation and enabled advocates of cancer and AIDS patients to present their viewpoints. As a result of the Committee's efforts, NCI and FDA are meeting monthly and have established a joint fellowship to provide physician training in clinical oncology and drug development and regulatory matters. Dr. Broder stated that future meetings with FDA will address the possibility of broadening the labeled indications for a new drug, and continue to discuss appropriate endpoints for development and approval of new drugs without having to use mortality as the approvable endpoint for New Drug Application (NDA) status. Efforts will be coordinated to hasten the NDA submission for pentostatin in hairy cell leukemia. Dr. Broder informed the Board that FDA had approved Group C status for levamisole in the treatment of Duke's C colon cancer. Other drugs scheduled for consideration of NDA approval are carboplatin, flutamide, and mitoxantrone, and cytokines such as erythropoietin and colony-stimulating factors. Dr. Broder also noted that because of encouraging preliminary results using suramin to treat certain solid tumors, in particular, prostate cancer, Phase II extramural trials will be initiated. Cancer centers that submit appropriate protocols will be provided with this drug, which is thought to act by affecting autocrine growth factors or growth factors specific to the tumor.

Referring to the cancer centers, Dr. Broder called the Board's attention to the Institute of Medicine's report entitled *A Stronger Cancer Centers Program.* Dr. Broder underscored the incomparable value of the cancer centers and their vital importance to the National Cancer Program. He asserted that the biological revolution offers unprecedented opportunities for applying research advances, in which NCI anticipates that the cancer centers will take an increased role. Because of current budget constraints, Dr. Broder said that five center core grants in both FY89 and FY90 will not be able to be funded. The Executive Committee has reviewed all priority scores for cancer centers competing for available funds in FY89, and a special effort will be made to support all centers with fundable priority scores at 85 percent of peer review recommended levels. The cancer centers, as well as many other NCI activities, are challenged by fiscal realities.

Dr. Broder reiterated that the by-pass budget provides the mechanism for a professional assessment of needs for the Cancer Centers Program and other components of NCI. The by-pass budget clearly documents NCI's strong commitment to centers in the context of a balanced national cancer program. Because of the importance of the Cancer Centers Program, Dr. Broder announced that NCI, in consultation with the NCAB and other external advisors, would develop a 5-year plan for the Program. Dr. Roper will lead the planning effort, assisted by Ms. Judith Whalen, NCI Planning Officer.

Dr. Broder commended the efforts of the NCAB Subcommittee on Cancer Centers, chaired by Dr. John Durant, and noted, in particular, the subcommittee's consideration of the issue of comprehensiveness. He expressed the view that the designation as a comprehensive cancer center should be time limited and an inherent part of the core grant peer review. NCI and the NCAB Subcommittee have developed proposed new criteria for comprehensive cancer centers, which if approved by the Board, would have to be translated into appropriate application and peer-review guidelines. Dr. Broder also noted that he is reviewing the entire organizational structure of the Institute, including the location of the centers program. He stated that NCI would continue to involve the centers in special initiatives and priorities, encourage their independence and diversity, and work with them as a crucial foundation for the National Cancer Program.

Dr. Broder stressed that institutions with cancer centers receive substantial amounts of NCI support from the research project grant pool, contracts, and cancer control funds, which all serve

to enhance the cancer center. The FY89 budget includes $101 million for cancer centers, while the by-pass budget sets needed funding at $135 million. Dr. Broder expressed concern that the number of cancer centers will decrease and requested assistance in addressing the problem. Related issues include the lack of construction funds for centers and staffing for this program, which is affected by Institute personnel ceilings and unfavorable salary structure. Dr. Broder acknowledged the contributions of other NCI personnel who work with the centers program staff and promised to continue the tradition of devoting personal attention to the program.

In concluding his report, Dr. Broder said that as part of the effort to address cancer incidence and mortality in persons over age 65, he had met with Dr. Frank Williams, Director of the National Institute on Aging, to explore collaborative projects. One joint project that is already scheduled is a conference on July 10-13 on dietary energy intake and aging and diseases. Other projects suggested by Dr. Williams are being considered by the NCI Executive Committee.

Dr. Broder announced that initiatives are also being undertaken to address the problem of cancer incidence and mortality in blacks and other minorities. The position of a Special Assistant to the Director for Minority Affairs has been created, and Dr. Claudia Baquet will head an effort to increase recruitment of minority scientists. Noting that Dr. Reed Tuckson would be addressing the Board, Dr. Broder announced that the District of Columbia, along with six other city health departments, had been awarded a 7-year cooperative agreement under which NCI would provide guidance and technical assistance. The use of RFAs for minority supplements for cancer centers is also being explored.

As his final point, Dr. Broder underscored the crucial importance of science education, both for the advancement of science and technology and as a means for young people to break through the barriers of poverty. He pledged to work with academia and the private sector to create new approaches to promoting science education.

In response to a question about cancer incidence and mortality in those over age 65, Dr. Broder reiterated that both the bad news and the good news about cancer are causes for redoubling the effort. He acknowledged that statistics demonstrate the need to target the over-65 population and minorities as priorities.

BUDGET UPDATE

Dr. Broder stated that the original FY89 appropriation was about $1.570 billion. The 1990 President's budget provides $1.494 billion for cancer and $151 million for AIDS for a total of $1.646 billion.

V. LEGISLATIVE UPDATE--DR. MARY KNIPMEYER

Dr. Knipmeyer began her report by listing congressional visits: Senators Dale Bumpers and Howell Heflin and staff to the Senate Committee on Labor and Human Resources. She noted that Senator Heflin had introduced a bill to protect animal research facilities by making it a Federal offense to break into animal research laboratories. A person found guilty of a charge under the proposed legislation would be liable for damages and subject to a fine of up to $5,000 or imprisonment for up to 1 year. Another bill would require Federal agencies to justify the use of animal toxicity tests.

Dr. Knipmeyer stated that more than 22 bills relating to tobacco issues have been introduced. These deal with continued restriction of smoking on airlines, passive smoking, and restrictions on advertising, especially advertising aimed at young people.

Other bills focus on cancer screening, including one introduced by Representative Mary Rose Oakar to increase the reimbursement cap on screening mammography from $50 to $60. Another bill introduced by Representative Barbara Kennelly would provide for payment for screening mammography equal to that for diagnostic mammography. Dr. Knipmeyer noted uncertainty about what effect such changes would have on the quality of and access to screening mammography.

Other proposed legislation mentioned by Dr. Knipmeyer included the following:

- Nutrition Monitoring Act--Regular issuance of nutrition guidelines requiring approval by both the Secretaries of Agriculture and Health and Human Services.

- Treatment--Additional funding to enhance studies of treatment outcome or effectiveness in research.

- Worker notification--Workers in certain occupations to be notified that they may be at increased risk, and the establishment of centers to provide education, training, and technical assistance to physicians and other health professionals.

- AIDS--Issues associated with discrimination and extramural funding.

In concluding her report, Dr. Knipmeyer expressed gratitude for her 7 years of interactions with the Board.

