Department of Health and Human Services

Public Health Service

National Cancer Institute

National Cancer Advisory Board

Summary of Meeting
September 28-30, 1987
Building 31, Conference Room 6
National Institutes of Health
Bethesda, Maryland

Department of Health and Human Services
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September 28-30, 1987

The National Cancer Advisory Board (NCAB) convened for its 63nd regular meeting at 8:30 a.m., September 28, 1987, in Building 31, 6th Floor, Conference Room 6, National Institutes of Health (NIH). Dr. David Korn, Chairman, presided.

Board Members Present

Mr. Richard A. Bloch
Dr. Roswell K. Boutwell
Dr. Victor Braren
Mrs. Nancy G. Brinker
Mrs. Helene G. Brown
Dr. Ed L. Calhoon
Dr. John R. Durant
Dr. Gertrude B. Elion
Dr. Bernard Fisher
Dr. Phillip Frost
Dr. Geza J. Jako
Dr. David Korn
Dr. Enrico Mihich
Mrs. Barbara Ingalls Shook
Dr. Louise C. Strong
Dr. Louis W. Sullivan
Dr. Howard Temin

Absent

Mrs. Irene S. Pollin

President's Cancer Panel

Dr. Armand Hammer

Absent

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

Ex Officio Members

Dr. Dorothy A. Canter, NIEHS
Dr. Mary Ann Danello, FDA
Dr. Richard J. Greene, VA
Mr. Richard A. Lemen, NIOSH
Dr. Lakshmi Mishra, CPSC
Captain Stephen R. Veach, DOD
Dr. James B. Wyngaarden, NIH
Dr. Ralph E. Yodaiken, DOL, OSHA

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

Liaison Representatives

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

Dr. Robert Frelick, representing the Association of Community Cancer Centers.

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

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

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

Dr. Carl A. Olsson, Professor and Chairman, Department of Urology, Columbia University, New York, representing the Society of Urologic Oncology.

Dr. Warren H. Pearse, Executive Director of the American College of Obstetricians and Gynecologists, Washington, D.C., representing the American College of Obstetricians and Gynecologists.

Dr. John Potter, Director, Lombardi Cancer Center, Georgetown University, Washington, D.C., representing the Society of Surgical Oncology.

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

Dr. Eve Ida Briles, Assistant Program Director for Cell Biology, representing the National Science Foundation.

Ms. Yvonne Soghomonian, Associate Director, Candlelighters Childhood Cancer Foundation, Washington, D.C., representing the Candlelighters Childhood Cancer Foundation.

Dr. Stephen Schiaffino, Executive Officer, representing the American Society for Clinical Nutrition.

Dr. Sidney Winawer, Director, Division of Gastroenterology, Memorial Sloan-Kettering, representing the American Gastroenterological Association.

Members, Executive Committee, National Cancer Institute, NCI

Dr. Vincent T. DeVita, Director, National Cancer Institute
Dr. Peter J. Fischinger, 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. Alan Rabson, Director, Division of Cancer Biology and Diagnosis
Executive Secretary, Ms. Iris Schneider, Assistant Director for Program Operations and Planning

In addition to NCI staff members, meeting participants, and guests, a total of 31 registered members of the public attended the meeting.

I. Call to Order, Opening Remarks, and Consideration of the May 26-27, 1987, NCAB Meeting Minutes--Dr. David Korn

Dr. Korn, Chairman, called the meeting to order and welcomed Dr. James Wyngaarden, Director of the National Institutes of Health (NIH), members of the Board, the President's Cancer Panel (PCP), liaison representatives, guests, staff of the National Cancer Institute (NCI), and members of the public. He introduced new Board member Dr. Howard Temin, professor at the McArdle Laboratory at the University of Wisconsin and Nobel Prize winner. Members of the public who wished to express views on items during the meeting were invited to submit written comments to Mrs. Bynum, Executive Secretary of the National Cancer Advisory Board (NCAB), within 10 days after the meeting.

Approval of the May NCAB minutes was postponed until the Wednesday, September 30, session.

II. Future Board Meeting Dates

Dr. Korn called the Board members' attention to the following confirmed future meeting dates: November 16-18, 1987; February 1-3, 1988; May 9-11, 1988; September 26-28, 1988; December 5-7, 1988; February 6-8, 1989; May 15-17, 1989; September 18-20, 1989; and December 4-6, 1989.

III. Remarks of the Director, National Institutes of Health--Dr. James Wyngaarden

After greeting the Board, Dr. Wyngaarden announced that a major meeting of the Director's Advisory Committee will be held on November 18 and 19 to address the role of biomedical research in combatting AIDS. He noted that a new AIDS Advisory Committee, requested by the NIH, will participate in the November meeting if organizational details are completed.

Next Dr. Wyngaarden summarized the results of two recent reviews of the Government's efforts in AIDS. The largest was the review conducted by the Institute of Medicine, National Academy of Sciences, which produced a major publication and advice on strategy in the areas of biomedical research and public education. That review was helpful to NIH in setting priorities and identifying areas needing additional attention.

Dr. Wyngaarden said the other review, mandated by Congress, examined NIH programs. The review was conducted by a committee chaired by Dr. Charles Carpenter of Western Reserve and concluded that the Government research effort is vigorous in addressing all important areas, is proceeding at a good pace, and is well supported at this stage. He added that NIH recognized from these two reviews the potential value of an ongoing panel to help in evaluating the AIDS program and requested that an AIDS Advisory Committee be chartered.

Dr. Wyngaarden reported that the Director's Advisory Committee met recently to address the general topic of the health of the extramural biomedical research community, which conducts 80 to 90 percent of the research supported by NIH. This meeting focused primarily on NIH's interactions with the administrative structure of the extramural research-performing institutions.

Dr. Wyngaarden said a number of areas were discovered where there was less than complete understanding of the complexities of NIH and the dilemmas inherent in public advocacy of programs. It was also found that NIH mechanisms were not fully understood. As a consequence, four regional hearings are planned where representatives of several components of NIH (including administrative staff and advisory boards and councils) will meet with scientists from the research community for an exchange of information.

Dr. Wyngaarden stated that NIH had already taken action to improve overall relationships with the extramural community and strengthen the research structure. He commended NCI for taking the lead with its Outstanding Investigator Grant program. Dr. Wyngaarden said the frequent meetings will focus not only on enlisting vigorous support of the extramural research community to help facilitate the operation of NIH, but also on clarifying the respective roles and responsibilities of NIH and the scientific community.

Dr. Wyngaarden next discussed allocation of resources on campus, particularly with respect to the Clinical Center. He noted that some beds have been down for remodeling purposes, that AIDS research has placed added stress on the Center (beds used for AIDS research have come from existing allocations), and that shortages of nurses and support space have prevented full use of all existing beds. Dr. Wyngaarden said the decision had been made to increase the number of beds available for research, particularly to the NCI, and that after a review of past assignments and use patterns, it was agreed to restore to NCI its original high number of 149 beds. He announced that arrangements are in progress to rapidly transfer the 26 beds in 12 East to NCI, which will increase the number of beds for AIDS research without compromising the existing level of activity on more specifically cancer-related projects. He noted that NCI's bed use pattern in the Center is the highest of any NIH component and the action should bring the distribution back to a more appropriate level.

Next, Dr. Wyngaarden discussed the ongoing assessment of the NIH's involvement in the human genome project. A survey of all Institutes indicated that NIH supports $300 million worth of research (about 2,000 projects) having components related to studies of human and complex genomes, with about one-third devoted to mapping and sequencing activities. In addition, NIH has been involved, along with other Federal agencies, in managing a data base of sequences. In 1979, the Los Alamos Laboratory began a DNA sequence data base, largely supported by NIH through the National Institute of General Medical Sciences (NIGMS). Dr. Wyngaarden said the data bank has been unable to keep pace with the acquisition of data in spite of NIH support in the amount of $3.5 million over the past 5 years. He noted that the human genome project was fully considered at a spring meeting in Heidelberg where plans were made to improve and enlarge the data bank and to coordinate more effectively with Japan.

Dr. Wyngaarden said the Director's Advisory Committee had also addressed the issue of NIH's role in human genome activities at a recent meeting and made recommendations. As a first priority, the Committee recommended improved handling of data, and in response, NIH has released a program announcement through the National Library of Medicine. In addition, Congress is studying the problem of biotechnology information handling.

The Director's Advisory Committee also emphasized the need for improved methodology in human genome research. Dr. Wyngaarden reported that NIH has released a program announcement, with NIGMS as the lead agency, to direct more attention to the general problem of methodology.

The Director's Advisory Committee agreed that NIH should proceed as fast as possible with physical and genetic mapping, and Dr. Wyngaarden noted that the FY 1988 budget includes funds to move in that direction. Hovever, though there was a general consensus among the Advisory Committee that an all-out sequencing effort was very high priority, it was agreed that such an effort could be more effectively undertaken when the other recommendations had been implemented. As to a lead agency to accomplish these goals, Dr. Wyngaarden said the consensus was that progress was limited by resources, not organizational structure, although effective coordination is necessary among agencies, between government and the private sector, and among countries.

Dr. Wyngaarden turned next to the FY 1988 budget, noting that NIH will operate on a continuing resolution until the final budget is passed. In the House markup, the total for NIH is $7.05 billion ($1.5 billion for NCI), compared to the FY 1987 budget of $6.18 billion, and it includes support for 6,500 new and competing awards (about 200 of that total for AIDS research). The House markup treats the AIDS budget as a separate component and puts all the funds in the Secretary's office, although it specifies Institute amounts. It also adds $50 million of flexible funds to the NIH request of $422 million for AIDS activities, although it specifies that $30 million must be used for AIDS infrastructure and $20 million for four or five multidisciplinary centers. Research training is supported at the present level of about 11,000 trainees. The House bill also includes $30 million in the NIGMS budget for gene mapping with $4 million for expansion of the gene bank. Dr. Wyngaarden said if this sum were allocated in that manner, an attempt would be made to instigate trans-NIH participation in the systematic mapping of the human genome.

