NATIONAL CANCER ADVISORY BOARD

convened on February 9-10, 1999, at the:
National Institutes of Health
Building 31-C, Conference Room 10
Bethesda, Maryland 20892a

TABLE OF CONTENTS

Cancer Surveillance Program: Update — Dr. Barbara Rimer

- Brief Overview of SEER; Dr. Brenda Edwards
- Cancer Surveillance Series: Trends in Prostate Incidence and Mortality; Dr. Benjamin Hankey, Dr. Eric Feuer
- Update on Geographic Patterns of Cancer Morality in the United States; Dr. Susan Devesa
- Surveillance Implementation Group Report; Dr. Robert Haitt

Update on Innovative Award Mechanisms — Dr. Richard Klausner

- Phased Innovation Awards; Dr. Carol Dahl
- Questions and Answers
- Rapid Access to Intervention Development (RAID); Dr. Edward Sausville

Annual Report on Gender and Minority Accruals to Clinical Trials — Dr. Marvin Kalt

Minority Reports

- Institute of Medicine Report; Dr. M. Alfred Haynes
- NCI Response to the Institute of Medicine; Dr. Richard Klausner
- Update on Office of Special Populations Research; Dr. Otis Brawley
- Opportunities for Sociocultural Research; Dr. Sherry Mills
- Questions and Answers

Subcommittee Reports and New Business II

- Planning and Budget; Ms. Ellen Stovall
- Cancer Centers; Dr. Ivor Royston
- New Business II; Dr. J. Michael Bishop

Office of Cancer Complementary and Alternative Medicine — Dr. Robert

	Dr. Jeffrey White
Extramural Policy Issues • Modular Grant Awards • Peer Review of Program Project (P01) Applications	Dr. Marvin Kalt
Status Report: Division of Cancer Prevention	Dr. Peter Greenwald
Adjournment	Dr. J. Michael Bishop

ATTENDEES

The National Cancer Advisory Board (NCAB) convened for its 109th regular meeting at 9:00 a.m., February 9, 1999, in Conference Room 10, C Wing, Building 31, National Institutes of Health.

NCAB Members
Dr. J. Michael Bishop (Chairperson)
Dr. Richard J. Boxer
Dr. Kay Dickersin
Dr. Alfred L. Goldson
Dr. Elmer E. Huerta
Dr. Frederick P. Li
Dr. Susan M. Love
The Honorable James E. McGreevey
Dr. Sandra Millon-Underwood
Dr. Arthur W. Nienhuis
Dr. Larry Norton
Dr. Amelie G. Ramirez
Dr. Ivor Royston
Dr. Philip S. Schein
Dr. Phillip A. Sharp
Ms. Ellen L. Stovall
Dr. Vainutis K. Vaitkevicius

President's Cancer Panel
Dr. Harold P. Freeman (Chairperson)
Dr. Paul Calabresi
Ms. Frances Visco (absent)

Alternate Ex Officio NCAB Members
Dr. Steven K. Akiyama, NIEHS
Col. Louis F. Diehl, DoD
Dr. Michael Hodgson, NIOSH
Ms. Rachel Levinson, OSTP (absent)
Dr. Alison Martin, FDA
Dr. Hugh McKinnon, EPA
Dr. Lakshmi C. Mishra, CPSC (absent)
Dr. T. G. Patel, DVA
Dr. Eugene Schwartz, DOL
Dr. Michael Viola, DOE

Members, Executive Committee, National Cancer Institute, NIH
Dr. Richard Klausner, Director, National Cancer Institute
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Dr. Martin Abeloff, External Advisor and Co-Chair, Clinical Sciences Subcommittee A of the NCI Intramural Board of Scientific Counselors; Professor

and Director, Johns Hopkins Oncology Center
Dr. Norka Ruiz-Bravo, Acting Director, Division of Cancer Biology
Dr. Ellen Feigal, Deputy Director Division of Cancer Treatment and Diagnosis (DCTD)
Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics
Dr. Peter Greenwald, Director, Division of Cancer Prevention
Dr. Paulette Gray, Deputy Director, Division of Extramural Activities (DEA)
Ms. maryAnn Guerra, Deputy Director for Management NCI
Dr. Joe Harford, Associate Director for Special Projects, NCI
Mr. John Hartinger, Associate Director for Budget & Financial Management, NCI
Dr. Marvin Kalt, Director, Division of Extramural Activities (DEA)
Dr. Alfred Knudson, External Advisor, Special Advisor to the NCI Division of Cancer Epidemiology and Genetics; Acting Director, Intramural Genetics Program; Senior Member, The Institute for Cancer Research, Fox Chase Cancer Center
Ms. Sandy Koeneman, Executive Secretary, NCI Executive Committee
Dr. Edison Liu, Director, Division of Clinical Sciences
Dr. David Livingston, External Advisor, Chairperson of the NCI Extramural Board of Scientific Advisors; Professor of Medicine, Dana-Farber Cancer Institute
Dr. Sherry Mills, Chair, NCI Extramural Advisory Board (EAB)
Ms. Cherie Nichols, Assistant Director for Science Planning and Assessment, OSP, NCI
Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS)
Dr. Matthew Scharff, External Advisor and Co-Chair, Basic Sciences Subcommittee A of the NCI Intramural Board of Scientific Counselors; Professor, Albert Einstein College of Medicine
Dr. Susan Sieber, Associate Director for Special Projects, NCI
Dr. Margaret Tucker, Chairperson, Intramural Advisory Board, Board of Scientific Counselors
Dr. George Vande Woude, Director, Division of Basic Sciences
Ms. Susan Waldrop, Assistant Director for Program Coordination, OSP, NCI
Dr. Allen M. Weissman, chair, Intramural Advisory Board (IAB), NCI
Dr. Robert Wittes, Deputy Director for Extramural Science, NCI
Dr. Maureen O. Wilson, Executive Secretary of the President's Cancer Panel

Liaison Representatives
Dr. John Currie, American Association for Cancer Education, Inc.
Dr. Edwin A. Mirand, Association of American Cancer Institutes
Dr. Margaret Foti, American Association for Cancer Research
Dr. Marc E. Lippman, American Association for Cancer Research
Dr. Robert Martuzza, American Association of Neurological Surgeons
Dr. Robert W. Frelick, Association of Community Cancer Centers
Ms. Kerrie B. Wilson, American Cancer Society
Dr. John Stevens, American Cancer Society

Dr. Stanley Zinberg, American College of Obstetricians and Gynecologists
Dr. Bernard Levin, American Gastroenterological Association
Dr. Edward P. Gelmann, American Society of Clinical Oncology, Inc.
Dr. Eli Glatstein, American Society of Therapeutic Radiologists
Ms. Laura Liebermann, Candlelighters Childhood Cancer Foundation
Dr. Lovell A. Jones, Intercultural Cancer Council
Dr. Armin D. Weinberg, Intercultural Cancer Council
Ms. Katharine R. Boyce, Intercultural Cancer Council
Ms. Martha M. Kendrick, Intercultural Cancer Council
Ms. Jean Ard, Leukemia Society of America
Ms. Dorothy J. Lamont, National Cancer Institute of Canada
Dr. Robert A. Phillips, National Cancer Institute of Canada
Dr. Eve I. Barak, National Science Foundation
Dr. Linda U. Krebs, Oncology Nursing Society
Dr. Jeffrey Norton, Society of Surgical Oncology, Inc.
Dr. Marston Linehan, Society of Urologic Oncology

CALL TO ORDER, OPENING REMARKS, AND CONSIDERATION OF MINUTES OF PREVIOUS MEETINGS
Dr. J. Michael Bishop

Dr. Bishop called to order the 109th meeting of the National Cancer Advisory Board (NCAB), and introduced guests representing cancer education and research associations and advocacy organizations. He welcomed members of the public and the press and invited them to submit in writing, within 10 days, any comments regarding items discussed during the meeting. A motion was requested and made to approve the minutes of the December 1998 meeting. They were approved by the Board unanimously. Dr. Bishop introduced and welcomed new members, Dr. Susan M. Love, The Honorable James McGreevey, and Dr. Larry Norton, who were attending for the first time.

FUTURE BOARD MEETING DATES
Dr. J. Michael Bishop

Dr. Bishop called Board members' attention to the meeting dates listed in the agenda. Dates have been confirmed through 2000. Members were asked to report conflicts with tentative dates listed for 2001.

REPORT OF THE DIRECTOR, NATIONAL CANCER INSTITUTE
Dr. Richard Klausner

Dr. Richard Klausner, Director, NCI, presented an update of the FY 2000 budget development, reviewed the status of the new extraordinary opportunities being developed for the next 3-year cycle of Bypass Budgets, and described the Institute's proposed follow

up to the reports of the disease-specific progress review groups for breast and prostate cancers.

