National Institutes of Health

National Cancer Institute

NATIONAL CANCER ADVISORY BOARD

Minutes of Meeting

November 30-December 2, 1981
Building 1
Wilson Hall
NIH Campus
Bethesda, Maryland

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

Minutes of Meeting*
November 30 - December 2, 1981

The National Cancer Advisory Board was convened for its 40th regular meeting at 8:30 a.m., November 30, 1981, in Wilson Hall, Building 1, National Institutes of Health, Bethesda, Maryland. Dr. Henry C. Pitot, Chairman, presided.

Board Members Present

Dr. Ames
Dr. Amos
Dr. Henderson
Dr. Hickey
Dr. Katterhagen
Mrs. Kushner
Ann Landers
Dr. Leffall
Dr. Pitot
Dr. Powers
Dr. Rowley
Mr. Samuels
Mr. Schrier
Dr. Seitz
Dr. Selikoff

Ex Officio Members

Dr. Dorothy Canter, OSTP
Dr. Allen Heim, FDA
Dr. F. Kash Mostofi, DOD
Dr. Denis J. Prager, OSTP
Dr. Peter Preuss, CPSC
Dr. David Rall, NIEHS

Representatives of the President's Cancer Panel

Dr. Amos
Dr. Hammer

Board Members Absent

Mrs. Lombardi
Dr. Shubik
Dr. Wogan

Liaison Representatives

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

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

---

* 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 (continued)

Dr. Virgil Loeb, Jr., Professor of Clinical Medicine, Washington University, St. Louis, Missouri, representing the American Association for Cancer Research and the American Society of Clinical Oncology, Inc.

Dr. J.W. Thiessen, representing Dr. Charles W. Edington, Acting Director, Office of Health and Environmental Research, Department of Energy, Washington, D.C.

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

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

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

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

Members, Executive Committee, National Cancer Institute

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

In addition to staff, participants, and invited guests, 20 registered members of the public attended this meeting.

I. Call to Order and Opening Remarks--Dr. Henry Pitot

Dr. Pitot called the meeting to order, and members and guests were welcomed. It was announced that this NCAB meeting is a program review meeting, and there would not be an opportunity to introduce each of the many visitors. However, many of them would be making a presentation and would be introduced at the appropriate time.

II. Consideration of Minutes

The minutes of the previous Board meeting were approved.

III. Future Board Meeting Dates

Future Board meeting dates that were confirmed were: February 1-3, 1982, May 17-19, 1982, October 4-6, 1982, November 29-December 1, 1982.

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

Dr. Hammer was sworn in as Chairman of the President's Cancer Panel on October 5, 1981. On October 27, the Panel had its first meeting, at which time Dr. Vincent DeVita and the NCI staff made presentations. The panel intends to take seriously its mandate under the National Cancer Act: "to monitor the development and execution of the National Cancer Program." Dr. Hammer stated that the Panel has expressed concern and intends to oppose the 12 percent budget cut that has been imposed on the NCI. The Panel received an extensive briefing by Dr. Jack McDonald, the Associate Director of Cancer Treatment at NCI, concerning the Washington Post series of articles. He invited all Board members to attend the next meeting of the Panel on December 3 which will include a discussion by Dr. Amos on appointments to the NCAB and some thoughts on improving the appointment process. Dr. Hammer enthusiatically spoke about breakthroughs in the area of hybridomas and announced that the Salk Institute in La Jolla, California, is planning to hold a hybridoma seminar in March 1982, to which as many scientists as possible have been invited from all over the world.

Questions and Comments. Dr. Harold Amos clarified two agenda items for the December Panel meeting. A question whether the NCAB is a legitimate issue for the Panel to get involved in is being raised, and the Panel recognizes the need to have some supplemental changes in the grants review mechanism.

V. Report of the Director, NCI -- Dr. Vincent T. DeVita, Jr.

Dr. DeVita reported on the following items:

Survival Statistics. Discussion concerning the relative survival rate has thus far been based on the Public Health Service Report No. 5 published in 1976, which reflected survival data between 1967 and 1973. New figures on relative survival are based on advances that have taken place since 1973. These figures were derived by the Surveillance Epidemiology and End Results (SEER) Program. The low figure for survival rate among whites for the period 1973 to 1978 is 46 percent. The high figure is 50 percent. This is a 12 percent advance in the relative survival rate.

Budget. In 1981, the actual budget level was $989,338,000. Congress passed a continuing resolution that covered the budget from October to November 20, 1981. The President's 1982 budget was $1,025,000,000. Subsequent to the submission of this budget figure, the President proposed a 12 percent budget cut across the board for the agencies, which would have reduced NCI's budget to $903,000,000. The Congress passed another continuing resolution, effective through July, that would have allowed the NCI to operate at the lower of the House and Senate levels, with a caveat that all budgets would be reduced by 4 percent, not 12 percent. The NCI would have been reduced from $1,025,000,000 by 4 percent, which would be the current level. However, the President vetoed this proposal. The NCI is now back at the continuing resolution level of $989,000,000, less 12 percent. All of the NCI deliberations that took place during the year, however, were based on the President's budget of $1,025,000,000, so proposals and projects that will be presented at this Board meeting must be adjusted by the cuts the Institute has to take when Congress and the President reach a compromise.

Funding Policies. NIH was issued the following policies by the administration to deal with grant programs in a consistent manner during this interim period. Noncompeting grant applications are being taken as continuations of grant applications, so that if a grant started before December 1, it is being moved to a December 1 start date to extend beyond the continuing resolution. Noncompeting grants are being renegotiated at a 12 percent reduced level. No new awards are being made and new grant applications that are approved with a good priority score are being delayed until the budget decision is made. Competing renewals are being funded at the levels of the preceding years. No new supplements will be awarded during this interim. All new investigator awards (R23s) will be awarded at the recommended levels when the NCI commences to award them. If they are competing renewals, they will go through the small grant application procedure. CORE grants--P30s, R01s, and P01s are being renegotiated at the 12 percent reduced level.

Hearings and Publicity. According to the television series "20/20," there was no improvement in cancer survival between 1955 and the present time. This conflicts with the SEER data just presented to the Board.

Concerning the Washington Post series of articles, the NCI was disappointed by inaccuracies, such as representing the National Cancer Program as a drug development program when in fact the drug program is only 4 percent of the entire NCI budget. The two major issues that were raised in the articles were the therapeutic intent in Phase I trials and informed consent.

The hearings conducted by Senator Paula Hawkins with the Senate Investigation and General Oversight Subcommittee on November 3 covered the issue of drug development.

The second hearing on November 6 was a joint hearing of the House Subcommittee on Health, chaired by Congressman Henry Waxman, and the House Oversight Committee on Science and Technology, chaired by Congressman Albert Gore. At this hearing, the NCI strongly affirmed it complies with the FDA regulations and that the NCI's relationship to the FDA is quite good. The main point concerning the issue of adverse drug reactions was whether in 1978 the NCI

should have alerted the FDA to the possible adverse reactions from methyl-CCNU when it was in the workup phase. According to FDA regulations, the NCI should have notified the FDA prior to the drug's workup. The issue of informed consent has to do not only with written informed consent but also with how physicians explain particulars to patients.

It was concluded that in spite of all the adverse publicity the National Cancer Program has received, the press coverage, in general, has been accurate and fair.

The NCI has been asked to attend, as scientific witnesses, hearings to be held in January 1982 that will focus on food safety.

Questions and Comments. When asked whether the SEER data were complete and could be used as outcome data for comparative purposes, Dr. DeVita replied that the data should be used for incidence and frequency of disease, rather than as outcome data, which are yet to be released. Dr. Amos posited that the Board should be "unalterably opposed" to budget cuts for the NCI, however, it was pointed out that only half the Board responded to the request to prioritize programs in view of future budget cuts.

Annual Report to the National Cancer Advisory Board. The fourth meeting of the NCAB will be in the form of an annual report to the NCAB by Division Directors and by the Chairmen of their Boards of Scientific Counselors. The purpose of the report will be to present all the business of the Institute to the NCAB, to keep the Panel and Boards informed on how the Institute operates so that they can make decisions based on actual knowledge; and to bring out transactions of great concern that have traditionally not been called to the Board's attention.

NCI Changes. Dr. DeVita presented an overview of 22 months of activities that have occurred since he assumed his position in January 1980. Many of these activities were in response to the Hatch Hearings, the Inspector General's 1978 Report, and the Post-Audit Inspector General's Report.

