

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH  
NATIONAL CANCER INSTITUTE  
NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting  
May 7-8, 1996**

**Building 31, Conference Room 10  
National Institutes of Health  
Bethesda, Maryland**

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**The National Cancer Advisory Board (NCAB) convened for its 98th regular meeting at 8:00 a.m., May 7, 1996, in Building 31, C Wing, 6th Floor, Conference Room 10, National Institutes of Health (NIH).**

NCAB MEMBERS Dr. Barbara K. Rimer (Chairperson)

Dr. J. Michael Bishop  
 Dr. Richard J. Boxer (absent)  
 Mrs. Zora K. Brown  
 Dr. Kenneth K. Chan  
 Dr. Pelayo Correa  
 Dr. Robert W. Day  
 Dr. Kay Dickersin (absent)  
 Mrs. Barbara P. Gimbel  
 Dr. Alfred L. Goldson  
 Mrs. Marlene A. Malek  
 Dr. Philip S. Schein  
 Dr. Ellen V. Sigal  
 Dr. Vainutis K. Vaitkevicius (absent)  
 Dr. Charles B. Wilson

PRESIDENT'S CANCER PANEL Dr. Harold P. Freeman (Chairperson)

Dr. Paul Calabresi  
 Ms. Frances M. Visco

ALTERNATE EX OFFICIO NCAB MEMBERS Dr. Alison Martin, FDA

Ms. Lynn Jenkins, NIOSH  
 Dr. Marilyn A. Fingerhut, NIOSH (absent)  
 Capt. Bimal C. Ghosh, DoD  
 Dr. Hugh McKinnon, EPA  
 Ms. Rachel Levinson, OSTP  
 Dr. Lakisma C. Mishra, CPSC (absent)  
 Dr. Kenneth Olden, NIEHS

Dr. Paul Hoffman, DVA (absent)  
Dr. P.C. Srivastava, DOE  
Dr. Ralph E. Yodaiken, DOL

MEMBERS, EXECUTIVE COMMITTEE, NATIONAL CANCER INSTITUTE, NIH Dr. Richard Klausner, Director,  
National Cancer Institute

Dr. Alan Rabson, Deputy Director, National Cancer Institute  
Dr. Edward Sondik, Associate Director, Strategic Planning  
Mr. Philip D. Amoruso, Associate Director for Extramural Administrative Management  
Ms. MaryAnn Guerra, Associate Director for Intramural Administrative Management  
Dr. Faye Austin, Director, Division of Cancer Biology; Chairman, Extramural Advisory Board  
Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics  
Dr. Peter Greenwald, Director, Division of Cancer Prevention and Control  
Dr. Marvin Kalt, Director, Division of Extramural Activities  
Dr. Philip Pizzo, Acting Director, Division of Clinical Sciences  
Dr. Robert Wittes, Director, Division of Cancer Treatment, Diagnosis, and Centers  
Dr. George Vande Woude, Scientific Advisor to the Director for Basic Sciences; Director, Advanced BioScience Laboratories, Inc., NCI-Frederick Cancer Research and Development Center  
Dr. Claude Klee, Chairman, Intramural Advisory Board, Board of Scientific Counselors  
Dr. David Livingston, External Advisor, Chairman of the NCI Extramural Board of Scientific Advisors; Professor of Medicine, Dana-Farber Cancer Institute  
Dr. Martin Abeloff, External Advisor and Co-Chairman, Clinical Sciences Subcommittee A of the NCI Intramural Board of Scientific Counselors; Professor and Director, Johns Hopkins Oncology Center  
Dr. Edward Harlow, External Advisor and Co-Chairman, Basic Sciences Subcommittee B of the NCI Intramural Board of Scientific Counselors; Member, Massachusetts General Hospital  
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  
Mrs. Iris Schneider, Executive Secretary, Assistant Director for Program Operations and Planning  
Dr. Maureen O. Wilson, Executive Secretary of the President's Cancer Panel

LIAISON REPRESENTATIVES Dr. John Currie, American Association for Cancer Education, Inc.

Dr. Marc E. Lippmann, American Association for Cancer Research (absent)  
Dr. Robert Martuza, American Association of Neurological Surgeons (absent)  
Dr. John Laszlo, American Cancer Society (absent)  
Ms. Kerrie B. Wilson, American Cancer Society  
Ms. Elaine Locke, American College of Obstetricians and Gynecologists  
Dr. Stanley Zinberg, American College of Obstetricians and Gynecologists (absent)  
Dr. Bernard Levin, American Gastroenterological Association (absent)  
Dr. Edward P. Gelmann, American Society of Clinical Oncology  
Dr. John Glick, American Society of Clinical Oncology (absent)  
Ms. Julie Taylor, American Society of Clinical Oncology  
Dr. Stanley Order, American Society of Therapeutic Radiologists (absent)  
Dr. Edwin A. Mirand, Association of American Cancer Institutes  
Dr. Robert W. Frelick, Association of Community Cancer Centers  
Mr. James Kitterman, Candlelighters Childhood Cancer Foundation (absent)  
Mr. Thomas Brandt, Intercultural Cancer Council  
Dr. Ronald Jones, Intercultural Cancer Council  
Ms. Jean Whalen, Leukemia Society of America, Inc.  
Ms. Dorothy J. Lamont, National Cancer Institute of Canada (absent)  
Dr. J. David Beatty, National Cancer Institute of Canada (absent)  
Dr. Margaret Foti, National Coalition for Cancer Research  
Dr. Tracy Walton, National Medical Association  
Dr. Eve I. Barak, National Science Foundation

Dr. James Brown, National Science Foundation (absent)  
Ms. Kathi Mooney, Oncology Nursing Society (absent)  
Ms. Roberta Strohl, Oncology Nursing Society  
Dr. Jeffrey Norton, Society of Surgical Oncology, Inc. (absent)  
Dr. Marston W. Linehan, Society of Urologic Oncology (absent)

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### **CALL TO ORDER AND OPENING REMARKS**

Dr. Rimer called to order the 98th meeting of the National Cancer Advisory Board (NCAB). She introduced guests representing several cancer education and research associations and institutions as well as Federal agencies involved in cancer-related issues. Dr. Rimer welcomed members of the public and invited them to submit in writing any comments regarding items discussed during the meeting. Comments should be submitted within 10 days of the meeting to Dr. Marvin Kalt, Executive Secretary of the Board.

Dr. Rimer referred to the confirmed meeting dates for 1996, 1997, and 1998, as listed in the agenda, and asked Board members to report any conflicts with future meeting dates as soon as possible. She indicated that 3-day meetings have been scheduled, but meetings are anticipated to last only 2 days. Except for the September 1997 meeting, which starts on a Wednesday because of space constraints, all meetings begin on Monday night with meetings of the subcommittees.

Dr. Rimer called for approval of the minutes of the February 27-28, 1996, meeting. The motion was seconded and the minutes were approved. Dr. Rimer announced that future minutes will be available earlier through e-mail.

Dr. Rimer announced that the meeting agenda was full and asked that all members be in attendance for voting, particularly because the new Board members had not yet been formally appointed. By law, a quorum of Board members—a minimum of 10 appointed members—is required for every vote, whether in open or closed session. Dr. Rimer thanked recently retired NCAB members Dr. Kenneth Chan and Mrs. Marlene Malek for coming to this meeting to help meet the requirement for a quorum.

Dr. Rimer asked that requests to have grant applications discussed during the closed session be given to Dr. Kalt before or during the morning break. She announced that those wishing to follow up on any of the communications received from scientists in the community or on any item identified in the Board books also should contact Dr. Kalt.

Dr. Rimer announced that subcommittee meetings would be held during and following lunch. She then reviewed the list of presentations scheduled for the day's Board meeting.

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### **SPECIAL RECOGNITION OF DR. PHILIP PIZZO**

On behalf of the NCAB, Dr. Rimer recognized and honored Dr. Philip Pizzo for his two decades of service to the National Cancer Institute (NCI). Dr. Rimer praised him as one of the NCI's most gifted and compassionate clinical researchers. She expressed particular gratitude for the collaborative way in which Dr. Pizzo had worked with the Board as a liaison to the Navy Committee. Dr. Pizzo has been Acting Director of the Division of Clinical Sciences (DCS), and he will be leaving the NCI to become physician-in-chief at Children's Hospital of Boston. Dr. Rimer presented Dr. Pizzo with a proclamation, which the Board had approved by acclamation. Dr. Pizzo accepted the proclamation and thanked the Board.

Dr. Rimer introduced Dr. Harold Freeman, Chairperson of the President's Cancer Panel (PCP) to report on recent activities of the Panel.

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### **REPORT OF THE PRESIDENT'S CANCER PANEL**

Dr. Freeman announced that, in his brief remarks, he would be issuing a challenge to the members of the NCAB to assist and to guide the PCP over the next few months. The Panel is about to embark on a series of meetings with

research, clinical, academic, pharmaceutical, advocacy, patient, and other concerned groups across the nation to hear first-hand about the impact managed or captivated care is having on the initiation of Phase I clinical trials. Dr. Freeman explained that the Panel had chosen to investigate Phase I trials because the NCI, through the excellent work of Dr. Robert Wittes and Ms. Mary McCabe, is focusing its efforts with the Civilian Health and Medical Plan of the Uniformed Services (CHAMPUS), with the cancer centers, and with clinical trials investigational groups on this issue as it relates to Phase II and III trials.

The Panel's first meeting is scheduled for July 30 in Seattle, Washington, where the Panel hopes to hear from concerned groups and individuals who are experiencing the impact of managed care. Dr. Freeman characterized Seattle as an area that is dominated by health maintenance organizations like the Group Health Association and larger corporate care organizations like Aetna's Northwest Regional Services. He added that Seattle also is the home of the Fred Hutchinson Cancer Center and the University of Washington, both of which are vested in the support of Phase I trials. The remainder of the 1996 meetings are scheduled for September, October, and November and will address concerns about managed care, as well as other issues.

Dr. Freeman stated that the question of Phase I trials affects many Board members immediately, and everyone ultimately, through its impact on initial support from which the nation will derive future treatment and prevention choices. He therefore invited Board members to pose specific questions for the Panel to investigate during the course of the next few months. He also invited the Board to join the Panel members in the investigative process. He asked those wishing to participate to contact Dr. Paul Calabresi, Ms. Frances Visco, himself, or Dr. Maureen Wilson.

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## **QUESTIONS AND ANSWERS**

### **Report of the President's Cancer Panel**

In response to Dr. Sigal's question about the outcome of the investigation, Dr. Freeman stated that the Panel would make recommendations after all data had been collected.

Dr. Rimer asked how the Panel planned to publicize the hearings in a city like Seattle, to ensure that people have the opportunity to attend them or to testify. Dr. Freeman acknowledged the validity of her question and stated that past efforts in this regard have not been very good. Although routine notices are sent, Panel meetings often do not attract people locally as they should. Dr. Freeman indicated the need for Panel members and the Executive Secretary to discuss how better to publicize the meetings, because some of the issues addressed are extremely important and the Panel meetings feature presentations by experts that should be heard by a larger public.

Dr. Rimer suggested to Dr. Philip Schein that the Subcommittee on Clinical Investigations might want to take this opportunity to pursue some of its concerns through the hearing mechanism used by Dr. Freeman and the Panel. She suggested that the committee think about specific questions that could be posed to the PCP for consideration during the hearings. Dr. Calabresi agreed, and he suggested that the committee work closely with Dr. Wittes, Ms. McCabe, and the Panel. Dr. Calabresi stated that limiting the coverage in the CHAMPUS agreement to Phase II and Phase III was a choice made by the Department of Defense (DoD) in the negotiations. The NCI is conducting ongoing and productive discussions with other agencies, private insurers, and providers with the ultimate goal of obtaining commitments for the support of all participation in clinical research.

Dr. Freeman agreed and stated that the Panel intends to combine forces. He raised the issue, however, that Phase I/II/III-related limitations of research are not the only effect of managed care on the outcome of cancer care in America. The Panel will combine forces on the Phase I aspect, but will also look at the total effect on the American public with respect to cancer outcome and managed care. Dr. Rimer conveyed the interest of the Board in working with the PCP on this issue, and she asked to be kept informed of the cities where the hearings will be held.

Dr. Freeman emphasized that this effort is of concern to the entire scientific community, in particular, but also to the entire American public. He indicated that all interested individuals in the NCAB and the NCI will be brought in to help plan these meetings.

Dr. Calabresi noted that the meetings will be held in different quadrants of the country, including the west coast,

northeast, and south. The belief is that although excellent work has been done in Phase II/Phase III and IV studies, particularly with the CHAMPUS initiative, there will be a gap at the Phase I level, where translational research takes place. Phase I studies should not be interpreted as being just clinical studies, but also as preclinical studies leading to Phase I and Phase I/II studies.

Dr. Rimer expressed interest in the upcoming hearings and thanked Dr. Freeman for his presentation. She introduced Dr. Klausner to present an update on activities in the NCI.

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## REPORT OF THE DIRECTOR, NATIONAL CANCER INSTITUTE

Dr. Klausner reported that the Department of Health and Human Services (DHHS), which includes the NIH and the NCI, is currently operating under a continuing resolution and would continue to do so through the end of FY 1996. The NCI is funded at a level of \$2,250,084,000, which is a 5.8 percent increase over the FY 1995 level—AIDS monies are included in this total. Dr. Klausner explained that AIDS funds were not distributed through the Office of AIDS Research (OAR) this year but were given directly to the Institutes as a result of the agreement made early in the year.