Finally, the House markup includes $15 million for extramural animal facilities, restores the biomedical support grant at the level of $60 million, provides $40 million for new clinical trials, but provides no funds for extramural construction. Dr. Wyngaarden noted that the NIH budget request included $1.542 million in construction funds for NCI.

Dr. Wyngaarden said the Senate markup, which is still in Committee, is about $6.8 billion, compared to the House total of $7.05 billion, and is systematically less for almost all activties. The Senate version allocates AIDS funds directly to the individual Institutes and contains only a few million dollars for gene sequencing activities.

In response to a question, Dr. Wyngaarden clarified that the AIDS Advisory Committee is an NIH committee and there will be cross representation and coordination if similar committees are formed in other agencies.

To another question about the nursing situation, he answered that as a consequence of two recent policy changes (more use of opportunities in the PHS Commissioned Corps and a more flexible system of payment for weekend

and night work), the Clinical Center's nursing deficit has been reduced from 43 to 25. NIH's starting salaries for nurses are now competitive in the Washington and Baltimore area, but the general problem is a nationwide shortage. However, the expectation is that recruitment will be successful for the expanded cancer component and has aready proven easier for AIDS-related research projects.

In response to a question about funding for AIDS patient care, Dr. Wyngaarden noted that NIH funding is primarily for research which includes drug evaluation. For that purpose, 18 AIDS treatment evaluation units (ATEU) have been established where clinical trials on about eight agents are presently underway. He stressed that although the ATEUs could treat more patients, 1,700 or 1,800 patients are currently on trials, and NIH's responsibility is to evaluate the efficacy and safety of the new agents and not to reach the maximum number for the purpose of health care delivery. He added that trials are behind schedule due to the need to redesign all of the clinical trials when AZT was released. The new trials will compare the use of new agents with AZT-treated patients, a more complicated procedure than the original trials that compared use of new agents in untreated patients.

In response to a question about the kind of information NIH is seeking at the regional meetings, Dr. Wyngaarden explained that NIH wants to find out what the extramural community perceives can be done to simplify scientific research and make it more effective, more responsive, and more equitable. The meeting will focus on helping NIH respond to the needs of the extramural community systematically, while stressing the constraints on NIH actions. He acknowledged the complexity of the present system due to the steps taken over the years to increase accountability and listed recent internal measures taken to strengthen the program: 1) simplification of the research grant application; 2) introduction of programs (such as the Career Development program) for first-time investigators, which stress training at levels beyond training grants and fellowships; 3) introduction of programs to reduce complexities for mid-career scientists, such as the new MERIT award, which assures up to 10 years of support for designated recipients.

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

Dr. Hammer thanked Dr. Wyngaarden for his informative report on NIH and conveyed the regrets of absent Panel members, Drs. Longmire and Montgomery. He reported that the June PCP meeting was cancelled and the next meeting is scheduled for Pittsburgh on October 23. One of the last two meetings on the PCP schedule may be held at NCI.

Dr. Hammer stated that he had had the privilege of speaking at the first NCAB Public Participation Hearing held on September 22 at the Los Angeles County Medical Society and that he wanted to go on record as endorsing the idea of such meetings. He noted that the PCP found its meetings held at cancer centers around the country to be very valuable. Dr. Hammer said the Los Angeles meeting marked a good beginning for the new undertaking, and he expressed the hope that the hearing report would receive wide distribution.

Next Dr. Hammer summarized the update he received from Dr. Steven Rosenberg on trials using the interleukin-2/lymphokine activated killer cell (IL-2/LAK) therapy. Of a total of 222 patients with metastatic cancer who had been treated, 16 had complete elimination of tumors, some for up to 3 years; 26 had at least 50 percent remission; and 20 had 20 to 50 percent remission. Thus, about 30 percent of these patients, who were considered terminal and had not responded to other forms of treatment, showed successful remission. About 38 cancer centers are now permitted by the Food and Drug Administration to treat patients with Dr. Rosenberg's protocol.

Dr. Hammer said further evidence of IL-2/LAK efficacy has come from work published in the New England Journal of Medicine by Dr. William West and his colleagues at the Biological Therapy Institute in Memphis, Tennessee. Dr. Rosenberg is continuing to improve the IL-2/LAK protocol to decrease the toxicity, and he is studying the synergy between IL-2 and the tumor necrosis factor, monoclonal antibodies, and colony-stimulating factors. Dr. Hammer predicted further developments in the next 10 years, which will lead to the elimination of cancer as it is known today.

Dr. Hammer reported that the October 23 Panel meeting at the University of Pittsburgh School of Medicine will include presentations by Dr. Bernard Fisher on the results of the National Surgical Adjuvant Cooperative Group study on colon and rectal cancer. He noted that Dr. Fisher's successful work in the treatment of breast cancer has led to a new national clinical trial in colon cancer. Dr. Hammer stressed the need to enroll a maximum number of patients in these clinical studies and recommended expansion of the clinical trials program and increased levels of support for the NCI. Dr. Hammer said the Panel hopes in its meetings to disseminate information about the need for more patients to be enrolled in clinical trials and to encourage physician and patient participation as a way of bringing new therapies to a wider segment of the population. To that end, Dr. Robert Wittes of the NCI will present his recommendations at the Pittsburgh meeting for optimizing the conduct of high priority clinical trials.

In conclusion, Dr. Hammer emphasized the responsibility of all who are involved in the National Cancer Program to make the latest advances available to cancer victims throughout the country.

V. NCI's Director's Report--Dr. Vincent T. DeVita

Dr. DeVita thanked Dr. Wyngaarden for his presentation and welcomed Dr. Temin to the Board. Dr. DeVita announced that the Year 2000 Award had been given to Mrs. Mary Lasker in recognition of her many contributions to biomedical research. He praised her foresight in stimulating research in NCI and other Institutes. The cover of the October issue of the Journal of the National Cancer Institute will have a portrait of Mrs. Lasker, the first issue ever to have anyone's picture on the cover.

Dr. DeVita noted the following staff changes: Ms. Martha Fewell, his new secretary; Dr. Daniel Nixon, Associate Director for Prevention in the Division of Cancer Prevention and Control (DCPC); Mr. Stephen Hazen, replacing Mr. Larry Ray, as Administrative Officer in the Division of Extramural Activities; Ms. Eleanor Nealon, formerly science writer in the Director's office, moved to Chief of the Reports and Inquiries Branch, Office of Cancer

Communications; Ms. Clarissa Wittenberg, new science writer in the Director's office; and Dr. Jerome Yates, leaving NCI as Associate Director for Centers and Community Oncology (DCPC), to go to Roswell Park. He announced that in February 1988 all NCI extramural staff will move into a newly leased office building.

Follow-up Items

Frederick Cancer Research Program

Dr. DeVita said the recompetition for the Frederick Cancer Research Program (FCRP) had been completed and contracts signed. Program Resources, Inc. (PRI) provides services and support for the intramural program and contractors. Biomedical Research Institute (BRI) has the basic research contract, and Owen Sprague-Dawley is the contractor for the animal program. Data Management Services (DMS) provides computer and library services. Dr. DeVita pointed out that this Government-owned, Contractor-operated (GOCO) contract is the largest contract in the Department of Health and Human Services. It is run parallel to NCI's intramural program except that NCI and its advisors provide the scientific stimulus for the contract. Dr. DeVita noted the many accomplishments of the program, including the work on the molecular biology of oncogenes, the new supercomputer, the crystallography program, and much of the AIDS work. A group at Frederick recently cloned one of the genes for reverse transcriptase and is producing large quantities of the enzyme, which should be useful in developing AIDS treatments. The Cancer and AIDS Drug Development Programs are also at Frederick.

Dr. DeVita acknowledged the efforts of Dr. Peter Fischinger, Mr. Phil Amoruso, and Mr. Ron Defelice for their skilled handling of the recompetition process.

IL-2/LAK Cell Program

Dr. DeVita called attention to the handout summarizing results of both intramural and extramural trials of IL-2/LAK treatment. He stated that nearly 400 patients have been treated. The first phase of the program was treatment of 218 patients by Dr. Rosenberg. The second phase was a national study in which the study was transferred from the intramural program to six centers to try to confirm Dr. Rosenberg's work. Another national study in phase three used a modified approach of a continuous infusion rather than a bolus administration to reduce toxicity. The fourth phase is a new trial, coupled with a Group C designation trial, to make IL-2 available at centers around the country.

Dr. DeVita summarized the general results: complete remissions in about 10 percent of patients with kidney cancer and melanoma in the intramural trials. When complete remission is achieved, there is rarely relapse so the problem is how to increase the complete remission rate. The first national trial confirmed that IL-2/LAK was an active therapy in renal cell cancer and melanoma, although there were some differences in response rates. In the national study modifying the approach, toxicity was decreased but so was the clinical activity. The new trial uses the intensive bolus therapy and a new schedule, and the Group C program uses Dr. Rosenberg's original protocol.

Dr. DeVita stated there is fairly good consensus that IL-2/LAK is the best single treatment available for patients with metastatic renal cell cancer. It is probably also the best therapy for widespread metastatic melanoma. In addition, Dr. DeVita said that in new studies the response rate in a small number of patients with lymphocytic lymphoma is extremely high. There have also been responses in small numbers of patients with breast cancer and colon cancer.