FY 2000 Budget. Dr. Klausner reported that the request submitted to Congress by the President asked for an increase in the NCI budget of approximately $70M or a 2.4 percent increase over FY99, compared with the 14 percent increase received in FY98. A 2.1 percent increase or $320M was requested for NIH, overall. In addition to funding for the categorical disease for each institute, a second component of the NCI budget and those of the other institutes is AIDS funding that is distributed through the NIH Office of AIDS Research. AIDS funding in the amount of $224M has been proposed for the NCI, a 1.9 percent increase over FY 1999.

Dr. Klausner then discussed planning and projections related to the research project grant (RPG) pool based upon the President's proposed budget for FY 2000. Because of the growth in size of the grant pool in the last several years, the funding commitment for noncompeting grants as projected would absorb 80 percent of the proposed 2.4 percent increase for the NCI. This is based on the expectation that approximately 1,230 new and competing grants will be funded in FY99—compared with 1,040 in FY98—for a total in the RPG pool of about 4,100 grants (an increase from about 3,700 in FY98) and an overall success rate of about 30 percent. With the 2.4 percent increase proposed in the President's budget, the number of new and competing grants that could be funded in FY 2000 would decrease by about 10 percent according to current projections. Projection modeling for RPGs based on the 1,230 competing grants expected to be funded in FY99 indicates that maintaining a 30 percent overall success rate in the outyears for these grants from FY 2000 through FY 2003 would require annual growths in the NCI budget ranging from 9.7 percent to 11.5 percent. Achieving a 35 percent overall success rate for RPGs would require annual growths ranging from 14 percent to 16 percent. Major variables in the projection models are average cost increase per year for competing grants and annual growth in applications received.

Bypass Budget. Dr. Klausner explained that the Bypass Budget, which is specified in the National Cancer Act, describes the NCI's priorities and planning and guides NCI efforts in discharging its responsibilities as mandated. One important area of the Bypass Budget is called Extraordinary Opportunities for Investment. It was agreed, when this area of the budget was initiated, that changes or additions should be made on a 3-year cycle because of the magnitude of these planning opportunities. Planning for the FY 2001 Bypass Budget, which marks the beginning of the second 3-year cycle, has involved a year-long process of evaluating the progress toward achieving the goals represented by the four current extraordinary opportunities and inviting suggestions from all within the cancer community for new opportunities to consider. Dr. Klausner reported that, on the basis of this evaluation, a decision was made at the December Bypass Budget planning meeting to transition the four current opportunities into a new category of ongoing opportunities. He then summarized NCI progress in the four research areas that constitute this first cycle—Defining the Signatures of Cancer Cells, Imaging Technologies, Preclinical Models of Cancer, and Genes and Gene Environment—and reviewed plans and objectives for expanding or changing their scope and/or direction. Dr. Klausner announced, that after

careful review of the hundreds of suggestions received, three new extraordinary opportunities were agreed on by the planning committee. The new research goals to be added to FY 2001 Bypass Budget are: (1) molecular targets; (2) tobacco and tobacco-related cancers, and (3) cancer communication.

Progress Review Groups: Update. Dr. Klausner reminded the Board that the Progress Review Groups (PRG)—committees of external experts and consumers—were organized to focus specifically on the diseases for which the NCI has responsibility, beginning with breast and prostate cancer. The needs to be addressed were to refine and prioritize scientific questions and to assess the current NCI portfolios in those diseases. An additional need was to test whether the planning approach embodied in the Bypass Budget, which focuses on overarching scientific opportunities that cut across all cancers, adequately and accurately addresses issues for specific diseases. Dr. Klausner briefly reviewed the organization in 1997 and operations of the Prostate Cancer PRG (PCPRG), which culminated in the development of a report entitled "Defeating Prostate Cancer: Crucial Directions for Research." This summation of PCPRG recommendations was submitted to and accepted by the Advisory Committee to the Director (ACD) in August 1998 and the NCAB in September. Since then, NCI staff have reviewed scores of recommendations in both the breast and prostate cancer reports and prepared responses. The NCI actions in response to the PCPRG and Breast Cancer PRG (BCPRG) reports were to identify the recommendations that could be addressed by ongoing NCI initiatives, refocus ongoing initiatives to address specific questions as recommended, and develop new initiatives where possible. Dr. Klausner reported that the NCI has initiated an extensive advertising campaign to encourage investigators to attach applications to the questions contained in the PRG reports, which have been published on the Web and in professional journals. This new approach to addressing broad questions is in lieu of writing disease specific Requests For Applications (RFAs) or Program Announcements (PAs). Applications that respond to PRG recommendations have first priority for funding as exceptions if they do not automatically get funded through the paylines of peer review. In addition, NCI has published a comprehensive prostate cancer research announcement on the Web outlining 20 new or ongoing opportunities tied to the major recommendations of the PCPRG. A similar announcement is planned for breast cancer research. The announcements describe the funding mechanisms and directs investigators to individual program staff at the NCI for help in linking their research to the available infrastructures. Dr. Klausner then presented examples of how ongoing NCI initiatives such as the Mouse Models of Human Cancer Consortium and Cancer Genome Anatomy Project (CGAP) are being used as a foundation for focused research in prostate cancer. Other new initiatives implemented in response to PRG recommendations were the new mechanism Quick Trials for rapid initiation of early clinical trials and a broad prostate cancer biology PA, tied to exception funding, which will be issued in conjunction with the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK). In summary, Dr. Klausner noted that these broad approaches to responding to disease-specific plans are an experiment, which the NCI will monitor and report on in the next year. The results of the experiment will help clarify whether the type of overarching planning represented by the Bypass Budget can be tailored and linked to the needs of researchers who work in addressing specific cancers.

Dr. Klausner concluded that the work of the breast and prostate cancer PRGs has proven to be: (1) useful in the process of organizing and validating the NCI portfolio; (2) a basis for establishing criteria for organizing NCI portfolios across different diseases; (3) a useful outline for planning and decision-making processes across multiple federal agencies; and (4) useful in elucidating the effectiveness of the interface between scientific opportunity planning and disease- need planning. There are no immediate plans for creating additional disease-specific PRGs, pending an evaluation of these current approaches to linking planning, infrastructures, and funding opportunities to answering specific questions related to breast and prostate cancer.

QUESTIONS AND ANSWERS

Mr. McGreevey expressed concern that the Bypass Budget area of extraordinary opportunities may be becoming too broad and asked whether the item related to imaging technologies might be a focus for the private sector. Dr. Klausner commented that the NCI works closely with industry and leverages that interaction for complementary initiatives. On the broader issue of the impact of expanding NCI budget priorities, he noted that the Bypass Budget is a mandated professional judgment budget and is important, not only to articulate priorities in NCI's presentations to Congress before legislation is enacted, but also as a process by which priorities are set for expending the budget that is enacted. Dr. Bishop commented on the value of this section of the Bypass Budget in redirecting the attention of the scientific community to research identified by the NCI as important to the national effort. In response to Mr. McGreevey's question about the linkage between tobacco settlement dollars accruing to several state legislature and NCI research efforts, Dr. Klausner described a major new NCI initiative in state and community tobacco control that has been approved.

Dr. Frederick Li asked about the availability of researchers trained in cancer control. Dr. Klausner agreed that the need for a trained workforce has been linked to many of the extraordinary opportunities and the NCI has had to integrate training opportunities with many of the new research infrastructures and mechanisms that are being developed. The expectation is that this practice will continue to be necessary. Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS), added that the NCI is working to bring new types of investigators into cancer communications and is considering the development of initiatives and resources that would be available to the larger scientific community nationwide.

From his perspective as a member of the BCPRG, Dr. Norton commented that the activity was characterized by an extraordinary degree of communication and should prove to be productive in leading to new initiatives and a redirection of thought in the areas of cancer control, communications, and environmental studies as well as cancer research. He recommended the continuation of the PRG process now that the operational procedures have been streamlined.

Dr. Kay Dickersin commented that the extraordinary opportunities aspect of the Bypass Budget must be kept relevant to issues that Congress and the public sees as important, as well as the scientific community, even as the list expands. Dr. Klausner stated that this issue has been central to planning for the second edition of the budget, and opportunities as described will be made relevant and accessible to people at risk for and with cancer, as well as funders. In addition, questions about the burden of disease will be addressed as they relate to levels of investment.

REPORT: AMERICAN ASSOCIATION FOR CANCER RESEARCH
Dr. Webster K. Cavenee

Dr. Webster K. Cavenee, President, American Association for Cancer Research (AACR), reported on AACR membership and programs, public education activities, and new initiatives being planned for early implementation. Dr. Cavenee noted that AACR scientists see their organization as a catalyst for discovery and innovation in cancer research, with an impact on all segments of the cancer community—survivors, advocates, industry, academia, and government. Major programs are: scientific journals; multidisciplinary annual meetings; special conferences on timely issues; career support through science education, mentorship, and scholar awards; and training workshops for young investigators; scientist-survival programs; public education; and public outreach. Another major program fosters the careers of women and minorities in cancer research in partnership with the NIH and industry.