Dr. Klausner provided some of the details of the 1997 President's budget, which had been submitted to Congress since the NCAB met in February. The total increase proposed for the NIH was 3.9 percent, or \$467M. The NCI's proposed FY 1997 budget represented a 1.3 percent increase over FY 1996. Dr. Klausner explained the apparent disparity in funding increases for the NIH and the NCI. There has been a significant change in policy, determined by the Office of Management and Budget (OMB), based on negotiations concerning the agreed-upon need for the NIH to address the crumbling infrastructure of the NIH Clinical Center. The OMB determined that renovation of the Clinical Center should be paid for completely with funds in the year in which the construction was to be approved. Dr. Klausner noted that the NCI had initially negotiated for multiyear funding, but the decision was made to have all funding available for a major construction project at the time of the approval. Dr. Klausner stated that the actual cost for the Clinical Center is almost \$310M and the difference between \$310M and the \$274M listed in the NCI budget is offset by decreasing the NIH buildings and facilities fund. Without the buildings and facilities funds, the total increase for the NIH research is \$193M, or 1.6 percent over the FY 1996 budget. This NIH increase of 1.6 percent contrasts more favorably with the 1.3 percent proposed increase for the NCI.

Dr. Klausner next addressed the distribution of funds among the various funding mechanisms in the President's budget for FY 1997. An increase in the Research Project Grants (RPG) line from \$1.02B to \$1.06B is proposed. This would represent 46.5 percent of the total NCI budget. The Cancer Centers line would remain flat at \$167M in this proposal; however, Dr. Klausner emphasized, the budget process is in early stages. Cancer Centers would maintain the increase that was made in FY 1996; most of the changes made in FY 1996 would be continued.

Dr. Klausner pointed out that the intramural research budget decreased from 18.5 percent of the NCI budget in FY 1995 to 18 percent in FY 1996 and would decrease to 17.5 percent in the budget proposed for FY 1997. Research Management and Support would continue at \$100M. He noted the possibility of changes, because of reprogramming that was not completed in time to be incorporated in the recommendations to the President's budget.

Dr. Klausner stated that the description of the intramural research budget contained in the FY 1997 President's budget accurately reflects all contracts and all support received from the Frederick Cancer Research and Development Center (FCRDC). Additional discussion of the intramural research budget was postponed until the response to the Bishop-Calabresi Report scheduled later in the meeting.

Dr. Klausner pointed out that the NCI's actual FY 1996 budget total as shown on the slide did not reflect the fact that the NIH Director, Dr. Harold Varmus, exercised his 1-percent transfer authority and redistributed a total of \$25M to the Institutes. The NCI received \$10M of that \$25M for its successful proposals in cancer genetics and in development of an informatics infrastructure for the National Clinical Trials System. The NCI thus received a net increase of \$7M over the original allocation for FY 1996.

Dr. Klausner reviewed the status of the RPG budget line as proposed in the FY 1997 President's budget: noncompeting

grants would increase by 290 (7.2 percent increase); competing grants would decrease by 129 (8.8 percent decrease); Small Business Innovation Research (SBIR) grants by law would increase; the total number of grants would increase from 3,444 to 3,605. Dr. Klausner noted that Congressman Porter's hearings in Congress questioned some aspects of the SBIR budget and final word on that appropriation has not been received. Without further budget changes, the R01 percentile funding line—the payline—would drop from the current 23rd percentile to the 21st percentile, and the success rate, calculated to be 29 percent this year, would be 27 percent for FY 1997. By contrast, the R01 payline in FY 1995 was 15 percent. Program project grants (P01) would have a payline at the 31st percentile and begin at a priority score of 140; small research grants (R03) would begin at a priority score of 200.

Dr. Klausner reminded the Board that these figures represented the budget at the beginning of deliberations of the President's proposed budget. The final status of the SBIR and the Small Business Technology Transfer Research (STTR) grants will depend on the deliberations of Congress. Significant changes have been effected in the NCI AIDS budget, which, Dr. Klausner stated, would be described in the scheduled report on progress in the implementation of the Bishop-Calabresi Report. The changes include reprogramming AIDS monies and rethinking how funds are coded.

Dr. Klausner reported that appropriation hearings held since the February NCAB meeting went quite well. Members of the House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies were aware of the changes the NCI has undergone and were supportive.

Since February, the first meetings were held of the NCI's two advisory boards—the Board of Scientific Counselors (BSC) for the Intramural Program and the Board of Scientific Advisers (BSA) for the Extramural Program. Dr. Klausner stated that the membership rosters are complete, and the Boards have been chartered. They are reviewing NCI operations, and participating in the planning and implementation of programs. Dr. Klausner deferred further discussion of advisory board activities until the discussion of the NCI's implementation of the Bishop-Calabresi Report.

Dr. Klausner announced that the Bypass Budget has been completed and will be released soon. Staff members throughout the DHHS have responded to the Budget with enthusiasm. DHHS Secretary Shalala has requested that the NCI and DHHS collaborate to ensure that the Bypass Budget undergoes widespread public discussion to clarify the role of the NCI and to show that the budget reflects NCI's strategies for progress against cancer based upon scientific opportunities for discovery. Dr. Klausner thanked members of the NCAB and representatives of extramural organizations for their comments, which had been reviewed and incorporated. He expressed satisfaction with the development process for this year's budget and indicated that it would continue to be a part of the NCI's planning activities.

**Director's Review Groups**—Dr. Klausner reported that, since February, the BSA-based review groups have continued to make progress. The report of the Cancer Centers Program Review Group will be presented later in the meeting by Dr. Joseph Simone. First meetings were held of the Clinical Trials Review Group, chaired by Dr. James Armitage, and the Prevention Review Group, chaired by Dr. Edward Bresnick. Organization of the Developmental Therapeutics Review Group, co-chaired by Dr. Susan Horowitz and Dr. Stuart Schreiber, and the Cancer Control Review Group, chaired by Dr. David Abrams, is progressing, and the groups are expected to be operating within the next few months.

Also, two Director's Working Groups are being formed, with broad representation from the research community, to operate in an ad hoc capacity when the NCI reaches out to the community for expertise from a wide range of constituents. They will not be charged with producing reports about specific programs; rather, they will help the NCI develop strategies with the scientific community to address critical and pressing issues, some of which might be identified as investment opportunities in the Bypass Budget.

The first working group, which has already met, is the Developmental Diagnostics Working Group, chaired by Drs. Arnold Levine and Eric Lander. Its goal is to help the NCI move into the post-genome world, as it applies to cancer. Three subgroups of this working group will advise on Technology Development and Dissemination, Clinical Resources, and Informatics. The Subgroup on Technology Development will bring together many individuals from industry and academia who are involved in the development of relevant technologies. The Subgroup on Clinical Resources will address such questions as: What do we want and what do we need? How will we deal with tissue

banks, DNA banks, etc. so that they are aligned with—rather than hindering—developments in technology? The Subgroup on Informatics will focus on the informatics base needed to deal with the enormous amount of information that will be generated.

The second working group that met is the Cancer Genetics Working Group, chaired by Dr. Alfred Knudson and Dr. Barbara Weber. This group will discuss the NCI on the nature of the national infrastructure that will be needed to facilitate the access of individuals to information about and the actual performance of genetic testing for cancer susceptibility. The question to be addressed will be: How can the NCI facilitate a national infrastructure to provide this access in the context of informed consent and counseling, and at the same time facilitate a research base for what is an increasingly complex and growing problem? Dr. Klausner reported that this group supports the creation of a cancer genetics network, which would be a disseminated informatics and education-based network available throughout the country. The NCI will ask its advisory bodies to consider a NCI-sponsored network that would also involve health care providers and would be a source where individuals could receive information about counseling for genetic susceptibility testing and about the testing itself. The network would be embedded in an extremely simple research base that, in essence, would be a registry contained in a longitudinal observational study. Information in the registry would be rendered anonymous and would be completely protected and confidential. Without such a registry, Dr. Klausner observed, the NCI would not be able to integrate the identification of genetic susceptibility in individuals with the opportunity to address their individual questions and to provide for them the possibility of entering clinical studies and clinical trials.

The Cancer Genetics Working Group has now been divided into three subgroups. The first, chaired by Dr. Kenneth Offit, will help create national protocols with widespread collaboration. The protocols will be used for decision trees about counseling and testing for different predispositions and different syndromes. The second subgroup, chaired by Dr. Kenneth Buetow, is already working on a structure for this interactive, two-way education information and informatics system. The third subgroup, co-chaired by Dr. Judy Garber, Ms. Mary Jo Kahn, and Dr. Reed Pyeritz, will identify the activities of relevant professional societies—through liaisons with these organizations—to create a database for educational materials, to identify what educational materials have to be developed, and to learn to interface those educational materials with the distribution and dissemination system that the NCI will establish through this network.

**Organizational Changes**—Dr. Klausner announced that Dr. Faye Austin has accepted the position of Director, Division of Cancer Biology (DCB), and that Dr. Joseph Fraumeni is Director, Division of Cancer Epidemiology and Genetics (DCEG). The search for a candidate to replace Dr. Pizzo is in progress, and an offer is expected to be made within the month. Dr. Carmen Allegra has agreed to be Acting Director until the new director is appointed (Dr. Edison Liu, University of North Carolina, has since been named to this position).

**Update on Accelerated Executive Review (AER) for Grants**—Based on 2 months of experience, the program of Accelerated Executive Review (AER) is "working spectacularly," according to Dr. Klausner. Sixteen applications have been reviewed; 10 have resulted in awards—the majority of these are for patient-oriented research. Dr. Klausner expressed conviction that AER is an experiment that should be continued because it provides a way to deal with the problem created by the payline and the queue for amendment. The percentiles of the grants that have been paid range from 23.5 to 28.2 (as opposed to the current payline of 23). Dr. Klausner concluded that the response from the community has been very positive. Even though applications are coming in at a significant rate, the NCI program staff has been able to process and manage them all. He congratulated the program staff on the extraordinary job they are doing.

**NIH Shannon Awards**—The NCI has received approval from the NIH for an experimental program of year-round Shannon Awards. These are 2-year, \$100,000 awards, of which no more than \$20,000 can be allocated for indirect costs. Dr. Klausner reported that the program is working well, and the NCI would like to continue the program after the 1-year experiment ends. Eleven awards have been approved—current estimates are that about 30 will be awarded this year—and the NCI has applied to Dr. Varmus for cost sharing between the NIH and the NCI.

**Intramural Program**—Dr. Klausner reported that much has happened in the Intramural Program that will be reviewed in a later presentation. He announced that although there are many scientific topics to report on, he would

focus on epidemiologic data that have been published or that have emerged from new analysis of the latest Surveillance Epidemiology and End Results (SEER) data. He recognized the work of Dr. Brenda Edwards and her staff in the Cancer Control Research Program, which maintains this national resource and works with the extraordinarily valuable information that comes from it. He reported that Secretary Shalala would be announcing the analysis of 1993 data for breast cancer mortality rates at a press conference later in the day.

The 1993 data show that mortality rates for breast cancer continue to fall. For the first time, a small but significant decrease has been seen in the mortality rates in African-Americans, particularly in young women.

Other interesting information derived from analysis of 1993 SEER data includes a decline of about 11 percent in prostate cancer incidence in white men. In African-American men, the incidence continued to increase, but the size of the increase was significantly lower. It is assumed that these results reflect a saturation of incidence due to PSA testing.

Dr. Klausner announced the release by the NCI of a very important SEER monograph entitled *Racial/Ethnic Patterns of Cancer Incidence in the United States: 1988-1992*. In the monograph, 11 ethnic and racial groups are analyzed in terms of the incidence of and mortality from all cancers, as well as by specific sites. Dr. Klausner noted that this monograph promises to be a valuable resource in identifying research questions that the NCI will need to ask. He announced that an Office for Special Populations will soon be established in the Office of the Director and that he will be appointing an associate director to oversee that office and help in designing a research agenda aimed at special populations and underserved minorities.

In another action since February, the NCI has established an office to deal with survivorship issues, both short- and long-range, and Dr. Anna Meadows has been appointed to oversee that office. Dr. Meadows, Chair of Oncology at Children's Hospital of Pennsylvania, has considerable interest and expertise in this area, particularly the issue of late effects of treatment and second cancers in childhood. Dr. Klausner cited the growing need for a research agenda concerning the many medical, social, psychosocial, and epidemiologic issues that face cancer survivors, because of the increasing number of long-term survivors after the original diagnosis of cancer. As a first order-of-business, a working group will be convened to solicit advice from the extramural community about creating a research agenda across the Institute for the issue of cancer survivorship.

**Mammography Workshop**—Dr. Klausner announced that the NCI plans a workshop on mammography in the fall. The impetus for this workshop was the presentation at a meeting in Sweden of recent data from five trials in Sweden, as well as updated analyses from other trials, specifically looking at the issue of mammography screening in women from 40 to 49 years of age. Dr. Klausner commented that the NCI is interested in looking at the Swedish data in the context of peer review. He announced that he has invited the Swedish investigators to submit their work in an accelerated fashion to the *Journal of the National Cancer Institute*. The NCI workshop in the fall will involve the Swedish investigators, and the data, if not yet published, will be made available to all participants. Both current and complete evidence on many issues related to mammography, including mammography screening in women below the age of 50, will be examined.