Management Initiatives Accomplished. The entire business management of the Institute is now centralized in the Office of the Director, NCI, within a corporate decision-making body known as the Executive Committee. Each Division has a Board of Scientific Counselors. The contracts management system was moved to the Grants Financial Management Branch, and the Contracts Branch was geographically consolidated.

Senior Personnel Appointments. Appointments made in the Office of the Director include the following: Associate Director for Administrative Management (Executive Officer), Mr. Philip Amoruso; Deputy Director (Acting), Dr. Jane Henney; Associate Director, Dr. Peter Fischinger; and Assistant Director, Dr. Elliott Stonehill. Appointments to Divisions include: Mrs. Barbara Bynum, Director, DEA; Dr. Peter Greenwald, Director, DRCCA; Dr. Richard Adamson, Director, DCCP; and Dr. Bruce Chabner, Acting Director, DCT.

Space. An analysis was done of all NCI space, with program consolidation and reallocation of space against program requirements. There was closure of off-site laboratories, and space at the Frederick Cancer Research Facility is now being utilized for intramural personnel.

Program Changes. The Division of Cancer Control is now the Division of Resources, Centers, and Community Activities, and has been consolidated into one space. Its scientific mission is to develop prevention and community clinical oncology programs and to develop chemoprevention programs. The Biologic Response Modifier Program (BRMP) was established in 1980 by the Secretary, HHS. The National Toxicology Program was moved to the National Institute for Environmental Health Sciences. Four new laboratories were established in the DCCP. As a result, the emphasis was shifted in the intramural program from viral carcinogenesis to a mixture of viral and chemical carcinogenesis. The Radiation Research Program is in the process of being approved. Some $4,000,000 in grants from the NIGMS for imaging research is being transferred to the NCI. The Baltimore Cancer Research Program was converted from intramural to extramural with the concurrence of the Board. The VA Medical Oncology Branch was moved to the Naval Hospital.

Uniform Business Practices. The Grants Administration and Grants Financial Management Branches were transferred to the Associate Director for Administrative Management so that, as a policy is instituted, it will impact equally on both the contracts and business management level.

Position Review. The entire NCI is undergoing a staff review to reallocate positions against high-priority programs. Since the National Cancer Act was passed in 1971, the budget has grown by more than 200 percent, but the number of positions has only increased by approximately 25 percent. Positions have had to be reallocated to all the new NCI programs since no new positions are forthcoming.

Role of the Board of Scientific Counselors. The BSCs have budget overview responsibilities requiring an appropriate mix of individuals from different specialities to reflect the responsibilities of the Division. They perform concept review of all new and current programs, including interagency agreements. BSCs select groups of advisors from outside the NCI to conduct two to three-day site visits of intramural branches. They also have responsibility for expanding their subcommittees in order to develop new programs.

Contracts. Dr. DeVita provided copies of the following documents to each Board member: The National Cancer Institute Contracting Process, and The Peer Review of Contract Proposals at the National Cancer Institute. The NCI did a contract cost analysis and pulled $40,000,000 from contract programs and redistributed it to other programs. Also, the Frederick contract is being reduced by 29 percent. The $20,000,000 allocated for intramural resource and support contracts is being reduced by 20 percent. Contracts that supply resources to the extramural program have been put on a payback provision.

Contracting processes have changed in three areas: review, program management, and contract management. Concept merit review is now required of all contract projects. All contracts reviewed are handled uniformly in DEA, and new peer review groups have been established. Contract categories were reclassified

to conform to the review process. The Contracts Review Branch was created with appropriate staffing. The position of Chief Project Officer was created in each Division to ensure that the Project Officer adheres to contracting procedures. The Justification for Non-Competitive Procurements, was made more restrictive. The NCI established Contract Administration Review Teams (CART) to audit contracts management in the Contracts Review Branch. The tracking information systems for annual progress and financial reports are being updated. Procurement planning has been improved because concept review by BSCs enables the Research Contracts Branch to plan for the year. Project Officers have set up plans for site visiting contractors. Advice of peer reviewers on contract programs is now uniform.

Corporate Budget Formulation and Decision-Making Process. This process involves two three-day retreats. In February, the Director of NCI and the Division Directors and their main administrators meet to discuss general budget policies and Division Directors begin formulating their program budgets and setting their program priorities. At the July retreat, the same staff meet to review each of the Division's budgets and priorities, each contract being proposed, new RFAs, and new program plans, and to shift money between Divisions. In September and October, the Divisional BSCs meet to review Divisional budgets and the NCAB reviews the budget. In November, Division Directors and BSC Chairmen present annual reports to the NCAB.

Budget and Priorities. From 1979 to 1980, NCI's budget was increased by 6 percent--from $931,000,000 to $998,000,000. The year 1981 resulted in a budget decrease of nine-tenths of one percent to the current level of $989,338,000. The cumulative increase between 1979 and 1981 is 5.7 percent.

NCI priorities are research projects, R01 and P01 grants, because they support innovative investigative research. In 1979, contracts were $231,014,000 in 1980, $231,346,000; and in 1981, $201,431,000 (a reduction of 12.9 percent). Research contracts dropped from $76,261,000 in 1979 to $38,428,000 in 1981, a reduction of 49.6 percent. Resource contracts dropped from $111,412,000 in 1979 to $103,860,000, a 6.8 percent reduction. Ongoing contracts were substantially reduced to allow for the creation of new programs. Interagency agreements have been reduced by 18 percent. Intramural research has received the same priority as recent projects and has had an 18 percent cumulative increase over two years. The most vulnerable part of the NCP is the day-to-day supplies and services of the laboratories on campus. A 12 percent cut in the intramural program would reduce other projects approximately 30 percent. The current budget level is $989,338,000; however, the Divisions have been operating all year at the level of $1,025,000,000. The DCBD has seen a substantial increase due to research trends in the area of hybridoma. Grants within this Division get good priority scores and are widely funded. The DRCCA and the DCT are relatively flat in funding growth. Within the 37 percent increase based on the President's budget, research grants would go up 4.6 percent, cancer center grants would increase by 5.8 percent, and the Organ Site Programs would be reduced by about 3.3 percent. Clinical cooperative groups remain stable. Research Career Awards and the Clinical Education Program would receive about a 5.3 percent increase, and in-house operations, which include the intramural program, the DEA, and the OD are increasing by 8 percent.

NCI Business Practices. NCI business practices include the following: a weekly Director's scientific seminar; a daily OD staff meeting to implement policy related to OD programs and to conduct day-to-day business; a weekly Executive Committee meeting to discuss policy, budget, resources, and allocations; and a biweekly meeting of the Director and Associate Director for Administrative Management with the Administrative Officer and the administrative staff.

Budget Allocation. NCAB and the Panel are responsible for budget allocation and setting program priorities. Program development of the budget is done by the Divisions and their BSCs. Allocation of resources for individual projects is done according to merit by the DEA, its peer review groups, and the NIH's peer review groups.

Frederick Cancer Research Facility (FCRF). Some 18 months ago, the divisional BSCs decided to recompete the Frederick facility contract. The contract is being recompeted at a 29 percent reduced level. Because of the criticism in the Inspector General's report, it is being split into five component parts, two of which will be small business set-asides. Alternate science proposals will be considered. The facility is managed by an Associate Director in the Office of the Director. A resident manager position has been instituted and all scientific programs have been integrated into one. Through these reductions, intramural scientists from off-site locations could be relocated to the Frederick facility. The Biologic Response Modifier Program and a small clinical unit are now located there.

Report on the Frederick Cancer Research Facility--Dr. Peter Fischinger
This is the last year of the five-year contracts for the Frederick Cancer Research Facility, which employs 854 Litton Bionetics (LBI) employees at a cost to the NCI of $19,500,000. The LBI contract for science deals with five different scientific programs, which represent parallel ongoing programs at the Institute. A major function of the FCRF is support of the NCI intramural program.

The NCAB and BSCs will be involved in establishing numerical ratings for the absolute quality relative to the revision process of the scientific portion of the contract. The quality of the scientific work at Frederick must be compared to the NCI intramural program and redundancies eliminated. Steering committees composed of chartered members (scientific experts), Board members, and members of BSCs, will make reviews in May. The incumbents are likely to submit proposals for the scientific, support, and animal production facility programs. Alternate proposals, due December 14, are being accepted to widen the scope of science. In addition to LBI, a local university is expected to submit a proposal for the scientific portion of the contract.

Questions and Comments. There is a fiscal lid under which offerors must work. The question of salaries of LBI employees who transfer to another bidder's company was posed; the NCI does not interfere in specific salary negotiations. The legality of the staffing practices being followed by offerors in response to the RFP was questioned. The response was that this is a non acceptable service-type contract. Further questions addressed what

criteria would be used to evaluate the staffing and scientific quality of an offer, if, hypothetically, all offerors can list a staff identical to the present one.

