Department of Health and Human Services

Public Health Service

National Cancer Institute

National Cancer Advisory Board

Summary of Meeting
February 2-4, 1987
Building 31, Conference Room 6
National Institutes of Health
Bethesda, Maryland

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February 2-4, 1987

The National Cancer Advisory Board (NCAB) convened for its 61st regular meeting at 8:30 a.m., February 2, 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. Irene S. Pollin
Dr. Louise C. Strong
Dr. Louis W. Sullivan

President's Cancer Panel

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

Absent

Dr. Armand Hammer

Ex Officio Members

Dr. Dorothy A. Canter, NIEHS
Captain Stephen R. Veach, DOD
Dr. Ralph E. Yodaiken, DOL, OSHA
Dr. Richard J. Greene, VA
Dr. Lakshmi Mishra, CPSC

Absent

Dr. Tim Lee Carter
Mrs. Barbara Ingalls Shook

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

Liaison Representatives

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

Dr. Judi Johnson, Cancer Services Coordinator, North Memorial Medical Center, Robbinsdale, Minnesota, representing the Oncology Nursing Society.

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

Ms. Elaine Locke, Associate Director for Practice, American College of Obstetrics and Gynecologists, Washington, D.C., representing the American College of Obstetrics and Gynecology.

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

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

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

Members, Executive Committee, National Cancer Institute

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, Cancer Biology and Diagnosis
Executive Secretary, Ms. Iris Schneider, Director of Staff Operations

I. Call to Order, Opening Remarks, and Consideration of the December 8-10, 1986, NCAB Meeting Minutes--Dr. David Korn

Dr. Korn, Chairman, called the meeting to order and welcomed 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. Members of the public who wished to express views on items discussed 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.

Dr. Korn announced that, due to the short time interval between the December 1986 and this meeting of the Board and to the length of the December 1986 NCAB meeting minutes, distribution of the minutes had been delayed until shortly before the meeting. Several corrections to the minutes were distributed to the Board members, and a vote for approval of the minutes was delayed until Wednesday, February 4. As a quorum of 12 members was not present on February 4, a vote for approval of the December minutes will be deferred until the May 26-27, 1987, NCAB meeting.

Dr. Korn also announced that in his absence Dr. Louise Strong would chair the February 4 session of the meeting.

II. Future Board Meeting Dates

Dr. Korn called the Board members' attention to the following confirmed future meeting dates: May 26-27, 1987; September 28-30, 1987; November 16-18, 1987; February 1-3, 1988; May 16-18, 1988; September 26-28, 1988; and December 5-7, 1988. He noted that one member had a conflict with the May 1988 dates, and that Mrs. Bynum would investigate changing the dates to May 9-11, 1988.

III. Report of the President's Cancer Panel--Dr. William P. Longmire

In Dr. Armand Hammer's (Chairman, PCP) absence, Dr. Longmire read Dr. Hammer's prepared report.

Dr. Hammer cited the upcoming 50th anniversary of the NCI to be celebrated in May 1987, designated as NCI's month in the centennial year of the National Institutes of Health (NIH). He also noted that 1987 marks the 15th anniversary of the signing of the National Cancer Act by former President Richard Nixon, and the inception of the NCAB and the PCP. He congratulated the NCI on its anniversaries and expressed pride in being associated with Dr. DeVita, the NCI staff, and members of the Board.

The PCP held its final meeting of 1986 on December 15 at the University of Chicago Cancer Research Center. Consistent with their theme for the year of exploring innovations in cancer treatment, the Panel heard presentations on new approaches to cancer therapy, developments in biological response modifier programs, and more precise diagnosis and treatment via

molecular analysis. Dr. Hammer stated that the reports clearly illustrated that promising research was being conducted in all of these areas.

Dr. Hammer referred to the chromosome work performed at the University of Chicago under the leadership of Dr. Janet Rowley, a former NCAB member, and noted that Dr. Rowley was a recent recipient of an Outstanding Investigator Grant for her research. Reports that the Panel had received on developments in breast and ovarian cancers and the use of radiolabeled monoclonal antibodies in T-cell lymphomas indicated that research with monoclonal antibodies continues to show promise as both a therapeutic and a diagnostic tool. A presentation by Dr. Richard Fisher of Loyola University concerning clinical and laboratory studies with IL-2/LAK cells to duplicate Dr. Steven Rosenberg's intramural trial reported encouraging results. In contrast to an editorial by Dr. Charles G. Moertel of the Mayo Clinic in the December 12, 1986, issue of the Journal of the American Medical Association (JAMA), criticizing the IL-2/LAK cell protocol for its toxicity, Dr. Fisher reported that this toxicity could be ameliorated by dose manipulation and careful patient selection and was rapidly reversed within 24 to 48 hours of discontinuance of treatment. Dr. Hammer expressed confidence that the IL-2/LAK cell therapy will have a major impact on cancer treatment and cited a recent Hammer Workshop at the Salk Institute, which was attended by Drs. DeVita and Rosenberg, as well as representatives from the centers pursuing the IL-2/LAK cell protocol extramurally and many research scientists in the field of immunology.