A steering committee has been assembled to define the workshop goals as well as research questions and evaluation issues, and to ensure that this workshop has broad participation from individuals with many perspectives. The committee includes Dr. Laszlo Tabar, Swedish investigator from one of the five studies; Dr. Robert Smith, American Cancer Society; Dr. Gillian Newstead, New York University; Ms. Amy Langer, National Alliance of Breast Cancer; Dr. Barbara Rimer, Duke University; Dr. Sam Shapiro, Johns Hopkins University; Dr. Douglas Kamerow, Agency for Health Care Policy and Research (AHCPR); Dr. Edward Sickles and Dr. Lawrence Bassett, American Association for Cancer Research (AACR); and Drs. Barnett Kramer, Edward Sondik, Leslie Ford, Philip Prorok, and Richard Klausner, NCI. Dr. Klausner noted that conclusions presented at the meeting from all of the Swedish studies demonstrated a 23 percent reduction in mortality that was statistically significant. He expressed hope that the data will hold up to rigorous analysis and peer review.

Dr. Day asked if the SEER data had been analyzed to determine reasons for the change in breast cancer incidence and mortality. Dr. Klausner answered that the NCI is reporting only the changes at this time; the NCI has no clear data readily available to explain these changes. He observed that the drop in mortality is seen not only in the United States but also in Canada and the United Kingdom—in the United Kingdom, the drop is about 12 percent. The changes begin about 1990, and that date is consistent with an effect of altered medical intervention, particularly, treatment. Dr. Klausner maintained that determining to what extent these decreases are due to early detection, early diagnosis, better treatment, or different combinations of these is going to be difficult. He asked Dr. Edwards to comment. Dr. Edwards added that her staff have been looking for explanations. The evidence, as far as can be seen, can vary by different age groups, and there are multiple explanations. Dr. Schein commented that concern has been expressed in the Bishop-Calabresi Report about the extent to which the total NCI budget is supported by AIDS research. He asked if the NCI had any contingency plans for phasing out the AIDS program and maintaining the financial integrity of the Institute in the process. Dr. Klausner responded that the NCI has shifted, in 9 months, from 16 percent of the total AIDS budget in the RPG pool to 47 percent. A system has been created for coding what is AIDS, what is AIDS-related, and what is fundamental to understanding AIDS. The NCI has recoded its entire AIDS research portfolio—including intramural research—according to the new classification system.

Dr. Klausner expressed the view that, based on the Levine Report, which clearly defines priorities and approaches to AIDS, the NCI will continue to, play an important role in AIDS research. A major focus for the NCI is AIDS malignancies, which complicate 30 percent of AIDS cases. Moreover, AIDS is the setting for a significant percentage of total cancer incidence, at least in men below age 55, and an important confluence exists between the interests of NCI and the interests and needs of the AIDS Program in terms of virology and human immunology.

Dr. Bishop asked whether the NCI's funding would be affected if Representative Porter's attitude prevailed. Dr. Klausner expressed the opinion that there would be little effect. Dr. Klausner reported, a broad-based group called the AIDS Malignancy Working Group, chaired by Dr. Ellen Feigal, has been instituted. The working group has met and has been advising the NCI on a long-range research program for AIDS malignancies.

Dr. Goldson commended the NCAB's national conference in January on recruitment and retention of minorities to clinical trials. He expressed the opinion that the January conference and regional programs that are being planned will dovetail with the SEER monograph on racial and ethnic patterns of cancer in the United States. The monograph will assist the Board in identifying high-risk areas and forming protocols that will help these groups. He noted that thousands of lives would be saved if all that is accomplished is an increase in black survivorship to match white survivorship. He stated that the Board was moving in the right direction, and that its actions will be a help in the community and affect the way the Board is viewed.

Dr. Rimer thanked Dr. Goldson for his commendation and Dr. Klausner for his presentation. She introduced Ms. Dorothy Tisevich, NCI Legislative Liaison, to present the legislative update.

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## LEGISLATIVE UPDATE

Ms. Tisevich reported that the number of departing Congressional members continues to increase to about 13 departing senators and more than 40 departing congresspersons. The result of these changes is a more junior makeup of both the House and the Senate, significant turnovers in members and staff, and education on an ongoing basis for new members of the Congress.

Dr. Klausner had several opportunities to meet with members of committees important to the NCI; these meetings focused generally on discussions of the changes at the NCI, the new Bypass Budget approach, and scientific opportunities. One important hearing was held on April 24 before the House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies, chaired by Representative John Porter (R-IL). Several questions asked during the hearing focused on issues that had been raised during preliminary visits: the changes taking place at the NCI, the funds shifted into research project grants, and emerging areas of scientific opportunity.

Dr. Klausner testified as part of the panel on cancer and genetics during a reauthorization hearing before Senator Nancy Kassebaum (R-KS), which was held on March 7. Concern about potential abuses of genetic information was prevalent.

A copy of Dr. Klausner's testimony before the committee was provided to the Board.

On May 14, Congressman Porter (R-IL) and several members of the subcommittee and staff were scheduled for a brief visit to the NIH. A hearing featuring a panel of Nobel Laureates was scheduled in the afternoon to gather further testimony on emerging areas of science and the role of the NIH in supporting this research.

The Senate appropriation hearing for the NIH was scheduled for May 23.

Ms. Tisevich briefly mentioned several other issues. At this time, the reauthorization bill for the NIH has not been introduced. Genetic information continues to be an item of great interest, and legislation on health insurance reform was recently passed in both the House and Senate.

Ms. Tisevich reported that, although it is unlikely that comprehensive health care reform legislation will be passed during this Congress, the bill that has passed and is waiting for conference action establishes some steps toward access to care by individuals and would possibly—in the House version—allow for medical insurance accounts that would be tax free.

Ms. Tisevich noted that the Women's Health Equity Act has been introduced in several past Congresses. This is an omnibus bill that includes several pieces of legislation related to women's health. On March 27, Representative Louise Slaughter (D-NY) introduced the Women's Health Equity Act of 1996. This bill is a compilation of 36 separate pieces of legislation that address issues related to areas of interest to women's health, including breast cancer research, employment opportunities for women scientists, cardiovascular disease research, ovarian cancer research, and many others. She noted that experience in past years has shown that the omnibus bill may not be enacted, but individual pieces of legislation, particularly authorizing legislation, often are pulled out and passed separately.

Ms. Tisevich reported that the National Technology Transfer and Advancement Act of 1995 has been passed and signed into law. This legislation addresses several changes in technology transfer activities at the NIH. One provision in the area of reassignment of patent rights now permits the government to reassign the title to patent applications back to the inventor if the government decides to discontinue patent prosecution and otherwise not pursue commercialization. A second provision increases the royalty cap from \$100,000 to \$150,000 for earnings to individuals on royalties. In a third provision, the use of the license royalty revenue by the government has been expanded. In a fourth provision, unused royalty revenues may be maintained for 2 fiscal years. Previously and until the bill passed, all unused royalty revenue was to be returned to the Treasury after 1 full year. Ms. Tisevich commented that this provision permits the NIH much greater flexibility by making royalty funds available for an additional year.

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## **QUESTIONS AND ANSWERS**

### **Legislative Update**

Dr. Rimer asked if anything had been added to the Kennedy-Kassebaum bill that would cause President Clinton to veto it. Ms. Tisevich indicated that medical trust fund issues have been a topic of much discussion and conference deliberations are under way.

Referring to Clinical Center construction costs, Dr. Sigal asked whether the law required that these funds be written off in 1 year. Ms. Tisevich stated her understanding that a budget request is required to provide for all construction costs at once. Dr. Sigal asked if Ms. Tisevich had any information on how the Senate and House appropriations for the NIH would come out in this regard. Ms. Tisevich referred Dr. Sigal to Dr. Klausner's earlier report that the President's budget, as proposed, is a starting point for congressional deliberation. Dr. Klausner explained that the requirement to provide for all construction costs in 1 year is OMB policy. The President's budget reflects a decision made by OMB in negotiations with the DHHS and Dr. Varmus. The original plan was for an appropriation spread over 4 years. Dr. Sigal suggested that there might be some flexibility or opportunity for discussion if the requirement is not a law.

In response to a question from Dr. Sigal, Ms. Tisevich noted that the Harkin-Hatfield bill has not received much attention recently, and its status is unknown.

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## NEW BUSINESS-SESSION I

Dr. Rimer opened the floor for identification of items to be discussed at the second new business session on the following day. She also called for draft resolutions or items of special public concern that need to be brought before the Board. Dr. Rimer suggested as an agenda item the request from the Center for Health Advancement regarding support for tobacco counseling as a Health Plan Employer Data and Information Set (HEDIS) indicator; information on this request was included in a packet mailed earlier to all Board members. She expressed the view that this item presents the Board with an opportunity to use its imprimatur on an action that changes the way medicine is practiced in managed care organizations. Dr. Rimer then introduced Dr. Joseph Bertino, Program Chairman for Molecular Pharmacology and Therapeutics, Memorial Sloan-Kettering Cancer Center, and immediate past president of the AACR to discuss recent events and future plans of the AACR.

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### REMARKS FROM THE PAST PRESIDENT, AACR

Dr. Bertino stated that he finished his term as president of the AACR as of the 87th annual meeting held in Washington, D.C., during the previous week. He characterized the AACR as a dynamic and vibrant society, which has grown in membership at an annual rate of about 10 percent for the last 6 or 7 years. He announced that he would report on some AACR activities and plans for the future.

Dr. Bertino explained that the AACR currently has 11,300 members. The AACR mission is to foster research in cancer and to contribute to the understanding of cancer etiology, diagnosis, treatment, and prevention.

The AACR publishes four journals ranging from epidemiology to clinical research, with the flagship journal being *Cancer Research*. The AACR also holds annual meetings and small, focused special conferences. The 87th annual meeting held in May attracted 7,800 participants. Six to eight small focused special conferences are held each year. Public education, under the leadership of the Public Education Committee; government and media relations; science education and training programs for young investigators; and international outreach all are important activities of the AACR.

Dr. Bertino described AACR's scientific scope as unique in that it bridges the gap between the laboratory and the clinic. Membership includes scientists, both M.D.s and Ph.D.s, who are expert in both basic and clinical research, epidemiology, prevention, and especially translational research.

Having completed this brief background summary, Dr. Bertino reported on the status of AACR activities over the past year and outlined new initiatives that are planned for early implementation. Dr. Bertino reviewed the focuses of major AACR initiatives undertaken during the last year of his presidency: (1) strengthening the clinical research programs in the AACR; (2) providing training programs and opportunities for young investigators; (3) promoting the professional advancement of women and minorities in cancer and biomedical research; (4) collaborating with relevant scientific societies in the United States and abroad; (5) introducing new electronic media; (6) enhancing communication and collaborations with industry, in part by forming an Industry Advisory Council; (7) emphasizing public education and government relations; (8) enhancing media relations as a mechanism for increasing grassroots support for cancer research among the lay public; and (9) developing a strategic plan for the AACR.

A particular interest in the AACR has been to strengthen clinical programs, emphasizing translation from research to the bedside. A Clinical Research Committee has been organized to oversee the very active clinical programs of AACR. As noted previously, clinical presentations at the AACR annual meeting have increased, and special conferences now include clinical and translational topics. In this regard, Dr. Bertino noted, the conference on prostate cancer, chaired by Dr. Donald Coffey, proved to be one of the most exciting and productive conferences held by AACR during the year.

Another initiative in 1995-1996 was institution of a new award for clinical research accomplishment, entitled the Joseph H. Burchenal Award, which is sponsored by Bristol-Myers Squibb. The first recipient was Dr. James Armitage, current president of the American Society of Clinical Oncology (ASCO). Dr. Bertino stated that AACR has worked to incorporate clinical research into the public education agenda, and one outcome of that effort is active collaboration

with ASCO on two annual events. One jointly sponsored event is a Clinical Methods Summer Workshop, which will be useful for training young investigators to understand methodology in clinical research. In the second collaboration, a series of annual special conferences is planned to explore the basic and clinical aspects of one organ-specific topic each year.

Dr. Bertino listed training programs and opportunities initiated by the AACR for young investigators. Under a new program of research fellowships, three awards have been made during the past year to young investigators. AACR has an annual Gertrude Elion Cancer Research Award for junior faculty, which is supported by the Burroughs-Wellcome Glaxo Company. AACR increased its level of support for awards to young scholars for travel to the annual meeting and funding of more than \$75,000 is now allocated for this program. Another new opportunity for young investigators is the recently instituted Associate Member Council, composed of young associate members and charged with advising the board of directors on the needs of young investigators.

Dr. Bertino reported that AACR training programs include educational sessions at the annual meetings and summer workshops. In addition to the workshop on Methods in Clinical Cancer Research, two other summer workshops over the past several years were Histopathobiology of Neoplasia and Molecular Biology in Clinical Oncology. Another committee, chaired by Dr. Michael Gottesman, is attempting to develop science education programs to attract high school and undergraduate students to careers in cancer and biomedical research. AACR also sponsors programs to increase professional advancement opportunities for women and minorities in cancer research.