VI. Report of the Director, DEA -- Mrs. Barbara Bynum

The DEA's responsibilities include the administration and coordination of the peer review activities for NCI grants, cooperative agreements, and research, resource and intramural support contracts. The Grants Review Branch and the Contracts Review Branch have responsibility for assignment, review, and preparation of summary statements and summary reports.

NCI Review of Grants. A grant is initiated by the investigator, although it may originate in response to a Program Announcement. The NIH Division of Research Grants then assigns the application to a categorical BID and to an IRG, which may be one of the DRG's chartered study sections or one of NCI's five chartered grant review committees.

When NIH receives a grant application, an NCI health scientist administrator within the appropriate Divisional program is designated as the application's Program Administrator (PA), and is responsible for following the progress of that application through the review process, and, if an award is made, through the post-award period. The PA negotiates, advises, and advocates the grant, evaluates the relevance of the research, considers the appropriateness of the IRG, and makes recommendations to this Board. The IRG reviews the application for technical merit and forwards its recommendations to the NCAB, which completes the review process. All applications that request more than $35,000 per year require NCAB concurrence. NCI staff then meet with Division Directors to discuss and review recommendations and make funding decisions. Site visits may take place prior to the chartered review group meeting or after the meeting. This review cycle, which takes about 10 months, occurs three times a year.

NCI Review of Contract Proposals. Additional administrative and legal requirements for the award of contracts are governed by Federal and departmental procurement regulations. An NCI program staff member develops a concept for a project which is subjected to a series of internal program clearances and to review by the Boards of Scientific Counselors. Concept review includes appraisal of the substance of the proposed effort, as well as consideration of its level, scope, and the most effective and appropriate funding instrument.

Once the concept is accepted and recommended for implementation, a project plan is formulated by the Project Officer in the Research Contracts Branch. A Request for Proposal (RFP) is prepared, defining the scope of the work and the evaluation criteria. All proposals received are checked by the contracting and program staffs to ensure completeness and are then forwarded to the Contracts Review Branch for supervision and administration of the technical merit review.

A contract proposal is reviewed for scientific content and technical requirements by one of the five chartered peer review committees or by an ad hoc committee. A Source Selection Group then advises the Contracting Officer on a competitive range based on both scientific and financial considerations.

The Contracting Officer makes the final decision and arranges for negotiation with the prospective contractor. The total contracting cycle requires upwards of eight or nine months.

There is also an authorized committee of Federal employees which reviews intramural support activities; it comprises two subcommittees. This committee is formed as dictated by conflict of interest considerations, by the need to adapt to excessive workloads, or by the need to be responsive to a particular contracting requirement.

Questions and Comments. It was asked how the chartered committee balances the science of a proposal against its cost. Mr. James Graalman explained that there is no formula for weighing technical scores and capabilities against the cost. The question of estimating costs for a proposed piece of work was clarified by pointing out that when BSCs review the concept of a proposed project, the dollar amounts postulated are estimates. Dr. Janet Rowley asked if the BSCs that approve a concept have additional input regarding whether a project clearly addresses the original concept. Since BSCs serve for four years, they see the results of a project when it comes up for recompetition. A Board member queried whether the time frame for funding could be reduced if a project was urgent. Proposal time and selection time could be condensed, but technical evaluation time could not. The issue was raised concerning favoritism of the incumbent, as exemplified by the Frederick contract. If a contract is recompeted, it will be done without favoritism.

A Board member asked if approved concepts should be published in advance of an RFP, since some potential offerors learn late that an RFP has been issued. To respond to this situation, NCI is considering extending the period from issuance of an RFP to its final submission acceptance date. However, in most instances, the 45- to 60-day turnaround time has been adequate.

VII. Division of Cancer Treatment Program Review - Dr. Bruce Chabner

Dr. Chabner presented an overview of three basic aspects of the activities of the DCT: its scientific program, its administration, and its budget development for the past year and for 1982.

Scientific Program. The DCT is organized into six program divisions and the Board of Scientific Counselors, which formulates scientific objectives and approves new initiatives. The programs are: Clinical Oncology Program/Medical Oncology Group; Cancer Therapy Evaluation Program; Cancer Treatment and Therapy Evaluation Program (CTEP); Developmental Therapeutics Program; Radiation Research Program; and Biologic Response Modifier Program (BRMP).

The CTEP includes contract, cooperative group and grant activities, and is designed to support therapeutic research and the various modalities of treatment. The Developmental Therapeutics Program is both intramural and extramural. The Radiation Research Program includes a diagnostic branch, a low-level radiation branch, and a therapeutic radiation research branch. It was decided to terminate the Baltimore Cancer Research Program; its funds have been shifted from a P50 grant to an extramural Cancer Center grant.

The BRMP was initiated two years ago to investigate the use of naturally occurring agents such as interferon that modify post-responses to tumors. It is administered through the Frederick Cancer Facility with both grant and contract extramural and intramural components. The total budget for the Therapeutics Development Program is $68,000,000. The largest portion of this program is in drug development where about $45,000,000 is spent on research contracts and $7,500,000 on the early drug trials in the cooperative agreement program. The budget for the developmental aspects of the Biologic Development Program is $8,000,000. The budget for new therapy development in the Radiation Research Program is $5,000,000. There is a small contracts budget of $2,000,000, primarily designated for disease-oriented studies. The entire budget for extramural-supported research is $163,000,000: $120,000,000 for grants and $38,000,000 for cooperative agreements. The total budget for the intramural program is $45,000,000. This budget is evenly split between the Clinical Oncology Program and the Basic Science Research Program.

Administration. The early portions of drug, biologic, and radiation development programs are primarily operated through contracts supported by intramural research and by ideas that come through the grants program. As agents are developed, they enter into limited clinical trials, conducted intramurally by the Clinical Oncology Program and extramurally by the CTEP. Later, large-scale clinical trials of compounds are conducted mainly through the cooperative agreement mechanism, but may be conducted under program project grants. There is also an intramural component for largescale clinical trials, supported through the Clinical Oncology Program.

Budget. The Board's ideas are channeled into the budget process through a review by the Associate Director and senior NCI personnel. After approval by the program staff, a concept will be reviewed by the BSCs and issued either as an RFP or RFA. The budget process begins in January, when special issues and ideas are taken into consideration in projecting the next year's budget. In May, the plans for the subsequent year's budget are conceptualized and finalized in an annual review by the Director and Associate Directors. Program Directors submit and defend their budget proposals and draw up a tentative budget. This budget is presented in July at the annual NCI Director's retreat where all Division Directors defend their Divisions' programs. The budget formulated at this retreat is presented to the BSC in October at the beginning of the fiscal year, when contract concept review is continued and additional concept review is begun for the subsequent year's contracts. The budget agreed to by the BSCs is presented for final approval at the December NCAB meeting.

Questions and Comments. Dr. Amos asked if the BSC is informed about the non-contract intramural program and the grants extramural program. Dr. Chabner pointed out that the BSC is made aware of the intramural program through the site-visit program that occurs on a four-year cycle basis. They are made aware of the total budget for grants. Areas of major support are systematically examined by special Board presentations. A question was raised concerning whether major internal organizational changes are done in consultation with a board. Both Divisional BSCs and the NCAB are presented with options under consideration. In response to a question concerning the appropriateness

of expertise and the capabilities of BSC to do a concept review for OD contracts, it was explained that a program temporarily housed in the OD, such as the Radiation Research Program, may need to be BSC reviewed for the OD but once it is in place within a Division, Divisional BSCs have the appropriate expertise to review the proposed project's subject matter.

Administrative and Scientific Highlights. The Baltimore Cancer Research Program will phase out in the spring of 1982. A $1,900,000 P50 grant for funding this Center was approved at the close of business FY 81. In the CTEP, a number of active new drugs were identified in the Phase I and Phase II trials with several drugs showing serious toxicities. The toxicology protocol was revised, streamlined, and approved by the FDA in October, and the cooperative agreements were initiated in August 1981. Issues raised concerning cooperative agreements include the right to disapprove protocols that were not safe or presented undue risks to the patient, and the right to withhold funding for studies that duplicated ongoing work. Under the revised procedure for reporting adverse drug reactions, NCI advises FDA immediately.