VI. NCI INITIATIVES ON CANCER IN MINORITIES AND THE MEDICALLY UNDERSERVED

INTRODUCTION--DR. SAMUEL BRODER

Dr. Broder stated that the purpose of the presentation was to provide information on the differential burden of incidence and mortality in blacks and certain minority populations. Although no action would be required of the Board at this time, Dr. Broder said that the Board can expect several proposals and initiatives over the next few years.

CANCER MORTALITY IN THE DISTRICT OF COLUMBIA: POSSIBILITIES FOR THE FUTURE--DR. REED TUCKSON

Dr. Tuckson began by stating that while in many respects, Washington, D.C., is a prototypical urban community of 640,000 people, it is atypical in that 75 percent of the population is black. Nationwide, there are 60,000 premature excess deaths among the various minority groups; in other words, if these persons had the same health status as white Americans, they would not have died before age 70. Dr. Tuckson identified the six leading causes of these deaths as heart disease, cancer, diseases of chemical dependency, the triad of homicide, suicide, and accidents, infant mortality, and diabetes. Last year in the District of Columbia, there were 1,463 premature excess deaths attributable to those six causes.

Dr. Tuckson expressed concern that all these causes of death have two common characteristics: 1) they are diseases related to how people behave, what choices they make, what chances they take, and how they relate to their environment, and 2) they are diseases related to access to basic primary care and screening health resources. He suggested that with behavioral determinants so embedded in society, the convergence of all these social forces is most clearly reflected in health. Dr. Tuckson said that when he admonishes young people not to smoke because 23 percent of all deaths in the District are caused by cancer and lung is the leading site, their response is that with the violence around them, only the present is important; they have no vision of the future.

Dr. Tuckson asserted that there is no biological reason why blacks in the District, both males and females, smoke cigarettes at twice the rate of whites. He questioned how to respond to the targeted marketing of tobacco and the message that smoking narrows the gap between contemporary social reality and the purported "lifestyles of the rich and the famous." Dr. Tuckson stated that while education and prevention are very important, that message alone is not sufficient--a whole agenda of issues must be addressed to convince people of the value of their own lives.

In turning to the issue of access to medical care, Dr. Tuckson pointed out that of the District's population of 640,000, 117,000 people have no health insurance. The disease burden continues to increase even without the added burden of AIDS. Dr. Tuckson indicated his expectation that Federal and local resources to deal with these problems will remain limited. In addition, many Americans, particularly in the cities, are disenfranchised from health care systems, which will require reorienting of public health practices to get people aware and involved.

Dr. Tuckson acknowledged the assistance of NIH in establishing a cancer control registry in the District of Columbia. He said that the implications of the data collected are understood, and now the effort must be to translate that understanding into action. Dr. Tuckson stated his view that the community-based organizations--churches, fraternities and sororities, civic groups--offer the best opportunity for reaching the population. In addition, the private sector must be more creatively involved in the effort. Dr. Tuckson noted that the District Health Department has hired persons whose job is to "cause a parade to occur around them." A health fair is set up where the crowd gathers, and if a problem is discovered through screening, people are taken directly to clinics. Three hospitals in the District perform mammograms for $25, and Dr. Tuckson said he is trying to find funds to underwrite even that reduced cost for persons with no resources. Posters have been placed on buses to emphasize the importance of mammography, and through the involvement of the private sector, people are matched to services. In return for municipal bond financing for the hospital industry, the District has been able to arrange for in-kind health care and screening services for persons living in low-income housing.

Dr. Tuckson reiterated the need to address the fundamental and pervasive problems in urban societies. Without that perspective, he cautioned that even the most innovative programmatic ideas will fail.

In response to a question about the cooperation of black business leaders, Dr. Tuckson noted that many of these persons first need to make personal lifestyle changes. Black business leaders exercise less and smoke more than their white counterparts and do not accord to their health the same high priority as whites. In addition, because of the many competing needs for resources, Dr. Tuckson stated that it is necessary to impart the message that the fights against cancer, heart disease, AIDS, and other diseases are not in conflict. Dr. Tuckson identified other potential

contributions of business leaders as influencing young people to value their lives and believe in their futures; supporting outreach activities, which can increase clinic visits for cancer screening by 12 percent; and changing the types of food sold in supermarkets and convenience stores. He cited the publication of a tabloid newspaper to be placed at the checkout stands in supermarkets as a new cancer education effort.

As to the role of the schools, Dr. Tuckson said that an effective curriculum, "Know Your Body," is available, but to only about 5 percent of students in the District. The curriculum is very much anti-cancer, anti-heart disease, and anti-substance abuse and smoking and conveys the values of self-worth, being healthy, and making informed decisions about life. Budgetary constraints prevent the expanded use of the curriculum. Responding to a question about the food served in school cafeterias, Dr. Tuckson indicated that this is an area of concern and noted the illogic of Federal food programs giving out cheese, when high cholesterol levels are such a big problem among minorities. He suggested the involvement of parent-teacher associations (PTAs) to help educate parents about appropriate food choices.

Responding to a question about whether the cost of cigarettes affects smoking behavior, Dr. Tuckson contended that cost is probably not an important determinant of whether a young person smokes. The appeal of smoking is the image that it is thought to convey, and it is the perception of that image as desirable that needs to be changed. Dr. Tuckson noted the pervasive influence of tobacco and alcohol advertising in black institutions, including business, the media, the arts, and even nonprofit fundraising efforts. He pointed out, however, that other advertisers will be needed to replace tobacco and alcohol advertising.

TRANS-NCI-SUPPORTED MINORITY PROGRAMS--MRS. BARBARA BYNUM

As introduction, Mrs. Bynum pointed out that in the 1940s, the public health community first became aware of the disparity in cancer mortality between minority groups and the rest of the U.S. population. In 1972, the *Journal of the National Cancer Institute* published a report describing a "cross-over" in cancer rates between blacks and whites, followed by a series of definitive studies to address this disparity. Mrs. Bynum said that since the 1970s, NCI increasingly has targeted programs towards minorities and other underserved populations. This trend is represented both in the Comprehensive Minority Biomedical Program (CMBP), which addresses training and research, and in other NCI programs that address critical aspects of cancer in minorities. She then indicated that the subsequent speakers would discuss several such ongoing programs within the Institute.

COMPREHENSIVE MINORITY BIOMEDICAL PROGRAM--DR. LEMUEL EVANS

Dr. Evans recalled that at the 56th NCAB meeting, he had outlined a series of specific approaches to expand NCI's minority efforts along the lines of the Institute's programmatic thrusts. The purpose was to enable the Institute to more directly address issues of manpower development, involvement of minority populations, and implementation of intervention programs, as well as specialized training for minorities and the development of centers of excellence around the nation. Dr. Evans identified the objectives of the CMBP as to

- Promote broadened participation by minorities in cancer-related research and training activities

- Contribute to the support of NCI clinical cooperative groups to better enable NCI's research to reach and support minority populations that are particularly susceptible to cancer

- Provide additional funds to NCI-supported investigators who wish to engage minority investigators in their research.

The earliest mechanism implemented was the Minority Investigator Supplement (MIS), which is designed to encourage participation of ethnic minorities in cancer-related research activities by providing supplemental funds to NCI grantees who involve minority researchers in their projects. Twenty-five awards have been made from 53 applications. Dr. Evans noted that this mechanism has been adopted by NIH, and he called attention to a recent program announcement in the *NIH Guide for Grants and Contracts*. This announcement extends the opportunity to graduate and undergraduate students.