Dr. Bertino announced that AACR has moved into the electronic age with the introduction of Cancer Research on CD-ROM this past year. In addition, AACR's new World Wide Web site has been launched and has attracted much attention ([HTTP://WWW.AACR.org](http://WWW.AACR.org)).

Dr. Bertino outlined public education initiatives that have been a major focus of recent AACR activities. These include: AACR Public Education Committee, chaired by Dr. Anna Barker; a network of state legislative committees that deals with the individual legislative bodies; public policy sessions at the annual meeting; development of progress statements with a disease orientation as information resources for lay advocates and educational resources for legislators; testimony before the House and Senate Appropriations Subcommittees each year; links with survivor groups through which leaders of the groups give presentations at AACR meetings (e.g., Ms. Francis Visco and Ms. Ellen Stovall); membership in the National Coalition for Cancer Research and the Food and Drug Administration (FDA) Council; celebration of the 25th anniversary of the National Cancer Act at the 1996 annual meeting; and input into the format and content of the Bypass Budget.

Dr. Bertino reviewed events that were part of the celebration of the 25th anniversary of the National Cancer Act during the 1996 annual meeting in May: a congressional briefing on the value of cancer research as an investment opportunity, which was attended by more than 100 congressional aides and associates; more than 25 visits by AACR delegates to members of Congress; a Contact Congress booth, where more than 1,000 letters supporting cancer research were generated; a speech by Congressman James Moran (D-VA) at the plenary session; and a congressional reception on Capitol Hill highlighting the presentation of public service awards to Senators Mark Hatfield (R-OR) and Tom Harkin (D-IA), and Congressman John Porter (R-IL).

On behalf of the AACR, Dr. Bertino expressed approval of the 1997-1998 Bypass Budget, and he congratulated Dr. Klausner and his associates for preparing a document that meets the special challenge of informing the public, Congress, and the Administration about the value of and opportunities for cancer research, as well as the resources needed to achieve the goals of the National Cancer Program.

Dr. Bertino stated that AACR—as part of its public policy agenda—will continue to press for funding for cancer and biomedical research, support legislation for revitalization of the National Cancer Act, support the Hatfield-Harkin Health Research Fund (a major priority in 1996-1997), support the Clinical Research Act, promote FDA changes that will increase the availability of new and more effective cancer therapies to the population, and continue to be involved in the translation of genetic research results to the clinical arena—a major priority.

To implement its public policy agenda, Dr. Bertino noted, AACR has developed a strategic plan with the objectives of increasing AACR's leadership role in fostering cancer research through its own scientific programs and on a national

level; using the expertise and broad scientific perspective of the membership to identify national scientific priorities in cancer research; developing a proactive public education strategy in support of these scientific priorities; and strengthening communication with AACR members, lay public, Congress, and the NCI with respect to cancer research issues and policies. Dr. Bertino expressed satisfaction that Dr. Klausner has used AACR membership and expertise widely in the NCI's committees and programs.

Dr. Rimer commended AACR activities related to educating the public about the need to support science at all levels. She noted that this has been the theme of many other NIH Advisory Councils and is a very important function. Dr. Klausner voiced approval of the sense of accomplishment, enthusiasm, and optimism that pervaded the annual meeting, as well as of the number of young people who attended.

Dr. Rimer announced that Dr. Klausner's summons to a meeting at the White House necessitated a change in the timing of the executive session and subcommittee meetings. The executive session was rescheduled to begin at 12:15 p.m., followed by subcommittee meetings.

Dr. Rimer introduced Dr. Joseph Simone, Medical Director, Hunterman Cancer Foundation and Institute, University of Utah, to present a progress report on the Cancer Centers Working Group.

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### **PROGRESS REPORT ON THE CANCER CENTERS WORKING GROUP**

Dr. Simone, Chair, Cancer Centers Working Group, reported that this was the first of the Director's Review Groups convened by Dr. Klausner and that several meetings have been held. He briefly described the progress made by the Working Group. Dr. Simone stated that Dr. Klausner emphasized, in his charge to the Group, that the NCI function is fundamentally discovery and that each working group should consider potential changes and favor substance over precedent and principle over process. Dr. Simone listed the names and affiliations of Group members and noted that a list with addresses would be provided by Dr. Paulette Gray, who is Executive Secretary of the Group.

Dr. Simone explained how the Working Group viewed its charge from Dr. Klausner, who had asked the Group to consider the following issues: What should cancer centers look like? What should their structure be? What can they achieve? What can they not achieve? What should they not be engaged in? How is it best to evaluate the Centers? He explained that the Cancer Centers Program is peculiar among research programs in that it is intended and was developed historically to provide infrastructure for research, not to provide direct funds for research. Thus, it supports various shared resources within an institution and a variety of functions. One of the dilemmas for committees reviewing cancer centers is the charge to review not the science, but rather how these resources are shared, and effectively how they are used. Because this is an almost impossible task, the Working Group is considering the issue of how best to fund these cancer centers based on the evaluation of the review committees.

Dr. Simone stated that the Working Group received many comments from the extramural community addressing the issue of flexibility and accountability. Dr. Simone referred to the report on general principles for cancer centers produced by the Institute of Medicine (IOM) some years ago, which the Working Group has consulted. He noted that the Working Group has been charged with producing a more focused evaluation, with considerably more detail, than that of the IOM, as well as with considering the question of new initiatives and funding.

Dr. Simone presented the five basic areas that constitute the framework of this review. The first area involves considering what the goals should be for the individual centers and for the NCI Centers Program as a whole. Related questions are: How should the Centers Program be viewed? How should it be evaluated programmatically overall?

The second area deals with the structure and function of the three types of centers. Currently, comprehensive centers have programs in the areas of basic science, clinical research, and population-based research; clinical centers have both basic science and clinical research; and basic science centers conduct only basic science research. Related questions include: Is this the right mix? Are these the right designations for cancer centers? What is needed in the armamentaria of the cancer centers? The NCI program has approximately 55 cancer centers—about 12 are basic science centers; about 26 are comprehensive centers; and the remainder are clinical cancer centers.

The third area of the Working Group review focuses on the guidelines, review criteria, and process of review. Dr. Simone noted that these are some of the major issues raised in the testimony received from people in cancer centers and the Group is spending considerable time discussing them. A key question deals with how to review an organization for productivity if the science is not being formally reviewed.

The fourth area focuses on distribution of the cancer centers' funding. The Working Group is looking at the whole area of how funds might be applied, keeping in mind that flexibility cannot be so great that there is no way to measure productivity.

Dr. Simone stated that the fifth area of discussion—that of centers in relation to regional and national resources—has been the most difficult. He gave the example of tying these organizations together with sophisticated informatics and sharing perhaps very expensive resources like tissue and organ banks.

Dr. Simone stated that the Group has met several times and has reviewed extensive reports from the NCI cancer centers staff, presentations from a variety of cancer center directors and interested parties, and communications from a number of people who were invited to comment. The information is now being collated and organized. Dr. Simone anticipates a few more monthly meetings before the draft report can be formulated.

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## **QUESTIONS AND ANSWERS**

### **Progress Report on the Cancer Centers Working Group**

Dr. Rimer stated that she had received calls and letters from people in the cancer prevention and control community who are concerned that cancer prevention and control is not adequately represented on the Group. She asked Dr. Simone to comment. Dr. Simone gave assurance that the Working Group is cognizant of this and is paying much attention to cancer prevention and control. He pointed out that several members of the Group have a cancer prevention and control orientation, and he stated that the Group has made it known that comments continue to be welcomed.

Dr. Bishop asked Dr. Rimer whether the source of this concern is inadequate representation on the Working Group for research on prevention and control or for implementation of prevention and control measures. He explained that this gets to the issue of whether the centers, in the past, have been expected to go beyond discovery. Dr. Rimer presumed that the concern was about the research mission, and that the Group lacks sufficient appreciation of the role of cancer prevention and control research as an inherent part of cancer centers. Dr. Simone added that the Group is sensitive to this issue, and that discussion has focused on whether cancer centers should exist that do not have a mandate for population-based research. An issue that has not been resolved and is still open to discussion is whether there should be only two kinds of centers—those engaged in the spectrum of cancer research, including population-based research, and those focused on a single area.

Dr. Chan asked for clarification of regional expectations with respect to community outreach and whether the Working Group sees the need to look into minority involvement. Dr. Simone stated that the issue of regional expectations for a cancer center is very complex, because of the differences in geography and the nature of the institutions. An institution like Duke University, for example, which is located in a low-population area, has a different agenda or different possibilities than a cancer center based in New York City or Los Angeles. All comprehensive cancer centers have community outreach programs as part of the requirement for comprehensiveness, and many of the clinical cancer centers also have outreach programs—although they may not have funded research in those areas. The question is whether the existence of community outreach activity in the centers should be formulated into some kind of general policy. Dr. Simone noted that scientists in the basic centers communicate internationally so their physical location is less of an issue. In response to Dr. Chan's question about minority issues, Dr. Simone explained that the Group is sensitive to the problem of reaching minority patients. Some cancer centers succeed and others have difficulty engaging minority populations in cancer research programs in their region.

Dr. Freeman asked whether applied research is a major element being considered by the Working Group, particularly because research, broadly defined, extends from basic to applied. He acknowledged the difficulty in defining research, but voiced his opinion that research that will affect people directly must be addressed. Dr. Simone stated that without question the Group is sensitive to this issue. He pointed out that the Group is broad based, and many are pragmatists

with respect to meeting both the needs of patients who enter their institutions and the needs of the community. The centers have difficulty in trying to encompass everything in the spectrum of research. The Group believes that, although some institutions cannot excel at everything, all have an obligation in applied research areas. Dr. Simone noted that virtually all of the cancer centers are engaged in some type of applied research and are uniquely placed and qualified to engage in that kind of activity, because they have a broad charge in the community.

Dr. Freeman asked Dr. Klausner if, at another level (perhaps not the cancer center level), there is still a concern that investigators must study real people in communities. He expressed the belief that the NCI, NCAB, and the PCP have a moral responsibility to try to influence research in that area. Dr. Freeman urged that, along with the discussion about discovery and the NCI as a discovery institution, the NCI's concern that the ultimate effect the NCI must have is on the American public should not diminish.

Dr. Klausner responded that the areas comprising cancer centers, as defined by NCI funding, are parts of large institutions. When defining goals for cancer centers, the NCI must ensure criteria are established to put the limited resources to the best possible use, so that they will have potential for larger effects. Dr. Klausner added that the NCI recognizes all things cannot be accomplished with one approach or one institution, but the NCI must ensure that what is accomplished is of high quality and that the accomplishments can be integrated into and amplified by other activities. He expressed concern that continuing to demand more than is doable and placing those demands on every NCI program results in dissociation from the scale of NCI's resources. Dr. Klausner noted that the Working Group is struggling to strike a balance in this difficult problem, for which there is no perfect solution.

Dr. Freeman stated that, at a certain point in the process, discovery must be transcended and transformed into real meaning for real people. Although it could be argued that this is not the cancer centers' responsibility, at some level, whether it is at the NCI level or that of the PCP, influence must be brought to bear on the total effort that benefits the public with respect to cancer. Dr. Freeman expressed concern that the NCI should continue to do everything possible for all people with what is already known. Dr. Rimer thanked Dr. Freeman and noted that the Board shared his concern.

Dr. Schein noted that one of the Working Group's agenda items relates to managed care, particularly as it will affect cancer centers in their fulfillment of the overall mission, which is to deliver not only new but clinical scientific information to the community. He referred to the concern that free-standing cancer centers might look increasingly too expensive to third-party payers—despite the fact that they have an important clinical research mission for the country—and that the clinical programs in some centers may have to be phased out. Dr. Schein asked what kind of response the Working Group is preparing and what type of recommendations will be proposed to maintain at least the current level of clinical investigation at these centers.

Dr. Simone stated that this issue was one of the first raised at the initial meeting, and he agreed that the problem differs for the categorical cancer centers, which are very specialized in cancer-related activities, and the university-based matrix centers, which have a broad spectrum of patient care activities. He pointed out that both types have problems, depending on their local environment, and that their access to patients is clearly being threatened and reduced. Many kinds of mergers have been discussed, out of fear that clinical programs may not be sustainable at their current level. Beds are closing, and the critical mass that is required in certain kinds of clinical programs is reaching a crisis level in some areas. Dr. Simone gave assurance that the Working Group is aware of the situation and will be addressing the questions, but he speculated about whether the Group had any more intelligence as to what to advise in this area than anybody else. He noted that the Group met with Dr. Wittes and his staff about the CHAMPUS negotiations and discussed whether those negotiations could be extended.

Dr. Correa noted that the benefits of science are not reaching society to the extent that they could, and he suggested that the Board consider whether this perception is well founded. He suggested that, because the NCI is a research institution, perhaps the way to address this perception in a research environment is by asking why the benefits of science are not reaching society. He voiced his opinion that the Institute is somewhat weak in behavioral research, and if behavioral research is not in the charter of the NCI, then perhaps it should be stated. He pointed out that although the basic, clinical, and epidemiologic science may have a behavioral component, behavioral research does not have its own identity.