AACR's rapidly growing membership—expected to reach 25,000 by 2005—is affiliated primarily with academia (83%), industry (9%), and government (8%). Attendance at the annual meeting also is increasing, with registration for the 1999 meeting at about 11,600. About 5,000 papers were received for consideration by the program committee. Dr. Cavenee noted that the AACR has emphasized the strengthening of clinical and translational research within its programs through an increase in presentations at the annual meetings, special conferences, a clinical cancer research award, a special committee to oversee the clinical programs of the AACR, the formation of a clinical/translational cancer research working group with the AACR, incorporation of these topics into the public education agenda, and collaboration with the American Society of Clinical Oncology (ASCO) on matters of mutual interest. Support for young investigators includes grant writing training, travel awards for scientific meetings, a research award, the mentorship program, summer training workshops, fellowships, and career development awards for junior faculty. These cancer researchers in training receive numerous fringe benefits as associate members of the AACR.

Efforts to address the problem of underrepresented populations have resulted in an increase in membership of minorities and women on all AACR committees. In addition, the 10- year-old Minority Issues Committee is working to strengthen existing programs and develop new ones, such as the year-round program for young scientists that is being discussed in the context of the NCI Minority Mentorship Program. The Science Education Committee also sponsors a program to foster careers in cancer research for minorities, and the AACR and NCI have partnered in awards to faculty from historically Black colleges and universities under that program. In an affiliation with the Women in

Cancer Research organization, the AACR is working to foster professional advancement of women in research.

AACR's international efforts have been expanded over recent years with consequent increases in international membership and attendance at AACR annual meetings. Currently, almost 30% of the members reside outside the United States. Special conferences and workshops have been held outside the United States or in collaboration with international associations. The AACR recently became a co-sponsor, with the NCI and European Organization for Research and Treatment of Cancer (EORTC), of the annual drug development meeting held alternately in the United States and Europe, it will hold a summit meeting of International Cancer Research Association leaders in Bangkok in December 1999.

Major public policy initiatives of the AACR have advocated: (1) a dramatic increase in funding for cancer and biomedical research; (2) revitalization of the National Cancer Act with an emphasis on the special authorities of the NCI to coordinate the National Cancer Program; (3) a rational approach to genetic privacy issues and ethical concerns regarding genetics research; (4) emphasis on universal access to quality care and on other concerns of patients and advocates; and (5) novel approaches to accelerating progress in cancer research. AACR public education and policy initiatives have been carried out through position papers on matters of research and public health policy, relationships with advocacy and survivor groups, involvement with key community leaders, interactions with the Administration and Congress, dialogues with NCI and other agencies, and clear messages to the national and international media. The AACR played a significant role in the organization and execution of The MARCH ... Coming Together to Conquer Cancer, as well as in developing the report from The MARCH Research Task Force.
Dr. Cavenee concluded with a brief summary of the many ways the AACR and the NCI have worked together, commented on the comprehensiveness and vision of the current Bypass Budget, and looked forward to continuing to work with the NCI toward common goals.

OMB CIRCULAR A-110 AND THE FREEDOM OF INFORMATION ACT (FOIA) RESOLUTION

Dr. Marvin Kalt, Dr. Wendy Baldwin, Dr. Philip Schein

Dr. Marvin Kalt, Director, Division of Extramural Activities (DEA), opened the discussion on the implications of the Notice of Proposed Rule Making (NPRM)—Circular A- 110: Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations, which has been issued by the Office of Management and Budget (OMB) as mandated in the Omnibus 1999 Appropriations Bill. He introduced Dr. Wendy Baldwin, Deputy Director for Extramural Research, NIH, to review the events leading to the NPRM and present the NIH view on implications of the proposed amendments to Circular A-110.

Dr. Baldwin reminded the Board that the NPRM was the next phase in the series of events following passage of the Omnibus 1999 Appropriation with its directive that the OMB amend Circular A-110 to extend the Freedom of Information Act (FOIA) to

"require Federal awarding agencies to ensure that all data produced under an award will be made available under the FOIA." The NPRM sets forth the OMB interpretation of the law and planned implementation. Issuance of the NPRM is followed by a 60-day public comment period in which the community is asked to submit concerns with the amendment as proposed and suggest further issues to address. Dr. Baldwin emphasized the need to ensure that the scientific community understands the issues raised in the NPRM and understands the need for engagement during the 60-day period. She presented for Board information a series of questions that in the view of the NIH need further clarification before the rule is finalized. The questions related to the breadth of the NPRM definition of data, how costs of compliance would be recouped, and whether sufficient protections for privacy are provided under the FOIA. The intent in developing these questions was to provide a framework for in-depth consideration of the issues, with the expectation that individual communities would elaborate on them and join the NIH in helping OMB focus on the rule in a way that is constructive. These questions will be publicized on the Web. Dr. Baldwin emphasized the need for the scientific community to discuss these complex, but important, issues relating to data sharing whatever the outcome of this NPRM.

Following a brief discussion by members of the implications of Circular A-110, Dr. Philip Schein presented drafts of a letter to the OMB and a resolution, which were prepared by an *ad hoc* subcommittee for consideration as the NCAB's response to the request for comment contained in Circular A-110. The letter summarized the NCAB's position on the potential threat posed by the amendment and concluded with a request that the public comment period be extended to allow for full consideration and discussion of the matter. The draft resolution called on "national legislators, health professionals, and scientists to support recision of the revisions to Circular A-110." The resolution further expressed NCAB support for "purposing an amendment to the circular to allow individual agencies, institutions, and researchers to retain fees from requesters equaling the full incremental cost of obtaining the data in response to FOIA requests." It was decided that action on the letter and resolution would be postponed until the New Business II session the following day.

LEGISLATIVE UPDATE
Ms. Dorothy Foellmer

Ms. Dorothy Foellmer, Director, Office of Legislation and Congressional Activities (OCLA), reviewed early proposals by members of the 106th Congress that would support increases to the NIH appropriation for FY 2000. The first, a resolution expressing the Sense of the Senate, supported a $2B increase in the Federal investment in biomedical research, with provisions to minimize the financial impact on other programs in the Labor and Health and Human Services (HHS) bill. The second would provide for a continuation of the Federal research investment in a fiscally sustainable way, double this investment over a 12-year period from FY99 through FY10, and require a comprehensive accountability study by the National Academy of Sciences (NAS) to develop methods for evaluating federally funded research. The third would create a National Fund for Health Research supported through a graduated health premium set aside. As an indication of

how these proposals to supplement NIH's yearly appropriation might fare when put to the vote, Ms. Foellmer reviewed the legislative history of similar attempts by the 103rd, 104th, and 105th Congresses.

Ms. Foellmer then presented an update on recent efforts by the Food and Drug Administration (FDA) to regulate the sale and distribution of cigarettes and smokeless tobacco to children and adolescents. The final rule stating the FDA's intent to regulate these products was published in the *Federal Register* in August 1996; youth access provisions went into effect in February 1997; a challenge in the U.S. District Court was upheld in April 1997; this decision was reversed in by the U.S. Court of Appeals in August 1998; a petition seeking a rehearing was filed by the Justice Department in September 1998 and denied in November. In January 1998, a petition was filed with the Supreme Court seeking a review of the August ruling. The petition cites that tobacco products fall within the FDA's jurisdiction as intended in the Food, Drug and Cosmetic Act. The FDA is currently awaiting the ruling from the Supreme Court on whether it will hear the petition. Youth access provisions remain in effect pending action by the Supreme Court.

ANNUAL DELEGATIONS OF AUTHORITY
Dr. Marvin Kalt, Ms. Maryann Guerra

Ms. MaryAnn Guerra, Deputy Director for Management, reminded Board members that as the advisory council for the NCI, the NCAB is asked annually to vote on the continuation of the legislative authorities granted to the Director, NCI, to establish specialized training and educational programs as specified in the Public Health Service Act. These authorities apply to fellowships that are sponsored at the NCI and the training takes place in NCI laboratories and programs. The NCI's multifaceted approach to training includes comprehensive pre- and postdoctoral training fellowships, general educational programs that support NCI mission, targeted training programs developed specifically to address special needs, and a formal clinical training program that spans a range of disciplines. Ms. Guerra presented a summary description of the Cancer Research Training Award, which is the universal training program for all NCI domestic in-house fellows and the umbrella appointing mechanism for NCI specialized fellowships. This was followed by descriptions of the specialized fellowships, which respond to special needs identified in NCI programs and are available in the areas of cancer epidemiology and biostatistics, cancer genetics and epidemiology, cancer prevention, health communications, and technology transfer. The total NCI and NIH inhouse fellowships increased from about 1,000 in FY97 to 1,100 in FY98. In response to recommendations of the Intramural Advisory Board (IAB), which has been studying the issue of minority recruitment in NCI's tenure track scientists and fellows, the NCI is developing plans to target an improved recruitment to fellowship and training programs and will report to the Board at a later date.