As to future studies involving IL-2/LAK, Dr. DeVita said that the Board of Scientific Counselors of the Division of Cancer Treatment will consider the following questions:

- Should IL-2/LAK be used as an adjuvant to surgery in patients with better prognoses than those who have been treated to date?

- Should adjuvant studies be delayed until there is more information on the use of IL-2/LAK with interferon and chemotherapy with monoclonal antibodies?

Physicians' Data Query (PDQ) System

Dr. DeVita, noting the Institute's satisfaction with PDQ, said that the American Medical Association (AMA) had contacted NCI about having PDQ on the AMA network through a gateway program to the National Library of Medicine. He thanked Dr. Calhoon for sustaining interactions with the AMA.

Dr. DeVita said that continuing medical education (CME) credits are now available for PDQ use. PDQ usage has increased and a contract has been signed to explore making PDQ available on CD-ROM which would not require telephone link-ups. A system that operates out of the Netherlands has put PDQ online, and negotiations are in progress with other major data base distributors.

Review of P01 Grants

Dr. DeVita recalled that a committee, headed by Dr. Paul Rambaut, had assessed the process for review of P01 grants and recommended, among other changes, that a single special review committee for each competing application be used. Although NIH had been informed of this assessment, when NCI was about to announce the plan, as approved by the NCAB, NIH expressed concern that this procedure might be construed as deviation from the peer review process as described by the NIH reauthorization. Dr. Wyngaarden has agreed to review the issue.

Clinical Center

Dr. DeVita praised Dr. Wyngaarden's efforts to make more beds at the Clinical Center available to NCI. It is expected that the 12 East Ward can be fully operational and fully occupied by NCI by December 1987. Dr. DeVita acknowledged the efforts of Ms. Kathy Thaney, Head of Cancer Nursing, in building morale and reshaping the nursing program. Another issue involving the Clinical

Center is consideration of bed reconfiguration or closing beds. Dr. DeVita stated that the Clinical Center beds are precious clinical resources to researchers and any reconfiguration of beds would impact on NCI.

AIDS

Because of the immediacy of the AIDS problem, Dr. DeVita said that the scientific portion of the November NCAB program review would be dedicated to AIDS. The first day of the meeting will be the usual program review by Division Directors and the second day will be the review of NCI's AIDS program.

Dr. DeVita said contract negotiations had been completed on three AIDS drugs, dideoxycytidine, dideoxyadenosine, and dideoxyinosine, all compounds related to AZT. Dr. Samuel Broder has patients who have received AZT for as long as two years with encouraging results. Dr. DeVita said in a new study by the Pediatrics Branch, 20 patients with AIDS (70 percent with neurologic deficits), who were treated with AZT, had all improved.

Dr. DeVita said the AIDS drug screening program would soon reach its full capacity of screening 8,000 compounds per year. About six or eight new compounds have already been identified for possible development for clinical use.

Nutrition Laboratory

Dr. DeVita announced that a search committee had been established to select a chief for the intramural Nutrition Laboratory, which will support Dr. Greenwald's nutrition program in prevention. The NCI Executive Committee approved a 10-year plan for the laboratory, which will be housed at Frederick.

Cancer Centers

The review of the Cancer Centers Program has been initiated by the NCAB Cancer Centers Subcommittee in response to a request from a center that it be considered for designation as a comprehensive cancer center. Dr. DeVita said the review will include a redefinition of centers and delineation of the responsibilities of NCI and the Centers in developing national initiatives.

Extramural Surgery Program

Dr. Joseph L. Skibba, from the Medical College of Wisconsin, will be responsible for the extramural surgery program.

Budget Update

In beginning his budget update, Dr. DeVita stated that NCI was still operating under the consolidated apportionment concept, whereby adjustments amongst budget categories require approval from NIH or OMB. Dr. Wyngaarden had written a letter requesting that OMB return to the old system of apportioning funds directly to the Institutes, but a response has not been received yet.

In FY 1987, funds available to the Institute total $1.402 billion, including AIDS ($1.341 billion without AIDS). Dr. DeVita said that in FY 1987, NCI had requested permission to fund additional competing grants and had been approved to award 8 more for a total of 1,061. The full House and the Senate subcommittee have marked up the FY 1988 budget. The Senate level is about $15 million less than the House proposal which is $1.448 billion plus $93 million for AIDS (proposed to be provided to the Office of the Secretary). The House increase to NCI is about $107 million for cancer research and $32 million for AIDS research. Two-thirds of the increase is to support research projects and smaller increases are to the cancer centers, cooperative groups, contracts, intramural research, and cancer prevention and control. No funds are allocated for construction. The increase in AIDS research is about 52 percent. Dr. DeVita said that because of space and resource constraints on intramural programs, the addition of AIDS money diminishes intramural cancer research to some degree. There may need to be consideration of contracting out some intramural research to outside laboratories. With proposed levels of funding, negotiations of about 8 percent will be required for competing research project grants in FY 1988. In response to a question, Dr. DeVita said NCI's priority scores are similar to those of other Institutes, although some Institutes use percentile funding. He said there is a recommendation that all of NIH go to percentile funding.

Because of the heavy emphasis on the allocation of monies on the basis of numbers of grants, Dr. DeVita said NCI receives less of a percent increase than other Institutes. The NCI has many special initiatives--such as cooperative groups and cancer prevention and control--that are not supported through research project grants. Although NCI's 1989 by-pass budget will exceed $2 billion, approximately 90 percent of the budget is a continuing commitment. Dr. DeVita said NCI is faced with a continuing dilemma of how to allocate the limited uncommitted resources to various programs. He suggested that a 21.9 percent increase for NIAID and 9.3 percent increase for NCI represents underfunding of the Cancer Program, particularly in view of the cancer-related resources that are being applied on behalf of AIDS that are not being reimbursed.

Dr. DeVita said the 1989 by-pass budget had gone to OMB and differed from the budget discussed at the May NCAB meeting only in that some funds had been added to expand clinical trials of biologics and to modernize and upgrade the facilities at the Frederick Cancer Research Facility. The total 1989 by-pass budget is $2.080 billion. The President's 1989 budget will not be made public until January 1988 when the budget is submitted to Congress.

Discussion

The following points were raised in discussion:

- When the dose of IL-2 was decreased in the second phase of IL-2/LAK studies, therapeutic effectiveness was diminished (there were no complete remissions).

- Weight gain occurs with IL-2 treatment because of capillary leakage. There is some evidence this phenomenon is related to the therapeutic effect.

- The genetically controlled autocrine motility factor is being studied as a potential means of preventing metastases.

- Through Congressional action, the Department of Energy has allocated the first $3 million of an $18.2 million challenge grant to start a cancer center affiliated with the Medical and Dental School of New Jersey.

- The use of IL-2/LAK and other biologics as adjuvant therapy may be especially effective because of the limited number of cancer cells. However, the treatment's toxicity must be considered when it is not known whether the patient's tumor will recur.

New Items

Surveillance for the Year 2000 Goals

Dr. DeVita announced that a system for surveillance for the Year 2000 goals has been established. Dr. Edward Sondik will report on this system at the November NCAB meeting. Some initial data indicate that progress toward the smoking cessation goals has been greater than anticipated.

Organ Systems Program

Dr. DeVita stated that in February 1988 the Board must decide how to proceed with the Organ Systems Program. The following suggestions were presented to the Organ Systems Subcommittee:

1) The Program should assume as part of its mandate some concern for the cancer control objectives as these might be related to the various organ systems.

2) The Organ Systems portfolio should be diversified to the Program Directors in the Divisions responsible for those areas of science.

3) Organ Systems workshops and meetings should be held in Bethesda to facilitate staff coordination.

4) Criteria should be developed for discontinuing Organ Systems working groups as well as for establishing them.

5) The Organ Systems headquarters function should be internalized within NCI, but with external advisory bodies maintained. This would save about $1 million a year.

Dr. DeVita said NCI would prefer to run the program in-house, but would abide by the Board's advice. There was some discussion from Board members of whether the savings would be as great as $1 million a year since the expenses of the working groups would still have to be paid.

Clinical Trials Program

Dr. DeVita said that NCI had undertaken an initiative to expand the

Clinical Trials Program by doubling the number of patients who go on clinical trials by 1992 and doubling the number of patients who go on colorectal trials within the next two years. Clinical trials are effective in decreasing mortality from specific cancers. For example, in pediatric malignancies, most children with cancer have been enrolled in trials and mortality in this age group has fallen precipitously. Dr. Wittes will be working with investigators in the extramural program to develop ways of encouraging patients to participate in clinical trials. Dr. DeVita said his future reports to the NCAB will include information on accrual of patients to important national protocols. The President's Cancer Panel will meet in Pittsburgh to highlight the fact of a positive colon study as a means of encouraging patient participation. Dr. DeVita said the issue was one of interfacing with practicing physicians.

Government Accounting Office Studies

Dr. DeVita said that two requests had come from Congress for Government Accounting Office (GAO) studies. The request from Representative Henry Waxman relates to clinical trials and survival and mortality--specifically, the time it takes for therapy to get into medical practice. NCI's position is that the study should be done by looking at the identified new therapies and tracking their use rather than looking at old data. The request from Representative Ted Weiss is to review the mechanism by which IL-2/LAK therapy was moved to the Group C designation.

Prevention

Dr. DeVita called Board members' attention to an excerpt from the September 9, 1987, Congressional Record, entitled "Are We Losing the War Against Cancer" by Dr. Samuel Epstein. Dr. Epstein proposes a complete reshaping of the National Cancer Program.