Important scientific activities of the BRMP include initiation of the genetically engineered interferon trials and issuance of several RFAs dealing with monoclonal antibodies and lymphokine research. Major administrative actions include transferring the Laboratory of Immunodiagnosis to the DCT; initiating the inpatient unit at Frederick Memorial Hospital; and consolidating BRMP extramural and intramural operations in Frederick. Important scientific developments of the Developmental Therapeutics Program include isolating the T-cell lymphoma leukemia virus and phasing out contract acquisition of new plant derivatives from the Drug Development Program. The $2,500,000 pulled from this program will be used to develop centers for drug development research in universities and institutes. Most of the active compounds received by the NCI are voluntary submissions of plant products, although the NCI also has 400 discrete commercial agreements for synthetics. The NCI is examining a cost-sharing relationship with industry for drug testing. A laboratory of experimental pharmacology has also been created.

In the clinical program, major scientific achievements include therapy of soft tissue sarcomas and characterization of hormone-resistant mutants. Important administrative actions include opening new laboratories in an outpatient area and establishing the Radiation Research Program.

Budget. For 1981, the total budget was $272,000,000. One major component is the Radiation Research Program ($44,000,000). The BRMP budget was $14,000,000, and will increase by $7,000,000 in 1982. The Baltimore Cancer Research Program's budget of $5,800,000 will decrease to $3,600,000 in 1982. The CTEP budget (clinical arm) was $89,000,000 and is estimated to be $88,500,000 in 1982. The Clinical Oncology Program will have a budget of about $500,000 less in 1982. The Developmental Therapeutics Program will be reduced in FY 82 to $92,000,000.

The grant portion of the budget was $159,800,000 in 1981. The overall grant budget for 1982 is $125,400,000, due to $35,000,000 being shifted to the cooperative agreement. The 1982 cooperative agreement budget is $44,000,000. The contracts budget for 1982 will be decreased by $5,500,000. The intra-

mural research budget will decrease by $2,700,000 to $274,000,000.
Questions and Comments. A question was raised whether it would be more economical and efficient to have some extramural contract work done intramurally. NCI does not have the positions available, and, because the work flow varies, it would not necessarily be economical to hire permanent staff. Furthermore, the NCI information system needs are so extensive that they could not be supported by an intramural staff. A question regarding the travel of patients and their families to treatment centers was clarified by describing the Special Ambulatory Care Program in which travel monies are budgeted for each of the clinical branches of DCT. A proposal was made that certain protocols be identified that could be performed in centers near the patient's home.

CCIRC is newly organized into two study groups. One will review the new regional cancer center groups as one package. The clinical trials applications will be reviewed randomly by both groups. Previously supported nutrition work is being phased out.

VIII. DCT Board of Scientific Counselors--Dr. Samuel Hellman

Members of DCT's Board of Scientific Counselors have expertise in various basic sciences and clinical specialties associated with cancer. The Board is appointed by the Director of DCT in consultation with the Chairman of the Board, and serves terms of 2-4 years, after which a year must elapse before possible reappointment. There are two ad hoc subcommittees: the Surgical Oncology Research Development Subcommittee and a Subcommittee on the Biological Response Modifier Program. The Board advises on new program initiatives; evaluates the intramural scientific program and performs site visits; reviews the concepts for grants; hears scientific presentations of interest to the DCT, advises on problems presented to the Board; and initiates some new activities.

Implementation of Site Visits. Site visits of intramural programs are done every four years; a report is written and presented to the BSC in a closed session. The results of the BSC's discussion are made known to the head of that program, who is responsible for relating the Board's recommendations to the specific laboratory chief. Follow-up is presented to the Board.

Science and Program Review. Scientific presentations have been made to the Board on the BRMP, the GI tumor study group, science under way in the intramural program, soft tissue sarcoma protocol, drug development review, toxicology protocol, the particle beam theory, bovine ocular carcinoma, and the human protein index.

Concept Review. The BSC reviews a concept to ensure that it meets the goals set forth and is an important part of the program, that the mechanism of the contract is appropriate, that funds are adequate, and that the time for the contract is reasonable.

Questions and Comments. Board members stated they would take budget cuts selectively if they could. Areas singled out as being least meritorious for support were nutrition, disease-oriented contracts, and the Baltimore Program.

A Board member questioned whether any DCT programs support nurse oncologists, and was told that cooperative group funds have been appropriated for support of statisticians and chemotherapy nurses. It was then proposed that a nurse oncologist be appointed as a member of a BSC. The response to whether the cuts can be made only from the areas of low priority was that if there is a 12 percent cut, not all good contracts or grants could be spared. Contracts would be cut first, the grants and intramural programs would be treated equally and would take sizable cuts, and excess funds from the Drug Development Program would be cut. Dr. William Powers asked if and when the BSC was involved in producing the cooperative agreement document and why Phase I and II trials were not considered part of the cooperative agreement. One of the major leaders of the cooperative agreement was a BSC member; the BSC has had input throughout the formulative stages and in its modifications and final approval.

IX. DCT Scientific Presentation -- Dr. Robert Gallo

Some of the major efforts put forth by DCT to determine how cells become leukemic and what the essential differences are between leukemic and normal cells were discussed. Several years ago, DCT began studying Type-C viruses that cause leukemia and lymphoma in chickens, wild mice, cats, cows, and the gibbon ape. For several years, evidence of any relationship of these viruses to human leukemia was inconclusive. Within the last five years, it has been established that the Type-C virus is not transmitted as an extracellular virus, but rather by cell-to-cell contact. The T-Cell growth factor that was found approximately five years ago allowed researchers to grow mature T-lymphocytes in vitro.

Researchers found that the first two isolated human viruses were the same. After numerous tests, it was concluded that the virus could not be an animal laboratory contamination. Moreover, the patient was found to be the source of the virus. The next step discerned that the virus was not endogenous to humans or to specific populations. Researchers are now looking in various parts of the world for antibodies specific to proteins of this particular virus as evidence that a given patient has been actively infected and probably has integrated sequences. Thus far, there has been limited success in linking viruses to particular geographic regions. Researchers are trying to probe two major points: that the virus is always present; and that when penetration, synthesis, and integration of the provirus occur and it integrates upstream for the T-cell growth factor, the cell proliferates at an abnormal rate and is involved in the first stages of disease. Advances in this area are expected during 1982.

X. Association of Community Cancer Centers (ACCC)--Dr. Herbert Kerman

Dr. Kerman outlined the ACCC's objectives and goals: 1) to contribute to improved care for cancer patients in all areas of cancer intervention; 2) to encourage and assist with the development of community cancer programs; 3) to exchange information related to community cancer program establishment and improvement; and 4) to provide a national forum and a unified voice for causes of community-based cancer institutions and health care professionals. Representatives of institutions or organizations having multidisciplinary

The National Cancer Act of 1971 promoted the designation of cancer centers. The cancer centers are broadly classified as comprehensive cancer centers (20), specialized clinical centers (about 50), academic clinical centers (123 or 124 medical schools), and more than 1,000 community cancer centers accredited by the American College of Surgeons (ACOS). The ACCC has developed from this resource of organized community, clinical oncology groups. Necessary to initiate a community cancer center program is a "change agent," in individual, group, or committee who can develop a cooperative multidisciplinary and multimodal technology with facilities, resources, and services to apply in all intervention areas. Guidelines specify a community cancer center program requires a multidisciplinary cancer committee responsible for a tumor registry, tumor conferences, consultative, diagnostic, and treatment services including surgery, radiation therapy, and medical oncology, and quality-of-care evaluation. The ACCC program also has optional components for ideal comprehensive community cancer centers: patient management guidelines, outpatient clinics, psychosocial support, hospices, rehabilitation, cancer patient education, community education, education for professionals, allied health professionals, and community outreach, pain clinics, family support groups, and screening groups.

The ACCC delegate institutions served 135,000 new cancer patients in 1981, an increase from 115,000 in 1980. An estimated 20 percent of all U.S. cancer patients are treated in ACCC delegate institutions. Twelve percent of these institutions receive Federal funds for participation in cooperative study groups or supplemental funding by cooperative groups, or participate in the Comprehensive Cancer Centers Program. Two receive funding through the Community Oncology Program. Twenty-three are funded from the Community Hospital Oncology Program (CHOP). Most activities are funded by each institution's own reimbursement sources.

Liaison activities of the ACCC are reflected by its Board's inclusion of representatives from the Oncology Nursing Society and the Association of American Cancer Institutes (AACI). The ACCC president is a liaison member of the ACOS Commission on Cancer. Indirect liaison activities relate to the NCI, American Cancer Society, the American Association of Cancer Research and ASCO. Joint activity, as with the AACI Progress in Cancer Control meetings, is increasing. ACCC has also expended effort in continuing support of the National Cancer Program (NCP). This is accomplished through influence that resulted in emphasis on community care in the 1978 amendments to the National Cancer Act.