Dr. Evans described the Minority Satellite Supplement Program as a new initiative undertaken jointly by CMBP and DCT to address the issue of low minority patient accrual to trials conducted by cooperative groups. Through Minority Enhancement Awards to cancer centers, NCI hopes to enable centers to broaden their operational base to facilitate the expansion of cancer control activities and increase the involvement of primary care providers to minority populations. Three such awards are anticipated to be made during the current fiscal year, and Dr. Evans noted that one approved project focuses on breast cancer screening, smoking cessation, dietary intake of fiber and fats, and prostate cancer. Another project proposes to expand the understanding of the knowledge, attitudes, and practices of Mexican Americans and American Indians with respect to cancer. Dr. Evans underscored NCI's clearly increasing commitment to supplement-type CMBP activities.

In keeping with NCI's major emphasis on cancer prevention through control, education, and innovation, Dr. Evans said a special black college initiative is being undertaken to heighten awareness about cancer risk and prevention among black Americans and to develop and disseminate information on controlling or reducing cancer risks in blacks. Awards are expected to be made to two historically black colleges.

Future efforts will be aimed at increasing the number of minority undergraduates participating in summer research at NCI, expanding the number of Minority Enhancement Awards to support the inclusion of minorities in cancer control studies, increasing efforts to promote minority patient accrual, and increasing the number of awards to black colleges to increase awareness about cancer prevention among blacks. New approaches will focus on manpower development targeted toward minority shortage areas of specialization, involvement of affected minority populations in the implementation of intervention programs, and specialized research training for minorities at cancer centers.

In discussion, it was pointed out that differences in cancer incidence and mortality exist among various minority groups. Dr. Baquet noted that the major risk factors--tobacco, alcohol, and health system variants--apply to all groups, but there is evidence that some biologic factors, which may contribute to host vulnerability, may have a genetic basis.

Dr. Evans, in replying to a question about how to get minorities to go into biomedical science careers, identified a minority apprenticeship program, sponsored by the Division of Research Resources. This program enables high school students to participate in research at

institutions that have certain kinds of grants. Dr. Evans suggested that efforts were also needed at the elementary school level to broaden the base of those who choose science careers.

CANCER THERAPY EVALUATION PROGRAM (CTEP)--DR. MICHAEL FRIEDMAN

In reviewing statistical data, Dr. Friedman pointed out an excess incidence of some cancers among blacks and, in some cancers with no excess incidence, a greater mortality among blacks. He listed the number of studies currently open in the Clinical Cooperative Group system and stated that in 1988, 9,400 patients were accrued to 174 active protocols from a population estimated at more than half a million patients. Only 5,280 patients were accrued to adjuvant trials, where cure was an expectation. Dr. Friedman acknowledged a generic problem accruing patients, not only minorities, to clinical trials. He also noted that the cooperative groups generally do not collect racial data and therefore complete information on minority accrual is not available. Nevertheless, he said the highest percentage of minority patient accrual was in the major pediatric oncology groups. For other groups for which there are racial data, minorities represent between 19 and 9 percent of the total number of patients accrued. Among the minority medical institutions, full membership and participation in cooperative groups is limited.

Dr. Friedman reiterated that DCT will be assisting the CMBP in administering the Minority Satellite Supplement Program to increase the accrual of minority patients to DCT-sponsored protocols. Short-term supplemental funds are provided to established or new investigators via the group's cooperative agreements, and at the time of the group's competitive renewal, the grants are consolidated and reviewed. In 1987-88, $570,000 in supplements were provided to 15 institutions with approximately 111 patients accrued. Dr. Friedman indicated that this result was not considered satisfactory, and ways of improving the effectiveness of the approach are under consideration. In concluding his remarks, Dr. Friedman mentioned possible approaches for enhancing minority patient recruitment into clinical trials: 1) provide per case reimbursement for accrual; 2) enlist new institutions (e.g., Veterans Administration facilities, public health hospitals) that have not been members of groups but have a high percentage of minority patients; and 3) formalize relationships between cooperative groups and minority medical schools. He requested the Board's assistance in addressing this issue.

In discussion, Dr. Friedman clarified that in the accrual data, all minorities are grouped together. He also stated that the money for the supplements is used to support the salaries of data managers, nurse clinicians, and investigators to cover research costs and costs of recruiting patients into clinical trials. It is not available for future reprogramming. In the per case reimbursement model, funds are not expended until a patient enters the trial, but the cost per case for minority patients may be higher than for some other patients. Mrs. Bynum noted that the principal investigators who manage the Minority Satellite Supplements will discuss these and other issues at a June 7, 1989, meeting with NCI staff. Other points raised in discussion included the following:

- The Community Clinical Oncology Program (CCOP) has been effective in accruing patients, and a system for accruing minority patients might follow the model for the clinical cooperative groups.

- Supplemental funds are used to help support the research activity.

- Care must be taken in administering any per case reimbursement program so that it is not perceived as a kind of bounty.

- A minority-based community clinical oncology program initiative is scheduled to be implemented shortly.

- The involvement of minority physicians and staff of minority medical schools in leadership roles enhances the credibility and acceptability of programs to increase minority accrual to clinical trials.

ENVIRONMENTAL EPIDEMIOLOGY BRANCH--DR. ROBERT HOOVER

Dr. Hoover suggested that epidemiologists have been in the forefront of cancer research among minorities because epidemiologists study population groups, defined by certain attributes including race and ethnicity groups, and cancer rates in an attempt to find clues about cancer etiology. In the 1970s, Dr. Joseph Fraumeni acquired data tapes from the National Center for Health Statistics that allowed the quantification of mortality by cancer site and racial group over a 20-year period. This led to a series of descriptive studies on cancer mortality among various ethnic groups. The *Atlas of Cancer Mortality Among U.S. Non-Whites* was published in 1977 and gave rates for specific racial subgroups by geographical area. The most recent study is a chapter by Drs. Fraumeni and Hoover, Epidemiology of Cancer (Racial and Ethnic Differences, 1975-1985), in the third edition (1989) of Dr. DeVita's textbook, *Cancer: Principles and Practice of Oncology*. In graphically portraying cancer incidence, Dr. Hoover pointed out that the excess total incidence among blacks obscures important racial variations for individual cancer sites.

Dr. Hoover next described several of a larger number of analytic studies in which a minority group was the focus of the study. For esophageal cancer, a well-known problem among blacks, cancer maps showed high rates in urban areas, especially northern urban areas and coastal areas of South Carolina. To investigate the first observation, a next-of-kin interview survey was initiated among blacks in Washington, D.C., in the mid-1970s. The risk factors identified from this study--alcohol and tobacco consumption--were the major risk factors identified in other studies of esophageal cancer. However, nutritional findings from the Washington study indicated that black men who consumed relatively small amounts of fruits and vegetables had a 2-fold excess risk compared to those who consumed relatively high amounts of those foods. Dr. Hoover said there was a consistent finding of increasing risk with decreasing consumption of several food groups associated with "good" nutrition, these being fresh or frozen meat and fish, dairy products and eggs, and fruits and vegetables. These risks were independent of each other, so that persons who consumed relatively low amounts of foods from all three of these groups had about a 13-fold excess risk compared with those who consumed relatively high amounts of those foods. Speculation about the biological mechanism has focused on nutrients, particularly some micronutrients, and, in fact, when the nutrient content of the reported diets was analyzed, risk increased with decreased intake of vitamins A, C, and riboflavin.