The first 1987 meeting of the Panel will be held March 16 at the University of California at Los Angeles. Board members were invited to attend.

The following points were raised in discussion of Dr. Hammer's report:

- It was clarified that Dr. Moertel's criticism of the IL-2/LAK cell protocol appeared as an editorial in JAMA, not as an editorial issued by the American Medical Association (AMA).

- Dr. DeVita agreed to send Board members the recently instituted periodic reports analyzing the results of the intramural and extramural trials of the IL-2/LAK cell protocol.

IV. Director's Report, National Cancer Institute--Dr. Vincent T. DeVita

After welcoming Board members to the meeting, Dr. DeVita announced that Ms. Nina Hyde, fashion editor of the Washington Post, had donated $170,000 primarily for AIDS research to the Director's Gift Fund on behalf of the Washington Fashion Group.

Dr. DeVita also announced that Dr. Lillian Gigliotti will serve as the new Associate Director for Cancer Control Science.

Dr. DeVita congratulated Mrs. Nancy Brinker, the recipient of the first Ultra magazine humanitarian award, for her work in creating the Susan Komen Foundation and her fight against breast cancer.

Budget Presentation

Dr. DeVita began his budget report by explaining the significance of the concepts "extended availability" and "advanced appropriation." In the President's 1988 budget, $64 million of NCI's 1987 budget is proposed to become available in 1988. The effect is to reduce the increase in funds granted by Congress between 1986 and 1987. Thus, since the NCI has been functioning under a continuing resolution budget of $1.403 billion for 1987 and has already funded the first round of grants in 1987, reductions are required in the second two rounds of grants. This includes decreases below recommended levels of approximately 18 percent for competing applications and approximately 5 percent for noncompeting applications.

Of the 1988 budget of $1.8 billion, $508 million is an advanced appropriation to fund FY 1988 competing grants for the life of their awards. The money is not obligated in FY 1988 for future years, but is obligated in annual increments. Thus, the 1988 obligational budget is $1.8 billion, minus the $508 million in advanced appropriations, plus the $64 million moved forward from 1987, or $1.366 billion.

Dr. DeVita said he will be defending NCI's 1988 budget at hearings in the House of Representatives on March 5. The question of whether or not the extended availability of 1987 funds to 1988 violates the intent of Congress to give the NCI a 14 percent increase in budget from 1986 to 1987 will be considered. Congressional consideration of the 1987/88 budgets will likely take several months.

Dr. DeVita reported that the 1987 budget estimate designated for Small Business Innovation Research awards is $13.6 million. The 1988 estimate reduces this set-aside by a small amount as it is a percentage of the total extramural research and development budget.

In response to a previous request from Dr. Calhoon, Dr. DeVita also presented a breakdown of funding for NCI clinical activities. Approximately 10 to 12 percent of the NCI budget is devoted to these activities, including R01 and P01 grants, support for the Clinical Cooperative Groups, prevention trials, and intramural research. The estimate for both 1987 and 1988 is about $190 million, reflecting an increase of about 13.7 percent between 1986 and 1988 and paralleling the increase in the total NCI budget over this period. A hard copy of Dr. DeVita's slide detailing funding for clinical activities was distributed to the Board.

Turning to the budget for AIDS research, Dr. DeVita reported that the NCI AIDS budget for 1987 includes $61.6 million and for 1988, $84.8 million. The major responsibility for immunologic research lies with the National Institute of Allergy and Infectious Diseases (NIAID) and that for virology with NCI; epidemiologic research responsibility is evenly split. NIAID will be the lead Institute for clinical trials and vaccine

development and will support the AIDS Treatment Evaluation Units (ATEU). NCI's responsibility is preclinical drug development, including a full-scale screening program within the Developmental Therapeutics Program (DTP), with $3.5 million transferred from NIAID to support this effort. The understanding is that by about 1992, the NCI will begin transferring responsibility for preclinical drug development back to NIAID.

AIDS

Dr. DeVita said the focus on AIDS research resulted in the decision to transfer Dr. Robert Gallo's laboratory, the Laboratory of Tumor Cell Biology, from the Division of Cancer Treatment (DCT) to the Division of Cancer Etiology (DCE), which conducts the rest of NCI's viral oncology programs. The vaccine development program at the Frederick Cancer Research Facility (FCRF) under Dr. Fischinger, Deputy Director of the NCI, will also be transferred to DCE. An Associate Director in DCE for Biological Carcinogenesis will be recruited to head this program.