Motion. A motion was made to extend the legislative authorities of the NCI to support programs of education and training (including continuing education and laboratory and clinical research training). The motion was seconded and unanimously approved.

Dr. Kalt then requested NCAB approval for extending the delegations of authority that pertain to the extramural program as specified in the Public Health Service Act. Delegation A permits the Director, NCI, to appoint not more than 151 special experts or consultants; delegation B allows the Director to appoint one or more advisory committees of private citizens or officials; and delegation C permits the Director and NCI staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards recommended by the Board.

Motion. A motion was made to extend the delegation of authorities that pertain to the extramural program for another year. The motion was seconded and unanimously approved.

NEW BUSINESS I
Dr. J. Michael Bishop

Dr. Kalt presented for NCAB approval a proposed procedure for expediting Board review of grant applications that fall within established paylines and that have no concerns or other bars to awards that must be resolved prior to payment. The procedure if approved would permit expedited funding of such awards and would be activated for applications received for Board concurrence in September 1999 and thereafter. In response to questions, Dr. Kalt clarified that Council/Board operating procedures are being streamlined similarly across the NIH and that the en bloc concurrence procedure provides that any Board member can request full discussion of any application destined for automatic consideration.

Motion. A motion was made to approve the proposed procedures for expediting NCAB review of grant applications that fall within established paylines and that have no concerns or other bars to awards that must be resolved prior to payment. The motion was seconded and approved unanimously.

Items of business scheduled for action the following day were: (1) recommendations of the Subcommittee on Cancer Centers related to revising the Cancer Center Support Grant Guidelines; (2) the draft letter to the OMB in response to the request for comment contained in OMB Circular A-110; and (3) the NCAB Resolution related to OMB Circular A-110.

CANCER SURVEILLANCE PROGRAM: UPDATE
Dr. Barbara Rimer

As background, Dr. Rimer explained that NCI's cancer surveillance program, with the Surveillance, Epidemiology, and End Results (SEER) program as its foundation, is continuously changing and expanding due in part to new tools made possible by advances in technology and is becoming increasingly a national effort. Over the last few years, surveillance staff at the NCI have made their new tools more widely available to the

research community, with provisions for training in the use of the tools. Initiatives such as the new "Stat Chats" are making the annual presentation of statistics more accessible and other innovations are being pioneered. Dr. Rimer stated that update would include a brief overview of NCI's cancer surveillance strategy, an examination of prostate cancer trends and the new cancer atlas, and a review of recommendations from the Cancer Surveillance Implementation Group.

Brief Overview of SEER

Dr. Brenda Edwards, Associate Director, Cancer Surveillance Research Program (CSRP), DCCPS, stated that the work of the CSRP is anchored in the Surveillance Epidemiology and End Results Program (SEER) population laboratory, which makes it possible to monitor the cancer burden on the population through the measurement of cancer incidence, mortality, and survival. Beyond SEER, data are collected to assess individual, societal, and health services factors both directly and indirectly. Seven surveillance program databases ranging from primary prevention to terminal cancer/death produce the information used to explain the trends of cancer burden in the United States. American Cancer Society (ACS) figures, which are based to a large extent on SEER data, estimate that the U.S. cancer burden in 1999 will be more than 1.2M new cases and 563,000 deaths. More detailed information on the U.S. cancer burden has been published in the *Journal of the National Cancer Institute (JNCI)*. The report entitled "Annual Report to the Nation on the Status of Cancer, 1973-1996, with a Special Section on Lung Cancer and Tobacco Smoking" is a joint effort of the NCI, Centers for Disease Control and Prevention (CDC), ACS, and National Center for Health Statistics (NCHS). The report summary shows that cancer incidence and mortality continue to decline for all sites combined. Differential patterns of cancer burden, however, are seen when the data are analyzed according to the factors that have been shown to influence rates—race/ethnicity, primary site, sex, age, stage, geography, and social economic status (SES). Dr. Edwards presented information from the report to illustrate the differential patterns when incidence data are analyzed for racial/ethnic diversity, primary site and sex; when cervical cancer data are analyzed by race/ethnicity, stage, and age; and when lung cancer mortality is analyzed by sex and SES.

Next, Dr. Edwards summarized a landmark study published in 1998 that addressed the question of whether it is possible to establish a national cancer surveillance program that meet the needs of all people. Only 14 percent of the country is included in SEER areas. The study focused on pooling registries, both SEER and non-SEER, as the central core unit for collecting data on cancer burden. She concluded with a brief description of the Cancer Statistics Review Seminar Series also known as "Stat Chats."

In discussion and in response to questions, it was noted that these cancer surveillance strategies describe what is happening and produce the data needed to identify more accurately where prevention and treatment interventions research should be targeted. Dr. Rimer stated that the next presentations would illustrate how the NCI attempts to understand and explain cancer trends, using the example of prostate cancer.

Cancer Surveillance Series: Trends in Prostate Incidence and Mortality

Dr. Benjamin Hankey, Chief, Cancer Statistics Branch, CSRP, DCCPS, informed the Board that a Cancer Surveillance Series was established recently in the *Journal of the National Cancer Institute* with the expectation that peer-reviewed manuscripts on four to five topics will be published each year. Three manuscripts on interpreting trends in prostate cancer are expected to be part of the new series. Dr. Hankey summarized the findings included in the first manuscript in this prostate trilogy entitled "Evidence of the Effects of Screening in Recent Prostate Cancer Incidence, Mortality, and Survival Rates." This work addressed the question "What are the tracks that screening has left in our cancer statistics?" The purpose of the analyses was to discuss the likelihood that prostate specific antigen (PSA) testing has had an effect on prostate cancer mortality which for the total United States has been observed recently to be decreasing. Conclusions reached from this study were that (1) the incidence of moderately differentiated tumors is driving the incidence trend; and (2) trends for distant-stage disease (histologic grade and survival) show that the best prognosis cases are being shifted out.

Dr. Eric Feuer, Chief, Surveillance Modeling and Methods Section, CSRP, DCCPS, discussed the findings in the second manuscript entitled "Cause-of-Death Misclassification and Potential Effects on Mortality." This study attempted to find out whether cause-of-death misclassification could explain why the rise and fall seen in U.S. mortality rates for prostate cancer in white males in the early 1990s appeared to coincide with the rise and fall in incidence rates as reported in SEER. Ordinarily, the impact on mortality of a change in incidence is usually not seen for many years. The study suggested that misclassification of reported cause of death for prostate cancer cases may be contributing to the observed rise and fall of mortality but more information is needed. Two special studies in SEER areas are ongoing to gather that information.

Dr. Feuer then discussed the findings of the third study entitled "Modeling: Quantifying the Link Between Population PSA Testing and the Recent Declines in Prostate Cancer Mortality." The conclusion from the study using a prostate cancer simulation model to project the number of PSA-prevented deaths was that PSA screening may be responsible for some part of the decline in mortality especially, if the lead time is relatively short, but more information is needed on the natural history of the disease. Collaborations are ongoing with other groups of investigators who have developed more detailed simulation models of the natural history of prostate cancer to gain further insight into national trends. Taken together, these studies suggest that a single factor (*e.g.*, PSA screening) is unlikely to be totally responsible for current trends in incidence and mortality. Dr. Feuer noted that these surveillance studies have been the impetus for a concept for an RFA cooperative agreement, which is currently going through the NCI review process. The RFA would establish a working group called CISNET—Cancer Intervention and Surveillance Modeling Network—to elucidate trends.

In response to Dr. Li's question concerning the extent to which extramural scientists outside the SEER areas use the SEER database for research, it was noted that use of the

database is growing as a result of new ways of providing and accessing files. About 1,500 public-use files are currently being provided to researchers in conjunction with software that greatly facilitates the ability to analyze. Dr. Klausner added that the NCI and the Agency for Health Care Policy Research (AHCPR) are forming a working group to monitor changes identified through prostate cancer surveillance studies nationwide and worldwide to better inform public health decisionmakers.