Dr. Hoover said a study of esophageal cancer in coastal South Carolina was initiated in the early 1980s, with findings published in December 1988. Persons who consumed more than 7 ounces of moonshine whiskey per day were found to have a 3.5-fold excess risk of esophageal cancer, after adjusting for tobacco and ethanol consumption. The moonshine is being analyzed for potential carcinogens.

As follow-up to these studies, Dr. Hoover said that he and Dr. Linda Pottern had initiated a study of four different cancers that are excessive in blacks in three different SEER areas. For esophageal cancer, patients are being interviewed and blood samples are being evaluated for differences in nutrients and micronutrients among blacks and whites in the same area.

Several studies have been conducted on cancer of the uterine cervix, which has a high incidence in blacks and Hispanics. Blacks have an excess risk by a factor of five or six established for this cancer. In a Washington, D.C., study of cervical neoplasia, infection with human papillomavirus was found to be three times more prevalent among black controls over age 35 than among whites. Dr. Hoover said that although these findings do not indict human papillomavirus as the specific cause of cancer, they provide useful information about the biological explanation for the risk difference between races.

Dr. Hoover said that the Division of Cancer Etiology's (DCE) approach is to describe cancer differences in different minority groups, follow up with analytic studies to identify possible risk factors, and, if appropriate, perform interdisciplinary studies to identify relationships that may underlie the risk factors and give insights into the mechanisms of human carcinogenesis. Future initiatives include the publication of the *Atlas of Trends in Cancer Mortality Among Non-Whites* in the summer of 1989, a study of excess breast cancer risk among black women under age 45, a study of nasopharyngeal carcinoma in Chinese and Chinese-Americans, and a study of genetic polymorphisms and other biochemical and molecular epidemiologic explorations of racial differences in cancer risks.

SPECIAL POPULATION STUDIES BRANCH--DR. CLAUDIA BAQUET

Dr. Baquet recalled that in 1985 NCI had convened a working group of experts on black health who advised that NCI should have a cancer control objective specifically in response to the dramatic cancer rate differentials in the black population. That objective is to "reduce and eliminate the differentials in cancer incidence, mortality, and survival between blacks and whites by the year 2000." Milestones in the development of the special populations initiative include the publication of the DHHS Secretary's Task Force Report on Black and Minority Health (1984), an inventory of NCI's intervention activities (1984), and a series of working group meetings to assist in developing a national research agenda. The Special Population Studies Branch was established in 1986 and to date has funded extramural research programs for Alaskan natives, American Indians, Asian Americans, blacks, blue collar groups, the aging population, Hispanics, low income groups, and native Hawaiians.

Dr. Baquet stated that all the special populations experience high rates of some cancers, although not necessarily all cancer. Interventions are possible for a number of these cancers, but the special populations are underserved in terms of cancer prevention and control, as well as access to state-of-the-art treatment. Therefore, Dr. Baquet said, the Branch supports multidisciplinary cancer intervention research; identifies both internal and external research resources; develops and implements rapid response initiatives; identifies populations with special needs; collects, analyzes, and disseminates data; and collaborates with various groups, including community grassroots and advocacy organizations.

Dr. Baquet summarized the intervention research program for the black population, which was first funded in 1986 and now includes 13 intervention trials. Primary prevention activities include the development of long-term, culturally specific tobacco interventions. Other studies are intended to identify key factors, such as behavioral/cultural factors and health system barriers, that contribute to avoidable mortality from specific cancer sites. Dr. Baquet cited the Washington, D.C., initiative as a collaborative effort among various components of NCI and DCPC to address the dramatic differentials in cancer rates among blacks and whites in the District.

The Intervention Research Program for Native Americans addresses the cancer prevention and control needs of American Indians, Alaskan Natives, and Native Hawaiians. Dr. Baquet said RFAs have been issued on primary prevention and avoidable mortality in these populations. She noted that the Branch had benefitted from the advice of representatives from these groups on cultural sensitivity issues. An interagency agreement between NCI and the Indian Health Service, with some support from the Centers for Disease Control, will serve to develop and monitor intervention studies and identify leads for future intervention trials.

Dr. Baquet said the DCPC Board of Scientific Counselors had recently approved an intervention research program for Hispanic populations. RFAs are expected to be issued by the winter of 1989.

Among new initiatives, Dr. Baquet mentioned the development of primary prevention, screening or treatment protocols for 500 community and migrant health centers that serve large numbers of low income patients. Efforts are also in progress to identify ways of increasing recruitment of underrepresented minorities in scientific careers. Further, Dr. Baquet noted that the National Black Leadership Initiative on Cancer is soon to embark on its follow-up phase. In conclusion, she emphasized the need to make use of internal and external expertise to develop culturally appropriate cancer intervention programs for special populations.

Mrs. Bynum commented that in closed session the Board would be asked to approve the second phase of the National Black Leadership Initiative on Cancer. She also pointed out that the Department of Health and Human Services, through the Office of Minority Health, has established multi-agency working groups to address minority health issues. NCI is the lead agency in the Working Group on Cancer and Minorities and on a continuing basis reports to the Department on the Agencies' activities in this area. Mrs Bynum offered to provide this information to the Board as well.

VII. STATUS OF CLINICAL TRIALS ACCRUAL

A CRITICAL COMMENTARY ON CLINICAL TRIALS: DILEMMAS RESULTING FROM THE SUCCESS OF THIS RESEARCH MECHANISM--DR. BERNARD FISHER

Dr. Fisher opened his presentation by outlining annual funding and accrual figures for the National Surgical Adjuvant Breast and Bowel Project (NSABP). He stated that in the previous year (2/1/88-1/31/89), the NSABP received $1.9 million in NCI funding, which would have been sufficient monies to enter 1,090 breast cancer patients and 515 colorectal cancer patients on trials. However, the NSABP actually accrued 1,947 patients, which would require $2.3 million instead of $1.9 million, leaving a deficit of almost $400,000 by January 31, 1989. For the current year (2/1/89-1/31/90), the NSABP projects that patient accrual will be slightly less than the previous year. However, their cooperative agreement calls for the group to receive $1.8 million, which is 4 percent less than the previous year, adding a further deficit of $391,000, or a total deficit for subcontracts of $785,000 by January 31, 1990.

Dr. Fisher questioned how such a flat budget and resultant deficits can be reconciled with NCI's stated goals to double patient participation in clinical trials from 25,000 to 50,000 per year and to provide extra funds for accrual to high-priority trials. He emphasized that to meet these goals the clinical trials program will require increased funding and pointed out that the annual NCI budget for the clinical cooperative groups has remained essentially the same since 1987. He shared with the Board two statements made in a letter from Dr. Harris Busch, President of the American Association for Cancer Research (AACR), to Senator Lloyd Bentsen:

> More money has been spent on defense R&D in the past 18 months than has been spent on medical research by the NIH in the past 100 years. As a nation, we spend well over a billion dollars a day on health care (approximately 11 percent of the Gross National Product) but we allocate less than 0.34 percent for our research programs.