Dr. DeVita urged the Board to consider the institution of a Board Subcommittee on AIDS to coordinate the cross-divisional research efforts on AIDS. He noted that this group could interact with the NIAID Council Subcommittee on AIDS and that both might be represented on the NIH AIDS Executive Committee, which coordinates the entire NIH AIDS research effort. He suggested that ad hoc consultants prominent in the AIDS research field be sought until a future Board vacancy arises to allow inclusion of such an expert as an NCAB member. This new Subcommittee of the NCAB perhaps would meet more frequently than other Board subcommittees and not necessarily in conjunction with Board meetings.

In response to a question regarding the pace of AIDS research, Dr. DeVita expressed his belief that AIDS research has progressed with great speed. He cited the example of the development of AZT into a widespread clinical trial in an 18-month period. Other anti-AIDS agents, such as suramin (which proved to be too toxic) and dideoxycytidine, have also been investigated during this period.

Follow-up Items

IL-2/LAK Cell Therapy

Referring to Dr. Hammer's comments about Dr. Moertel's editorial in JAMA about the IL-2/LAK cell therapy, Dr. DeVita stressed that this is an investigational therapy and is not being proposed as suitable for general practice as Dr. Moertel seemed to assume. The results of the trials, particularly in renal cell carcinoma and melanoma, showed promise, and that further studies are being pursued in those diseases. He noted that in the 1920s and 1930s radiotherapy was thought to be too toxic, but that improved technology has allowed its continued use and effectiveness, and now it is probably responsible for saving about 180,000 lives per year in the United States.

NCI's Role in Nutrition Research

In response to a request by Dr. James Wyngaarden, the Director of NIH, for NCI and NHLBI to organize a meeting on nutrition and health, Dr. DeVita and Dr. Claude Lenfant (Director of the National Heart, Lung, and Blood Institute) contacted Dr. Samuel O. Thier (President of the Institute of Medicine) regarding IOM sponsorship of such a meeting. The NCI will be actively pursuing this in conjunction with Dr. Peter Greenwald. He noted that Dr. Greenwald's afternoon presentation would focus on dietary issues. (See discussion in Section IX. below.)

New Items

Dr. DeVita reported that responses to the announcement for applications for small instrumentation grants were due March 20, 1987, and that the Board will have the opportunity to review these applications at their closed session during the May Board meeting. The grants will be awarded in September.

The Government Accounting Office (GAO) has conducted a study on cancer statistics by interviewing physicians about progress in 12 different cancers, and will issue their report soon. Copies of the GAO report and NCI's reply will be sent to Board members upon publication.

Dr. DeVita called for a meeting of the Subcommittee on Environmental Carcinogenesis, NCAB, in May to consider recent studies on formaldehyde, acrylonitrile, and methylene chloride conducted by the NCI. He stressed that the Subcommittee needed to evaluate the issue of maintaining a proper balance in the relationship between the NCI, the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, industry, and unions.

Dr. DeVita expressed his concern over inaccuracies in a recent article in the New England Journal of Medicine by Dr. Robert Oldham. Dr. DeVita pointed out that Dr. Henry Mihich was the real founder of the NCI Biological Response Modifiers Program (BRMP) as he had chaired a subcommittee of the DCT Board of Scientific Counselors, which worked for a year and produced a monograph, published in 1979, which outlined the framework and agenda for such a program and is a guide for the development of biologics to this day. Subsequently, Dr. Oldham was hired to be the first Associate Director for the BRMP. Dr. DeVita also noted that what Dr. Oldham terms patient-funded research, unlike some other private sector-funded research, is really the sale of an unproven method. It is not going to do anything to advance a new method so that it can be marketed.

Turning to organizational issues, Dr. DeVita explained the proposal to dissolve the position of Associate Director for the Office of Program Planning and Analysis (previously held by the late Mr. Louis Carrese). The planning and evaluation function will be moved to the Office of the Director under Ms. Iris Schneider. The Management Information System Branch has been made part of the Office of Administrative Management under Mr. Philip Amoruso.

Next, Dr. DeVita called the Board members' attention to the concern over the lack of visibility of the Cancer Centers program expressed in meetings

by leaders of the Association of American Cancer Institutes and other Center directors. A meeting of the Board of Scientific Counselors of the Division of Cancer Prevention and Control, the Division that includes the Centers Program, will be held in early May, and comments raised in their discussion of this Program can be presented to the NCAB meeting in late May. Such a discussion could include review of possible organizational changes. Options are establishment of a new division to encompass the Cancer Centers Program, the Organ Systems Program, and training or the establishment of an associate director's position in the Office of the Director.