Dr. Klausner agreed that behavioral research should be on the NCI agenda and should be incorporated into the NCI planning and policymaking process. For this reason, Dr. Klausner stated, one of the five major review groups—the Cancer Control Working Group—will be charged with advising the Institute on mechanisms and priorities in the area of cancer control and on long-range problems in psychosocial and biobehavioral research. Dr. David Abrams, a behavioral scientist, is chairing that committee. In this regard, Dr. Rimer mentioned that Mrs. Malek would report later on an April 1996 meeting that focused on making recommendations in the area of behavioral research. Dr. Rimer noted that the Board has an important window now to strengthen this whole area.

Dr. Calabresi observed that many of the concerns expressed by the Board relate to the interface of science and research discovery with application to the community and people. He seconded Dr. Schein's question about the Working Group's recommendations to deal with the impact of managed care because of the danger that major breast cancer centers will become isolated from the primary care networks that affect a variety of patients and people. Dr. Calabresi pointed out that the fourth overarching recommendation in the Subcommittee to Evaluate the National Cancer Act Program (SENCAP) Report stressed many of the points mentioned by Dr. Chan and Dr. Correa. A related question would be: Is there any opportunity to form networks of cancer centers? Because it has been noted that some centers specialize in different areas, Dr. Calabresi suggested that encouraging cancer centers to collaborate and providing incentives for those that work together in a network would allow research results to be applied more rapidly to a larger and more diffuse population.

In response, Dr. Simone contended that cancer care is a local issue. Although cooperation could be achieved at the informational level, at the research level, or even at the resource level, having an impact on patient care is a local regional issue. He emphasized the importance of finding ways for existing cancer centers, or possibly new centers, to develop their own networks so that they can touch people as broadly as possible where they are located. He pointed out that the centers know best what the issues are, the particular mix of their populations, and their own capabilities. He agreed that the actual application of research must emanate from the centers in a regional way.

Dr. Calabresi agreed with the overall focus described by Dr. Simone but expressed concern with the statement that some of the centers are going to be more specialized in one area or another. Dr. Simone explained that the Group's position is not for more specialization, but rather to recognize the fact that some cancer centers excel in a smaller spectrum rather than the entire spectrum, and these excellences should be used to the advantage of other centers. Dr. Rimer conveyed her understanding of the foregoing discussion, namely, that the Group is recognizing that even within an area like prevention, areas of excellence need to be developed. The Working Group recognizes that that all cancer centers cannot be all things to all people and excel in all kinds of research.

Dr. Freeman agreed and asked if all centers cannot do all things, and that some centers can be given as much respect for excelling in cancer control research with modest basic research as is given to those centers doing basic research with very little cancer control research. The point was well taken. Dr. Freeman stated that he sees cancer centers that are fundamentally basic research centers, and which are doing an excellent job at basic research, and say they are reaching the community—but they probably are not to any extent. He emphasized the need for promoting this other kind of research—no matter its name. He suggested the possibility of building up basic research capabilities at the sites excelling in community outreach research so that both types of centers could be working on the problem from opposite ends of the pole and reaching toward each other.

In that regard, Mrs. Brown related that she and Dr. Goldman had convened the directors of all centers in the Washington, D.C. area to discuss the need for a cooperative cancer control initiative. The initiative would take advantage of the fact that community hospitals, which have the population base, could collaborate with research institutes, which have the specialized expertise. Mrs. Brown suggested that there is a way to apply such a strategy to the cancer centers problem and that the time has come for the Board to encourage a move in this direction. She recognized that any application of such a strategy would require tailoring it to the needs and resources of the different communities. Dr. Rimer agreed and noted that this suggestion is particularly salient in communities where there is more than one cancer center, and where the need to determine areas of specialization is important. She expressed the view that, as the Working Group is writing its report, the Board has the challenge of preparing its response to the report, deciding how to review the recommendations, and thinking about implementation. She charged Dr. Day as head of the Cancer Centers Subcommittee and Dr. Bishop with helping to guide the Board.

Dr. Rimer relinquished the floor to Dr. Kalt for the introduction of Dr. Wendy Baldwin, Deputy Director for Extramural Research, NIH.

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## UPDATE ON NIH EXTRAMURAL REINVENTION ACTIVITIES

In his introduction, Dr. Kalt reminded those present that reinvention in the government started officially when Vice President Gore announced the initiative, and he noted that the announcement served as a reminder to NIH scientist administrators in the NIH extramural programs. Measures of that progress can be found by logging onto the NIH home page or the NCI home page or by using the EDISON invention reporting system. Dr. Kalt introduced Dr. Wendy Baldwin, Deputy Director for Extramural Research in the Office of the Director, NIH, and commended her for her success in moving the NIH toward the 21st century. Dr. Kalt announced that Dr. Baldwin would present an update to the Board on the continuing array of activities that have been going on in the reinvention process.

Dr. Baldwin thanked Dr. Kalt for his introduction. She welcomed the opportunity to review the extent of the changes that have taken place since the NIH started its reinvention activities in response to the National Performance Review (NPR) plan and Vice President Gore's announcement of the initiative. The statement had indicted the system, not the federal worker, and set very clear goals that provided an opportunity to make some changes in a system where the basic mission had become obscure over the years. Dr. Baldwin observed that Dr. Varmus easily identified the NIH mission as that of finding and supporting the best science. Armed with many goals and objectives, the NIH staff began the task of reinventing and making the system work for the NIH and for the scientific community. The first step was to form a cascade of committees that were charged with thinking about reinvention. She noted that one tenet of reinvention was that changes would be required in practices based on culture and tradition, but not laws or regulations. By that reasoning, it was quite likely that many of the changes the NIH would want to make would not require congressional action, although the NIH was prepared for that too.

Dr. Baldwin reported that many pilot projects are in progress. She noted that her occasional encounter with a reinvention activity that she is not familiar with means that the system is working exactly as planned. When reinvention was started, the sheer complexity of the NIH was found to be both a plus and a minus. On one hand, "a thousand flowers" had been left to bloom, possibly to the NIH's detriment. On the other hand, the fact that the NIH does have many different components and different levels means that it has not been necessary to change the whole process in one wave. This has been particularly important for extramural research, because reinvention does not mean a one-size-fits-all strategy that can be applied for extramural programming across the NIH. Because of the legitimate variation that exists across the NIH, it has been necessary to ensure flexibility to accommodate the different needs that range, for example, from those of the NCI (with its size, complexity, and longevity), to those of the National Institute of Nursing Research (NINR) (which is very new, establishing itself, and much smaller), and finally to those of the National Center for Human Genome Research (NCHGR) (which is quite different from all other institutes).

Dr. Baldwin explained that it has been necessary to make sure the extramural community can interact with the NIH as a whole, without having to relearn a different system for each Institute. As reinvention activities move into the area of electronic interfacing, this same uniformity will be essential among all government agencies. Extramural institutions have been concerned that each agency would reinvent processes in its own way. Dr. Baldwin gave assurance that several levels of interagency committees are working to ensure that this does not happen.

She reported that reinvention activities began with peer review and is now moving into grants management and will then move to all areas of extramural programming. Dr. Baldwin explained that changes to the grant application review system have led to a "streamlined" review process using triage to identify applications that reviewers believe are in the top half, which then are discussed and scored. Streamlined review is now universal throughout the Division of Research Grants (DRG); no bias was found for young investigators, women, or minorities. Dr. Baldwin stated that this process was adopted to focus discussion at review meetings on those applications which required most discussion. The process has also saved money.

Another streamlining innovation is to send applicants the original reviewers' comments rather than the synthesized summary of reviewers' comments. This innovation was well received in the scientific community and effected an

enormous change in the workload for NIH staff. The final innovation in streamlined review is the direct mail-out of reviewer comments. In addition, every effort is being made to identify other stages in the review process that can be made more efficient.

One innovation currently in a pilot stage is the Just-in-Time concept, which is based on the premise that institutions should not be required to submit certain kinds of information until the information is needed. Data that are important for the award but not important for the scientific review, such as budget details, are not collected until an award is likely to be made. The NIH is now looking into the feasibility of expanding the Just-in-Time concept into the area of human subjects and animal welfare reviews. Dr. Baldwin stated that the NIH is moving carefully on this innovation.

Dr. Baldwin next described the Electronic Research Administration (ERA) initiative, which she characterized as the essence of the NIH electronic exchange function. ERA represents a commitment to improving administrative operations between the NIH and the grantee community through information technologies and reengineering of the administrative process. A key feature is to maintain the information required for various NIH processes within a client-server "common file" database. For example, a Common Application File would provide a way for the NIH and authorized awardee institutions to review and add information as required. This would eliminate the need for individuals to convert information—which now exists electronically in the institutions—into hard copy and send it to the NIH, where it is then rekeyed. The NIH would be able to provide application-specific information such as the assignment and the score to the electronic file.

Dr. Baldwin commented that feedback from institutions which receive information electronically from other sponsoring agencies indicates that 80 percent of their contacts with the agencies are eliminated if it is possible to tap into an electronic file and obtain a status report for an application. Notice of grant award as one piece of information should be available within the year through the common file.

The Grants Policy Statement, which can be accessed through the NIH Home Page, provides the most current information on deadlines, policy, and background in an organized, structured format. Dr. Baldwin noted that the NIH Home Page had been envisioned as a cornerstone for electronic communication, and it proved to be an invaluable lifeline during the government furlough and shutdown.

Dr. Baldwin emphasized that the NIH reinvention activities are an evolving operation, which will continue to rely on the valued input of all interested parties. The NIH is attempting to make information available that will help the components of NIH find useful processes and procedures to best achieve the overall mission of finding and supporting the best science. Dr. Baldwin commended the NCI's AER as an example of finding new ways to address the underlying issues that slow up the grant application process.

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## **QUESTIONS AND ANSWERS**

### **Update on NIH Extramural Reinvention Activities**

Dr. Day observed that confidentiality is going to become more of an issue and he asked how the NIH plans to manage it. Dr. Baldwin responded that the issue was raised when the NIH started to develop EDISON for electronic invention reporting, because the information involved required confidentiality. To that end, the NIH developed a three-level layer of security, and counted on having affordable encryption technology available when the system was ready for full-scale operation. Dr. Baldwin concluded that confidentiality is an issue that has been dealt with in other arenas of electronic commerce; the NIH has given it a high priority, and it is a manageable issue.

Dr. Goldson asked Dr. Baldwin if she thought the full implementation of electronic reporting and electronic grant submissions will affect staffing requirements negatively, in terms of full-time equivalents (FTE). Dr. Baldwin responded that efficiency would probably improve and that staffing needs on both the NIH and the Institute side would change. Whether the overall change results in fewer people needed is unclear, in part because of the level of support required to keep any kind of electronic system running.

Dr. Chan observed that the front pages of applications now contain the investigator's Social Security number. He asked whether existing policy dictates that this information must appear on the front page and how confidentiality would be

maintained with outside reviewers. Dr. Baldwin responded that the NIH always makes the distinction between information that is available widely or not available, whether or not it is received and maintained electronically.

Dr. Schein asked if the NCI has any plans to transmit—by CD-ROM or some other electronic means—the voluminous materials now contained in the Board books. Dr. Kalt replied that the NCI has been piloting the electronic submission of the summary statements with several Board members and has the capability to put the whole Board book online, but there are several limiting factors. One is that different Board members have both different computer systems and different degrees of comfort with operating in an electronic environment. Another is that, for applications, specific conflicts are sorted out for each individual member. A third factor is whether members of the Board wish eventually to have hard copy of some items. Dr. Kalt stated that the NCI can eliminate paper and plans some pilot experiments in the future. Dr. Rimer confirmed that the task is confounded by the fact that Board members have different preferences in formats or vehicles for receiving information. She pointed out that Dr. Kalt and his staff in DEA have been trying to respond to everybody and tailor materials to their needs.

Dr. Baldwin predicted that a best-practices document will be available in the next 6 to 9 months with information from the Institutes that have experimented with different ways of making information available electronically, and the NCI will be able to weigh the pros and cons concerning different strategies.

Dr. Day referred to a legal suit working its way through the system having to do with manuscript review and a sequence that was used for a patent that actually appeared in a manuscript. He indicated that the suit has ramifications, particularly for progress reports, which might contain process information that would not be going to publication at that point, but might be of great commercial interest. He predicted many changes because of the nature of the information that has to be protected when electronic communication replaces paper. Dr. Day acknowledged that paper does not necessarily guarantee confidentiality, but he emphasized the need for awareness as information goes out in a system that is widely susceptible to hacking.

Dr. Baldwin agreed with Dr. Day's concern that moving the electronic side of reinvention forward must be done very carefully. Dr. Rimer offered the services of the Board in piloting reinvention activities as appropriate. Dr. Baldwin commented that the NCI already has a large investment in reinvention activities, and she expressed appreciation for the time people have spent bringing their Institutes' perspective to bear and helping to define better ways for doing business.

Dr. Correa asked how the electronic system is being developed with other entities such as the American Cancer Society (ACS) or the National Science Foundation (NSF). Dr. Baldwin explained that a Research Managers Group has been formed including herself and representatives from the NSF, the Department of Energy (DoE), DoD, and the Air Force to ensure uniformity among the agencies. A Business Practices Group is operating at a much more practical level, and Dr. Baldwin described some types of business practice agreements that are being worked out with other agencies. She explained that Web-based activities can accommodate interaction with an individual investigator and with institutions holding one or two grants, but they are inadequate for clients such as Johns Hopkins—with whom the NIH does about \$300M worth of business. Therefore, a system called the EDI, the Electronic Data Interchange, is being developed, which is building a common format in the commercial sector to ensure that the NIH and these types of clients can have computer-to-computer exchange of information. Another example of interagency collaboration is software that converts a Lotus spreadsheet in the NIH format to NSF format or vice versa with the flip of a toggle switch.