Essential to the NCP research effort is the sustained flow of patients into clinical trials. Eighty-five percent of cancer patients are now being treated in community hospitals. ACCC has now appointed a Clinical Research Core Committee which has developed a needs assessment and consensus of support for Community Clinical Oncology Programs (CCOPs).

The 1980s role of the community cancer centers is to better identify high-risk cancer profiles and to target screening and preventive measures. These measures are associated with selected occupational and environmental groups and increase public and professional awareness of cancer. They become an added dimension in research as well as control.

Dr. DeVita said that conducting research with cancer control funds posed no problems in the past if it occurred under the supervision of a particular advisory council. Further concerns were raised: 1) community hospitals' problem of getting sufficient numbers of patients with particular forms of cancer, 2) dividing the national protocols to suit various community cancer centers, 3) referrals from unofficial physicians, and 4) organizing cooperative ventures to study certain therapies.

XI. American Association of Cancer Institutes (AACI)--Dr. Richard Steckel

Founded in 1959 by a group of cancer center directors to share ideas on the development of cancer centers nationally, the AACI meets twice annually. Nationally the AACI includes 65 centers (45 specialized and 20 comprehensive) and several corresponding centers overseas. These centers foster interdisciplinary research collaboration and multidisciplinary patient care. They serve as a focus for professional education, community cancer control activities, and public information. Data from clinical admissions are shared among all 20 comprehensive centers and an institution in Seattle, where the Clinical Cancer Patient Data System (CCPDS) and intercenter research projects are being promoted. AACI focuses on academically based centers and categorical research institutes rather than on community cancer centers.

Basic Research. Dr. Peter Magee, Director of the Fels Research Institute, defined a "cancer center." It is a distinct entity dedicated to discovering new knowledge about cancer. It is either a component of an existing university or other educational institution, or may be a freestanding entity, interdisciplinary in nature. Centers provide a focus of activity on cancer research and participate in education on new approaches to cancer prevention and treatment. It will never be possible to reduce all exposure levels of detectable carcinogens to innocuous levels; therefore, methods should be developed to prevent cancer promotion. This includes agents that would inhibit activation of clinical carcinogenesis. In the area of treatment, great basic research advances have been made in anesthesia and patient support in surgery, knowledge of basic cell kinetics in radiation therapy, synthetic and natural chemical agents in chemotherapy, and development of monoclonal antibodies in immunotherapy.

Patient Research and Clinical Care at Cancer Centers. Dr. Gerald Murphy of Roswell Park presented a summary self-assessment by 47 of the cancer centers within the AACI. It reviewed activities of those extant prior to 1971 and of all since 1978. Of 1,800 specific achievements reported, 52 percent were in basic science, 40 percent in clinical investigation, with some overlapping in both areas. Approximately 57 percent of those considered outstanding in clinical areas specialized in treatment; 29 percent in detection and diagnosis. Forty-three percent involved work of more than one person or group within the centers. In some cases the presence of a center program has led to involvement in Phase I and II trials that otherwise would not have been attempted.

Demonstration programs developed at centers have become group projects that further promoted cancer care. New developments cited as specifically center-related include interferon, the Biological Response Modifier Program (BRMP)

stimulated by NCI, bone marrow transplantation, advances in hypothermia, the neutron program, and LET. The Drug Development Program, DCT, is the foundation for drug development in the centers.

The Importance of the Core Grant. Dr. Steckel commented that the core grant at a center, whether for research or control, is justified only by the existence of program research and individual projects at that center. It binds the diverse efforts of the 40 or more specialized and 20 comprehensive centers around the country and provides central administrative support. Core grants undergo rigorous multidisciplinary peer review and are an element of stability. They draw additional support for the centers from the community and the institutions themselves. Despite this, they are presently being funded at considerably less than the recommended level. Several questions regarding the future of core grants were raised. 1) What, if any, is the optimal number and distribution of cancer centers nationally? 2) Is geographic setting more important for clinical centers than for basic science centers? 3) Is there a need to optimize patient resources and to avoid underserving patients? 4) Can the mechanisms for peer review be improved?

In a discussion of possible funding cutbacks, a liberal phase-out plan was recommended. Current phaseout support is being given those programs within the previous year's pay range, but there is no support for phase-out of those programs below that range.

There is a question of whether to support all present centers at a decreased level or to limit the number of centers. Optimal funds will be provided to those considered more valuable. Centers need to use core grants while seeking alternatives to Federal funding. It was emphasized that the NCI program has been considered uniquely successful by international groups in developing comprehensive cancer centers associated with community cancer centers. Efforts are being made to duplicate the program.

XII. Report of the Subcommittee on Planning and Budget--Dr. Frederick Seitz

The Subcommittee met November 30 to discuss the 1982 budget; it is hoped the cutback will be no more than 4 percent. There was almost unanimous agreement that any cuts should be selective, rather than across the board; however, there was disagreement on the desired pattern of cuts. Discussion of the R01, P01, and center funding cutoff levels did not resolve the issue of the role of centers, which, in serving the community, in turn encourage community support for cancer programs.

XIII. DCBD Program Review--Dr. Alan Rabson and Dr. David Korn

The Division of Cancer Biology and Diagnosis (formerly the NIH Intramural Program), is the oldest of the Divisions, having always had a Board of Scientific Counselors to review intramural laboratories, then having expanded to include extramural programs, contract programs in diagnosis, and the Breast Cancer Task Force. DCBD science focuses upon regulating gene expression and the immune system (particularly defense against tumors) and, in diagnosis, imaging research concerned with detecting and demonstrating the products of abnormal regulation.

Organization. The Division is headed by the Office of the Director, its Board of Scientific Counselors, and administrative offices, and then is divided into an Extramural Program, comprising the Cancer Biology Branch (Tumor Biology and Immunology Programs) which receives $110,000,000, the major part of the budget, the Diagnosis and Breast Cancer Coordinating Branches; and the Intramural Program, which includes the Immunology Branch (Laboratories of Immunology, Immunodiagnosis, Cell Biology), the Metabolism Branch (including the Laboratories of Pathology, Molecular Biology, Biochemistry, Pathophysiology, and Mathematical Biology), and the Dermatology Branch.

Research in Programs. Dr. Michael Potter and associates in the Cell Biology Laboratory were cited for the impact of their tumor research technology on all biomedical research, particularly on the development of hybridomas in mice. Major advances have been made in understanding gene regulation and the mechanisms by which it becomes aberrant after neoplastic transformation were described as technological breakthroughs in molecular biology, the ability to clone genes, and to sequence DNA rapidly. These are both intramural and extramural studies. The generation of T-cell mediated cell killing responses are being studied in the Intramural Immunology Program.

Extramural projects highlighted were the cloning of oncogenes within normal cells and cancer cells, protein transformation, tumor cell invasiveness, teratocarcinoma in embryology, the generation of diversity (GOD) in antibody production, natural cell-mediated immunity, monoclonal antibodies (involved in some 70 percent of tumor immunology grants) used in diagnosis, the complex immune response gene, the work on steroid (estrogen) receptors in breast cancer, and immunodiagnostic markers for diagnosis.

Program Plans. The DCBD will continue emphasis on investigator-initiated research, both intramurally and extramurally, through the R01 grant program.

XIV. DCBD Board of Scientific Counselors--Dr. David Korn

Prior to last year's revision of its role, the DCBD Board of Scientific Counselors served primarily as a group of site visitors meeting three times yearly to review intramural programs or the Basic Cancer Biology Program at Frederick. The Board is now taking part in all contract proposal reviews and reviews of RFA and RFP concepts. It was suggested that approval or disapproval of a concept be ranked since some ideas are very good but the issues are not well developed. In terms of intramural efforts, the Board's recommendations resulted in palpable results; however, the Board was frustrated at being able to review only a part of the total Frederick operation or only individual contracts as opposed to the total program supported by the Institutes, which may be duplicative. The BSCs are more effective than advisory groups because the Divisions are obligated to respond to the direction of their boards. Since there are questions about the long-term contracts' continuing usefulness, a group of outside experts is being assembled to review and pare them annually.

XV. DCBD Scientific Presentation--Dr. Thomas Waldmann

Understanding the control of antibody production at a molecular level via maturation of a primitive stem cell to a B-lymphocyte, its proliferation to a

plasma cell producing immunoglobulin molecule, aided or inhibited by helper T-cells or suppressor T-cells, is one facet of studying the aberrances in this normal immune process associated with neoplasia. A critical observation is that genetic material for immunoglobulin genes, as for many other proteins, is not a continuous stretch of DNA but chains made up of bits of genetic material quite separate from each other on the chromosome.