Dr. DeVita then described a year-long internal review leading to the decision to consolidate both NCI journals--the Journal of the National Cancer Institute (JNCI) and Cancer Treatment Reports--into one biweekly publication with the proposed title, The Cancer Journal: The Journal of the National Cancer Institute. In response to comments from Board members, Dr. DeVita emphasized that speed of publication of high quality articles is the number one priority of the new publication, which NCI hopes to launch in January 1988. Although time for peer review and authors' revisions can vary widely, the NCI would take steps to shorten time from submission to acceptance. The Government Printing Office (GPO) has agreed to establish a contract for printing the new journal, which would shorten the time from final acceptance of articles to publication to 3 months. Dr. DeVita noted that the establishment of the Journal of Clinical Oncology in the late 1970s had been one factor influencing the decision to combine the two NCI journals, particularly as Cancer Treatment Reports and the Journal of Clinical Oncology attracted very similar types of articles. He also stressed that the new journal would continue to allow flexibility to publish longer articles, as in the current JNCI publication of epidemiologic data. It was suggested that establishing special sections, such as on treatment or epidemiology, headed by distinguished associate editors, might enhance the new journal's quality and reputation. The final title of the new journal will be confirmed after the investigation of other journal titles and copyrights. Board members will be sent a package detailing plans for the new NCI publication.

At the conclusion of Dr. DeVita's presentation, Dr. Korn and other Board members stressed their concern over the 18 percent budget cuts to competing grant applications and the potential detrimental effects on academic research laboratories.

Legislative Report--Dr. Mary Knipmeyer

Dr. Knipmeyer gave a report on the legislative activities of the 100th Congress. An AIDS hearing held by Senator Edward Kennedy considered the timetable for vaccine development. AIDS bills were reintroduced related to control of the epidemic and the financial burden on AIDS patients. Members of Senator Kennedy's staff discussed the goals for the year 2000 with Drs. Greenwald and Edward Sondik, as well as Dr. Knipmeyer.

Of particular interest is the introduction of several tobacco bills. These include a bill to increase the excise tax on cigarettes to 32 cents per package and two bills related to passive smoking.

Representative Claude Pepper has reintroduced a bill on establishing a Breast Cancer Screening Program at the Cancer Centers. Dr. Knipmeyer clarified that this bill included a proposal that Centers offer mammograms at a cost of no more than $25 per patient. Representative Mary Rose Oakar has reintroduced a Medicare reimbursement bill that would provide for annual mammograms for Medicare participants. She has also reintroduced her informed consent measure related to the two-stage procedure for diagnosis and surgery for breast cancer patients.

There was continued discussion in Congress on the diethylstilbestrol (DES) issue, several occupational cancer bills, and the animal welfare issue. The heroin bill was reintroduced in the Senate.

The Office of Technology Assessment has begun a two-year study of unproven cancer methods. A Working Group is being established to evaluate, in particular, the IAT method used by Lawrence Burton in the Bahamas. The objective is to determine how best to evaluate these methods, not to come to decisions about their validity.

Dr. Knipmeyer concluded her report by referring to a statement and resolution by Mr. Pepper who introduced the bill to commemorate the National Cancer Institute during May. A series of Congressional breakfasts, including one to discuss the revolution in cancer cell biology in May, will be held as part of the NIH centennial celebration.

V. Report on the P01 Working Group--Dr. Paul Rambaut

Dr. Rambaut summarized the current review process for Program Project P01 applications and presented several revisions to this process proposed by a recent program project working group. He began by defining the P01 as an award for support of broadly-based, multidisciplinary research with a well-defined research focus. There are usually about seven projects within a typical P01. In FY 1986, NCI supported 144 P01s, at an average cost of $1 million in direct and indirect costs per P01 award. This support totaled $138 million and represented about 11.4 percent of the 1986 NCI budget.

Dr. Rambaut explained that in the current review system the NIH Division of Research Grants receives all P01s and assigns appropriate applications to the NCI. The NCI in turn assigns the P01 applications either to one of three chartered review committees (the Preclinical Program Project, Clinical Program Project, and Cancer Therapeutics Program Project Review Committees) or to a special review committee, currently 74 percent and 26 percent of applications, respectively. All applying institutions are automatically site visited, either by an organized site visit team that reports back to the appropriate charter committee, or by the special review committee. All applications are ultimately reviewed by the NCAB.

An NCAB subcommittee review of the P01 instrument in 1983 and 1984 had resulted in the key recommendations that all projects within a P01 program must contribute to the overall priority score and that no umbrella grants for core support of an institution be allowed. Dr. Rambaut noted that since

these guidelines have gone into effect, priority scores had become lower and POIs seemed more tightly focused. However, Dr. Rambaut reported that the current working group had cited several remaining problems, including:

- Poor information transfer from site visit teams back to the chartered review committees
- Increased review workload for staff (i.e., 8,000 units in 1986 and an estimated 10,000 units in 1987)
- Redundant report writing, necessitated by the two-tier process involving the special review committees and the chartered committees, which also allows midstream rebuttal of the first report obtainable under the provisions of the Privacy Act.