Dr. Fisher provided an overview of the history, mechanism, and recent accomplishments of clinical trials programs in an effort to address what he considers one of the greatest dilemmas of such programs: how to communicate to others what is involved in clinical trials. He expressed the opinion that the introduction of the prospective, randomized, controlled trials into clinical medicine represented one of the great advances of the previous 50 years. Clinical trials apply scientific method to clinical problem solving and provide definitive information about the worth of therapies prior to their widespread use in populations as a whole; they are mechanisms for conducting clinical research. Dr. Fisher remarked that the lack of knowledge and appreciation of clinical trials among the general medical community can be attributed partly to the lack of sufficient education about clinical trials in medical schools.

Next, Dr. Fisher explained the rationale for the conduct of randomized Phase III clinical trials. He emphasized that to evaluate a therapy, patients who receive the therapy must be as similar as possible to those who do not receive the therapy. That is, there must be assurance that variables such as patient age and prognostic indicators (e.g., number of positive nodes, tumor size) occur with equal frequency in the treatment and control groups. The process of randomization is a technique to eliminate all biases that could influence the findings of a clinical trial.

Dr. Fisher described a recent NSABP trial comparing a placebo with tamoxifen therapy in more than 1,000 patients in each group. He noted that because this was a double-blind study (i.e., neither the patients nor the physicians knew which patients received placebo or tamoxifen), there was little or no chance for any bias. He pointed out that, in this trial, as many patients receiving placebo as patients receiving tamoxifen complained of symptoms that were thought to be due to drug toxicity.

Dr. Fisher stressed that clinical trial research is not only a necessary corollary of laboratory research but is also a source of concepts and hypotheses in its own right. He illustrated that laboratory and clinical trials research represent a continuum of efforts and delineated the purposes of clinical trials to test hypotheses, to obtain information about the natural history of disease, to evaluate therapy, and, more recently, to determine the value of tumor markers. He also provided a brief overview of the historical background of clinical trials, including the applications of statistical techniques and the development of the sciences of pharmacology and bacteriology and the consequent availability of new therapeutic agents. He stated that the clinical trial of streptomycin for the treatment of tuberculosis conducted in 1946 by the British Medical Research Council is most frequently claimed to be the first trial.

Dr. Fisher expressed concern about the many years of delay in the acceptance of clinical trials, citing as possible reasons a perception of challenge to the doctor-patient relationship, the lack of recording and publishing of scientific information, the lack of remedies to evaluate, and the use of polypharmacy. He explained that the National Cancer Chemotherapy Evaluation Program, NCI, was established in 1957, and that several clinical trials of adjuvant chemotherapy were conducted.

Dr. Fisher then turned to a description of the development of the NSABP, which he has chaired since 1971, as an example of the evolution of a clinical trials group. The Project moved its headquarters from Buffalo, New York, to Pittsburgh, Pennsylvania, in 1971, where, at that time, there were 13 participating institutions at medical schools. Dr. Fisher interjected his thoughts that cancer centers and universities do not participate in clinical trials because these institutions have their own research plans. Thus, community physicians and hospitals have been encouraged to participate, and, as a result, in 1989 the NSABP headquarters at the University of Pittsburgh has a satellite group of 84 institutions and includes a Cooperative Group Outreach Program (CGOP) and Community Clinical Oncology Program (CCOP) network. He noted that the NSABP also supports subcontracts, which, however, are most affected by the NSABP budget deficit. Dr. Fisher reminded the Board that the other cooperative groups like the Eastern Cooperative Oncology Group also have similar networks of institutions that conduct clinical trials, and that, in fact, a massive network of this kind exists throughout the country. He cited such accomplishments of these combined networks as improved physician education, better patient care, and improved documentation and data collection. He explained that the results of NSABP trials are disseminated, before publication, to the group's network of 6,000 physicians, including 1,600 surgeons and stated that 20 NSABP affiliates receive grants and that all participants compete for cooperative agreements, subcontracts, CGOPs, and CCOPs.

Dr. Fisher then reviewed patient accrual of the NSABP. He pointed out that the accrual has risen steadily since 1971 with a few declines, which occur when unexpected findings occur or when trials close earlier than expected and there are no new trials to replace them immediately. He emphasized that, as treatments improve, the patient follow-up time increases, requiring long-term commitment of human resources as well as long-term financial commitment. He pointed out that follow-up procedures require processing data collection forms, which have, with the exception of 1983, steadily increased since 1978, amounting to a total of 116,000 forms in 1987.

Dr. Fisher explained that the Division of Cancer Treatment provides the majority of funding for the NSABP and that the Division of Cancer Prevention and Control provides some funding for the CCOP mechanism. He stated that over the first 10 years of the existence of the NSABP, funds awarded increased 1,140 percent and patient accrual increased 1,564 percent; in the last 6 years, there was a 62 percent increase in funds but an 88 percent increase in accrual. He added that pharmaceutical companies play a significant role in clinical trials research. For example, in the NSABP trials using tamoxifen, ICI provided 20 million tamoxifen tablets (worth approximately $25 million commercially) as well as several million placebo tablets.

Next, Dr. Fisher summarized the role clinical trials have played in altering the paradigm for breast cancer treatment from the use of the Halsted radical mastectomy to simple mastectomy to lumpectomy and/or radiation therapy. Specifically, controlled clinical trials showed that, after 15 years' follow-up, there is no evidence to indicate that simple mastectomy provides better results than radical mastectomy; also, a trial of mastectomy versus lumpectomy with or without breast irradiation has shown no difference in distant disease-free survival or survival between the treatment groups at 8 years after the trial closed.

Dr. Fisher also reviewed the development of adjuvant chemotherapy for breast cancer. He hypothesized that, as systemic therapy improves, the surgical and chemotherapeutic paradigms will converge and that surgery will partially or completely disappear from use in the treatment of breast cancer. At present, a study of whether or not preoperative chemotherapy can control disseminated disease more effectively than the same therapy after surgery is ongoing. This study was initiated based on three main hypotheses: Dr. Howard Skipper's research in the 1960s, which led to the concept that primary and secondary tumors respond differently to chemotherapy; his

own findings published in *Cancer Research* in April 1989, indicating that primary tumors perturb growth kinetics of metastases; and the Goldie-Coldman hypothesis, which suggests that, as a tumor cell population increases, drug-resistant phenotypic variants also increase. Dr. Fisher reported that he is awaiting the results of another trial to determine whether tamoxifen inhibits the antitumor effects of cytotoxic chemotherapy when the two are given together.

Dr. Fisher then described briefly the problems of identifying good markers, which have assumed a large role in research on solid tumors and he stated that the best marker for predicting response to treatment for breast cancer is still the number of positive regional lymph nodes. He emphasized that clinical studies must be conducted to properly evaluate markers such as estrogen receptors and nuclear and histologic grade, stating, however, that obtaining material to study all of these markers is becoming more difficult as tumors get smaller and smaller. In addition, he commented that protocols are closing with greater rapidity as patient accrual rates increase and that several protocols may close in succession before data become available and can be assimilated into the design of subsequent clinical trials.