To respond to Dr. Epstein, Dr. DeVita reviewed the recent history of cancer research. During the 1970s, the research emphasis was on initiation and promotion, the two-stage process of carcinogenesis. The most important influence was thought to be chemicals in the environment, with about 20 to 30 percent of cancers estimated to be caused by chemicals, particularly in the workplace. NCI was encouraged to identify initiators with the thought that they would be removed from the environment. Therefore the Bioassay Program was expanded in an attempt to screen chemicals as they came into the environment. Dr. DeVita said the problem was that only about 100 to 200 chemicals could be screened per year, yet 150,000 new chemicals were entering the environment. The study of viruses was also de-emphasized. Pass-through funds were routed through NCI to the National Institute for Occupational Safety and Health and the Occupational Safety and Health Administration. In 1978, the Cancer Act was amended to require that the NCAB include five members interested in environmental carcinogenesis.

During this time, there was no research on nutrition, no smoking prevention program, no chemoprevention program or trials, and no effector arm for cancer prevention. The Cancer Control Program was all treatment demonstration projects. The pass-through monies were not subject to NCI's normal peer review process.

Dr. DeVita said that in 1980 NCI made a conscious effort to reexamine prevention activities to emphasize approaches to interfere with promotion rather than prevent initiation which would be almost impossible. The conclusion was reached that the emphasis on chemicals had been too great and that the incidence of cancer related to chemical exposure was probably in the range of 5 percent. Smoking and diet were identified as the most important influences on cancer. NCI changed its focus to cancer prevention and support of basic research on cancer etiology. Dr. DeVita said that in support of this change NCI transferred the Bioassay Program to the National Toxicology Program of the National Institute of Environmental Health Sciences, moved into the area of smoking prevention, re-emphasized the work on viruses, placed the pass-through programs under the Division of Cancer Etiology's Board of Scientific Counselors, established a prevention-oriented division (the Division of Cancer Prevention and Control), established a nutrition research program, established a chemoprevention program, and reshaped the Cancer Control Program to emphasize research on prevention and control. In addition, the interpretation of environmental carcinogenesis was broadened to include viruses as environmental causes of cancer.

Dr. DeVita noted that these changes also brought various problems. The Cancer Control Program is not well understood and its budget suffers accordingly. Several of the prevention initiatives are controversial, and establishing applications in prevention continues to be difficult. The change in policy required eliminating treatment programs to build prevention programs, and although basic research, epidemiology, and clinical trials were increased, money had to be transferred out of the control budget, which NCI is now attempting to rebuild. Dr. DeVita emphasized that NCI does not intend to ignore occupational carcinogenesis. However, he suggested that the issue of whether occupational carcinogenesis is the major problem in the United States needs to be resolved publicly.

Dr. Korn noted that the Environmental Carcinogenesis Subcommittee of the NCAB had been reconstituted. Points raised in discussion included the following:

- Researchers in NCI's virus program recognized early the possible relationship of retroviruses to AIDS.

- Other Agencies, including the Environmental Protection Agency, the Consumer Product Safety Commission, the National Institute for Occupational Safety and Health, the National Institute of Environmental Health Sciences, and the Occupational Safety and Health Administration of the Department of Labor, have undertaken initiatives in environmental carcinogenesis.

- The National Toxicology Program (NTP) now studies multiple toxicological endpoints for each chemical, not only cancer. NCI continues to support the program through its system for nominating chemicals and its participation on the NTP Executive Committee and other committees.

- While the issue of using special review committees exclusively for POl reviews has yet to be resolved, other POl-related recommendations are in effect.

Due to time constraints, Dr. Knipmeyer was unable to present her legislative update. Board members were referred to the written report.

VI. NCAB Public Participation Hearings--Mrs. Nancy G. Brinker and Mrs. Helene G. Brown

Mrs. Brinker and Mrs. Brown reported the results of the first Public Participation Hearing, held in Los Angeles on September 22, 1987, which focused on cancer prevention and detection. Mrs. Brinker thanked Mr. Paul Van Nevel and his staff for coordinating the organization of the Hearing and Mrs. Brown for acting as chairwoman.

Mrs. Brinker outlined progress made at the Los Angeles Hearing toward the goal to increase awareness in the community about the National Cancer Program. She noted that more than 40 witnesses had provided testimony which spanned interests of major cancer centers, health professions, and various cultural groups. The Hearing received very wide media coverage, for example, from Cable News Network, Associated Press, and the Los Angeles Times. Mrs. Brown and Dr. DeVita had participated in an editorial board meeting of the Los Angeles Times. A business luncheon, including representatives from organizations such as ARCO, Union Bank, and Security Pacific Corporation, held before the Hearing, produced several constructive ideas for potential cooperative follow-up programs. Mrs. Brinker noted her appreciation for the Cancer Prevention Awareness Proclamation given by Los Angeles Mayor Tom Bradley and testimony given by Dr. Armand Hammer and Mr. Larry Hagman.

Mrs. Brinker also reported that the Hearing had promoted progress toward creating increased public involvement in and commitment to programs related to the Year 2000 goals. In addition, enough testimony had been gathered to compile a report of the Hearing, which will be included as part of the biennial report to the President and to Congress. Part of the Hearing report will also be disseminated to local and state organizations such as health departments, public health care institutions, and state legislators. Related NCAB recommendations will be developed for distribution to Federal agencies with responsibilities in health care and screening.

Mrs. Brinker announced that the next Public Participation Hearing will be held November 5 in Atlanta, Georgia, and will focus again on prevention and detection. Dr. Louis Sullivan will serve as chairman for the Hearing.

An eight-minute videotape, produced by Hill and Knowlton and Technical Resources, Inc., to summarize the Los Angeles Hearing was then shown to the Board.

Mrs. Brown emphasized the importance of encouraging participation of a wide range of community groups in the Hearings and of follow-up programs.

She noted that several groups had expressed interest in continued cooperative programs. For example, the local PTA had offered to coordinate a television monitoring project on the prevalence of smoking on television programs. At the business luncheon prior to the Hearing, the Union Bank Foundation expressed interest in a project to change the menus in the Los Angeles city school system to offer more nutritionally balanced meals.

Mrs. Brown and Mrs. Brinker concurred that follow-up projects, including distribution of the Hearing report, are vital components of the NCAB Public Participation Hearings project. Mrs. Brinker urged Board members to endorse the concept of planning for at least two further hearings after the Atlanta Hearing, as the preparation for each Hearing is very labor- and time-intensive.

A motion, passed by acclamation, was made to thank Mrs. Brinker and Mrs. Brown for their efforts in organizing the Los Angeles Public Participation Hearing.

In discussion following the presentation, Mrs. Brown clarified that although a representative of the California Medical Association had not testified at the Los Angeles Hearing, both the Los Angeles County Medical Society and the California Medical Association had played major roles in planning and hosting the Hearing. Dr. Braren congratulated Mrs. Brown on the inclusion of testimony from groups of Blacks and Hispanics in the Los Angeles Hearing.

In response to a question, Mrs. Brown emphasized that the testimony from the Hearing would be distributed to people and organizations involved in health planning, especially the local Los Angeles legislators. A discussion ensued as to the most effective forum for presentation of the Los Angeles Hearing report and videotape to Congress, and several Board Members suggested that Dr. Knipmeyer communicate this information to members of Congress, perhaps at the October 28, 1987, Congressional breakfast. On the question of monitoring follow-up projects, it was suggested that this be the responsibility of the Board member located in the city in which the Hearing is held.

The Board unanimously approved a motion to endorse the concept of planning for a January 1988 Hearing in Philadelphia and a March 1988 Hearing in Dallas.

VII. An Initiative to Involve the Nation's Black Leadership in NCI Programs --Dr. Louis W. Sullivan

Dr. Sullivan reported on the planning activities of the National Black Leadership Initiative on Cancer organized at the suggestion of Dr. DeVita and Board members to obtain more participation from the Black business community to mobilize the Black community for the Year 2000 effort. He noted that several planning meetings had been held with Dr. Claudia Baquet, Chief of NCI's Special Populations Studies Branch, and with staff of Technical Resources, Inc. (TRI), the support services contractor, and that an ad hoc group of three advisors from the Atlanta Black business community had been formed. At the first meeting of Drs. Sullivan and Baquet with the ad hoc advisory group

on March 25, 1987, it was noted that none of the executives was aware of the higher incidence of and poorer survival from cancer in Blacks. All agreed to support programs to involve the nation's Black leadership to decrease the incidence of cancer in the Black population. It was also noted that leadership in the Black community is not concentrated in the business community but includes clergy, educators, and civil rights leaders who should also be involved in this effort to reach the Black population. Dr. Dorcas Bowles, Dean of the School of Social Work at Atlanta University and an expert in Black community structure, was invited to join the ad hoc advisory group to advise on successful methods of reaching all segments of the diverse Black population.

As a result of several further logistics planning meetings, the plan for the National Black Leadership Initiative on Cancer was developed to include a series of regional meetings in six cities with major Black populations (Atlanta, November 20, 1987; Los Angeles, February 1988; Chicago, April 1988; New York, June 1988; Houston, fall 1988; Washington, D.C., 1988). Approximately 100 attendees, representing leadership from Black business, health/medical, political, and entertainment communities will participate at each meeting. Recommendations and proposed follow-up activities generated from each meeting will be submitted to appropriate local, state, and national agencies.

Dr. Sullivan explained that small local committees would organize each meeting and that the chairperson of each regional committee would serve on a National Steering Committee chaired by Dr. Sullivan. Commitments have been received from individuals to chair all of the regional meetings except the Mid-Atlantic/Washington, D.C., and the Southwestern/Houston, Texas, efforts. Written reports of each meeting will be integrated by the Steering Committee to develop final conclusions and recommendations.

In addition to NCI support of this effort, financial support will be sought from the private sector. Dr. Sullivan noted that the Association of Minority Health Professional Schools has agreed to co-sponsor the initiative.