The program project working group proposed that:

- An initial letter of intent to make an application should be made mandatory.
- No arbitrary limits should be set on the length or size of applications nor should the length of time for site visiting be limited to a single day.
- There should be more interaction between program staff and applicants and between program and review staff.
- The chartered committees should be eliminated, and a single tier of initial review by special review committees should be employed. These committees should be smaller, more focused teams that could use mail and other types of collateral review to supplement areas of missing expertise.
- The automatic site visiting of amended applications should be discontinued.
- New guidelines based on these recommendations would be implemented in approximately one year.

Dr. Rambaut cited the advantages of instituting these changes, one of which would be cost reduction. He reported that site visits include about 8 to 10 outside experts, at a cost of about $10,000 for the average site visit of 3 days.

In discussion of the recommendation to eliminate the chartered review committees and institute single-tier review, several Board members raised concerns that this change might weaken the peer review system. It was suggested that two experts per relevant discipline be included in each special review committee to avoid the possibility of individual biases. Persons who have experience and knowledge of the POI process should also be included on the special committees, when possible. Eliminating the high and low vote on priority scoring was also suggested. It was clarified that all POI applicants

are given the opportunity to notify the Executive Secretary coordinating site visits of persons whom they considered unable to provide an unbiased review. Dr. DeVita noted that some information on effectiveness of the P01 mechanism in general would be forthcoming from a contracted study to evaluate the sources (e.g., R01, P01, intramural, contract) of major discoveries in oncology.

A motion to approve the recommendations of the working group was unanimously approved. NCI staff will develop the details of implementation, which will be presented to the Board at the May meeting, resulting in the subsequent issuance of revised P01 program guidelines.

VI. Physician Data Query System (PDQ)--Mr. Richard Bloch

Mr. Bloch drew attention to an article about PDQ in the New England Journal of Medicine (February 5 issue) and cited it as evidence that progress is being made in extending the use of the system. To further extend the use and usefulness of PDQ, Mr. Bloch offered the following suggestions:

(1) The sole goal of PDQ should be the dissemination of complete, honest, and accurate knowledge.

(2) Independent private firms specializing in computer networking should be invited to make suggestions for ease and simplification of the system at no cost to the Government.

(3) Each segment of PDQ should be examined for usage, cost to maintain, and efficiency.

In discussion of the first suggestion, the difficulty of defining state-of-the-art treatment was noted. For some diseases, there are no state-of-the-art treatments and PDQ refers the user to investigational protocols. PDQ is updated monthly by an Editorial Board, which can respond quickly to data suggesting a need to modify the state-of-the-art statements.

The Division of Cancer Prevention and Control currently is evaluating PDQ with respect to users and patterns of use. While PDQ is becoming increasingly user-friendly and use is increasing, more advertising is needed to inform physicians of its existence and provide information on its usage. Mr. Bloch said he hoped every physician who calls 1-800-4-CANCER receives information on how to access PDQ. NCI has received inquiries from 36 medical schools about including use of PDQ in their curricula.

It was agreed that the Subcommittee on Cancer Information would follow up on Mr. Bloch's suggestions.

VII. Radical Prostatectomy for the Treatment of Prostatic Cancer with the Preservation of Sexual Function--Dr. Patrick Walsh

Dr. Braren introduced Dr. Walsh as the originator of a well-accepted and increasingly used surgical technique to treat prostate cancer. Dr. Walsh

reviewed the anatomy and function of the prostate and described the two diseases of the prostate that occur as men age. Benign prostatic hyperplasia, the most common neoplasm in men, begins around the urethra and causes symptoms of urinary obstruction. Prostatic cancer, the second most common malignancy in men, begins at the periphery of the gland and produces no symptoms until it is far advanced. This, Dr. Walsh said, underscores the importance of routine screening. (The American Cancer Society recommends yearly screening in men over 40.) While treatment for benign hyperplasia involves removal of just the central portion of the prostate, treatment for cancer necessitates the removal of the entire prostate and seminal vesicles. Dr. Walsh said that if the disease is detected early, radical prostatectomy can cure prostatic cancer; however, the surgical technique has involved postoperative side effects of urinary incontinence and impotence.

By locating the microscopic nerves of the pelvic plexus that innervate the corpora cavernosa, Dr. Walsh was able to modify the surgical technique to avoid the complication of impotence. The microscopic nerves were demonstrated to be constantly associated with a neurovascular bundle which can be visually located during surgery. The surgeon can determine whether nerves can be preserved or resected widely with the specimen. Dr. Walsh emphasized that the primary goal of the surgery must be resection of cancer. Preservation of sexual function is of secondary concern.

Pathological review of the modified abdominal technique compared to the standard retropubic technique and the perineal technique showed that at least as much tissue and possibly more is removed with the new technique. Identification of the neurovascular bundles allows wide resection on one side and preservation of the neurovascular bundle on the other side, which is sufficient to preserve sexual function. The pathologists concluded that the technique does not compromise the removal of cancer which is determined by the extent of tumor rather than the operative technique.