Dr. Fisher concluded his presentation by expressing concern that only $9 million has been allocated for breast cancer research through clinical cooperative group agreements, and for colorectal cancer, less than $6 million.

STATUS OF COOPERATIVE GROUP ACCRUAL ACTIVITIES-- DR. MICHAEL FRIEDMAN

Dr. Friedman presented a summary of accrual figures for the cooperative groups for 1988. Only 34 Phase I studies with 600 patient entries were performed in the cooperative group system. Phase II activities comprise the drug evaluation portion of the cooperative group activities, and the Phase III trials, described previously by Dr. Fisher, represent the largest number of patients studied by the cooperative groups. The CTEP also supports nontherapeutic trials (e.g., of markers, prognostic indicators) within the groups as well as providing some funding to the statistical center of the European Organization for Research on the Treatment of Cancer.

Dr. Friedman informed the Board that over the previous 3-month period, the number of ongoing Phase III studies had decreased. At the same time there was an increase in the overall accrual rate over the previous quarter. Hence the system is more efficient. The median duration of the Phase III trials decreased significantly over the past 2 years due to increased patient accrual.

Turning to the high-priority trials, Dr. Friedman stated that the colon cancer study had progressed at approximately three times the projected accrual rate. Two other high-priority studies were performing well above the projected rates, and overall there has been approximately a 20 percent increase over the number of patients projected for these high-priority trials.

Dr. Friedman listed the following changes in the cooperative group system between 1985 and 1988:

- The number of cooperative groups has decreased from 18 to 11.
- The budget increased from $51 to $58 million.
- The annualized accrual rates increased from less than 18,000 to more than 21,000.

- The number of studies open to group accrual decreased from 586 to 495.

Dr. Friedman stated that this streamlining of the clinical trials mechanism indicates that the groups are performing studies more efficiently, and he commended their efforts to perform in a highly efficient and effective manner. He concluded by expressing agreement with Dr. Fisher that unmet needs in the cooperative group budget must be addressed. He congratulated cooperative group participants and program staff for their work in improving the system to become more focused and effective over the past several years.

In the discussion, Dr. Friedman clarified that most of the top institutions from the cooperative groups that are no longer funded have become reaffiliated with other groups. In response to a question about accrual rates by each of the remaining 10 groups, Dr. Friedman stated that all groups must operate within their own budgetary constraints, and funding limitations prohibit entering excess patients on trials. Dr. Erwin Bettinghaus asked whether a breakdown of funding sources for a cooperative group trial could be made available. Dr. Friedman responded that although CTEP has been attempting to obtain such reports for the past 5 years, this has been extremely difficult because of the many different ways in which institutions fund principal investigators, nurses, and clinics.

VIII. ORGAN SYSTEMS PROGRAM--DRS. ALAN RABSON AND BRIAN KIMES

Dr. Rabson recalled that the origin of the Organ Systems Program was in 1966 with the Breast Cancer Task Force, which was originally part of the Division of Cancer Biology and Diagnosis (DCBD). This task force was established in response to concerns of Congress and others that NCI was placing too much emphasis on leukemia and lymphoma studies and not enough emphasis on common solid tumors. Subsequently, task forces to address other solid tumors were also formed. These task forces were organized to have a multidisciplinary approach to each particular cancer, as compared to the divisional programs focused on cancer causation, diagnosis, prevention, and treatment. Dr. Rabson said that NCI directors and the NCAB have been reviewing and modifying this program since 1973. He then introduced Dr. Brian Kimes to discuss the most recent review of the Program.

Dr. Kimes announced that a revised final plan for the Organ Systems Program (OSP) had been developed and the first stages implemented. At Dr. Broder's request, he and Dr. Andrew Chiarodo had reevaluated the Program and presented a plan to the Executive Committee in conformance with the following conditions: the plan should be realistic with respect to currently available resources, but reserve a potential for future growth; it should be flexible for addressing new scientific opportunities and high priorities of the NCI; it should preserve the working group concept and the creative role that bench scientists serve in advising the NCI; and it should provide for a prominent role of the NCI Director in overseeing its management. The Executive Committee has approved the plan, and the first changes that are required for organizational implementation are in progress.

Dr. Kimes emphasized that the focus of the program is the promotion of multi-disciplinary, investigator-initiated research in high-priority solid tumors as the key to further progress. The emphasis on research in etiology, biology, diagnosis, prognosis, and treatment, based on novel concepts, will continue, but the Program will not be involved in the design of new clinical trials. The Program will serve as an important focus for tracking, reporting, and evaluating information related to solid tumor research and addressing high priorities in the National Cancer Program. Further, the Program will promote dialogue and interactions across divisions of the NCI.

In describing some of the major operational elements of the new Program, Dr. Kimes stated that the Program will hold two major comprehensive workshops per year, each on a given type of cancer, with each type of cancer included in the OSP having a workshop every two or three years. The two cancers to be addressed this year are breast and prostate cancer. In addition, Dr. Kimes reported that there will be three focused workshops per year to address areas of immediate concern to the Institute.

To encourage investigator-initiated research, Dr. Kimes stated that Program Announcements (PAs) will be prepared in the seven areas of solid tumor research currently represented by working groups. He added that PAs will be considered for other types of cancer that do not have working groups at this time, for example, lung cancer, ovarian cancer, and melanoma.

Dr. Kimes suggested that the NCI also support, through the conference grant mechanism, regular biannual or triennial conferences that address each cancer in a multidisciplinary way. He said that these conferences can have more of a stimulatory influence than small working group meetings because they would bring together the most important scientists in the field.

Dr. Kimes emphasized that the Organ Systems Program will remain an important focus for reporting, information tracking, and evaluation activities dealing with the solid tumors. The OSP will also continue to produce regular organ systems reports, but these reports will be coordinated with the periodic comprehensive workshops rather than being issued yearly. Dr. Kimes stated that the OSP will remain the single most important informational focus for investigators who are interested in pursuing research objectives related to solid tumor research. The Program can direct these investigators to resources and program directors within the Institute. He added that the Program will represent for the Director of the Institute the single best source of data on solid cancers. Dr. Kimes emphasized that the NCI internal Organ Systems Committee will be preserved as it is an important link among divisions and is needed to facilitate cooperation for program planning and evaluation activities.

Dr. Kimes identified the important elements of the workshop process, which will apply to both comprehensive and focused workshops:

- Larger workshops may last for three or four days and smaller workshops will normally last a day-and-a-half.

- Substantial numbers of scientists and staff, representing all disciplines, will be invited.

- Working groups of approximately 15 participants will be assembled to help develop a publication that will clearly define the conclusions and consensus items and to help identify priorities and scientific opportunities that can be developed as program initiatives.

- These priorities will then be assessed by the Director and Executive Committee of NCI each year.

- Those priorities that eventually result in staff development of concepts for RFAs, PAs, and contracts will again involve the same nucleus of working group members to ensure continuity (the working group members may help to defend those concepts before the Boards of Scientific Counselors).

Dr. Kimes concluded that this process will generally work for the comprehensive, as well as the more focused workshops.