Dr. Rimer thanked Dr. Baldwin for her presentation and commended her for a job well done.

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## **PROGRESS IN IMPLEMENTATION OF THE BISHOP-CALABRESI REPORT**

Dr. Rimer reminded the Board of its request for an update on the NCI's progress in implementing the Bishop-Calabresi Report. She introduced Dr. Bishop to set the framework for Dr. Klausner's report by providing an overview of the committee's findings. Dr. Bishop observed that it has been just 1 year since this extramurally constituted Ad Hoc Working Group of the NCAB was asked to report on its evaluation of the Intramural Research Program (IRP) and make recommendations about how that program might be improved. He then reviewed the major issues that were

considered and the major recommendations that ensued.

First, strategic planning was felt to be inadequate with respect to consultation, and too remote from the substance of science. The Working Group recommended: (1) more abundant use of consultation with scientists—both from within the Intramural Program and from the extramural community; (2) maintenance and improvement of liaisons with the NCAB; and (3) regular attention by the NCAB to the balance between the IRP and the Extramural Research Program (ERP). The Working Group believed that improving and reforming strategic planning at the NCI might have substantial impact on how awarded funds were used.

The second group of recommendations related to the organization of NCI. The Working Group recommended strongly that the IRP and the ERP be completely separated rather than interdigitated—as they had been traditionally—and that there be explicit leadership for the each program. The Working Group recommended that there be fewer chiefs and a simplification of the organization within the IRP—perhaps two scientific divisions. The Working Group believed there was redundancy among the laboratories and room for improvement, and that careful attention should be given to the lower level organization. Dr. Bishop stated that the Working Group suggested a specific organizational plan as an exercise to prove that such reorganization would be worthwhile and to give the leadership of the NCI some sense of what was envisioned. There were no expectations that the reorganization would take the exact form that was recommended.

The third group of recommendations related to quality assurance in the IRP. The Working Group was concerned about the history of peer review and quality evaluation within the IRP. The administration of peer review was believed to be too close to the people who were immediately directing the research, hence the recommendation that the authority and administration be vested farther up the chain of command. The record of review with regard to site visits was a source of such concern that the Working Group devised a recommendation for written reviews to dramatize the concern. Included in this recommendation was a clear statement that standards should be high. Also, the Working Group was concerned that budgets had not been subject to sufficiently rigorous review and urged that this take place. The Working Group urged that a formal appeal and unified process be implemented throughout the IRP, a means by which anyone who had not fared well would be able to make a case in rebuttal.

The fourth set of recommendations related to stewardship review and tenure policy in the IRP. Dr. Bishop stated that the Working Group perceived what it called "ethos" as one of the largest problems encountered. The committee believed that the administration of funds and even the direction of research was executed in a top-down manner, and that inadequate independence existed among many of the younger scientists and at the lower levels of advancement. The Working Group urged that this be examined carefully, and that every effort be made to change the ethos—both by example and by practice. Among the recommendations was one for rigorous and regular stewardship review that was separate from scientific review, directed at the people who were in administrative control of units and who were responsible for younger careers.

The Working Group believed that available resources were such that—properly used and with the proper ethos—the Intramural Program enjoyed an advantage in recruiting young scientists that should be developed and exploited to revive and improve the IRP. The Working Group urged that younger scientists be given authority in practice as well as nominally over their own budgets. In that regard, the Working Group suggested institution of a modest-sized competitive grants program that would allow young scientists to compete for money by way of supplementing their activities and that would allow them to do this independently.

The Working Group made specific recommendations about how the careers of women and underrepresented minorities within the IRP could be fostered. In this regard, a longstanding recommendation was revived that an ombudsperson be available to the IRP for all manner of adjudication.

Clinical research in the IRP was the focus of the fifth set of recommendations. The Working Group made specific recommendations on how to improve peer review, ranging from establishing formal protocol review and monitoring committees—along the lines mandated in the extramural community by the NCI—to urging that the clinical programs acknowledge that the peer review and promotions review recommended by the Marks-Cassell Committee were reasonable for the clinical track if properly implemented. Specific recommendations were made about how many

resources might be better utilized. Dr. Bishop emphasized that clinical research in the IRP was a momentous matter. The Working Group believed that intramural clinical research represents an important scientific opportunity as well as an opportunity for the NCI to play a leadership role, and that it should receive immediate and searching attention.

Another series of recommendations related to drug development in the IRP. The Working Group decided that this program should continue, but that it needed improvement. Better peer review was recommended to evaluate suitability, quality, and redundancy of efforts. The committee further recommended that the drug development program needed to be better integrated into the larger mission of not only the NCI, but also the NIH as a whole. Dr. Bishop pointed out that other opinions have since been heard on this matter and resolution is uncertain, but he noted that the Working Group favored continuation of this effort, with the help of expert consultation.

Another series of recommendations related to the FCRDC. Dr. Bishop stated that the Working Group had difficulty understanding how the FCRDC was organized and exactly how it functioned. He noted that a series of specific recommendations were made as examples of what could be done, not necessarily as mandates. Dr. Bishop explained that the Working Group could see the prospects for improving the IRP, as well as for saving money, by rearranging the FCRDC. However, the recommendations were made with the understanding that some of them might not be feasible.

Dr. Bishop concluded his overview of the Bishop-Calabresi Report by noting that the final recommendation was that the NCAB receive a progress report a year hence, in May 1996. Dr. Rimer thanked Dr. Bishop for his excellent overview of the Working Group's findings, and she called for a report on the changes that have been implemented during the year since the evaluation was completed.

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## RESTRUCTURING AND REFOCUSING THE INTRAMURAL PROGRAM

Dr. Klausner thanked Dr. Bishop and Dr. Calabresi and all others who had participated in the evaluation. He praised the quality of the review and acknowledged its value as a blueprint. In particular, Dr. Klausner stated, the success and value of the Bishop-Calabresi Report was as a model that the NCI is using to change its fundamental nature and to create, for the first time, a culture of planning. The guiding principles are to formulate questions, include participants from all constituencies in the process, and ensure that advice is integrated into planning, implementation, and decisionmaking.

Dr. Klausner referred members to the Board books for a fully detailed, point-by-point description of the many accomplishments in response to each recommendation, as well as what is yet to be accomplished. He noted that a series of charts have been included that give particular information about the restructuring and about the composition of review and advisory committees.

**Strategic Planning at the NCI**—In response to the critique on strategic planning, Dr. Klausner reported that the NCI has moved to change its approach according to simple principles: planning by the NCI is to be undertaken with the larger scientific community; and critical areas in need of planning will be identified. Separate advisory committees have been established to oversee the two newly separated Intramural and Extramural Research Programs. They are the Board of Scientific Counselors (BSC) for the IRP and the Board of Scientific Advisers (BSA) for the ERP.

Dr. Klausner reported that two internal committees were created—from the staff doing the work of the Institute—in response to the critique that the NCI was not structured to seek and to heed advice about how it functioned in long- and medium-term as well as day-to-day activities. The first is the Intramural Advisory Board (IAB), chaired by Dr. Claude Klee, which includes representatives of the IRP at all levels of science and of career development. The IAB has formed a series of subcommittees to focus on the following issues: (1) core facilities and the interactions; (2) communications within the IRP; (3) the review process; (4) resource distribution; (5) recruitment; and (6) administration. The chairs and co-chairs of these subcommittees have been asked to present a brief annual report outlining accomplishments and tasks to be completed in each area. The IAB meets monthly, and new policies being considered by the NCI are presented to the IAB before they are codified, thus ensuring the input of the intramural scientists whom these policies will affect.

The second internal committee is the Extramural Advisory Board (EAB), chaired by Dr. Faye Austin, which deals with

issues in the ERP. Dr. Klausner emphasized that the chairs of the IAB and EAB sit on the governing body of the Institute—the Executive Committee (EC). The EC deals with overarching issues—for example, reviewing new initiatives, setting the payline, reviewing grants, managing the AER, and developing training programs. Micromanagement is no longer a function of the EC because of authorities that have been delegated to scientists. This was done to address the recommendation by the Working Group concerning the need for change in the areas of administration and science.

Dr. Klausner reported that the NCI is creating a culture and a set of mechanisms to elicit the best advice about issues from the larger community, as well as to raise questions that would not otherwise be raised. The NCI's major response to the recommendation about strategic planning recommendations was to create a planning process that involves the wisdom of the larger community in the planning and decisionmaking of the Institute.

**Organization of the Intramural Research Program (IRP)**—Dr. Klausner outlined the NCI actions taken in response to the critique that the structure of the IRP was complex, redundant, and administratively burdensome. As recommended, the IRP was almost completely separated from the ERP. Three divisions were created, not two as suggested by the committee, because of the size of the program and the very different science. The divisions within the IRP are the Division of Basic Sciences (DBS), Dr. George Vande Woude, Scientific Advisor to the Director; DCS, Dr. Philip Pizzo, Acting Director; and DCEG, Dr. Joseph Fraumeni, Director. The latter division also has an extramural component because of the nature of epidemiologic research—much of which is integrated collaboratively with the extramural community. Dr. Klausner stated that the reorganization has resulted in simplification in that 8 major programs, 8 branches, and 18 sections in the IRP and the ERP have been eliminated, and all division directors now report directly to him.

Responsibility for administrative management now resides in the Office of Intramural Management (OIM) in the IRP and the Office of Extramural Management (OEM) in the ERP. Administration for the entire IRP resides in the OIM under the directorship of Ms. MaryAnn Guerra, and administrative redundancies have been reduced. The six administrative management branches of the former configuration have been consolidated into the OIM and OEM, layers of review and permission for a variety of things have been eliminated, and the services to the scientific staff are now geographically dispersed through single multifunctional service centers of expertise. Dr. Klausner noted that the evaluation of individuals is now based not on the number of people they supervise but rather on the quality of service they provide to the scientists through the Administrative Resource Centers (ARCs). Dr. Klausner emphasized that the key to ensuring that everything that is done serves the science is to delegate authorities within the streamlined administrative structure. To that end, many authorities have been delegated to the ARCs. Additional procurement and technology transfer authorities have been delegated directly to the scientific staff. To help the scientific staff, the position of Laboratory Manager was created within each laboratory, and in this new configuration, the managers responsible for the administrative functions are an integral part of the laboratory. A training program has been developed to provide training in the specific skills needed for this new career track.

Dr. Klausner next addressed the reorganization of the FCRDC, which had previously included a mixture of contract and support services for both the IRP and ERP as well as independent research—some of which had never been reviewed. In the restructuring, all intramural research has been reorganized and transferred to the appropriate intramural divisions, and all the contracts that directly support that research are now part of the reviewed budgets. Dr. Klausner noted, however, that the FCRDC presents the NCI with an extraordinary opportunity to create an intellectual and service infrastructure—for both the IRP and the nation—in developmental therapeutics, developmental diagnostics, informatics and computation, animal models, and complex genetics. He stated that the NCI is working to develop a plan to turn the FCRDC into a national resource. Using a slide, Dr. Klausner delineated the new structure of the FCRDC, which has been placed under the leadership of Dr. Alan Rabson, Deputy Director, NCI. Services located there include the production facility, fermentation facility, drug discovery core, supercomputer, and animal production facilities.

**Quality Assurance**—Dr. Klausner stated that quality assurance for the IRP of the NIH as a whole has been a topic which he frequently addresses, and he agreed with the assessment of the Bishop-Calabresi Report. To that end, the chartered BSC and its subcommittees have received clear guidelines regarding the nature, format, and expectations of site visits. These guidelines have been formalized in the new booklet entitled *Intramural Organization and Principles*

(IOP). This booklet is key to quality assurance of activities in the NCI; for the first time, principles, expectations, structures, and design of processes are clearly written to be rigorous but fair. Both the reviewers and the reviewees know exactly what to expect, know what the process is, and know what to prepare. To coordinate the review process, the Office of Advisory Activities (OAA) has been established in the DEA, and it will facilitate effective implementation of all operations of the BSC and BSA, including oversight of site visits. Dr. Klausner referred Board members to the written report of the NCI's response for more explicit details about the site visit process. He emphasized that the IOP lays out specific criteria and a format for the review and each independent principal investigator presents his or her program and all resources. The report of the site visit committee is a narrative about the quality of the science in relation to available resources, containing a recommendation to the NCI for action in regard to allocation of resources. In addition, the IOP codifies a written response mechanism, which allows the individuals being reviewed an opportunity to defend their program and respond to the reviews.

Dr. Klausner stated that the decision was made to continue using a site review process that combines a retrospective review with current work and plans for future work. The site reviews are expected to be rigorous; the NCI is instructing the reviewers that the intramural researchers are to be held to the same rigorous criteria for valuable, creative, and innovative science as the extramural community. Dr. Klausner reiterated that the resources of each principal investigator, as well as the science, will be reviewed. In terms of resources, the NCI has established cost-management principles and zero-based budgeting. A key element is the fact that the budget and all resources are given to the principal investigators, including both those in the tenure track and the junior investigators. The budget built by each laboratory or branch chief is the sum of the budgets and resources of the principal investigators in that lab or branch, but the budgets and resources are the domain of each principal investigator. The laboratory or branch chief is the advocate of the principal investigators to the division director. The laboratory or branch budget also includes budgetary support for core facilities as well as for the general environment of the division.