Dr. Walsh said that 250 men have now been followed for one year or more after modified radical prostatectomy. By one year after surgery, 72 percent of the men were potent compared to 10 percent or fewer men who regain potency following the traditional surgery. The return of sexual function is related to the age of the patient--younger men regain potency more frequently--and pathologic extent of the tumor--patients with low volume disease confined within the capsule of the prostate are more likely to regain potency. In conclusion, Dr. Walsh expressed the hope that this curative technique, by reducing overall morbidity, would encourage physicians and patients to be more interested in diagnosing prostate cancer at an early stage.

Members of the Board congratulated Dr. Walsh on his presentation. Points raised in discussion included the following:

- Dr. Walsh's technique is being increasingly used by other surgeons with similar results.

- Recurrence rates following this modified surgical technique appear to be low and lower than following the traditional operations.

- The technique has not been used in children with prostatic rhabdomyosarcoma. The operation may not be possible because of the often large size of such tumors.

- Radical prostatectomy may be appropriate in young men with very focal cancer. About 100 percent of such men could be expected to regain potency. Without removal of the prostate, these men might suffer progression of the cancer.

- About 80 percent of prostate cancers are multifocal.

VIII. Public Participation Hearings--Mrs. Nancy Brinker

Mrs. Brinker provided Board members with the February 2, 1987, draft of the project proposal, Public Participation Program--Meeting the Challenge: Cancer and the Public's Stake. The Cancer Information Subcommittee met twice to refine and revise the proposal first presented at the December 6-8, 1986, NCAB meeting. Mrs. Brinker said the purpose of the program is to remind the public of the importance of basic research and to enlist the public in the massive effort needed to reach the goals for the year 2000. The essential action messages for the American public are early detection and prevention.

Six hearings would be held in selected cities across the United States. The resulting Hearings Report should provide NCAB members with a meaningful composite picture of individual and community involvement and commitment to the goal of reducing cancer deaths. Mrs. Brinker said the plan calls for pilot public participation hearings in Los Angeles and Atlanta, followed by an evaluation of the process and adjustments to the plan, if needed. If the pilot hearings are successful, another four hearings would be scheduled. She emphasized the flexibility of the plan and the involvement of regional committees in the process. A new report to update Decade of Discovery and other materials would be used in conjunction with the Public Participation Hearings and other NCI information efforts. Most of the effort described in the proposal would be accomplished between February 1987 and April 1988.

Points raised in discussion included the following:

- The hearings should provide the opportunity for the identification of gaps in service, availability, and accessibility of prevention and detection programs.

- There is a need to involve the public in the planning of programs that are implemented in their communities.

- The program should involve rural areas and minorities.

- The program could serve as an example of the practical application of science.

- Invitations to participate in the hearings would be based on the advice of the regional chairpersons.

- Evaluation of each hearing will occur shortly afterwards so that all involved parties can contribute.

- The Public Participation Program working committee will be the NCAB Subcommittee on Cancer Information and any other interested Board members.

- Merger of the Subcommittee on Cancer Information and the Subcommittee on Cancer Control for the Year 2000 should be considered.

It was moved, seconded and unanimously approved that the Public Participation Hearings Program be implemented.

IX. NCI Process Leading to Dietary Recommendations--Dr. Peter Greenwald

Dr. Greenwald traced the interest in nutrition issues back to the 1970s when the concern shifted from synthetic chemical food contaminants to dietary components. Epidemiologic studies showed patterns of variation in cancer incidence that were likely attributable to diet. Doll and Peto estimated that perhaps 35 percent of cancer might be related to diet. Research results that showed it was possible to inhibit carcinogenesis were complementary to the epidemiologic evidence and pointed to the need for a research focus on diet.

In 1981, the Board of Scientific Counselors, DCPC, was established with the intention of giving some research emphasis to diet. An NCAB ad hoc Subcommittee on Diet and Cancer, chaired by Dr. Maureen Henderson in 1982, advised NCI to give top priority to diet, nutrition, and cancer research. Dr. Greenwald said it was shortly after that that NCI began clinical trials in cancer prevention. The focus was on specific nutrients, some synthetic analogs of nutrients, and dietary patterns. Because of public interest in obtaining dietary information, NCI decided to develop a broad, moderate set of public information guidelines, rather than interpreting results of each individual study.

Dr. Greenwald reviewed the advisory structure for research relating to dietary recommendations, noting that in 1986, more than 100 experts advised DCPC. Four workshops were held related to the Low Fat Trials for Women at Risk of Breast Cancer and another was held on chemoprevention planning. The key sources for dietary recommendations include the National Academy of Sciences 1982 report, Diet, Nutrition and Cancer; a DCPC review of dietary fiber and colon cancer; Office of Cancer Communication planning research groups for the Cancer Prevention Awareness Program; an international symposium on dietary fiber (George Washington University 1984); a BSC, DCPC workshop on dietary fiber and cancer; and the recommendations of other national and international groups.