Update on Geographic Patterns of Cancer Mortality in the United States

Dr. Susan Devesa, Chief, Descriptive Studies Section, Division of Cancer Epidemiology and Genetics (DCEG), reviewed recent changes that have been made in the latest edition of the U.S. cancer mortality atlas. The new atlas has been expanded to show cancer mortality for the years from 1950 to 1994, with maps representing two time periods—1950 to 1969 and 1970 to 1994 for comparison of mortality data over time. The atlas will present many maps using the U.S. Census Bureau arrangement of the more than 3,000 U.S. counties into 508 state economic areas (SEAs) and some maps at the county level. After preparing all of the maps for the atlas, DCEG researchers have begun reviewing in detail the mortality patterns for cancer that have shown substantial changes in their geographic patterns. A manuscript focusing on the changing patterns of lung cancer mortality from the 1950s to 1990s was submitted to the *JNCI* as part of the new Cancer Surveillance Series, and is currently being readied for resubmission. For white males, lung cancer mortality showed a dramatic increase for the period, with differing elevations in rate and changing patterns over time for the northeast, southeast, and west coasts. In the recent time period, most areas with the highest rates were in the southeast quadrant of the country, and rates in the northeast and on the west coast have approximated the national rate. By comparison, rates in the northern plains and Rocky Mountain states have been relatively low over most of the time period. The same type of data for lung cancer mortality among women showed a sixfold rate increase over the 45-year period, but with less pronounced geographic patterns except for some urban-rural patterns. Of particular note was the absence of high rates in the southeast among women. These findings somewhat mirror the 1985 population survey at the state-level of the prevalence of cigarette smoking by gender. Overall, the study found different patterns among women compared with men and distinctive changes over time in the patterns of lung cancer mortality.

In contrast to the substantial pattern changes seen in lung cancer, breast cancer mortality patterns for the more than 40 years studied have remained relatively stable, with elevated rates in the northeast and midwest and some parts of the west coast and generally low rates across the south. Dr. Devesa noted that this finding suggests that recently introduced environmental factors are not playing a major role. DCEG researchers did a correlational analysis looking at the regional variation in the prevalence of risk factors and certain prognostic factors for breast cancer. They found that geographic patterns among breast cancer mortality rates were largely attributable to the variations in the prevalence of risk factors, although not totally.

Prostate cancer mortality rates also have been relatively unchanged over the 45-year period, but with distribution patterns for males distinctly different from those for lung and breast cancer. For white men, rates have been elevated not only in the northeast but also in the northern plains and Rocky Mountain states and west, with generally low rates across the south. In recognition of the smaller numbers and differing geographic distribution patterns for black populations, separate maps have been included in the new atlas for deaths since 1970. They show that prostate cancer mortality rates for black men were elevated along the southeastern coastal states (with generally low rates farther inland), certain areas of the northeast (although not necessarily the urban areas), and certain areas on the west coast. Some studies have suggested that agricultural exposures may play a role in prostate cancer among both white and black men.

Dr. Devesa noted that the new cancer atlas is expected to provide information on geographic patterns of cancer mortality that will be of interest for further study. It will be possible to study temporal trends, mortality patterns by gender, and comparisons of these among blacks and whites. The atlas will be published as a book, and the book plus all tables will be made available on the Internet, with downloadable map files and tables. As additional maps are prepared, they will be added to the Web site. The possibility of preparing a compact disk also is being considered.

In discussion, it was noted that smoking prevalence data from a 1992-93 survey has already been mapped; data from the 1995-96 survey will be mapped when complete data have been received. Together, these maps should strongly predict the lung cancer mortality rates of the future. In response to the question of how the American tendency to change residence frequently will influence these types of analyses, Dr. Devesa noted that all maps are based on mortality data which use the place of residence at the time of death. For some diseases like colon cancer, however, elevated mortality rates have not been seen in retirement areas chosen by people from the high-risk northeast, suggesting that risk may change fairly rapidly or that there might be differential migration.

Surveillance Implementation Group Report

Dr. Robert Hiatt, Deputy Director, DCCPS, presented a summary of the report of the Surveillance Implementation Group (SIG), which was organized to respond to the recommendations of the Cancer Control Program Review Group (CCPRG). The full report will be presented in March to the Board of Scientific Advisors (BSA). Dr. Hiatt noted that the CCPRG recognized that NCI's Cancer Surveillance Research Program (CSRP) performed high- quality data collection and its applied research was responsive to the reporting requirements of the National Cancer Act of 1971. The CCPRG noted, however, that additional measures of the total cancer burden were needed (building on the existing infrastructure) to measure progress in reducing this burden and to allow the NCI to properly plan and evaluate its research agenda. CCPRG recommendations were to expand the SEER program (taken to mean NCI's surveillance program in general) and use the SEER expanded data and expertise to produce a timely report card on the cancer burden. To plan the NCI's response, the 42-member SIG was organized, with co-chairs

Dr. Nicole Urban, Fred Hutchinson Cancer Research Center, Dr. Hiatt, and Dr. Edwards. After extensive discussion, the SIG reached consensus on a vision statement and an action plan outlining five priority areas and 12 research opportunities within those areas. The vision statement was based on the current record of progress and the SIG's view of how that could be enhanced to take full advantage of current opportunities.

As envisioned, NCI's CSRP would connect the SEER system to multiple other data collection mechanisms, as new tools are developed, to understand the causes of cancer, incidence rates, and trends in these rates over time. The populations defined in connecting other data sets in the SEER registries would enable the collection of data on prevention, risk factors, screening, and treatment outcomes. These data would be connected in order to answer specific questions concerning cancer rates. Expansion of the SEER or surveillance programs would be taken in concert with the NCI's partners in the National Coordinating Council for Cancer Surveillance in the context of a long-term National Cancer Surveillance Program. The strong research infrastructure already in place would continue with major methodologic efforts in modeling rates and trends to better understand the "why" questions, together with new efforts in geographic information systems and approaches to creating national estimates of the cancer burden. To implement this vision, the SIG implementation plan identifies five priority areas for action: (1) expand the scope of surveillance research through additional data collection and methods development; (2) expand the scope of surveillance by the addition of under-represented populations; (3) produce a national report card; (4) support molecular and genetic research; and (5) develop a strategy for training cancer prevention and control scientists. Dr. Hiatt concluded with a description of twelve specific recommendations for action in these priority areas and the proposed implementation initiatives of the SIG, together with the timetable to initiation.

In discussion, Dr. Sandra Millon-Underwood asked about the timetable for reporting on quality-of-life and cancer survivorship issues. Dr. Hiatt noted that the concern in surveillance research is to understand which are the best measures for quality-of-life for different cancers and stages of cancer, and which of these measures lend themselves to surveillance. These data are envisioned as being collected in cohorts of newly registered cancer patients over time, not by routine collection across the surveillance spectrum. Dr. Li asked whether there was a need for more widespread use of rapid case ascertainment systems, which already exist at some SEER sites. Dr. Edwards replied that this is an area of interest for the future especially because of the potential for use in special studies. Dr. Klausner concluded the update on NCI's cancer surveillance efforts by pointing out that the response to the SIG recommendations will begin this fiscal year, with funding from the Director's reserve.

UPDATE ON INNOVATIVE AWARD MECHANISMS

Dr. Richard Klausner

Dr. Klausner introduced Dr. Carol Dahl, Director, Office of Technology and Industrial Relations, and Dr. Edward Sausville, Associate Director, Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD), to present

information on the progress in implementing two of NCI's new funding mechanisms—Phased Innovation Awards and Rapid Access to Intervention Development (RAID)

Phased Innovation Awards

Dr. Dahl reviewed for the Board the Phased Innovation Awards that were created to provide a technology development support mechanism to address the limitations of the existing mechanisms in responding to near-term technology opportunities. The needs identified through discussions with the research community and in the recommendations of the working groups were: (1) a rapid turnaround review period from acceptance to award, (2) provisions for a feasibility phase, and (3) an expedited transition into the development phase. Thus, the Phased Innovation Award features a single submission that encompasses both the feasibility and development phases, using the existing R21 award (including measurable milestones) for the former and a new R33 award (including a credible development plan) for the latter. Other characteristics of the award are rapid review of applications, expedited transition from phase to phase, flexible budget levels, and flexible staging of the phases.

Dr. Dahl noted that the first implementation was a pilot study advertised through a PA calling for technology development suitable for *in vitro*, *in vivo*, and *in situ* analysis of: (1) alterations in genomic DNA; (2) expression of genes and gene products; and (3) cellular localization, modifications, and function of proteins. The technology also could be suitable for monitoring major signal transduction networks involved in cancer. A parallel solicitation was issued for Small Business Innovation Awards (SBIR) and Small Business Technology Transfer Research (STTR). A cap of $100K was applied only to the feasibility phase, and the built-in flexibility of the award permitted up to 2 years for the R21 phase and from 1 to 3 years for the R33, with a maximum award length of 4 years. Receipt dates were August 7 and December 10 in 1998 and April 9, 1999. The total of 46 applications (23 for Phased Innovation Award, 23 for SBIR/STTR) received by the August receipt date are in review. Taking advantage of the provisions for flexibility, 10 investigators applied for R33 awards only, and others applied for award periods of varying lengths. Concerns about the possibility of rapid expansion of the budget for the R33 phase were unfounded in relation to this first round. Assignment of applications was made to 9 branches or programs in 3 extramural divisions—Division of Cancer Biology (DCB), Division of Cancer Prevention (DCP), and DCTD. Molecular analysis tools for population science applications was the only area of science for which a significant number of applications was not received. The response of this first round of applications, in terms of the scientific areas solicited, was deemed successful; quality applications were received for both the Phased Innovation and SBIR/STTR Awards. Dr. Dahl noted that ongoing cooperative management across the divisions is planned because many of the applications have potential application across a number of programs. She announced that a larger number of applications were received for the December 10 deadline, and there is a continued level of interest for the April 9 date and beyond. Dr. Dahl noted that the mechanism has been successful in evoking an enthusiastic response from the research community, and the provisions for flexibility were justified in that applicants took full advantage of them. In response to interest on the part of extramural researchers and NCI

scientific program directors, this mechanism is being considered for a variety of other programmatic announcements.