Dr. Kimes noted that the Organ Systems Program will be given branch status within the DCBD and renamed the Organ Systems Coordinating Branch. He stressed that he and Dr. Rabson will ensure close communication with Dr. Broder about the Program. The current staffing levels of three health science administrators and two support staff will be maintained. Dr. Kimes suggested that while the new plan takes into account a realistic view of current fiscal challenges, the Program should become more visible and allow for future growth.

The following points were raised in discussion:

- The working groups of workshop participants will include extramural scientific experts and NCI staff.
- Program announcements may involve more than one division, and members from other Boards of Scientific Counselors may attend meetings of the DCBD Board.
- The working groups will include various scientific disciplines, and members will be involved for 12 to 24 months to help bring an initiative to reality.
- Ideas for workshops can originate from extramural scientists and NCI staff.
- Fiscal constraints precluded the continuing, simultaneous support of seven working groups.
- The advantage of having larger workshops and working groups is that there is a better chance of having a thorough discussion of all the issues.

IX. CANCER CENTERS PROGRAM

INTRODUCTION--DR. PETER GREENWALD

Dr. Greenwald stated that cancer centers, established as a primary means of achieving a stable environment for cancer research progress, represent a major accomplishment of the National Cancer Program. Because of budgetary constraints and other changes, it has been difficult to maintain the flexibility and strength needed for the growth and success of cancer centers. Therefore, several reviews were undertaken to determine how to best strengthen the centers. Dr. Greenwald identified these efforts as the President's Cancer Panel's hearings at a number of centers, a report by the Institute of Medicine prepared at the request of the Senate Appropriations Committee, and a review by NCAB's Subcommittee on Cancer Centers, chaired by Dr. John Durant.

REPORT OF THE SUBCOMMITTEE ON CANCER CENTERS--DR. JOHN DURANT

Before presenting the report, Dr. Durant observed that in spite of the inevitable urge to centralize and consolidate programs to improve their efficiency during times of financial stress, the heterogeneity of the centers should be recognized as an important asset worthy of preservation. For historical perspective, he recalled that the centers were originally funded by umbrella grants that subsumed individual research projects. The umbrella grant was replaced with a new funding mechanism, the core grant, which provided support for the infrastructure of

cancer centers. The NCAB assumed responsibility for the designation of comprehensive centers, considering applications after a core grant was awarded. Dr. Durant stated that the event precipitating the formation of the NCAB Subcommittee on Cancer Centers was a request from the University of Arizona that it be designated a comprehensive cancer center.

In beginning his report, Dr. Durant identified members of the IOM Committee to Study the Cancer Centers Program and noted the participation of representatives from the centers. Responding to a graph showing core grant support decreasing as a percentage of total NCI support to institutions with cancer centers over the years 1981-88, the point was raised that parent institutions and cancer centers are not synonymous. Dr. Greenwald added that funding information is available only for institutions that house cancer centers, not the centers themselves, except for information voluntarily provided by centers. However, for those institutions that receive center core grants, NCI provides a greater percentage of support through mechanisms other than the core grant than it does to institutions without center core grants. Most of the core grant funds support shared resources, with smaller amounts used to support the center's senior leadership, staff investigators and administrative expenses. Most of the shared resources support the laboratory science activities of the center.

Dr. Durant described the turnover of NCI-designated cancer centers, pointing out that the composition of the 61 in existence in 1988 is substantially different from the 64 that existed in 1977. Twenty-four of the original centers are no longer funded and 25 new centers have been added. These changes have occurred as a result of peer review and payline decisions.

Next, Dr. Durant discussed the Subcommittee's response to the IOM report's recommendations. He said the Subcommittee strongly believed that funding should not be reduced below the current 85 percent of the peer-review-recommended level. The Subcommittee felt that further reductions of the level of funding would negate peer review and that money should be sought to pay all centers with a fundable priority score. To address the issue of future planning, the Subcommittee supervised election of six center directors to advise Dr. Broder and NCI staff on issues of concern to centers. The Subcommittee also recommended that to strengthen the program organization and management, consideration should be given to creating a new division for cross-divisional programs, including the Cancer Centers Program. Dr. Durant acknowledged that the feasibility of that recommendation was dependent on whether it could be implemented due to administrative constraints like availability of personnel slots (FTEs).

Dr. Durant listed the proposed new criteria for NCI-designated comprehensive cancer centers:

1. Basic laboratory research
2. Basic/clinical research linkage
3. Clinical research
4. High-priority clinical trial research
5. Cancer prevention and control research
6. Education and training and providing updates on current technology
7. Information services.

Those applicants that request designation as a comprehensive cancer center would be evaluated according to guidelines that address these criteria, and the evaluation would be part of the peer-review of the core grant application. The NCAB oversees the review of core grants, as it does for all peer-reviewed applications. Dr. Durant said the Subcommittee specifically recommended that those centers that receive NCI support be called "NCI-designated" centers.

With respect to the IOM committee's recommendation that the NCI Director identify additional funds to solve short-term funding problems, Dr. Durant said the NCAB Subcommittee believed that the problems of the centers reflect problems in the infrastructure of biomedical science in the United States. Reprogramming of funds within the Institute can only temporarily address the interests of one constituency. The real need is to accord a higher priority to biomedical research overall.

Dr. Korn commended Dr. Durant for his leadership in the work of the Subcommittee and suggested that the Board address two issues: 1) consideration of the Subcommittee's report, including the proposed criteria for comprehensiveness, and 2) response to the IOM report.

Mrs. Brown moved approval of the Subcommittee report; the motion was seconded. Issues raised in discussion included the following:

- The value of the title "NCI-designated" should provide incentive to centers to maintain and apply for comprehensive status.

- The title "NCI-designated" would also be applied to the other types of centers, i.e. clinical, laboratory, and consortium.

- The NCI-designated cancer centers might adopt the logo of the National Cancer Institute to help define an identifiable network of institutions.

- Specific guidelines for applying the criteria for comprehensiveness will be written and will address such issues as minority concerns.

The Board unanimously approved the Subcommittee's report and recommendations, which included the new criteria for comprehensive cancer centers.

The Board next discussed the draft subcommittee statement on the IOM report. Dr. Broder recognized the vital importance of the cancer centers but urged that the IOM report not be used as precedent for different programs supported by NCI requesting reprogramming of funds to increase resources for their own activities. He stated that without an increase to the total budget, the request for additional funds for the cancer centers would pose a serious challenge. Dr. Broder suggested that the by-pass budget be used to focus attention on priorities, and he pointed out that the 1990 by-pass budget requests an additional $30 million for the cancer centers program. He underscored the importance of the by-pass budget as a realistic professional assessment of needs.

The following points were raised in discussion:

- The IOM report confuses funding mechanism with function and thereby gives disproportionate importance to the centers core grant.

- The statement on the IOM report should stress the interdependence of the parts of NCI and the need to pay attention to NCI's by-pass budget.

- A letter should be sent to members of the Senate Appropriations Committee expressing the Board's support of the by-pass budget and noting the overall deficit in the biomedical research budget.

It was agreed that Dr. Durant should revise the draft NCAB statement on the IOM report for the Board's further review.

Dr. Korn distributed a draft resolution endorsing the NCI Director's strong commitment to addressing the unequal burden of cancer in minorities as a high national priority. He asked that members review the resolution and consider whether it should be adopted.