Radiolabeling was used to probe genes to examine events occurring in human leukemias. The use of recombinant DNA is answering questions about diverse antibody generation and helping categoric leukemias.

Techniques have been developed in which poke weed mitogen simulates foreign antigens, stimulating B-cell to plasma cell transition; in combination with a helper T-cell; B-cell maturation and antibody production then takes place. It is thought suppressor cells may act to enhance tumor growth, interfering with normal immunological systems that would lead to tumor rejection. It now appears that some immunotherapeutic approaches to the treatment of neoplasia may have activated, rather than inhibited, the suppressor T-cells, although some chemotherapeutic agents are effective as eliminators of suppressor T-cell activity and as tumoricidal agents.

The suppressor T-cell system is critically important in that it prevents the body from making an immune response to its own tissue; when it fails entirely, it may be one of the causes of complex autoimmune disorders as systemic lupus erythematosis. Two approaches have been used to acquire the humoral product of suppressor T-cells that inhibits B-cell maturation: the first is cloning the progeny of a single T-cell, and selecting those clones that make large quantities of the desired lympokine that can inhibit antibody production alone; the second approach parallels in human cells Potter's hybridoma technology. In the future, biologically important agents made by these cells may help to manipulate the immune system.

XVI. Resolution Commending Dr. Garb for His Contributions to the National Cancer Program--Dr. Henry Pitot

The following motion was introduced at the beginning of the session:

"Whereas Solomon Garb, M.D., wrote A Cure for Cancer: A National Goal, published in 1968, a book which inspired the National Cancer Act of 1971;

And whereas Dr. Garb made major contributions to the Report of the Panel of Consultants on the Conquest of Cancer under its Chairman Benno C. Schmidt and Cochairman Sidney Farber, M.D.;

And whereas Dr. Garb's counsel as a pharmacologist, physician, hospital administrator, and scientific investigator has been sought by every National Institute Director since 1971;

And whereas Dr. Garb, as a citizen advocate, has effectively communicated to the Congress the needs of the National Cancer Institute for funds, and he has also documented, in terms of thousands of lives saved and through the history of research progress, the justification for appropriations for the cancer program;

Therefore, be it resolved that the National Cancer Advisory Board extends its gratitude and thanks to Dr. Garb for his extremely valuable public service and that these thanks be inscribed in a suitable document along with the Board's hope that the cancer program will benefit in future years from Dr. Garb's activities."

The resolution was passed unanimously by the Board.

XVII. DCCP Program Review--Dr. Richard Adamson

DCCP Mandate. Dr. Adamson explained that DCCP is responsible for planning and conducting NCI's program of coordinated research on cancer cause and prevention.

Managerial Initiatives. During the past year, DCP has undertaken 20 managerial initiatives. Three laboratories--Viral Carcinogenesis, Experimental Pathology, and Comparative Carcinogenesis--moved to the Frederick facility. The laboratories in Building 37 are in the process of consolidation so that laboratories that work together are close together. A space in Building 41 for the Laboratory of Chemoprevention has been identified. All DCCP staff positions have been reviewed in preparation for an Institute-wide review, and DCCP staff promotion review was performed. The intramural site visit procedures were improved and standardized to include laboratory reports on research initiatives, resources, and staffing. Other DCCP initiatives were designed to promote intradivisional communications and cost savings. The DCCP sponsored workshops in undeveloped research areas and held meetings with intramural and extramural branch chiefs as well as a meeting of the 53 section chiefs with the Division Director. Abstracts were compiled for the spring research meetings and circulated to all DCCP section heads and branch chiefs. The DCCP also instituted a payback system for resource contracts and an automated system for budget review for the internal laboratories.

The DCCP also established four new intramural laboratories: the Laboratory of Human Carcinogenesis will identify carcinogen DNA adjuvants in human specimens using monoclonal antibodies, and will perform studies of the metabolic balance between activation and detoxification of various carcinogens. The Laboratory of Cellular Carcinogenesis and Tumor Promotion was established to explore both models and mechanisms of tumor promotion. The Laboratory of Comparative Carcinogenesis (Frederick Campus), will look at interspecies comparisons of carcinogenesis and has a research group studying perinatal carcinogenesis. The Laboratory of Molecular Oncology will study the genetic elements required for molecular transformation and will consolidate within one laboratory interaction between chemical and biological carcinogenesis researchers and people using recombinant DNA techniques. Except for hiring three outside persons, all staff for the new laboratories were transferred from other positions in the Division or from other NCI divisions.

Budget. The DCCP budget expenditures for FY 1981 and estimates for FY 1982 were presented in several formats. FY 1982 estimates were based on the President's budget of $1,260,000,000 and did not reflect any proposed cuts. The program summary showed the following percentage and dollar changes from FY 1981 to FY 1982: Epidemiology, up 3 percent to $48,000,000; Chemical

and Physical Carcinogenesis, up 17 percent to $78,000,000; Biological Carcinogenesis, down 9 percent to $79,000,000; Nutrition up 24 percent to $8,800,000; and Preventive Oncology, up less than the cost of living. The overall budget figures projected a 3 percent increase from a FY 1981 budget of $206,000,000 to $216,000,000 in FY 1982.

The budget by organization within the Office of the Director shows a 3 percent increase in the FY 1982 estimate from the previous year in both the intramural and extramural budgets, up to $37,000,000 and $133,000,000 respectively. By mechanism, funding levels for P01s and in-house programs (covering staff salaries) are going up, while funding levels for contracts and conference grants are going down. R01 funding remains stable.

The Nutrition Program is divided into five or six different thrusts. Twelve P01 grants and 30 R01s were funded in FY 1981. There were approximately eight exceptions to the cutoff priority score for the past year, but none was more than 10 points below the cutoff. A total of 96 concepts was presented to the DCCP Board of Scientific Counselors for review. Of these, 89 were approved, with an estimated $24,000,000 per year passed on to the RFP preparation cycles. All 13 SEER concepts, a total of $10,000,000 annually, were reviewed and approved.

Workshops and Viral Oncology Support. The DCCP sponsored approximately 10 workshops in FY 1981. One conference brought together prominent viral oncologists, who advised the DCCP that it should support the Viral Oncology Program primarily through the investigator-initiated research of R01s and P01s. It is difficult to find grant support for large animal viral oncology models and studies. The insufficient priority for the bovine lymphoma leukemia models was cited as an example of such a problem within the peer review system. Whether or not NCI should continue to support viral oncology models that no researcher wished to use was questioned.

Second Primary Site Studies. Initial findings from DCCP and DCT studies do suggest a relationship between intensive therapies and second cancer risk. An expansion of adjuvant therapy and clinical therapy would thus increase public risk to future oncogenesis. A list for directors of chemotherapeutic trials to use in setting guidelines for patients by disease and therapy was seen as a useful action.

National Toxicology Program. The NTP has shifted to NIEHS, and NTP-related concepts listed in the DCCP review materials are no longer reviewed by the Division. NCI will not fund contracts as of FY 1982.

Epidemiology Program Support. The DCCP has had difficulties funding epidemiology research through the grant mechanism. The large number of epidemiology contracts and intramural projects as opposed to grants reflects this problem, although the SEER program is responsible for $10,000,000 in contract funds. Extramural epidemiology studies are funded through other NCI divisions and HHS agencies; the DCCP had only 34 competing epidemiology R01 grants in FY 1981. Of these, the DCCP funded 64 percent, as opposed to 39 percent of the entire DCCP R01 pool. This reflects the Division's commitment to building a base of epidemiology research in spite of low numbers of applications.

Other factors that tend to counterbalance DCCP's efforts to promote extramural epidemiology research are the proportionally small number of grant applications approved by the study section; the lower status and pay of epidemiologists as compared with clinical staff members; and the reduction of epidemiology training program support.

XVIII. DCCP-Board of Scientific Counselors Program Review--Dr. Peter Magee

Meetings and Other Activities. The DCCP Board of Scientific Counselors first met on October 17 and 18, 1978, and has subsequently met six times. The Board will meet three times a year beginning this year. At the 1981 meetings, a special committee of the Board considered using the cooperative agreement mechanism for the IARC Monographs, while another committee reviewed the SEER Program.

BSC members have participated in DCCP workshops, and several of these meetings have led to RFAs. These RFAs add more than $8,000,000 to the grants program per year.

Dr. Adamson was commended for strengthening the intramural program through reprogramming of resources and personnel and creating new chemical carcinogenesis laboratories.