Questions and Answers

In response to Dr. Nienhuis's question about the review process for the transition from R21 to R33, Dr. Dahl noted that a review will take place but it will be shortened considerably by the initial review of the milestones that accompany the R21 phase. Investigators will be held accountable for them at an appropriate level of review put in place by the management group. This could range from soliciting outside peer comments from the initial reviewers to a site visit, depending on the complexity of the milestones and magnitude of the effort.

Rapid Access to Intervention Development (RAID)

Dr. Sausville reminded the Board that this new mechanism provides preclinical resources to the academic investigators and, potentially, to the small business community to bridge the gap between the discovery of potentially useful therapies in academic laboratories and clinical testing. The program will allow access to NCI's R&D contracts for agents still in academic laboratories. Innovations include a format for applications in which the investigator provides an abstract, background information, hypothesis, specific requests, information to document the novelty of the proposed project, and a declaration of intellectual property issues. The originator does not request a budget; NCI staff estimate the budget based on the use of current contracts. Other innovations relate to the review process, which draws from a RAID reviewer pool; including PI's of R01 and P01 projects related to biochemical pharmacology and biologics; rapid progression from receipt of application to award (i.e., 3 months); the provision that all, some, or few elements of a RAID request can be supported; and the regular interaction with NCI staff to define goals and timelines. In the initial round received August 1, 1998, 30 applications were received, 29 were reviewed, five were recommended for full development, and 7 for partial development. Applicants were informed by November 1. Dr. Sausville estimated that the cost for these awards would be $6M if all of the funds that would be involved in these levels of support are committed over the life of the contracts, but the amount would be phased in over a period of 2-3 years. Projects approved for potentially complete development if milestones are met span the gamut of potential product areas—oligonucleotides, novel peptides, biological response modifiers, and a novel antifolate. Projects approved for partial assistance included classical chemotherapeutic agents, novel agents directed at inhibition of signal transduction, and gene therapy approaches. Dr. Sausville concluded that although the initial offering succeeded in attracting a broad spectrum of types of therapeutics, an overall assessment of the program is not yet possible. The hope is that RAID will lead to a more rapid development and initial clinical testing of novel agents that would allow well-defined scientific hypotheses to be addressed. Dr. Klausner added that the initial response to the two new funding mechanisms has been such that they are being considered as models for use in other areas of investigation, e.g., using the Phased Innovation Award to stimulate research in communication interventions.

ANNUAL REPORT ON GENDER AND MINORITY ACCRUALS TO CLINICAL TRIALS

Dr. Marvin Kalt

Dr. Kalt reminded members that the NIH Revitalization Act of 1993 requires that the Director, NIH, shall ensure that women are included as subjects in each project and that members of minority groups are included as subjects in such research. The NIH Office of Research on Women's Health prepares the summary report, which is to include the statement that the NCAB has reviewed the NCI procedures for implementation of NIH policy and the results of that implementation, and has determined NCI compliance. Dr. Kalt briefly reviewed the NCI procedures for implementing NIH policy and presented three summary tables showing enrollee distribution by race and gender, actual enrollment by race and gender, and gender distribution for NCI clinical studies active in FY 1996. Enrollee distribution in all active studies involving human subjects was found to be close to accrual targets except for the Native American population: 0.8 percent Native Americans; 11 percent Asian/Pacific Islanders; 7 percent Black; 6 percent Hispanic; 65 percent White; 11 percent not categorized. Because of major studies in breast cancer and reproductive tract cancers, women are well represented in aggregate clinical trial data, comprising 73 percent of clinical trial enrollment.

In discussion, Dr. Amelie Ramirez asked for additional information on recruitment of subjects from year to year to be able to track increases or decreases. Dr. Millon-Underwood asked for reports showing data from SEER, clinical cooperative groups, and cancer centers separately.

Motion. A motion was made to verify that NCI was in compliance with the NIH policy for inclusion of women and minorities in clinical studies. The motion was seconded and unanimously approved.

MINORITY REPORTS

Dr. Klausner introduced Dr. M. Alfred Haynes, Former President and Dean, Drew Postgraduate Medical School, and Former Director, Drew-Meharry-Morehouse Consortium Cancer Center, to present the Institute of Medicine (IOM) Report: Cancer Among Minorities and the Medically Underserved. The study was Congressionally mandated in the 1998 appropriations bill and was recently presented to the Labor, HHS, and Education Subcommittee of the Senate Appropriations Committee. Dr. Klausner noted that the presentation by Dr. Haynes, who chaired the IOM Committee, would be followed by his response to the report and presentations by staff members on NCI's program to address the differences in cancer incidence, mortality, and outcomes that exist among different U.S. populations.

Institute of Medicine Report

Dr. Haynes announced that he would focus his remarks on three of the most discussed recommendations of the IOM report on minorities and the medically underserved with the hope that IOM's position on these matters could be clarified in the ensuing dialogue.

The IOM Committee has recommended expansion of the SEER program with the purpose of including groups not adequately represented to date. A more formal relationship with state cancer registries that are not part of the SEER program was also recommended to move toward the goal of a national registry that is more broadly representative of the increasing diversity of the U.S. population. Uniform methods of data collection and analysis were recommended, including a change from the racial classifications to a system based on ethnic groups. Classification by large ethnic groups and subgroups was considered a better approach to studying the possible causes of cancer as they relate to lifestyle, customs, behavior, and other cultural characteristics.

Dr. Haynes noted that the Committee was asked to examine the allocation of resources to research on minorities and the medically underserved, which has implications in developing public policy. He stated that the Committee took a different position from that of the NCI in the categorization of expenditures for minority research. Whereas the NCI includes both the dollars for research specifically targeted toward minority populations and a percentage of the dollars for research targeted toward the general population but relevant to minorities in its calculation of total expenditures the IOM Committee would include only the former, because it does not believe that the percent relevancy method accurately accounts for the allocation. The Committee maintained that the accounting method should be based on the research question, which in this case meant the difference in the burden of cancer in the various groups, not the percentage of minorities in the studies.

Dr. Haynes identified priority setting as the third area of controversy. He noted that NCI documents state that research opportunity and the burden of cancer are the priorities that set the research agenda. The Committee believed, however, that, when significant population differences exist, scientific opportunity and the differential burden of cancer should set the priorities. The Committee concluded from oral presentations that it was NCI's view that there should be no difference in the approach and that any attempt to conduct separate differential studies would be a form of research segregation. The Committee believed that, regardless of ethnicity or income status, differential studies are justified as separate studies and should be based on the research question and differential burden of disease.

NCI Response to the Institute of Medicine

Dr. Klausner thanked Dr. Haynes for addressing a difficult issue that the Institute regards as important. He pointed out that the overwhelming amount of information that informed this study was produced from Institute programs that are established to target specific questions. In responding to the first issue identified by Dr. Haynes, Dr. Klausner briefly summarized the steps already undertaken to expand SEER in accordance with advice from experts secured through a long review process. NCI analysis of surveillance and burden of disease data has long gone beyond the five racial and macroethnic groups established in OMB Directive 15 for census and government reporting and now includes analysis according to socioeconomic status (SES), educational levels, and state economic areas. Current efforts are attempting to link SEER to the national system, and the pooling and publication of the pooled data is expanding.

Dr. Klausner then addressed the issue of how the NCI reports, oversees and monitors programs. The IOM report claimed that the NCI spends $24M on targeted research, $20M less than the $44M total of 128 projects targeted 100 percent to special populations that was submitted to the Committee. Because the list of projects was limited to RPGs as requested, the $44M total underestimated NCI's 100 percent targeted commitments by an additional $20M worth of projects not funded through the RPG pool—projects such as the Black, Hispanic, and Appalachian Leadership Initiatives, Minority Biomedical research Grants, Prevention Awareness Program for Hispanics, and Breast Cancer Among Asian American Women. Dr. Klausner noted that another $89M—47 additional projects—were accounted for as nontargeted research, which was defined as research having the ability to address specific questions relating to unequal burden of cancer. Examples of these studies, which were calculated as only partially targeted, are the Black/White Study in Prostate, Multiple Myeloma, Pancreatic, and Esophageal Cancer; a study of racial differences in breast cancer survival; the Multiethnic Minority Cohort Study of Diet and Cancer; epidemiologic studies of diet and cancer in Hawaii, and the SEER program. Dr. Klausner emphasized that knowing the outcome of the NCI investment in programs must be considered, and he cited the analysis submitted to the IOM Committee which showed that NCI- supported grantees produced 95 percent of the 358 peer-reviewed, published articles between 1995 and 1997 that answered questions specifically relevant to the unequal burden of cancer.