Dr. Greenwald emphasized that NCI's dietary recommendations are made in the context of the overall diet and focus on moderation and variety. The message is to eat a variety of foods that are lower in fats, cut down on calories, and increase fiber-containing foods from a variety of sources.

NCI recommends reducing fat to about 30 percent of total calories and consuming about 20 to 30 grams of fiber a day. These recommendations are similar to those of a number of expert groups, including a Senate select committee, the National Academy of Sciences, the American Cancer Society, Health and Welfare of Canada, and the Department of Agriculture and the Department of Health and Human Services (Dietary Guidelines). In addition, Dr. Greenwald said that most of the 131 dietary fiber and cancer studies reviewed supported increased intake of fiber as protective against cancer. The animal data on fat and calories are mixed on how much of an effect is due to reduced fat and how much to reduced calories. To keep abreast of new information, DCPC has established an internal Diet and Cancer Review Committee, chaired by Dr. Elaine Lanza.

The National Research Council of the National Academy of Sciences (NAS) is conducting a new study, Diet and Health, which will review the evidence on the relationship of diet to chronic diseases, including cancer. Dr. Greenwald said NCI intends to maintain its present recommendations unless there is new and compelling evidence for change. NCI will review the NAS report when it is finished in September 1988 and in consultation with the BSC, DCPC and coordinating with other groups, including the NIH Nutrition Coordinating Committee and the National Heart, Lung, and Blood Institute, will consider whether the recommendations should be changed. NCI will keep the NCAB informed of nutrition-related issues and the status of dietary recommendations.

In discussion, questions were raised about the Giant Food project, which Dr. Greenwald said would focus on how changes in the marketplace, e.g., shelf labeling, would influence people's purchasing behavior. About one hundred Giant stores in the Washington area will be compared to control markets in Baltimore. Shelf labels will identify foods as having high or low fiber, with 2 or more grams per serving considered to be high fiber. The program includes an evaluation parameter, combining surveys of people coming to the market and effects on levels of purchases. The program will be announced at a news conference on March 3, 1987.

Other points raised in discussion included the following:

- Where menu items were labeled as to cholesterol, fat, and caloric content, customers largely stopped ordering items high in cholesterol, fat, and calories.

- The nutrient content of foods varies widely, making it difficult to compare research results.

- NCI will report to the NCAB in May 1987 on plans to establish an intramural nutrition laboratory and in January 1988 on the Women's Health Trial.

- Dietary fiber occurs only in plants, mainly in the plant cell wall, and is not digestible by the usual enzymes in the digestive tract. About three-quarters of fiber is insoluble cellulose, hemi-cellulose and lignin.

- Diet is related to diseases other than cancer and perhaps also to aging processes.

- Many commercial enterprises have been responsible in helping to increase awareness of dietary recommendations.

- There is a need for physician education on diet and health issues.

X. 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 1,236, requesting support in the amount of $190,023,627. Of these, 1,058 were recommended for funding at a total cost of $129,278,977.

XI. Subcommittee Reports

Dr. Louise Strong chaired the final day of the meeting in the absence of Dr. Korn.

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

Ms. Brown presented the following statement, adopted by the Subcommittee, for approval by the NCAB:

> The NCAB recognizes study findings that screening mammography for women over age 50 can reduce breast cancer mortality by 30 percent. Public programs urging the use of screening mammography as a method of early detection of breast cancer should be encouraged.

Ms. Brown stated that BSC, DCPC had requested such a statement from the NCAB in support of the goals for the year 2000. The American Cancer Society is launching a widespread, broad-based program for the early detection of breast cancer through the use of screening mammography, emphasizing the importance of low cost mammography and the cooperation of diagnostic radiologists.

In discussion, the quality control issue was raised. Poor quality pictures and poor interpretations have contributed to an increase in the amount of surgery performed. Another consequence is likely to be the creation of a quality control industry. Organizations with some oversight in this area include the American College of Radiology, the Food and Drug Administration, and state agencies.

Another problem associated with screening mammography is microcalcifications, which have no true characteristics to indicate when a biopsy is needed. Also, increasing numbers of small *in situ* cancers are being found in women of all ages and their long-term clinical significance is unknown.

Ms. Brown noted that at the present time only about 15 to 20 percent of women over age 50 have ever had a mammogram. If a successful screening

program can be implemented, at least 80 to 90 percent of women over 50 should have mammograms. In the first few years of such a program there would be an increased detection of breast cancer with resulting increased medical and emotional costs.

A motion to approve the statement presented by the Subcommittee was made, seconded, and unanimously approved.

In continuing the report of the Subcommittee, Ms. Brown reported that Dr. Claudia Baquet (DCPC) and Dr. Lemuel Evans (Division of Extramural Activities) had presented information on cancer control studies and statistics in the black population and reviewed potential cancer control interventions. Dr. Evans also discussed minority support programs for professional education and patient accession through the Clinical Cooperative Groups and for research by minority investigators through supplemental grant mechanisms. The Subcommittee decided to establish a small planning group to investigate the possibility of recruiting black business people and others who have an income base in the black community to meet with NCI and enlist their participation in strategies for addressing control goals for the year 2000 in black populations. The primary issue to be addressed is smoking.