Streamlining Contract Cost Evaluation. A question was raised regarding the procedure for arriving at proposed dollar amounts for contracts. The NCI staff estimates what it will cost to do a project and present the concept, but the total costs are subject to change. The NCI Budget Office has taken steps to make more uniform costing, including factors such as man-years and indirect costs, part of the project plan.

Cancer Risk Assessment. The BSC was discussed as a possible group to review occupational cancer risk and make recommendations, but not official pronouncements, from carcinogenesis and epidemiological data. Part of the problem in determining risk is the insensitivity of protocols to distinguishing between potential carcinogens and general processes. Regulatory agencies or international boards were viewed as an appropriate place for such discussions. Risk assessment was termed an art rather than a science in most areas--a methodology of choosing between models where a scientific research base does not yet exist.

XIX. DCCP Scientific Presentation: Viral Transformation and the Molecular Elements of Malignancy--Dr. George Vande Woude

There has been much controversy over whether viruses or genetic insults to normal cells initiate the cancer process. Present knowledge of the molecular elements of malignancy suggests both are correct. Techniques have been developed to manipulate DNA and isolate genes responsible for transforming original tumor cells, and 12 acute transforming retroviruses have been isolated. An important feature on the viruses is the long-terminal repeat (LTR), which has transcriptional control properties allowing genes to be turned on, a situation analogous to transposition in eukaryotic transcription. Perhaps the most important feature of the viruses is that each possesses a sequence derived from the host chromosome and referred to as "onc" genes. By comparison of nucleic acids, these genes are shown to be neither

homologous nor related to each other, with one exception. Study of avian and mammalian viruses suggests they contain some similar, interspecies-related genes.

Experiments were designed to show whether Moloney sarcoma virus and its specific gene, "mos," have biological function, and if so, which portions, and whether retroviruses should be considered transposable elements. Tests of the internal portion of the viral sequence alone revealed low transforming efficiency; after reconstruction of the molecule containing the sequence, biological activity was restored 1000-fold; and high transformation efficiency was achieved in hybrid reconstructions between the LTR sequence froim the virus and the cellular mos gene, indicating that LTR alone was sufficient to activate the transforming potential of a normal cell gene. A number of different models have been developed from these data, and they have been utilized in meth-A tumor cells. Approaches of this kind will in the future provide information on genetic insult as a cause of tumorigenesis and on new reagents useful in clinical diagnosis.

XX. DCCP Program Review, Field Studies on Cancer Mortality--Dr. Joseph Fraumeni

Dr. Fraumeni presented cancer atlases that displayed geographic patterns of cancer incidence among particular populations. He began by explaining that tobacco smoking is a principal hazard to man. In addition, there is evidence that smokeless forms of tobacco are carcenogenic. One map for cancer of the mouth showed high rates among non-smoking women who live in rural southern counties.

Dr. Fraumeni pointed out that alcohol potentiates the effect of tobacco smoke on cancers of the mouth, pharynx, esophagus, and larynx. However, studies indicate that the risks for esophageal cancer are much higher among black males residing in urban areas. Results of a case control study of blacks in the Washington, D.C., area showed that the dominant risk factors were alcohol consumption and nutritional deficiencies, not smoking.

Ultraviolet radiation from sunlight is the major cause of skin cancers, including melanoma, and accounts for the high incidence in the southern part of the United States. Studies of several melanoma-prone families have identified a heritable precursor syndrome consisting of multiple large variably pigmented moles. In all, 31 new primary melanomas were detected; all but one are surgically curable.

High rates of lung cancer have been found among men in the urban Northeast, in rural counties along the Gulf of Mexico, and along the southeast Atlantic Coast. Case-control studies were undertaken in Georgia, Virginia, and Florida. Findings showed high risk among shipyard workers who were heavy smokers.

The distribution of bladder cancer also appears to be influenced by the location of certain occupational groups. The map for white males showed that rates for workers in the chemical industry were high in New Jersey, in urban areas around the Great Lakes, in southern Louisiana, and in rural areas of New York and New England. Case control studies have been undertaken to examine the possible influence of saccharin and the role of drinking water quality.

International correlations and migrant studies suggest that dietary factors may contribute to a large proportion of certain cancers. As a result, a study of colon cancer in Southern retirement areas has begun in an attempt to shed light on nutritional determinants and other possible influencing factors.

XXI. DRCCA Program Review--Dr. Peter Greenwald

Dr. Greenwald, who recently assumed his position as Director of DRCCA, listed the Division's key elements: cancer centers, community oncology, education, and, in the future, preventive medicine programs.

The DRCCA program is based on belief in the scientific method, i.e., close observation, measurement, and quantitative analysis, which can be applied to preventive medicine, management, the laboratory, and the clinical sciences. The program is aiming for a good quantitative basis and scientific method in the field of cancer control. The program believes in building on cancer control improvements, as in treatment, mammography, increases in the number of medical oncologists participating in the NCP, increases in worker awareness of carcinogens, decline in cervical cancer, and reductions in smoking among middle class men.

National Priorities. The program is in the process of setting national priorities in terms of measurable goals. This can be done with cervical cancer, lung cancer, smoking, some occupational areas, and wherever there have been clear improvements in treatment. Where information is insufficient for setting long-term objectives, more specialization and step-wise thought processes are needed. For instance, Phase I in applied cancer prevention and screening would be development of a hypothesis or screening methods. Phase II would be to test the components or technology in order to conduct case control studies, to establish cause and effect relationships, and to conceptualize the population impact for a realistic, cost-effective program. Data systems on studies in progress need to be tuned to track research efforts.

Organizational Structure. A model organizational structure for a successfully applied research effort could be found in Bell Laboratories. There are three planks to their success: in-house capability for leadership, strong interface with research conducted elsewhere, and a clearly stated mission. At present, approximately 3 1/2 percent of the Division's budget is allocated to in-house funds, which is not an adequate proportion.

Within each of the three major programs, the Division proposes to have a biometrics group in order to learn what exists, to monitor progress, and to aid in analysis and a chemopreventive and nutrition program. In chemoprevention, only RFA's for grant-supported research are planned. A program is planned to ensure that hypotheses are being tested and refined for the sites, areas, and populations where observational leads exist. A laboratory component is needed that bridges efforts of identifying inhibitors with what is safe, what is toxic, and what is a dose level. Individuals need to be recruited to fill three Associate Directors' positions.

The Preventive Medicine Program is largely geared toward screening efforts and radiation safety. The Behavioral Medicine Program is mainly focused

on the smoking problem and on other areas such as attention to pain. The Occupational/Cancer Program is largely focused on providing information to workers in a way that they can react to it. The Centers and Community Oncology Program is composed of the Cancer Centers Branch, the Research Facilities Branch, the Organ Site Program, and the Community Outreach and Rehabilitation Branch.

The Community Clinical Oncology Program was developed by a committee of the Division's BSC. The Program has the following specific objectives: to bring the highest quality cancer care to the American community; to bring the resources of the community hospitals and clinics into national clinical cancer control research programs; to develop and improve methods for transfer of cancer management technology from academic centers to community clinics and hospitals; and to conduct cancer control research at the community level.

Possible CCOP objectives are setting and implementing national cancer control treatment priorities; considering self-selection and its impact; testing the diffusion hypothesis; and developing a professional public education network. The educational program is composed of the Educational Research and Evaluation Branch, which includes cancer information services; the Clinical Manpower Branch, which provides support for schools building new oncology training programs; and the Research Manpower Branch, which supports research fellows. A Career Development Branch may be developed in which intensive training programs would be conducted.

Evaluation of large programs is also under consideration. A Divisional name change is being considered. The BSC is conducting in-house site visits of every aspect of the program and is actually developing some concepts. Some thought should be given to the overlap of functions of the Divisional BSC and the NCAB.

Questions and Comments. The monograph developed for physicians and physicists on basic radiation criteria and mammography was actually produced under contract with the National Commission for Radiation Protection.

The long-term follow-up of the breast cancer screening project will be continued to a point of statistical determination at which data are developed in an interpretable way. The annual expenditure for this project will be about $3,006,500. It was pointed out that in 1972, some 280,000 women were recruited for this project, but in 1977, the parameters of the project were changed so that only 59,000 women would be followed--mainly by postcard. Many of the women in this project feel cheated. The critical issue raised in 1977 by the Bioethics Subcommittee under Sister Farley's direction was that mammography itself might have caused cancer and, in view of this, free follow-up examinations should be conducted. Much of the data collected for this demonstration project were in response to public pressure, rather than good scientific judgment, so what is now being done is an attempt to interpret data from a poorly designed project. Over five years, $15,000,000 will be expended on this demonstration project.