Dr. Sullivan also described a tentative agenda for the meetings, which will include presentations by Dr. Sullivan on the general purpose of the program, by Dr. DeVita on the NCI and Year 2000 goals, and by Dr. Baquet on the cancer problem in Black populations. These presentations will be followed by afternoon working group sessions chaired by local committee members to discuss the issues and foster active involvement by the participants in cancer prevention and control activities. An evening performance by a well-known entertainer will complete the program as a further incentive for attendance.

Noting concern that Black organizations continue to receive significant financial resources from tobacco and alcohol companies for their conventions and other activities, Dr. Sullivan stressed that efforts to reach the Black community should emphasize education on the dangers of smoking and drinking and other health behaviors rather than be an attack on tobacco companies. He also urged that assistance be given the Black community in obtaining alternative sources of funding for their activities, as proposed by Dr. Reed Tuckson, Commissioner of Health for the District of Columbia, at a roundtable discussion on smoking and cancer at the September 24, 1987, Congressional Black Caucus Legislative Weekend.

In discussion following Dr. Sullivan's presentation, the following points arose:

- The National Black Leadership Initiative on Cancer should be coordinated with AIDS educational efforts in the Black community by using the same format for organization of the community while keeping the two messages separate.

- The importance of including rural Black leadership in the initiative was raised and should be considered when inviting meeting participants from the regions served by the host cities.

- Inclusion of athletic personalities in the initiative may be helpful in reaching the young Black population, particularly on the issue of smoking.

A written report on the National Black Leadership Initiative on Cancer, including a regional breakdown by state for each meeting and a tentative agenda for the November 20, 1987, meeting in Atlanta, was distributed to the Board.

VIII. Women's Health Trial: Introduction--Dr. Peter Greenwald

As background, Dr. Greenwald stated that in 1984 the Division of Cancer Prevention and Control (DCPC) had invited cooperative agreement grant applications for a multi-institutional trial of a low fat diet (20 percent of calories from fat) to test whether it would reduce the incidence of breast cancer in high risk women. He noted that both the DCPC Board of Scientific Counselors and the NCAB had considered the rationale strong enough to develop this research project. Dr. Greenwald said an outstanding group of investigators had been gathered and much work has been done on the feasibility of the trial.

Dr. Greenwald noted that since the initiation of the trial, several new epidemiologic studies had been published and some new ideas in carcinogenesis research had come forward. He said that the investigators involved in the Women's Health Trial have carefully considered this new information, and he emphasized that NCI is very satisfied with the work of the investigators.

Dr. Greenwald said the presentation to the NCAB was to provide an update on the trial and to ask for advice on whether the trial should proceed to full scale or be stopped. He said the DCPC Board had considered the issue with mixed feelings. Dr. Greenwald then introduced the first speaker, Dr. Paul Engstrom, who chairs the DCPC Board of Scientific Counselors (BSC) and the Policy Advisory Committee(PAC), a subcommittee of the Board that has been overseeing the trial. He indicated that the other speakers would be Dr. Maureen Henderson, a leader of the project who heads the Seattle clinical research unit that is entering women into the trial, and Dr. Ross Prentice, who heads the trial's statistical unit and has done much work on the design of the trial.

DCPC Board of Scientific Counselors' Report--Dr. Paul Engstrom

Dr. Engstrom said that the Policy Advisory Committee had worked closely with the trial investigators to work out problems. During the past two years, the PAC recommended workshops on diet and markers and supported the establishment of a blue ribbon panel of epidemiologists to review the evidence that is the basis for the Women's Health Trial. In addition, site visits were made to each of the investigators' programs to ascertain how each related to the trial. Dr. Engstrom said the PAC also recommended appointment of a steering committee that would enhance the efficiency and administration of the trial. This steering committee includes investigators, as well as DCPC staff. Dr. Engstrom said a revised protocol was submitted to the PAC in June 1987 and consideration of that protocol led to the PAC's recommendations which were provided to the NCAB.

Dr. Engstrom next described the revised protocol. He stated that the premise of the Women's Health Trial, based on epidemiologic and animal studies, is that dietary fat is implicated in the promotion phase of female breast cancer. The study's hypothesis is that a change in diet from the usual diet in the United States, which is made up of 40 percent of calories from fat, to a diet made up of 20 percent of calories from fat would decrease the relative risk of breast cancer by about 50 percent after 10 years. Dr. Engstrom said this translates into a 17 percent reduction in breast cancer incidence for the intervention versus the control group of women.

An early phase, the Vanguard, tested some aspects of the trial, such as whether the diet was tolerable and whether women could adhere to the diet. Within a few months of entering the trial, women were able to achieve the low-fat intervention diet and stayed on the diet for at least the 12-month follow-up period. Dr. Engstrom pointed out the trial was really a feasibility or efficacy trial in that if there was found to be a relationship between fat and breast cancer incidence, the next step would be a community-wide trial.

Dr. Engstrom said the PAC had presented its recommendations to the DCPC BSC at the September 1987 meeting. The PAC recommended that the full-scale Women's Health Trial, as described in the June 22, 1987, protocol, not be approved or funded. Dr. Engstrom summarized the reasons for the recommendations as follows:

- The trial's assumptions about the rate and extent of reduction in breast cancer relative risk are questionable.
- There are no objective measures of dietary compliance.
- There is insufficient information on possible mechanisms for the effect of fat on breast cancer etiology.
- The trial's assumptions about recruitment and maintenance of the intervention are questionable.

- The potential for increased use of estrogens and progestins in post-menopausal women, the availability of cholesterol-lowering agents and other drugs, and new dietary recommendations might be confounding factors that would make it difficult to identify dietary effects.

Dr. Engstrom said that when these reasons were considered with the estimated direct cost, about $90 million over 10 years, the PAC felt that additional preliminary studies should precede full implementation of the trial. The PAC recommended that the current investigators continue to follow the 12,000 women now in the trial to learn more about the long-term effects of the diet. The PAC also recommended that a committee be established by the Director of DCPC and the Chairman of the DCPC BSC to develop a research agenda for breast cancer prevention.

Dr. Engstrom noted that the BSC defeated a motion to accept the PAC recommendations by a vote of 6-5-1. The BSC also defeated a motion to fully implement the Women's Health Trial by a vote of 7-4. The BSC approved a motion that a small group of the BSC review the various issues with the study's investigators to try to work out a compromise to permit continued research in breast cancer prevention.

Issues raised in discussion included the following:

- Women in the intervention group lost weight, raising questions about the role of caloric intake.

- Since the trial had been initiated, information had not become available to clarify some of the original uncertainties and assumptions of the Women's Health Trial.

- The PAC was established after the initiation of the trial when it became apparent that the original concept of 6,000 women in a 5-year study and an unspecified diet was not appropriate.

Intervention and Feasibility Study--Dr. Maureen Henderson

Dr. Henderson said that the critical question of the trial is whether a dietary intervention, not a drug intervention, to reduce and maintain fat intake at about the level of 20 percent of daily calories, will reduce the incidence of breast cancer. In addition, by creating a group of women with an average fat intake of 20 percent of daily calories, the trial would create a group that does not exist naturally in the United States. Dr. Henderson pointed out that the trial is randomized so that unexpected background changes in the population will happen in the same way to both the control and intervention groups. She also stated that the projected costs are based on the actual costs of the recruitment, screening, and intervention that have already been done. Dr. Henderson said that it was intended from the beginning that information on mechanisms of dietary effects would come from separately funded ancillary studies.

Dr. Henderson described the intervention as based on principles of changing and maintaining changes in food use behavior. It is not based on a prescribed diet. Each participant has about 6 to 8 hours of homework in addition to a 2-hour class in each of the first 6 weeks of the trial. Participants learn how to budget and monitor their daily and weekly consumption of grams of fat. Dr. Henderson said that while women have flexibility in developing their individual food plans, the intervention strategy and materials are rigorously standardized, as is the training protocol for the nutritionists who deliver the intervention. Therefore, Dr. Henderson said, the intervention would be exactly the same in every new clinical unit.

Because the trial is an efficacy trial, Dr. Henderson said that a purposeful effort was made to select women expected to be compliant. However, Dr. Henderson said a community-wide trial with this intervention was not intended because the intervention was designed specifically for the group of women now in the trial. To extend the trial would require developing suitable instructional material for other groups of women. Dr. Henderson said that if there is a biological effect, it would not have to be tested in different groups of women.

Dr. Henderson next explained the initial decision to cut total fat intake. She said it is the easiest dietary change to make, and total fat consumption has the strongest statistical correlation with breast cancer incidence in international data. In addition, animal studies suggest that different types of fat have different effects on mammary tumor development. Dr. Henderson said it was thought that the most conservative approach would be not to change the relative proportions of different types of fat in the intervention and control groups.

Dr. Henderson stated that it was agreed from the beginning not to manipulate weight. The dietary instructions encourage the women to substitute foods as they change the composition of their diet and to maintain their calorie intake at the level at which they started. She stated that it was also agreed that even though participants weigh and measure everything they eat, write down every recipe, and the ingredients of every packaged food in completing a 4-day food record, this record cannot be used to compare the dietary intakes of individual women. These records can be used to compare average fat intakes of the control and intervention groups of women.