In regard to the issue of priority setting, Dr. Klausner referred to the extensive strategic planning that has been implemented in the years since his arrival at the NCI and pointed out that NCI planning in each program area always incorporates strategic plans specifically related to minorities and the underserved. He expressed the view that planning for the minorities and the underserved is best done within the context of planning for each research area. That process incorporates the most appropriate expertise and achieves the goals of specifically addressing the questions of unequal burden in all NCI research programs.

Update on Office of Special Populations Research

Dr. Otis Brawley, Director, Office of Special Populations Research (OSPR), NCI, reminded members that the OSPR, which was created two years ago, coordinates NCI special populations efforts, assures that pertinent scientific questions are being addressed, and serves as the liaison to special populations and those interested in research involving special populations. The OSPR has the advice and counsel of the intramural Special Priorities Advisory Group on activities and priorities related to special populations and women's health. A parallel extramural group to be called the Special Populations Working Group is being established as a subcommittee of the Advisory Committee to the Director to ensure that special populations issues are integrated into the research of every branch, program and division of the Institute. OSPR administrative activities include tracking accrual by race and gender in clinical trials, oversight of the NCI's funding from the NIH Office of Research on Minority Health (ORMH), which amounted to $8M for 27 projects in 1998, and monitoring NCI funding of projects targeted to special populations. Liaison activities recently have encompassed meetings with representatives of special population communities (Asian, Black, Hispanic, Native American) to better understand

concerns, set agendas, and review NIH/NCI portfolios of research in these areas. Communication of NCI efforts is maintained through print and Web-based publications (*e.g., Special Populations Exceptional Opportunities and NCI Initiatives for Special Populations*). Other outreach efforts are coordination of a soon-to-be established Special Populations Network for Cancer Awareness Research and Training and administration of the Cancer Control Academy, which features intensive course on cancer control and research.

Dr. Brawley outlined OSPR efforts to analyze available scientific data to identify what is known about special populations and minority health, what are the questions yet to be addressed, and what are the lessons that should be implemented. For example, it has been ascertained that there is racial proportionality on NCI treatment trials but a paucity of minorities and the poor on screening and prevention trials. Efforts to address this problem include 28 grants funded within the Institute through the Early Detection Branch and Comprehensive Minority Biomedical Program looking at minority inclusion issues as well as strategies for improving accrual to and retention in treatment and prevention trials. An analysis of the findings from these grants will be published in the *Annals of Epidemiology* in November or January. Dr. Brawley emphasized findings from NCI studies that equal treatment yields equal outcome regardless of race, and from NCI-sponsored patterns-of-care studies, which show that equal treatment does not prevail. Factors in the disparities are socioeconomic status, comorbid disease, and race. To illustrate this, Dr. Brawley presented data from the minority-based Community Clinical Oncology Program (CCOP) which shows that Blacks and Hispanics, aged 50 to 69, presenting cancer are more likely to have comorbid diseases than Whites. SEER data show that breast cancer mortality rates from 1991 to 1995 were very high for Blacks and Whites compared with Hispanics, American Indians, and Asian/Pacific Islanders. SEER data also show increasing disparities in breast cancer mortality for Black women driven primarily from deaths in older women (aged 50 to 70). Further analysis of these data show that the increasing mortality rates among Black women mirror the decrease in percentages receiving the standard treatment compared with White women. Dr. Brawley concluded that the fastest reduction in mortality can be brought about by addressing the societal issues of racism and deprivation and making the fruits of research available to special populations.

Opportunities for Sociocultural Research

Dr. Sherry Mills, Chief, Applied Sociocultural Research Branch (ASRB), Behavioral Research Program, DCCPS, reviewed expanded opportunities for research in sociocultural issues in cancer control. Established in October 1998, the ASRB has an extensive mission statement covering all aspects of grant program development and implementation; rapid-response initiatives; information collection, analysis, and dissemination; intervention evaluation; liaison activities; and research stimulation in the investigator community related to preventing and/or reducing cancer burden in special populations. These populations include ethnic and racial minorities; the elderly, rural, and physically challenged; and persons of low SES. The ASRB interacts with Dr. Brawley's office and serves on the Special Populations Advisory Committee to provide input on the

behavioral components of cancer control in special populations. The ASRB serves as a referral site within DCCPS for concepts that are going forward from a variety of NCI offices, to ensure that components of special populations needs are included in all NCI initiatives and will be appropriately addressed. Portfolio development of the branch is largely focusing on investigator-initiated research. To that end, the branch has been working with the NIH Center for Scientific Review to provide at least three standing committees for the appropriate peer review of grant applications in the behavioral and social sciences. The development of an R21 mechanism will be proposed to address the problem that many grants fail in peer review because they lack pilot data or appropriately tested hypotheses. The ASRB also is marketing to become the home for competing renewals by investigators with minority enhancement awards and attempting to interest minority supplement grantees in cancer control. Within the branch, a Fundamentals of Grant Writing Workshop is supported, a Web site is maintained for mentoring in cancer control grantsmanship, and a virtual technology assistance workshop has been piloted and is being debugged for reintroduction later in the year. Dr. Mills concluded with a summary of strategic planning activities that are ongoing within the DCCPS Behavioral and Surveillance Research Program to collaborate on the development of a geographic information system and with the minority CCOPs to introduce cancer control to those populations. A process for an annual evaluation of the ASRB portfolio is being proposed to identify gaps and help in priority setting. In the scientific area, the ASRB has begun a synthesis of tobacco interventions related to underserved populations to determine what are successful interventions and what the opportunities are to promote research in that area.

Questions and Answers

Dr. Bishop proposed that the Board discussion of the IOM report focus on three questions: (1) Is the NCI reporting its minority and underserved population research in an appropriate way? (2) Are efforts in this venue being planned appropriately? and (3) Should the NCI be working in a segregated or integrated manner with these problems? In discussion, an attempt was made to clarify what type of information the IOM Committee received and what they did with it. Dr. Haynes acknowledged that on the basis of the allocation made in the study discussed by Dr. Klausner, the NCI appeared to be under-reporting its cancer effort. Dr. Klausner explained the general problem encountered in coding studies when they address multiple questions coupled with the need to be as accurate as possible in discharging NCI's responsibility to Congress and to particular groups without over- or understating the numbers. Dr. Haynes suggested the need for the NCI to address the problem of making its coding system more accurately reflect what is being done. He explained some of the reasons behind the Committee's challenge of the NCI's percent relevancy estimates and suggested approaches to dealing with the coding problem. An attempt was made to clarify the effects of economics versus race in explaining the disparity in treatment received by Black breast cancer patients. Ms. Frances Visco suggested as a future Board topic the extent to which the NCI and the National Cancer Program should be involved in making certain the results of research are applied uniformly across all populations. Dr. Bishop proposed that the Board carry the discussion of the IOM report over to the next meeting. Dr. Ramirez proposed that an *ad*

hoc subcommittee of the Board be formed to address the issue of coding, with possible participation by representatives from the IOM Committee.

Motion. A motion was made to create an *ad hoc* working group of the NCAB to address the issue of coding for NCI research projects for ethnic minorities and the medically underserved. The motion was seconded and unanimously approved.

SUBCOMMITTEE REPORTS AND NEW BUSINESS II

Planning and Budget

Ms. Ellen Stovall presented the written report of the Planning and Budget meeting. During the meeting, a motion was made, and the Subcommittee voted, to recommend to the full Board that a letter be sent to members of Congress and the Administration expressing concern about the initial FY2000 budget request for the NCI. Ms. Stovall presented a draft of the letter for Board approval.

Motion. A motion was made to approve the report of the NCAB Subcommittee on Planning and Budget, which would subsume approval of the letter as drafted and concur with the Subcommittee's recommendations in this matter. The motion was seconded and unanimously approved.

Cancer Centers

Dr. Ivor Royston, acting for Chair Dr. Phillip Sharp, presented the written report of the Subcommittee on Cancer Centers and asked for full-Board action on three recommendations related to changes in the Cancer Center Support Grant (CCSG) Guidelines. The changes had been recommended by members of the parent peer-review committee in the September meeting with the Subcommittee to present their view on the effectiveness of the recently revised Guidelines. The recommended changes had subsequently been submitted for comment to NCI's cancer center directors, and their responses were considered by the Subcommittee in formulating the recommendations to be voted on. Dr. Royston summarized each of the three proposed changes and the supporting arguments in favor or against them. He entertained motions for each change in accord with the recommended action by the Subcommittee.