X. CLOSED SESSION

A portion of the second day of meetings was closed to the public because it was devoted to the Board's review of grant applications. A total of 1,244 applications were reviewed, requesting support in the amount of $237,801,137. Of these, 1,145 were recommended for funding at a total cost of $191,750,110.

XI. REPORT OF THE SUBCOMMITTEE ON PLANNING AND BUDGET--DR. LOUISE STRONG

Dr. Louise Strong presented the minutes of the Subcommittee on Planning and Budget meeting held on May 15, 1989, and a summary of the 1991 by-pass budget. A discussion of the by-pass budget followed. Concern was raised that in light of existing budget realities, the by-pass budget might be perceived to be unrealistically high. Dr. Broder stressed that the function of the by-pass budget is to present the best professional judgment of the needs of the NCI. The amount of money proposed in the by-pass budget is what the Institute believes it could spend soundly, wisely, and effectively for the important, substantive parts of a national cancer initiative. Dr. Broder added that it is the function of Congress to determine budget allocations and priorities, taking other national issues into account. It was suggested that emphasis be placed on the fact that a budget close to the by-pass budget was appropriated in 1984. Board members requested a comparison of allocated and by-pass budgets for the years 1984 to 1989, using constant dollars.

A motion to approve the 1991 by-pass budget was seconded and unanimously approved.

XII. NEW BUSINESS--DR. DAVID KORN

RESOLUTION TO ENDORSE DR. BRODER'S COMMITMENT TO ADDRESSING CANCER IN MINORITIES AS A HIGH PRIORITY OF THE NCI

The Board unanimously approved a motion to adopt the resolution to support the Director's strong public expressions of commitment to addressing cancer in minorities as a priority for the Institute, with an amendment that such a commitment provides a means for making significant progress towards the year 2000 goals. Mrs. Bynum will distribute copies of the amended resolution to Board members.

STATEMENT ON THE INSTITUTE OF MEDICINE (IOM) REPORT: *A STRONGER CANCER CENTERS PROGRAM*--DR. JOHN DURANT

Dr. Durant distributed an amended statement from the NCAB Subcommittee on Cancer Centers on the IOM report, *A Stronger Cancer Centers Program.* Dr. Korn explained that this statement describes the report as constructive but incomplete in that it fails to put the Cancer Centers Program in the context of research infrastructure support, a problem for the whole of

biomedical science. The statement also addresses the linkage of the centers to the totality of funding mechanisms of the cancer program as expressed in the by-pass budget.

After considerable discussion about the emphasis of the statement on the problem of support for U.S. biomedical science instead of strictly for the cancer program, the statement was amended to focus more on the centers and the NCI and on the by-pass budget, with reference to general support of biomedical research. Mrs. Bynum will send the amended statement to Drs. Korn, Gertrude Elion, and Roswell Boutwell and then circulate it to the entire Board. The statement will be retitled to indicate that it is a statement from the NCAB rather than a statement from the Subcommittee on Cancer Centers.

REPORT OF THE SUBCOMMITTEE ON AGENDA WORKING GROUP--
DR. LOUISE STRONG

Dr. Strong reviewed the goal of the Subcommittee on Agenda: to promote efficient use of meeting time to discharge NCAB's mandated review and advisory responsibilities. She noted that while the format changes that had already been implemented would be evaluated at the next subcommittee meeting, the Working Group, in preliminary discussions, favored the 2-day over the 3-day meeting. Other recommendations were:

- Begin subcommittee meetings no earlier than 6:00 p.m. on Sunday; have subcommittee meetings on Monday morning from 7:30 a.m. to 9:30 a.m.
- Begin the Monday morning plenary session at 9:30 and include on that agenda the President's Cancer Panel's and Director's reports and the legislative update
- Hold the closed session on Monday afternoon, followed by committee meetings
- Begin the Tuesday plenary session at 8:00 a.m. and schedule action items that call for extensive Board discussion, for which members had received prior detailed agendas; adjourn at 4:00 p.m.
- Hold the remaining subcommittee meetings on Tuesday afternoon; minutes would be mailed out and approved at the subsequent NCAB meeting.

In discussion, it was suggested that subcommittee meetings be scheduled early on Monday morning and the plenary session convened a little later (9:00 or 9:30 a.m.). The point was also raised that subcommittee meetings should be scheduled early enough to ensure that reports are presented and acted on before the NCAB adjourns. Mrs. Bynum pointed out that all subcommittees do not meet every time, and she suggested that those those subcommittees desiring to meet could so inform her and a schedule could be drawn up, after consultation with Dr. Korn, to avoid conflicts for those members who serve on multiple committees. She added that extended subcommittee meetings could be held on or off campus between regular NCAB meetings for efforts or issues that require more time.

Continuing with the subcommittee report, Dr. Strong said the group also discussed the desirability of receiving agendas that identify those items that require Board action and those that are for information only. She commented that the practice of sending out all grant information (e.g., rebuttal letters and special actions) had worked well for the closed session just completed in that members were able to read it in advance and dispense with addressing noncontroversial items at the meeting. She asked for concurrence on the subcommittee's recommendation that each

member receive only his or her assigned full summary sheets, as well as any others requested from the advance listing, thereby eliminating the need for the DEA to mail out unassigned summary statements. In discussion the Board concurred, and Mrs. Bynum agreed to implement that recommendation on a trial basis for the next meeting.

After summarizing discussions of the annual program review, Dr. Strong reported the recommendation that the format be changed to include in-depth presentations by only half of the divisions and their Boards of Scientific Counselors (BSCs) each year, on an alternating schedule, but that members receive summaries from all divisions. Mrs. Bynum reminded the Board that an all-encompassing presentation of concepts that had been reviewed by the divisional BSCs during the previous year had also been requested. Dr. Strong suggested that a similar list of concepts reviewed by the NCAB could be part of its annual summary.

Mrs. Bynum requested the Board's guidance on a procedural matter. Referring to the Board's request for advance copies of rebuttal letters, she asked if members also wished to receive copies of pre-award modifications requested by investigators (these adjustments can be made by program staff based on adequate justification of the request). The Board agreed that they need receive only those letters that change the results of the competitive review.

Finally, Dr. Strong emphasized the preliminary nature of these recommendations and said the subcommittee plans to cast them in a more final form. At a future and possibly final meeting of the ad hoc subcommittee, format changes that have already been implemented will be evaluated. In discussion, the global nature of NCAB's mandated responsibilities and the need for adequate meeting time to discharge them were emphasized. It was agreed that 3-day meetings might be warranted at times. Dr. Strong stated that minutes of the Subcommittee on Agenda Working Group meeting would be mailed to members, and Mrs. Bynum said that she would try to incorporate as many of the recommendations as possible in the planning for the next meeting. In closing, Mrs. Bynum thanked Dr. Paulette Gray and the staff of the Review Logistics Branch for improvements that had been noted in the current meeting.

XIII. ADJOURNMENT--DR. DAVID KORN

There being no further business, Dr. Korn adjourned the 70th meeting of the National Cancer Advisory Board at 2:43 p.m., Tuesday, May 16, 1989.

8/1/89
Date

Dr. David Korn, Chairman