Dr. Henderson then turned to discussion of the feasibility trial in which 100 women were recruited from each of three clinics. These women were recruited from those at highest risk--those with two or more relatives with breast cancer. With the approval of NCI, the clinical unit in Seattle investigated the effort and costs required to recruit women with different levels of breast cancer risk. Dr. Henderson said that after 2 years of measuring recruitment rates and costs in three different risk factor subsets of women aged 45 to 69 years, the 46 percent with 1.4 times the national average risk had proved to be the most logistically practical and cost-efficient group to recruit from. The women in this group have either a first-degree relative with breast cancer or are nulliparous or had a first child at age 25 or older or have had two benign breast biopsies. The women also must pass a

dietary screening test to ascertain whether their fat intake is above the median. In response to a question, Dr. Henderson said that in Seattle 5 percent of the women who are eligible on the basis of age and risk factor are randomized. She pointed out that the women are informed that this is a randomized trial requiring a 10-year commitment. Dr. Henderson emphasized that the Women's Health Trial is one of efficacy, not generalizability, of the intervention.

Using slides, Dr. Henderson showed that once the most efficient group to recruit from was identified, recruiting was at a higher rate than required. She noted the community collaboration in assisting with recruiting. Dr. Henderson suggested that to stop recruitment at the three centers would damage the credibility of both the centers and NCI and potentially damage the initiation of future trials.

In describing the intervention, Dr. Henderson said the women in the feasibility trial have been responsive; only 3 of the first 242 women asked to come in for their 24-month follow-up visit did not come in. Intervention women in the full-scale trial are also keeping their appointments for 12-month visits. Dr. Henderson pointed out that in the feasibility trial, the control group stayed at a level of about 40 percent of calories from fat and the intervention group reached and maintained an average of 20 percent of calories from fat. These differences were maintained at 24 months. The average decrease in calories was about 400 calories in the intervention group and 110 in the control group.

In response to a question about evaluating cholesterol levels in the control group, Dr. Henderson pointed out that this is a prevention trial of healthy women. Each woman must have her own source of medical care, as none is provided by the trial. The trial provides mammography, teaches breast self-examination, and monitors for any possible side effects of the dietary intervention. Dr. Henderson said that individuals with very high levels of cholesterol are not accepted into the trial. In addition, the trial does not identify cholesterol levels with individual women. A woman who wants to know her cholesterol level is advised to ask her personal physician. In conclusion, Dr. Henderson stated that the Women's Health Trial was needed to help resolve the controversy about the role of dietary fat in breast cancer. Responding to a question about the PAC, Dr. Henderson said she had expressed concerns about the changing composition of the group, their uncertainty about whether their role was to advise or review, and their heavy focus on the cost of the trial.

Design--Dr. Ross Prentice

Dr. Prentice described additional results of the feasibility trial since the last presentation to the Board in 1985. He pointed out that each of the clinics has enrolled between 500 and 600 women, although the original expectation was only 200 women. Dr. Prentice noted that the trial has been reviewed by several groups including a group of outside experts on statistics and epidemiology. These groups had not suggested a change in the basic design assumptions, which remained unchanged since January 1986. Dr. Prentice said that the PAC's recommendation in September 1987 to increase the sample size was the first time a design change had been requested.

Dr. Prentice then presented the following suggested changes based on the results of the feasibility study to date:

- 20 rather than 30 clinics to recruit the necessary number of women
- 32,000, rather than 30,000, women enrolled in the trial
- Direct cost estimate of $91.6 million, rather than $100 million.

Dr. Prentice reviewed the design assumptions on which the 17 percent reduction in breast cancer is based. The relative risk assumption is that a woman's breast cancer incidence will drop from an initial relative risk of 1 down to .5 at the end of 10 years of intervention. The hypothesis to be tested and the design assumption that gives rise to the sample size is that the dietary intervention, when administered for a certain period of time, will bring about a reduction in breast cancer incidence. Dr. Prentice said the ability to test the hypothesis is not absolutely dependent on linearity, but one reason for the linearity assumption is that in plotting age-adjusted breast cancer incidence in 22 countries versus percent of calories from fat, the result is an approximate straight line. Dr. Prentice said the assumed reduction in breast cancer incidence by a factor of 2 is conservative, compared to the international correlation data which assume a reduction by a factor of 4. When fat calories are compared to non-fat calories, only total fat calories show strong relationships with breast cancer incidence and mortality. Dr. Prentice said it is necessary to rely on population comparisons because in analytic epidemiologic studies in the United States, there is little variation in the percent of calories from fat. In addition, the kind of dietary assessment instruments that are practical to apply in large-scale studies have severe measurement errors. Dr. Prentice noted that migrant data are useful with respect to the length of time it might take to see a dietary effect. Women who go from a country with low fat intake to one with a high fat intake adopt the breast cancer incidence rates in the new country as a function of years from migration.

Dr. Prentice next discussed the trial's compliance assumptions: a 4 percent drift downward in percent calories from fat in the control group and a 6 percent upward drift in the intervention group would result in about 30 percent of the dietary change lost, on the average, by the end of 10 years. He reiterated that in the feasibility study compliance is a little better than anticipated in the intervention group and a little worse in the control group. In concluding the discussion of the trial's assumptions, Dr. Prentice said in Seattle a survey of health maintenance organizations (HMOs) was used to estimate the distribution of risk factors thought to correspond to the eligibility criteria. A competing risk assumption was based on national data. Other assumptions were made about the rate at which clinics will be able to recruit. Using epidemiologic data from large case control and cohort studies, estimates were made of breast cancer incidence at standard levels of dietary fat intake. Dr. Prentice said that by combining these assumptions, estimates of breast cancer incidence are 3.33 percent in the control group and 2.81 percent in the intervention group over the course of the trial for the expected 17 percent reduction in incidence. Using the standard sample size formula, 32,000 women would be allocated to the intervention and control groups in a 2 to 3 ratio.

Dr. Prentice emphasized in conclusion that the trial's cost projections are based on detailed experience and are not guesses. He said the investigators had developed a streamlined protocol with the expectation that important ancillary studies would be funded separately. In addition, Dr. Prentice said that the entirely new statistical design for processing the raw materials of the trial would save about $30 million.

In clarification of several points, Dr. Prentice said that the randomized trial enables comparison of the breast cancer incidence in the intervention group versus the control group. Additional analyses would be done to try to understand as fully as possible any differences in breast cancer incidence between the two groups. These analyses would be based on biennial food records, blood samples, and other information. Dr. Prentice said the investigators expect to be able to separate the effect of fat from other possible dietary factors.

Dr. Prentice next addressed two concerns expressed by the PAC. With respect to the concern about sample size, Dr. Prentice said that the original RFA instructed respondents to assume 6,000 total subjects. He said the only disadvantage of increasing the sample size is cost, but with a larger sample, it is possible to detect smaller impacts of dietary fat on the incidence of breast cancer. With respect to the concern about overestimation of the baseline incidence rate, Dr. Prentice said the estimate was based on raw data from a large case control study, national SEER data, and the Breast Cancer Detection Follow-Up Program, and risk factor distribution data from the HMO survey in Seattle. He said the power of the study is rather insensitive to a 10 or 20 percent change in the baseline incidence rate.

Dr. Prentice said the concern about the subjects being volunteers and possibly having less disease than other populations probably is not a factor in cancer studies. He cited as an example that cohorts using oral contraceptives have been found to have less cardiovascular disease than national age-specific data would indicate, but their cancer experience is much closer to the national data.

Dr. Prentice next discussed the USDA feeding study which he said produced the only new data from the time of the PAC's favorable report in July 1987 and the unfavorable report in September. Although the WHT Vanguard study does not include baseline standardized serum cholesterol measurements, comparison data on control and intervention groups are available at one year of the feasibility study. These showed an average 11.9 mg/deciliter reduction in serum cholesterol in the intervention versus the control group.
Dr. Prentice said the USDA study involved two groups of women who followed a diet intended to resemble the Vanguard protocol diet. The 25 women in the first phase experienced an average 24.3 mg/deciliter reduction in serum cholesterol. Another group of 22 women on the same Vanguard diet experienced a 9.7 mg/deciliter reduction, slightly less than the WHT Vanguard group.
Dr. Prentice said in another intervention trial in Toronto involving somewhat younger women, the average decrease in serum cholesterol was 5 mg/deciliter in one year. That study included duplicate meal preparations in conjunction with the 4-day food record, and the percentage of calories from fat was in

close agreement between the duplicate meals and the 4-day food record. In another Toronto study, premenopausal women consumed controlled diets containing 40 percent of calories from fat for 4 months and then 20 percent of calories from fat for 4 months, and their serum cholesterol decreased by 11.6 mg/deciliter. Dr. Prentice noted that formulas for predicting serum cholesterol reduction give reductions of 13 mg (Keyes), 20 mg (Hegsted), and 17 mg (Jacobs). He suggested that the USDA study should not be the basis for questioning the quality of the WHT's dietary intake data.

In referring to the PAC's concerns about extraneous confounding influences over the course of the trial, Dr. Prentice stated that such influences are likely to occur with applied research projects. He said that Dr. Brian Henderson had helped develop a plan to record intakes of estrogen, progesterone, and cholesterol-lowering drugs biennially. Data will be adjusted for evaluation of compliance and evaluation of endpoints concerning external influences.

Dr. Prentice stated that the investigators recognized that the divided opinion about the trial was based on reasons of cost and scientific uncertainty. He suggested that the cost is acceptable if compared to the cost of breast cancer treatment trials. Dr. Prentice said the reduction of scientific uncertainty would not be accomplished within the very near future, and in conclusion, he requested that the trial go forward.

Invited Comments--Dr. Brian Henderson

Dr. Henderson stated that while the scientific data are not consistent with fat as a specific nutrient as a risk factor for breast cancer, the data are consistent with weight being a risk factor. Fat, like other nutrients, has its effect as part of caloric intake and ultimately, of energy balance. Dr. Henderson said there was a plausible biological mechanism by which weight contributes to the amount of circulating estrogen and thereby to breast cancer risk. He next summarized the pathogenesis of breast cancer beginning at the onset of menarche when breast epithelial cell growth is at its maximum in response to estrogen from the ovaries. This rate of growth continues until the woman's first full-term delivery; the rate decreases and continues at about that level until age 40. The rate of growth decreases in the premenopausal period as ovulation becomes less frequent. After menopause when the circulating estrogen comes from body fat, the growth rate is only one-tenth of the initial rate. Dr. Henderson said a woman acquires a substantial amount of her breast cancer risk by the time she is 50. Therefore, primary prevention should start in adolescence or young adulthood.