Motion. A motion was made to recommend revision of the Cancer Center Support Grant Guidelines to **Change the scientific requirement for the comprehensive designation from a minimum of one center program in each of the areas of basic, clinical, and population to "reasonable depth and breadth of research" in each of the three areas.** The motion was seconded and unanimously approved.

Motion. A motion was made to recommend revision of the CCSG Guidelines to **Include language in the designation of clinical and comprehensive cancer centers that would encourage participation in the clinical cooperative groups.** The motion for this change was seconded and approved unanimously.

Motion. A motion was made to reject the proposal to change existing language in the Guidelines to **Include the word "Research" in all formal references to NCI designations (e.g., NCI- designated Comprehensive Cancer Research Center)**. The motion rejecting this proposed change was seconded and approved by a vote of six yeas to five nays, with one abstention.

In the discussion of this motion, members in favor of including "Research" in all formal references argued that: (1) not doing so represents a retreat from the effort to promote research and clinical research as excellence in cancer care; (2) failure to include research in the formal designation implies NCI approval of the level of care and may be misleading; and (3) centers were funded for excellence of research not clinical care based on their own design of the current guidelines. Arguments in favor of rejecting this motion were based on the Subcommittee's recommendation to defer to the rationale presented by the majority of cancer center directors surveyed that "research" in the title would disadvantage the center in the current health care climate. It was noted that more information from focus or marketing groups is needed to assess whether "research" in the title is detrimental to or helpful in the center's ability to attract patients. Dr. Klausner noted that the development of standards of advertising is being discussed with the cancer centers. This would be done by the interaction of cancer center directors and their marketing staff with the Office of Cancer Communication (OCC).

Motion. A motion was made to approve the written report of the NCAB Subcommittee on Cancer Centers as presented. The motion was seconded and unanimously approved.

New Business II

Dr. Bishop brought to the table and entertained motions on the items of unfinished business carried over from the previous day.

Motion. A motion was made to approve the proposed NCAB Resolution on Access to Grantee Data. The motion was seconded and unanimously approved.

Motion. A motion was made to approve the draft of a letter to be sent to the OMB conveying the sense of the Board in regard to the proposed rule making that would amend OMB Circular A-110 "Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations." The motion was seconded and approved unanimously.

OFFICE OF CANCER COMPLEMENTARY AND ALTERNATIVE MEDICINE
Dr. Robert Wittes, Dr. Jeffrey White

Dr. Robert Wittes, Deputy Director for Extramural Science (DDES), NCI, reported that the NCI has established the Office of Cancer Complementary and Alternative Medicine (OCCAM) within the Office of the Deputy Director for Extramural Science (ODDES) to coordinate the NCI's approach to complementary and alternative medicine (CAM) as it relates to cancer. Dr. Jeffrey White, Director, OCCAM, explained that this office functions as a liaison from the NCI to the National Center for Complementary and

Alternative Medicine ([NCCAM] the former NIH Office of Alternative Medicine) and as the interface with the public regarding CAM cancer research. The OCCAM also coordinates CAM projects throughout the Institute and is in the process of developing a proactive NCI CAM agenda. Dr. White noted that his office is working to develop a definition of CAM that can be actualized for different purposes, such as budget setting—one that defines this area as an integrated component of the cancer research portfolio and explains its connection to CAM-related areas such as dietary research and various areas of behavioral research.

Projects in which the OCCAM is currently involved are: (1) Phase III clinical trials of shark cartilage in patients with cancer; (2) evaluation of intensive pancreatic proteolytic enzyme therapy with ancillary nutritional support in the treatment of pancreatic cancer; (3) liaison with the University of Texas Center for Alternative Medicine Research; (4) an NIH RFA for Centers for CAM, with a January 1999 receipt date; (5) best-case-series reviews of patient data on alternative therapy received from CAM practitioners; (6) the Cancer Advisory Panel for CAM, which is advisory to the NCCAM; (7) co-sponsorship of a June conference "Comprehensive Cancer Care II: Integrating CAM Therapies;" and (8) an NIH RFA for Centers for Mind-Body and Health Interactions. Dr. White listed cancer research areas that are potential focuses for the OCCAM: (1)alternative systems of medical practice, including Chinese medicine and homeopathy; (2) bioelectromagnetic applications; (3) diet, nutrition, and lifestyle changes; (4) herbal medicine, manual healing, mind-body control; (5) pharmacological and biological treatments; (6) vaccines; and (7) chemotherapy modulators. Dr. Wittes pointed out that this area of medicine falls within the purview of the NCI because of the need to introduce and maintain scientific standards of evidence and evaluation for claims made in both the CAM clinics and laboratories. In response to a question from Dr. Vainutis Vaitkevicius, Dr. White noted that the NCCAM maintains a clearinghouse of information that is available for patients, physicians, and the general public. In addition, the OCCAM is trying to in trying to include specific CAM areas in the Physician Data Query (PDQ) system.

EXTRAMURAL POLICY ISSUES
Dr. Marvin Kalt
Modular Grant Awards

Dr. Kalt informed the Board that NIH has published the new modular grant award in the *NIH Guide*. This type of award is applicable to all applications that request no more than $250K in direct costs in any year. The budget process for the modular award has been streamlined in that applicants can request funding in $25K implements and the review committee will consider making budget recommendations in $25K increments. Administrative supplements, either competing or noncompeting, will continue to be allowed. Receipt dates are in April for SBIRs, May for area R15s, and June for R01s, R03s, and R21s so these applications will not be seen in NCAB's second level review process until 2000.

Peer Review of Program Project (P01) Applications

Dr. Kalt presented for Board approval a proposal for changes in the procedures for scoring P01 applications. He emphasized that the changes would not affect the number of

awards or total dollars allocated to P01s, nor would they require a change in applications or how they are written. Another difference is that paylines would be announced retrospectively, although target success rates will be indicated. Procedural changes include: (1) numeric scores for individual components; and (2) an adjectival range to indicate the synergy provided by a program as an integrated effort. Dr. Kalt concluded with an outline of measures to be taken to calibrate reviewers and noted that this approach to the review of P01s will be evaluated after three cycles.

Motion. A motion was made to approve the proposed changes to procedures for peer review of program project (P01) applications. The motion was seconded and approved unanimously.

STATUS REPORT: DIVISION OF CANCER PREVENTION
Dr. Peter Greenwald

Dr. Peter Greenwald, Director, DCP, reported on organizational changes in DCP. He reviewed for the members some of the research areas with the potential to have an impact on cancer prevention: (1) tobacco control, diet and nutrition, vaccination, and environment, which comprise a public health approach; (2) biomarkers and hormone modulation, chemoprevention, and infectious agent cancer prevention, which constitute a medical approach. Planning meetings undergirding the organizational changes were the Early Detection, Chemoprevention, and Nutrition Implementation Groups formed to respond to cancer prevention recommendations of the Progress Review Groups. Common themes in the reports were to strengthen the infrastructure for prevention, strengthen the basic science ties to translational research, and expand the training program. The report of the Early Detection Implementation Group has been completed and that resulted in the initiation of the Early Detection Research Network for identifying and validating biomarkers. Organizational, all hands orientation, strategic, and basic science planning for the new DCP have taken place in a series of intramural retreats. Objectives for the new structure were to strengthen ties to the basic science community within and external to the NCI and to broaden ties to the extramural research community to enhance the area of translational research.

Dr. Greenwald noted that the DCP is being organized as a matrix structure, with research groups and project teams replacing the former structure of programs and branches. The Foundations of Prevention Research Groups include Chemopreventive Agent Development, Community Oncology and Prevention Trials, Nutritional Science, Basic Prevention Science, Cancer Biomarkers, Early Detection, and Biometry. The Organ System Research Groups echo the focuses of the medical community: Breast and Gynecologic Cancer; Prostate and Urologic Cancer; Lung and Upper Aerodigestive Cancer; and Gastrointestinal and Other Cancer. A Coordinating Unit interfaces with the Research Groups and the Office of the Director to integrate the prevention effort. Another feature of the matrix structure are the project teams that are formed on an *ad hoc* basis to address particular scientific questions by assembling appropriate intramural and extramural expertise for as long as needed. An Office of Preventive Oncology operating out of the Office of the Director has responsibility for the preventive oncology training

program. Dr. Greenwald concluded with a summary of personnel assignments that have been made, noting that an active program of recruitment in ongoing.

ADJOURNMENT
Dr. J. Michael Bishop

There being no further business, the 109th meeting of the NCAB was adjourned at 12:40 p.m. on Wednesday, February 10, 1999.