Ms. Brown said the Subcommittee discussed merging with the Subcommittee on Cancer Information and decided to defer such an action, but recognized overlapping interests. The Cancer Control for the Year 2000 Subcommittee has a unique charge to address resource needs, which will be discussed at the next Subcommittee meeting.

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

Subcommittee on Planning and Budget--Dr. Louise Strong

Dr. Strong said that Dr. DeVita had presented an update on the President's 1988 budget and its implications for the 1987 budget. The Administration's proposal that $64 million of the 1987 budget not be made available for obligation until 1988 would apply to research project grants and would result in a reduction of about 116 competing grants. As discussed at the February 2, 1987, session of the NCAB meeting, competing grants would have to be negotiated down approximately 18 percent below recommended levels and noncompeting grants approximately 5 percent reductions. The Subcommittee felt that Board members could play a role in explaining the reasons for these reductions to grantees in appropriate forums. Board members expressed concern that the stability of funding for grantees is again being eroded. The increase to other mechanisms in 1988 is mainly for AIDS activities, which under Administration policy cannot be reduced. Dr. DeVita explained that the continuing controls of apportionment make the movement of funds among mechanisms difficult. Congress has asked the Director of NIH to submit a report on the effects of apportionment before the appropriation hearings, which will begin shortly.

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

Subcommittee on Surgical Oncology--Dr. Victor Braren

Dr. Braren first mentioned the informational items discussed at the Subcommittee meeting. Dr. Fred Avis has moved from his position as Coordinator of Extramural Surgical Oncology into the intramural program but will continue to act in the extramural position until a replacement is found. In discussing grants, Dr. Braren said there are now seven active T32 surgical training grants and three more are likely to be funded. This would bring to ten the number of institutional surgical oncology training grants, when a few years ago there were only two or three. Dr. Braren said six other institutions are considering submitting T32 applications for the May review. Within the past two years, 33 surgeons have submitted K08 individual surgeon development grant applications and 14 have been funded, for a funding percentage well above that for R01s and P01s. Dr. Braren announced that on June 15 to 17, NIH will hold a consensus development conference on low stage prostate cancer.

Dr. Braren then presented four recommendations from the Subcommittee:

(1) NCI should give serious consideration to elevating the position of Coordinator of Extramural Surgical Oncology to the level of a divisional associate director.

(2) NCI should continue to encourage surgical oncology training and increasing the number of surgical oncologists.

(3) NCI should consider issuing a program or other type announcement for a course on a topic of surgical oncology.

(4) Dr. Vincent Ansanelli should be invited to talk about his work on the use of lasers in breast cancer surgery.

In discussion, it was noted that NCI faces some constraints in elevating positions to the associate director level.

The Board unanimously accepted the report of the Subcommittee on Surgical Oncology.

XII. New Business

Format and Place of December Meeting

Dr. DeVita said that Board members' responses to his memorandum about the format and place of the December meeting indicated a preference for the traditional program review format. In discussion, several Board members voiced an interest in hearing presentations on intramural research efforts. It was suggested that a review of a program area be included as part of the second day of the NCAB meeting.

The general consensus was that a plan to include a program review in the second day session should be tried. There should be flexibility in

determining whether meetings should last two or three days. If the agenda is not too full, there might be an occasional two-day meeting. Board members will be polled about options for the meeting format and to determine what program area could be reviewed at the May meeting. However, because May is the anniversary of NCI, other activities may preclude a program review at that time. There was also a general consensus that the Board not meet at sites other than NIH unless there is a real need to do so.

Future Agenda Items

The following topics were suggested for inclusion in future agendas:

- Screening mammography, state regulations, and quality control issues
- Patient-paid research on not yet proven therapies
- Linkage of the goals for the year 2000 and the by-pass budget and status and function of NCI within NIH in light of the prerogatives afforded the NCI by the National Cancer Act
- Limitations and value of the Animal Welfare Act
- Protection of human subjects
- Use of lasers for breast cancer surgery
- Current status of tests for detecting cancer for both screening and diagnostic purposes
- In vitro screening for drug development
- Molecular characterization of tumors as a basis for selective therapy.

It was suggested that several of the topics be tied into a discussion of R01/P01 grants in progress in those areas.

One item--stabilization of the competing grant pool-- was deleted from the listing of future agenda items in the Board book.

There was also discussion of NCI's efforts to establish an NCAB subcommittee on AIDS, to include virologists and a public health expert.

XIII. Adjournment

The 61st meeting of the NCAB was adjourned at 10:00 a.m. on Wednesday, February 4, 1987.

April 21, 1987
Date

David Korn, M.D.