Dr. Henderson reviewed studies that documented the importance of weight as a risk factor. In the postmenopausal period, there is nearly a doubling of risk with a somewhat more than 10 kilogram difference in weight. Dr. Henderson said if American women could reduce to the weight of Japanese women at age 50, there would be no increase in the rate of breast cancer. This would require the sustained loss of about 30 pounds, which over 10 years would lead to about an 8 percent reduction in risk in a randomized trial. Dr. Henderson said that knowledge of how to sustain that large a weight loss

for that long a time is not now available. He suggested as an alternative design giving low dose tamoxofen, starting at age 35, to essentially eliminate ovulation, which would reduce the risk to one-quarter that of the overall population. He said such a trial has been proposed in very high risk women.

Dr. Henderson next showed a slide summarizing animal data that indicated that in mice, tumor incidence was most reasonably related to total calorie intake rather than to dietary fat per se. When dietary fat was kept constant, but calories were increased, there was an increase in tumor incidence. When calories were kept constant and fat was increased, no real change in tumor incidence was observed.

Dr. Henderson also presented data on efforts to alter the risk of breast cancer by impact in adolescence. He said studies have shown that the more energy expenditure by teenage girls, the less ovulation. Dr. Henderson suggested that if ovulation could be decreased by half during the 10 years before a woman's first full-term pregnancy, the lifetime risk of breast cancer would be reduced by half.

In response to a question, Dr. Henderson said he did not support the full-scale implementation of the Women's Health Trial as currently designed because he felt the wrong hypothesis, i.e., fat rather than total calories as a risk factor for breast cancer, was being tested. Dr. Prentice responded that considering standard risk factors on the basis of national measures, the data show a relationship with dietary fat. He also suggested that there is no conflict between fat being important and hormones being even a principal determinant of breast cancer. However, Dr. Prentice added that if hormones play a principal role, it would not be expected that male breast cancer rates in the U.S. are about five times the rate for Japanese males, just as the rates for U.S. females are five times higher than for Japanese females.

Comments--Dr. Marc Lippman

Dr. Lippman stated that although hypothetical bases for the role of dietary fat in breast cancer etiology can be put forward, there are several other factors that also require consideration. He said that dietary intervention to alter breast cancer risk seems plausible, but he questioned the assumptions of the WHT that the control and the treated populations will maintain an essentially stable dietary fat intake over a 10-year period. If these assumptions are not correct, Dr. Lippman said it would be unlikely that the study, as now designed, could detect any difference in breast cancer incidence. He said influences on women in the control group included pressure to reduce weight, more attention to a variety of special kinds of fat, emphasis on cholesterol lowering, trend toward exercising, etc. Dr. Lippmann also questioned whether compliance could be accurately assessed from self-reporting. He suggested that the most important factor lacking in the WHT is an objective measure of dietary compliance.

Discussion

Dr. Korn stated his opinion that because of the great complexity of

the issues associated with the WHT, the Board should not make a definitive decision about the future of the trial. He suggested that experts an the particular issues be asked to develop a proposal that would resolve the decision of whether to proceed with full-scale implementation of the trial.

Dr. Boutwell made the following motion: 1) that the Women's Health Trial be continued until the January meeting of the Board of Scientific Counselors of the Division of Cancer Prevention and Control; 2) that only the centers now operating will continue; 3) that a small group of consultants be convened to meet with Drs. M. Henderson and Prentice and develop a recommendation to present to the DCPC Board in January 1988. The motion was seconded.

The following were among the issues raised in discussion:

- No more data are likely to be forthcoming in the near future to facilitate making a decision about the WHT.
- Because breast cancer will be detected in both groups in the WHT earlier than in the general population, there might not be an effect on mortality within the time span of the study.
- If dietary fat is demonstrated to be a risk factor for breast cancer, this does not necessarily mean that women will change their diet to reduce their risk.
- The basic need is for a research agenda in breast cancer prevention.
- The trial is based on a hypothesis which requires testing; however, prevention trials, at times, appear to be held to more stringent criteria for testing than other trials.
- The trial should include objective measurements of body fat content.
- The trial may provide biological information that cannot now be foreseen.
- The trial may not be testing the right age of women.
- An objective means of monitoring compliance would enhance the trial.

Following a motion to call the question, the Board voted to approve Dr. Boutwell's motion by a vote of 15 to 5, with 1 abstention.

IX. Closed Session

The second day of the meeting was closed to the public as it was devoted to the Board's review of grant applications. The applications reviewed numbered 1,264, requesting support in the amount of $198,248,070. Of these, 1,140 were recommended for funding at a total cost of $151,559,779.

X. Report of the Subcommittee on Cancer Centers--Dr. John R. Durant

Dr. Durant presented the report of the Subcommittee on Cancer Centers, explaining that the Subcommittee has been charged with recommending new criteria for the designation of comprehensiveness and reviewing the Cancer Centers Program in general. To develop comprehensiveness criteria, the Subcommittee plans to seek assistance from a group convened by the AACI, NCI staff, and perhaps another group. In addition, a request for information and opinions will be sent to a variety of constituencies to elicit both qualitative and quantitative responses to the issues surrounding the Centers Programs. Dr. Durant referred to the initial draft of issues included in the written report and asked that the Subcommittee and other Board members individually review them and submit written suggestions for revisions so that the final list of issues can be formulated in the next few weeks. As a followup to the request for information, the Subcommittee plans to hold two workshops and submit a list of recommended criteria for Board approval at the May 1988 meeting. Dr. Durant said the issues of management and administration of the centers would be the subject of subsequent discussions, with a final report to NCAB tentatively scheduled for the fall meeting.

Referring to the list of representative constituencies to be queried, Dr. Durant noted that it would encompass a large group of people as it included all NCI grant holders as well as presidents of relevant organizations and numerous others. He added that a cover letter would be sent as a preamble to the list of issues under consideration.

Following Dr. Durant's presentation, Dr. DeVita emphasized the importance of the comprehensiveness issue and the need for a prompt resolution. With the reauthorization of the Cancer Act pending and with the Year 2000 goals in mind, there is also a need to clarify the role centers play in NCI's initiatives beyond performing basic research. Finally, Dr. DeVita said that testimonies at public meetings have revealed that people are often unaware of the existence of centers in their locality.

In the discussion, the issue was raised that failure by NCI to definitively designate comprehensive centers leaves a void often filled by self-designated centers, and other agencies are beginning to use the term for hospitals that serve several areas. The observation was made that until about 8 years ago, peer review determined whether institutions were comprehensive centers according to their operating characteristics.

Dr. DeVita noted that current criteria for comprehensiveness do not adequately describe what would be an acceptable center in today's context. It would be helpful, therefore, if work on the new criteria was approached as if NCI were developing a new cancer centers program and the ideal were considered in terms of current technological advances, technology problems, and opportunities available in basic research.

In response to a question, Dr. Durant explained that all of the approximately 3,000 grantees would receive a letter and list of issues under consideration with the aim of reaching all who wish to contribute to the

process. He added that Ms. Judith Whalen will develop a plan with possible computer assistance to compile the replies, whatever the number.

The Board unanimously accepted the report of the Subcommittee on Cancer Centers.

XI. Report of the Subcommittee on the Organ Systems Program --Dr. Bernard Fisher

Dr. Fisher referred Board members to the written report for a background review of the Organ Systems Program (OSP) and the list of issues for Board discussion. He said the Subcommittee is charged with presenting recommendations at the February 1988 NCAB meeting for the future directions of the Program, partly as a preliminary step to deciding whether to reissue the RFA for the Organ Systems Coordinating Center (OSCC), which is presently located at Roswell Park Memorial Institute.

Dr. Fisher emphasized that the Organ Systems Program has been valuable and performed well. The question now is how to improve upon it. Following a summarization of the development of an organ systems concept through the Program to a grant or contract award, Dr. Fisher listed the four issues identified for discussion as follows: 1) Should the OSCC continue as an outside activity and the cooperative agreement be recompeted for an extramural coordinating center, or should that activity be internalized in the NCI? 2) Should the organ systems grant portfolio continue to be administered separately by the Organ Systems Program or should the grants be included in the disciplinary programs of the NCI? 3) Should the working group's responsibilities be expanded to include cancer control activities in keeping with Year 2000 goals? 4) What should the criteria be for initiating new groups and phasing out existing groups?

Dr. Fisher said Subcommittee plans to facilitate Board consideration of these issues include a full report on the Program to be given at the November meeting by the chairman of the Organ Systems Coodinating Center, followed by a 1-day hearing to receive testimony from various participants in the Program. This latter group will include heads of working groups, the chairman of the OSCC, NCI staff, and investigators who have gone through the Organ Systems Program.

Issues and concerns raised in the discussion following Dr. Fisher's presentation included the following:

- The program might be weakened by internalizing the coordinating unit.
- A change in the portfolio's administration and management might be reasonable since the OSP grants represent a minority of the totals in the particular organ areas.
- If the external leadership in generating ideas is incorporated into a central source, diversity and visibility might be diminished.

- NCI already supports much cancer control activity.

In speaking to these concerns, Dr. DeVita stressed that the working groups would continue to be external and would remain intact; only relatively minor management details would be internalized. He added, however, that an opportunity would be missed in not involving the expert disease groups in the OSP for cancer control activities.