Dr. Klausner reported that allocating the budgets to the principal investigators using zero-based budgeting and cost-management principles has resulted in a reduction in intramural funding without any site visit review. Thirty-one out of the 45 intramural laboratories received decreases ranging up to 33 percent in their FY 1996 budgets. Dr. Klausner affirmed that the NCI will heed the advice received during the site review process. He emphasized the importance of ensuring that the research in the intramural laboratories of the NCI is of the highest quality and that the structure reflects the support of independent scientists at all levels of their careers.

**Stewardship Review and Tenure Policy in the IRP**—Dr. Klausner quoted the critique from the Bishop-Calabresi Report: "The IRP environment is not conducive to encouraging young investigators by rewarding creativity and excellence. Inadequate recruiting and promotion policies further undercut the scientific talent and diversity of the staff." Dr. Klausner outlined NCI's plans for addressing the issue of developing and renewing talent. Every 4 years, division directors will undergo an independent review conducted by the BSC to evaluate the degree to which they ensure appropriate stewardship of their resources. They will also be reviewed for their ability to recruit an outstanding and culturally diverse group of scientists and for implementing programs for career development, training, and mentoring of nontenured staff.

Dr. Klausner explained that, in the quadrennial reviews by the BSC, every laboratory and branch chief will be reviewed as a scientist and principal investigator, but they will also be reviewed in terms of their encouragement and facilitation of the development of independent scientists under their supervision; those criteria are clarified in the IOP.

Dr. Klausner stated that the NCI policy is to conduct nationwide and open searches for recruitment of tenured and tenure-track scientists for all scientific positions. Dr. Klausner also reported that the NCI is in the process of creating a new career development pathway for very young scientists, called the NCI Research Scholars Program. It is modeled after a Whitehead Scholars

Program and is aimed at providing an opportunity for outstanding young investigators to launch independent research careers at the NCI; these are not tenure-track positions.

Dr. Klausner announced that a career development office has been established under the leadership of Dr. Dinah Singer, an outstanding intramural scientist. New guidelines have been developed that codify promotion, tenure, tenure-

track, and recruitment policies. The NCI has also developed an Affirmative Action Plan to increase gender and ethnic diversity at the Institute. A new recruitment program—now being developed through this office—is targeted at identifying highly qualified individuals who are culturally diverse.

**Clinical Research in the IRP**—Dr. Klausner stated that he agreed with the Working Group's assessment that the IRP provides the NCI investigators with an opportunity for creative and important research that is unique in this country. Because of the lack of constraints and demands that the health care system places on this Institution, intramural scientists have an extraordinary opportunity to realize the ideal clinical research environment. The leadership of the DCS will be critical to this effort, and Dr. Klausner expressed confidence that the NCI will be able to recruit an outstanding individual to that position.

In line with the recommendations of the Report, a DCS Protocol Office is being created in conjunction with the Cancer Therapy Evaluation Program (CTEP), which is in the extramural Division of Cancer Treatment, Diagnosis, and Centers (DCTDC), to facilitate protocol development. In addition, a Protocol Review and Monitoring Committee (PRMC) was created, which has conducted a retrospective review of all of the active intramural clinical protocols. Dr. Klausner reported that the NCI had 266 open protocols at the beginning of the review, 190 of which were open for active accrual. As a result of the review, 50 of these were closed. Through the review process, the PRMC has identified an additional 55 requiring a second-level review, which is under way; 29 of the 55 have been reviewed, and 16 have been closed or recommended for closure. In addition, the PRMC has developed criteria for prospective review of new protocol concepts to ensure optimal scientific investment.

Dr. Klausner reported that the NCI also has established an Education and Mentoring Committee within the DCS. A handbook for mentoring has been developed and plans for developing a syllabus for training clinical investigators are under way. In addition, a training program in cancer genetics is being shared across all three intramural divisions.

Dr. Klausner stated that, through the site visit and review programs, the NCI will be assured that the clinical programs are as rigorously reviewed as any of the other programs. He noted that the FCRDC clinical program has been reviewed, and he would be presenting the recommendations of the review committee in the closed session.

**AIDS-related Activities of the IRP**—In FY 1995, the AIDS budget of the NCI was \$225M. Dr. Klausner stated that Dr. Rabson has the authority and responsibility for directing and coordinating AIDS research. Dr. Rabson will deal with issues raised by the Ad Hoc Working Group, such as how the NCI determines what are AIDS monies; what the NCI spends on AIDS research; what should be spent; and how AIDS research should be coordinated among the NCI, the other Institutes, and the OAR. Dr. Klausner noted that the major thrust of the NCI activities should and does relate to AIDS malignancies. As mentioned earlier, the AIDS Malignancy Working Group, chaired by Dr. Feigal, has met and made several recommendations, one of which is to identify the Institute's AIDS malignancy research. As a starting point, Dr. Feigal is compiling a handbook of the NCI's AIDS malignancy activities.

Dr. Klausner reported that the NCI has acted on a number of new AIDS initiatives. One important initiative began in August when a group of scientists developed scientific guidelines to define what the NCI considers to be AIDS and AIDS-related research within its various disciplines. He acknowledged the difficulty of this process, because the precise boundary of valuable scientific contributions to any area cannot be known. He cautioned against believing that advances against AIDS will be improved by the ability to define precisely where the progress will be. He noted the need, however, to be able to defend intellectually the choices made by the NCI. According to the guidelines, projects that involve working with HIV and AIDS patients were considered direct AIDS research and could be funded totally with AIDS money. Projects that were clearly applicable to AIDS research, such as research in central nervous system (CNS) lymphomas or Kaposi's sarcoma, even if they were not in the context of an individual infected with HIV, were to be examined on a case-by-case basis. These could be funded at a 30 to 70 percent level with AIDS money. A third category included projects embodying fundamental aspects of AIDS research related to virology and immunology. For this categorization, the committee found the Levine Report helpful for its recommendations about increased investment in human immunology and opportunistic infections, including infectious agents that may be involved in malignancy or malignant progression. Dr. Klausner stated that the NCI has used these criteria to adjust its coding and also to address the imbalance in the distribution of the AIDS monies between the IRP and the ERP. As a result of this review and recodification and in response to the Report of the NIH AIDS Research Program Evaluation Working Group, the

decision was made to shift more of the NCI's AIDS funding into extramural investigator-initiated research projects.

Dr. Klausner reviewed the significant changes in the NCI's AIDS budget estimates for FY 1996. He highlighted the following in the ERP funding estimates: (1) \$7M was moved immediately from the IRP into Research Project Grants; (2) using the process for coding the NCI projects as AIDS, AIDS-related, or fundamental to an understanding of AIDS, the NCI has arrived at the current estimate of \$96M, down from \$102M; (3) the Centers total includes a new program in AIDS malignancies; (4) funding to the cooperative groups has been increased in response to the recommendations from the AIDS Malignancy Working Group; (5) funding to the AIDS Malignancy Consortium and AIDS malignancy bank has been increased; and (6) funding has been included for the DCEG initiative to develop databases on AIDS epidemiology by linking AIDS and cancer registries in several areas of the United States. With these changes, NCI funding for the ERP has increased substantially.

Dr. Klausner pointed out changes in other lines of the NCI AIDS budget for FY 1996. The number of R&D contracts was reduced. AIDS funding in intramural research has decreased to \$44M. This constitutes a 44 percent decrease in 9 months in the amount of AIDS money in the IRP.

Dr. Klausner reported on another NCI AIDS initiative. To reduce redundancy found during a review of AIDS and AIDS-related projects, as well as to promote communication among scientists, the NCI is creating a consolidated AIDS program within the DBS, to be housed in a new research building in the FCRDC. Components of the new program are the basic research program at Advance BioScience Laboratories, Inc. (ABL), the Biomedical Supercomputing Center and AIDS Vaccine Development Program at Science Applications International Corporation (SAIC), the Laboratory of Leukocyte Biology (LLB), the Laboratory of Viral Carcinogenesis (LVC), the Laboratory of Molecular Oncology (LMO), and the Laboratory of Tumor Cell Biology (LTCB). A national search is under way for an outstanding scientist to lead this program; the search committee is chaired by Dr. John Coffin.

Dr. Klausner reported that a new laboratory has been created to integrate the AIDS malignancy and AIDS research efforts at the Clinical Center. This new laboratory, with Dr. Robert Yarchoan as Acting Director, unifies adult and pediatric approaches to AIDS research previously located in the Medicine and Pediatric Branches of the DCS.

Dr. Klausner announced that the DCEG has recruited an epidemiologist with 10 years of experience with the SEER Program, who is particularly interested in AIDS malignancy and AIDS epidemiology. This individual will work in DCEG to help coordinate the informatics and database efforts related to epidemiologic and multidisciplinary studies of AIDS-related malignancies.

**NCI at the Frederick Cancer Research and Development Center (FCRDC)**—Dr. Klausner referred to a diagram showing the new configuration of FCRDC and pointed out that the NCI responded to much of what was recommended in the Bishop-Calabresi Report. The entire program was disaggregated and all basic research programs have been relocated to appropriate divisions. Principal investigators who were on contract have been identified, and investigators with independent resources who have never gone through the recruitment process will be reviewed over the next year. The entire program at FCRDC will be reviewed this summer. The Biological Response Modifiers Program (BRMP) was discontinued as a separate program, but individual branches and laboratories have been relocated. The Clinical Research Branch is now part of the DCS, and all of the laboratories conducting basic research in immunology are under the DBS.

**Drug Development in the IRP**—Dr. Klausner stated that the drug development program is being studied by the Institute. NCI has a critical role to play in the discovery and development of new therapeutics. Because of the importance of that area and the complexity of the relationship among government, industry, and academia, the NCI has asked for a review to guide the Institute in determining future directions for its drug discovery and development efforts. The NCI will postpone making any decisions about developmental therapeutics until it is able to take a much broader and more detailed look at the program. Dr. Klausner reported that, in the meantime, the Developmental Therapeutics Program (DTP) has been disaggregated. The laboratories identified as clearly conducting intramural research are now part of the IRP in the DBS, but the DTP, with Dr. Edward Sausville as Associate Director, is part of the ERP in the DCTDC.

Dr. Klausner referred Board members to his written report for a more complete and detailed account of the NCI's

response to the Bishop-Calabresi Report. He observed that the changes in the NCI have been substantial, significant, and real. He acknowledged that changes of this magnitude raise great anxiety and uncertainty and noted that the NCI staff has dealt with those issues appropriately. He commented that everyone in the NCI community has worked with this program and all—not only staff members who helped formulate and implement it—are to be congratulated on their ability to deal with the enormous challenges.

In conclusion, Dr. Klausner thanked Dr. Bishop, Dr. Calabresi, and all members of the Ad Hoc Working Group for their help. He pledged the Institute's continued responsiveness to the recommendations of the NCAB and of the advisory groups that will help recreate an Institution that will be successful in fulfilling its mission.

Dr. Rimer thanked Dr. Klausner and commended the comprehensiveness of his report. Because she believed the Board could not adequately address all that had been reported in the limited time left in the meeting, she asked Dr. Bishop and Dr. Calabresi to review the written report over the summer, along with any updates received from the NCI, and lead a discussion at a future meeting after all members have had an opportunity to read and consider Dr. Klausner's full report. Dr. Calabresi agreed to the request. He commended Dr. Klausner and the NCI staff for the amount of work they had done in so short a time while implementing the recommendations in the Bishop-Calabresi Report, and thanked Dr. Klausner and everyone for their efforts.

Dr. Rimer opened the floor for a brief discussion in the time remaining before the executive session.

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## **QUESTIONS AND ANSWERS**

### **Progress in Implementation of the Bishop-Calabresi Report Restructuring and Refocusing the Intramural Program**

Dr. Chan asked about the optimal distribution of intramural versus extramural funds. Dr. Klausner pointed out that intramural funds over 1 year have decreased from about 18.8 percent of the NCI budget to 18 percent and are estimated to decrease to 17.5 percent of the total in FY 1997. He stated that further changes cannot and should not be made precipitously. He asked that the IRP be viewed for its outstanding accomplishments, ability to function well, efficient and effective use of funds, and support of extramural research rather than as a competitor with extramural activities. Dr. Day pointed out that the Working Group explicitly avoided specifying a number for funding and made the additional point that the number could be computed differently by including contract support; he noted that a major transfer of funds had occurred there. Dr. Klausner observed that calculating intramural funding proved to be difficult, and that the decrease was probably larger than described because of changes made in NCI contracts.

Dr. Day commented that he and a number of people have been concerned about the comparability between reviews of the IRP and the kind of review that a R01 or a P01 undergoes in intramural reviews. Dr. Klausner clarified that the NCI intramural reviews would be a mix of past and present accomplishments and plans for the future, as requested by the BSC. Dr. Day asked how the extensiveness and rigor of that review will compare with reviews conducted through the DRG mechanism. Dr. Klausner agreed that the two processes differ. Intramural laboratories will be reviewed during a site visit by expert and experienced extramural scientists who will be evaluating on the basis of one straightforward goal, namely, that the IRP be regarded as one of the great centers of science. Dr. Klausner emphasized that the site-visit process will be monitored and will change over time as needed to ensure that it works well. He pointed out that extramural investigators may have multiple sources of funding other than a particular R01, whereas, an investigator in the IRP has only the one source of funding. Thus, the intramural review process must be tailored to the nature of what is being reviewed—that is, the totality of a person's scientific career at a given moment as opposed to funding or partial funding for one of his or her projects.