Budget. The $57,600,000 cancer control share of the Division's $186,700,000 budget is distributed among centers, community oncology and the cancer control program (49 percent), prevention (32 percent), education (1 percent) and administration (8 percent). Major expenditures under prevention include radiation physics centers and DES programs, an interagency (with OSHA) worker awareness program, the anti-smoking behavioral program, cancer communications networks, and medical school prevention course development. In screening, breast cancer follow-up receives priority funding, followed by cervical cancer. The Cancer Centers Patient Control Data System is funded at $2,400,000, and further development of this resource is recommended. Community outreach programs receiving funding include the CHOPs, clinical cooperative groups, cancer center CORE grants, and organ site programs. Two nutrition awards and some grant-supported research in chemoprevention were also funded. Thirty-four percent of grant applications in cancer control were recommended for funding; the cutoff level priority score was 200.

XXII. DRCCA Board of Scientific Counselors--Dr. Stephen Carter

The membership of the DRCCA Board of Scientific Counselors comprises center directors, community physicians, and persons having background in education and psychosocial and epidemiologic research. Focusing its attention on cancer centers and their CORE grants, the Centers Committee has also addressed the issue of basic science CORE grants and will be considering the number and geographic distribution of centers.

Chemoprevention is a another area of interest, and workshops have been held on the subject. A variety of potential chemopreventive agents and preclinical chemopreventive compounds have been investigated. One decision to be made is the balance that should exist between clinical study of available compounds and a drug development program. Some 13 chemoprevention study protocols in the United States and abroad have been reviewed.

Cancer control has occupied the most of the Board's time and the Division budget and should remain a high priority of the National Cancer Program. The concepts of "defined populations" for cancer control and new guidelines for research are going to be extremely important. The newest resources for cancer control are the Community Clinical Oncology Programs (CCOPs), which represent symbiosis of patient care and clinical research; the CCOPs and Clinical Cancer Research Units (CCRUs) can further work together on defined populations whether geographic or specific target groups.

An Occupational Cancer Committee is now being formed to study that aspect of cancer and another committee will assess education efforts within DRCCA. In this manner, in-depth assessment of the Division's entire program is planned. It was suggested that the BSC and NCAB work together to avoid duplication of program efforts, and the cooperative efforts necessary by Divisions with overlapping interests were stressed. The length of time a project must be pursued, and therefore funded, to be valid was discussed. Inasmuch as it sometimes takes many years for a community program to become well-rooted, initial grants of at least five years are deemed necessary. The final decision on national protocols in clinical trials in cancer community control is not expected to rest entirely with the DRCCA, and the shared aims that cross divisions were again emphasized. Dr. DeVita responded to the comment

that the movement to establish new programs has been too rapid to be well planned. Dynamic programs, such as the community cancer oncology programs, are effective means of defending the cancer control budget and they are well researched.

XXIII. Closing Comments and Adjournment.

Dr. DeVita, Dr. Pitot, and Mrs. Bynum thanked the Board for participating in this NCI program review and thanked the staff for their well prepared presentations. The meeting was adjourned at 2:50 p.m.

Date

Henry C. Pitot, M.D., Ph.D.
Chairman
National Cancer Advisory Board

NATIONAL CANCER ADVISORY BOARD

CHAIRMAN

Dr. Henry C. Pitot 1982
Director
McArdle Laboratory for Cancer Research
University of Wisconsin
Madison, WI 53706

Dr. Bruce N. Ames 1982
Professor of Biochemistry
Department of Biochemistry
University of California
Berkeley, CA 94720

Dr. Harold Amos 1982
Professor
Department of Microbiology and
Molecular Genetics
Harvard Medical School
25 Shattuck Street
Boston, MA 02115

Dr. Maureen M. Henderson 1984
Professor of Health Services
Medicine
School of Public Health
and Community Medicine
University of Washington
Mail Stop SC-30
Seattle, WA 98195

Dr. Robert C. Hickey 1986
Executive Vice President
University of Texas System Cancer
Center
M.D. Anderson Hospital and
Tumor Institute
Texas Medical Center
Houston, TX 77030

Dr. Joseph Gale Katterhagen 1986
Director of Oncology for
Consolidated Hospitals
Department of Oncology
Tacoma General Hospital
Tacoma, WA 98405

Mrs. Rose Kushner 1986
Executive Director, Breast
Cancer Advisory Center
9607 Kingston Road
Kensington, MD 20895

Ann Landers 1986
Field Newspaper Syndicate
Chicago Sun Times Building
Chicago, IL 60611

Dr. LaSalle D. Leffall 1986
Professor and Chairman
Department of Surgery
College of Medicine
Howard University
Washington, DC 20060

Mrs. Vincent Lombardi 1982
550 South Ocean Boulevard
Manalapan, FL 33462

Dr. William E. Powers 1986
Chief
Radiation Oncology Center
Harper Grace Hospital
3990 John R. Street
Detroit, MI 48201

Dr. Janet D. Rowley 1984
Professor
Department of Medicine
School of Medicine
University of Chicago
Chicago, IL 60637

Mr. Sheldon W. Samuels 1984
Director
Health, Safety and Environment
Industrial Union Department, AFL-CIO
815 - 16th Street, N.W.
Washington, DC 20006

Mr. Morris M. Schrier 1984
Legal Consultant
MCA, Inc.
445 Park Avenue
New York, NY 10022

Dr. Frederick Seitz 1982
President Emeritus
The Rockefeller University
1230 York Avenue
New York, NY 10021

Dr. Irving J. Selikoff 1984
Director
Environmental Sciences Laboratory
Department of Community Medicine
Mount Sinai School of Medicine
The City University of New York
1 Gustave L. Levy Place
New York, NY 10029

Dr. Phillipe Shubik 1982
Green College
Oxford, England OX 26 United Kingdom

Contact: Elliott Graham
Suite 600
900 17th Street, N.W.
Washington, DC 20006

Dr. Gerald N. Wogan 1984
Professor of Toxicology
Department of Nutrition & Food Science
Massachusetts Institute of Technology
77 Massachusetts Avenue, Room 56-215
Cambridge, MA 02139

Ex Officio Members

Dr. John H. Moxley, III
Assistant Secretary of Defense
(Health Affairs)
Department of Defense
Washington, DC 20301

Dr. George A. Keyworth
Director, Office of Science
and Technology Policy
The White House
Washington, DC 20500

Mr. Walter C. Barber
Acting Administrator
Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Alternates to Ex Officio Members

Dr. F. Kash Mostofi
7001 Georgia Street
Chevy Chase, MD 20815
(DOD Representative - home address)

Dr. Denis J. Prager
Associate Director for Human Resources
Office of Science & Technology Policy
Executive Office of the President
Washington, DC 20500

Dr. John Todhunter
Assistant Administrator
Office of Pesticides & Toxic Substances
Environmental Protection Agency RD-675
401 M Street, S.W.
Washington, DC 20460

Ex Officio Members

Mr. Stuart M. Statler
Acting Chairman
Consumer Product Safety Commission
1111 18th Street, N.W.
Washington, DC 20207

The Honorable Raymond J. Donovan
Secretary of Labor
Washington, DC 20210

Dr. Donald L. Custis
Chief, Medical Director
Veterans Administration
Washington, DC 20420

Dr. Arthur H. Hayes, Jr.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dr. J. Donald Millar
Director
National Institute for Occupational Safety and Health, CDC
1600 Clifton Road, N.E.
Atlanta, GA 30333

Dr. David P. Rall
Director
National Institutes of Environmental Health Sciences
Research Triangle Park, NC 27709

Mr. Richard Schweiker
Secretary for Health and Human Services
Washington, DC 20201

Dr. Thomas E. Malone
Acting Director
National Institutes of Health, PHS
Bethesda, MD 20205

Alternates to Ex Officio Members

Dr. Peter W. Preuss
Associate Executive Director
Health Sciences
Room 700, 5401 Westbard Avenue
Bethesda, MD 20014

Dr. Victor Alexander
Medical Officer
Office of Technical Support
Occupational Safety and Health
Department of Labor
200 Constitution Avenue (N3656)
Washington, DC 20210

Dr. Hollis Boren
Assistant Chief Medical Director
Research and Development (15)
Veterans Administration
Washington, DC 20420

Dr. Allen Heim
Acting Deputy Associate Commissioner for Health Affairs (Science)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dr. Elliott S. Harris
Deputy Director
National Institute for Occupational Safety and Health, CDC
1600 Clifton Road, N.E.
Atlanta, GA 30333

Executive Secretary:

Mrs. Barbara S. Bynum
Director, Division of Extramural Activities
National Cancer Institute, NIH
Bethesda, MD 20205