The Board unanimously accepted the report of the Subcommittee on the Organ Systems Program.

XII. Report of the Subcommittee on Planning and Budget--Dr. Louise Strong

Dr. Strong presented the Subcommittee meeting report for Board review and explained that it dealt with the charge to develop and write the NCAB portion of the Second Biennial Report of the Director. Recognizing the opportunity of preparing a strong presentation of the National Cancer Program in a document that goes to Congress, the Subcommittee chose a new format that includes a general introduction and sections on NCAB concerns and recommendations, NCAB activities, and highlights of progress made by the Program in the areas of basic research, treatment, and possibly prevention. The section on NCAB activities would focus on the Subcommittees and the chairpersons and executive secretaries would be asked to prepare summaries. Dr. Strong requested that the Board as a whole review the list of recommended topics included in the written report and submit suggestions before the November meeting to herself, Ms. Judith Whalen, or Mrs. Barbara Bynum. The Subcommittee will make final decisions on content and format at the November meeting and present a draft for Board review in February.

In the discussion, the following points were raised:

- The Board is not bound by the same constraints as NCI executives and should take this opportunity to highlight areas of concern and support.

- The report could include a statement of concern about cancer statistics and their interpretation.

- Since the estimation of progress achieved by the Cancer Program is the most controversial, NCAB should make a positive statement of its position.

- The report should emphasize that a broader look at statistical data gives a different point of view (the National Academy of Sciences request to look at NCI statistical data should be helpful in that respect).

- The initiatives to appeal to Black business leaders should be included in the section on Subcommittee activities.

The Board unanimously accepted the report of the Subcommittee on Planning and Budget.

XIII. Subcommittee on Cancer Control for the Year 2000--Mrs. Helene Brown

Mrs. Brown said the Subcommittee on Cancer Control for the Year 2000 requested the Board's concurrence in at least the concept of the Draft Report of the Board of Scientific Counselors on Early Detection Guidelines. As recommended by the DCPC Board, a series of meetings, organized by Dr. Charles Smart, was held with professional societies to develop working recommendations for early detection of cancers at specific sites. Mrs. Brown emphasized that the recommendations are dynamic and expected to change from time to time. They are guidelines for early detection in physicians' offices, not recommendations for mass screening. Mrs. Brown said it was her understanding that the American Cancer Society would endorse these guidelines with some minor changes.

Dr. DeVita noted that in the past NCI had not issued recommendations, which had sometimes been interpreted as a lack of support for the American Cancer Society's recommendations. He stated the importance of having a mechanism for keeping such recommendations up to date. It was suggested that the next step be the development of early detection guidelines for high risk groups. Another suggestion was that third-party payers be educated about the importance of early detection.

The Board unanimously endorsed the concept and draft of the Early Detection Guidelines.

Mrs. Brown said the Subcommittee also discussed tracking the progress toward the Year 2000 goals with Dr. Sondik. Although there are many difficulties, some good tools, such as the SEER data, data from the National Center for Health Statistics, and the National Health Interview Survey, are available. In addition, Dr. Sullivan provided additional details to the Subcommittee about the Black Business Leaders' Conference.

The Board unanimously accepted the report of the Subcommittee on Cancer Control for the Year 2000.

XIV. Subcommittee on Contracts and Budget--Dr. Phillip Frost

Dr. Frost reported that the Subcommittee had approved funding for the following concepts: 1) support services for the Office of the Director; 2) a clearinghouse for ongoing research in cancer epidemiology; 3) a scientist-to-scientist information exchange program; 4) acquisition of CD-ROM technology.

The Board unanimously accepted the report of the Subcommittee on Contracts and Budget.

XV. AIDS Subcommittee--Dr. Gertrude Elion (for Dr. Howard Temin)

Dr. Elion reported that the Subcommittee had heard a review of the current NCI AIDS activities from Dr. Roper. In addition, the Subcommittee heard presentations from Dr. Chabner on the drug screening program and from Dr. Fischinger on the vaccine development program. In addition, Dr. Roper

presented an overview of the various committees within the Department of Health and Human Services involved in the coordination of AIDS research efforts. Issues discussed included the role of NCI in AIDS research, overall research on retroviruses, coordination of research with private companies, and transfer of some of the AIDS program from NCI to NIAID. Dr. Elion said the Subcommittee felt that NCI should take more of an activist role in dealing with industry, and comments to the press regarding achievements in AIDS research should be realistic and not so optimistic as to mislead the public. The Subcommittee also requested that in addition to the scientific presentations on AIDS at the November NCAB meeting, Dr. Fauci should be asked to present an overview of NIH and NIAID activity, and the role of the NCAB AIDS Subcommittee should be discussed.

Dr. Temin had expressed concern that there be wide availability of reagents to the scientific community after the reagents have been described in the scientific literature. Dr. Adamson noted that the DCE Board would discuss this concern at its October meeting.

Dr. Elion said that Dr. Fischinger had described the contract mechanisms for FCRF. The Subcommittee expressed concern that the early problems encountered in the Special Virus Cancer Program not recur in the AIDS program. Dr. Adamson and Dr. Gruber discussed several recent RFAs and RFPs issued by DCE.

Dr. Elion said another item discussed was peer review of intramural research on AIDS. Other intramural reviews occur through site visit teams which are usually appointed by the Boards of Scientific Counselors. This process will also be used for the AIDS research program.

The Subcommittee also discussed the importance of liaison with the NIH AIDS Advisory Committee to the Director. Dr. Elion said that expanded discussion of the role of the NCAB AIDS Subcommittee was deferred until November.

In discussion, it was requested that the AIDS presentation at the November NCAB meeting also provide information on Government-wide coordination on the AIDS problem and discussion of the impact on other research of increased funding for AIDS. There was also discussion of the fact that some states, in part because of concern about AIDS, are pursuing their own drug approval programs.

The Board unanimously accepted the report of the AIDS Subcommittee.

XVI. Consideration of the May 26-27, 1987, Meeting Minutes

The following changes were requested in the minutes of the May 26-27, 1987, NCAB meeting:

- Page 6: Add sentence explaining why animal research components were transferred to the Director's office
- Page 11: Reword first bullet: Fund 50 percent of approved research project grants at recommended levels

- Page 20: Reword to indicate that study on workers' exposure to benzene is being conducted on the Chinese mainland.

The minutes were then unanimously approved as corrected.

XVII. New Business--Dr. David Korn

New Initiative on PDQ--Mr. Richard Bloch

Mr. Bloch read a letter he had written to Ms. Susan Hubbard expressing his concern about the lack of knowledge among physicians about the availability of current treatment information. He proposed to finance a project to make tailored PDQ printouts widely available to physicians by supporting an 800 number that physicians could call for free cancer information. While CIS offices provide free PDQ printouts to physicians, Mr. Bloch expressed dismay that physicians were limited to one request and often did not receive customized printouts. He concluded by asking NCI to support his service in two ways. He asked that hard copy of the cancer information file be printed with one section on a page. This would allow his staff to file each section separately so they could assemble customized printouts from the files in response to physician requests. Secondly, he asked NCI and the NCAB to publicize the availability of his service throughout the country.

In response, Dr. DeVita reminded Mr. Bloch that PDQ was put on-line so that its currency could constantly be maintained and emphasized that the cancer information file should be used on-line rather than by developing hard copy files. He added that the staff of many Cancer Information Service (CIS) offices do customize PDQ printouts in response to requests. Ms. Hubbard pointed out that a file of hard copy information would be extremely cumbersome to maintain, and that staff would still have to log onto the on-line data base to get current protocol information. She said that CIS uses hard copies of state-of-the-art statements as a reference tool to assist staff respond to inquiries and to requests for complete statements. Mrs. Brown too expressed concern about the promotion of two 800 numbers by the Institute and recommended that the idea be referred to the information subcommittee for discussion prior to any decision.

A discussion of promotional efforts ensued and the following suggestions were made:

- NCI should identify more ways of advertising PDQ, such as videotapes that could be distributed widely to hospitals.

- NCI should report to the NCAB on its future plans for promoting PDQ once the long-range promotion plan is completed.

- NCI should do another videotape for nationwide broadcast and for use at state and local medical meetings.

It was agreed that the issue would be referred to the Subcommittee on Cancer Information for consideration. It was also agreed that the development of video training tapes would be investigated. The Board requested a short presentation on PDQ, including marketing initiatives, at the November meeting.

Future Agenda Items

The Board reviewed the listing of the proposed agenda items in the Board book and made the following changes:

- Deleted presentation by a State Department representative on the Administration's view on international science and foreign policy
- Deleted overview of mutagens in food processing (handout to be provided)
- Combined presentations on Year 2000 goals
- Include presentation on human cell lines in vitro drug screening as part of the November program review.

Future Public Participation Hearings

Dr. Korn asked about budget information for the first Public Participation Hearing. Mr. Van Nevel said the information would be available by the time of the November NCAB meeting. He said it was important to start planning for the Dallas and Philadelphia Hearings to begin to determine staff needs and organizational resources. Budget information on the National Black Leadership Initiative will also be presented at the November meeting.

Miscellaneous

Board members were invited to express concerns to Dr. DeVita about peer review issues as he is a member of the NIH-wide committee on peer review. Dr. DeVita said the use of mail ballots for the Outstanding Investigator grants was to be discussed.

Dr. DeVita asked that the Subcommittee on Environmental Carcinogenesis consider NCI's prevention program and its evolution over the past 10 years.

The Subcommittee on Surgical Oncology will meet in November.

XVIII. Adjournment

The open session of the 63rd meeting of the NCAB was adjourned at 10:26 a.m. on Wednesday, September 28, 1987.

11/12/87
DATE

David Korn, M.D.