Dr. Calabresi agreed that the NCI should follow the advice of the BSC and base reviews on past performance and future direction, but he urged that the NCI not duplicate internally what is being done externally. Dr. Klausner agreed and noted that a significant aspect of the intramural review will be retrospective, which is different than what has been done with an R01. He pointed out, however, that scientists prefer to focus on what they are doing now and where the research is going. If their projects are going to be risky, creative, and exciting, these intramural scientists will fare very well in these reviews. The NCI will attempt to strike a balance concerning past performance and future direction. Dr. Bishop expressed the view that the Working Group would not object to the change, because of the difficulty

experienced in reaching the original consensus on the recommendation that intramural review should be retrospective.

On behalf of the Board, Dr. Rimer commended Dr. Klausner and all other NCI staff for their accomplishments over the past year. She announced that the Board would move immediately into the closed session with Dr. Klausner, and she adjourned the open session of day one at 12:30 p.m.

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## U.S. POSTAL SERVICE-NCI BREAST CANCER INITIATIVES

Dr. Rimer convened the second day of the 98th meeting of the NCAB with the reminder that persons wishing to comment on any item of business could do so by writing to Dr. Kalt within 10 days after the meeting. She gave a brief overview of the day's business (announcement of the U.S. Postal Service-NCI breast cancer initiatives, reports from the subcommittees, forum on issues related to genetic susceptibility testing) and asked for comments from Dr. Klausner on his meeting at the White House the previous afternoon.

Dr. Klausner reported that First Lady Hillary Rodham Clinton chaired a session at the White House on breast cancer awareness, which featured testimony from survivors, activists, and representatives of the Administration. Mrs. Clinton used the opportunity to comment on the NCI's announcement the day before of new data demonstrating a further reduction in mortality from breast cancer, which expanded and extended a continuing trend to more segments of the U.S. population. She also communicated the Administration's commitment to research in breast cancer and to actions that ensure access by all to screening and treatment.

In her remarks introducing the first presentation, Dr. Rimer briefly reviewed Mr. Marvin Runyon's professional career before becoming Chief Executive Officer (CEO) and Postmaster General of the United States Postal Service (USPS) in 1992. She remarked that he now leads an organization with 750,000 employees that reaches every American, making the collaboration between the USPS and the NCI to promote awareness of breast cancer and breast cancer screening one of the largest outreach efforts ever launched. The initiatives to be undertaken include printing and disseminating 100 million breast cancer awareness stamps, publicizing the 800 number of the Cancer Information Service (CIS) (1-800-4-CANCER), making materials about breast cancer available at all local post offices, and sponsoring collaborations between local postal services and CIS outreach workers. Dr. Rimer showed a video based on a talk given by a postal worker, Ms. Diane Nannery, at the annual meeting of the CIS, which was also a 20th anniversary celebration. Dr. Rimer noted that the video was available for use locally.

Following the video, Dr. Klausner introduced Mr. Runyon. With this initiative, Mr. Runyon stated, the USPS would be throwing the full weight of its resources behind the cause. From June to October, it would be launching a national awareness campaign to battle breast cancer. He expressed confidence that USPS involvement could make a difference in the fight against breast cancer. He noted that although breast cancer is recognized as one of the leading health problems facing the Nation, much remains to be done because many Americans are still unaware of the life-saving value of early detection and treatment, and die needlessly.

Mr. Runyon credited Ms. Nannery with bringing the idea of the stamp to his attention, noting that she transformed her battle against breast cancer into a personal crusade to enlighten and empower others. Mr. Runyon reported that the initiative would begin on June 15 with the printing of 100 million stamps. In April, all postmasters received a promotion kit to guide their efforts to spread the message of early detection and treatment. The kits contained factual materials, lists of grassroots contacts, media materials, stamp artwork, and suggestions for hosting stamp ceremonies in communities across the nation.

Mr. Runyon acknowledged the help of a host of health experts and public service organizations in this initiative, and most importantly, the NCI. Help from the NCI included permission to print the toll-free cancer number on the border of each sheet of stamps, assistance in creating a link to NCI services with the USPS Internet home page, provision of information on breast cancer, and help with the development of many of the outreach materials. Mr. Runyon thanked the NCI staff for their help in facilitating and making possible these USPS efforts.

Mr. Runyon also cited the Susan G. Komen Foundation, as another important ally. The USPS is teaming with the National Race for the Cure, to be held in Washington, D.C. The stamp will be dedicated at the 5K race where Vice

President and Mrs. Gore will join 35,000 area runners and walkers in raising more than \$1M.

Mr. Runyon noted that the USPS is also teaming with the YMCA of the United States through the YMCA Encore Program to provide information forums and mammography screenings at selected post offices. The USPS is also working closely with organizations such as the National Alliance of Breast Cancer Organizations, ACS, and Y-ME National Breast Cancer Organization to sponsor local awareness activities. Finally, the 750,000 employees of the USPS are to receive information on breast cancer organizations to share with their families and friends.

Mr. Runyon expressed pride concerning these efforts and pleasure at having an opportunity to work with the NCI and so many other organizations, and Dr. Klausner and Dr. Rimer joined him in unveiling the breast cancer awareness stamp.

Dr. Klausner thanked Mr. Runyon and acknowledged the NCI's willingness to lead the fight to discover the cause of and cure for breast cancer. On behalf of the NCI, Dr. Klausner presented Mr. Runyon a certificate of appreciation for all that he and the USPS have done and are doing. Mr. Runyon accepted the certificate with thanks.

In another expression of thanks, Dr. Rimer read excerpts from a resolution passed by the NCAB in appreciation of the work of Mr. Runyon and the USPS. Dr. Rimer added her own appreciation for the work of the USPS and for the stamp.

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### **QUESTIONS AND ANSWERS**

#### **U.S. Postal Service-NCI Breast Cancer Initiatives**

Dr. Bishop noted that the USPS had recently unveiled a stamp in memory of a distinguished Black American scientist, and he commended the work of the USPS in helping to educate and sensitize the American public. He encouraged continuation of this type of initiative to promote recognition of the importance of science and medicine. Mr. Runyon agreed with Dr. Bishop's suggestion and thanked him. Mr. Runyon then related an experience during his TVA tenure as a member of the organization Leadership Memphis, when he was given the task of informing the group about AIDS. Being uninformed about AIDS, he approached the task of learning about the disease and about resources available in Memphis from the perspective of a person with AIDS. Dr. Runyon remarked that the experience so heightened his sense of the widespread need for AIDS awareness that he launched a successful campaign after he became Postmaster General to issue an AIDS stamp to get the word out to all parts of the country.

Dr. Rimer thanked Mr. Runyon on behalf of the Board and acknowledged the work of Mr. Paul Van Nevel and his staff for their work in the partnership.

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### **SPECIAL RECOGNITION OF DR. EDWARD SONDIK**

Dr. Rimer called attention to the departure of Dr. Edward Sondik—former Acting Director of the NCI and current Associate Director for Strategic Planning—to assume the position of Director, National Center for Health Statistics (NCHS), and advisor to DHHS Secretary Shalala. Dr. Rimer recognized the contributions made by Dr. Sondik during his long career at the NIH and the NCI with a resolution adopted by the NCAB, from which she read excerpts.

Dr. Klausner praised the grace and the amount of knowledge with which Dr. Sondik transferred the directorship of the Institute, and he acknowledged Dr. Sondik's continued invaluable assistance. Dr. Klausner applauded Dr. Sondik's appointment to head the NCHS as a well-deserved honor that recognized his skills and contributions.

Dr. Sondik thanked Dr. Klausner and the Board. He especially remembered the commitment shown by NCI staff to making a difference and reducing the suffering from disease. He expressed a strong belief that research is critical but liaisons must also be developed with those who can apply the research. Dr. Sondik cited the partnership with the USPS as exemplifying what can be accomplished, and he affirmed that his partnership with the NCI would continue in his new position.

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## **FORUM: SHOULD GENETIC SUSCEPTIBILITY TESTING BE LIMITED TO RESEARCH PROTOCOLS OR BE MADE GENERALLY AVAILABLE**

In introducing this forum, Dr. Rimer noted that the Board has been concerned about and would continue to monitor critical questions that surround recent advances in genetics research and, particularly, those questions that surround testing for genetic susceptibility. She read excerpts from two recent articles published in the *New England Journal of Medicine* to introduce some of the issues to be addressed in the forum.

Dr. Rimer noted that the three speakers were some of the most experienced scientists in the field of genetic susceptibility testing: Dr. Henry T. Lynch, Professor of Medicine, Department of Preventive Medicine at Creighton University School of Medicine; Dr. Francis S. Collins, Director, NCHGR, NIH; and Dr. Caryn E. Lerman, Associate Professor of Medicine and Psychiatry, Lombardi Cancer Research Center, Georgetown University Medical Center. Dr. Rimer introduced Dr. Lynch to make the first presentation.

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### **BRCA1 TESTING AND ITS CLINICAL AND PUBLIC HEALTH IMPLICATIONS**

Dr. Lynch outlined topics to be considered in preparing to incorporate genetic testing in oncology practice: the need to obtain a family history of sufficient depth to enable the physician to make a diagnosis of hereditary cancer syndrome—should one exist in a family; genetic counseling prior to conducting DNA studies; surveillance or management after DNA studies; and extension of the study to all at-risk relatives. Dr. Lynch cited the need for physician education to overcome the neglect often accorded family history as part of the medical evaluation of patients.

Dr. Lynch stressed that hereditary cancer is not rare, but the diagnosis of hereditary cancer is. Dr. Lynch estimated conservatively that, of the 1.2 million new cases of cancer that can be expected to occur in the United States, at least 5 percent or 50,000 patients will have a primary genetic factor. Because penetrance of the BRCA1 and BRCA2 genes or any other gene does not reach 100 percent (in the range of 85 to 90 percent for BRCA1 and BRCA2), all carriers will not develop cancer. Moreover, cancer is so common that most patients with breast cancer are sporadic cases and will not be germ-line carriers.

Dr. Lynch showed a slide listing genes that have already been identified in hereditary cancers, noting that the list already was obsolete. Dr. Lynch noted that clinicians must recognize the profound genetic heterogeneity—even within those carrying the same breast cancer predisposition gene—as well as the differing presentations of the inherited cancer syndromes. Much research is needed to identify sporadic presentations where BRCA1 and BRCA2 may play a role.

Dr. Lynch reviewed the stages in the paradigm for genetic susceptibility testing: clinical assessment; selection of individuals who want predisposition DNA testing; counseling and informed consent; predisposition testing; counseling prior to and at the time of disclosure of findings; and clinical surveillance. One problem to be addressed is the limited number of genetic counselors who are knowledgeable about cancer and who can provide appropriate counseling that integrates the importance of genetic risk and natural history of cancer in the patient's particular family. Patients should be informed of the advantages and disadvantages of available management options. Other requirements include psychotherapy for patients, assurance of confidentiality, and patient education and knowledge of long-term outcome studies. Dr. Lynch emphasized the importance of close collaboration between physician and counselor and noted that oncology nurses are assuming major roles in such counseling.

Dr. Lynch then described the genetic counseling experience that his institution's Hereditary Cancer Prevention Clinic has attained with several hundred patients over the past several years. One family, in particular, had been followed for 25 years and incidence of ovarian and breast carcinoma was histologically verified. Dr. Lynch noted that data gained from one of the kindreds was helpful in identifying the fact that BRCA1 was also linked to carcinoma of the ovary.

Dr. Lynch summarized the Clinic's protocol for management of individuals found to be BRCA1 mutation carriers. He explained that they received education about genetic risk and the natural history of cancer; were advised to perform regular self breast examinations and initiate mammography at age 25; were informed of the limitations of current testing for ovarian cancer and advised to consider prophylactic oophorectomy after their families were completed; and

made aware of sequelae, such as peritoneal cystadenocarcinoma.

Dr. Lynch noted that many families were observed over the years, but he would focus on the 14 BRCA1 families which included the individuals who actually received genetic counseling in the study. Of the total number of 3,678 individuals in the 14 families, 2,549 were blood relatives and the remainder spouses. Dr. Lynch noted that DNA sampling had been completed for more than 300 members of these families; 145 were found to be gene positive and 174 were gene negative. Of these, 181 individuals were counseled and given their gene status; 78 were gene positive, 100 gene negative, and 3 ambiguous. Dr. Lynch noted that although males are at equal risk for the gene, only 46 came forward for counseling. The mean age at the time of counseling was 42 and the primary reason for seeking risk assessment as cited by the 181 counseled individuals was concern about their children or loved ones. Other reasons were to maintain surveillance, satisfy curiosity, consider possible prophylactic surgery, relieve anxiety, and contribute to research. Emotional responses observed in those receiving the BRCA1-positive results were sadness, no surprise, guilt about the effect on offspring, anger, and relief. Several in this category received the results with no emotional response at all.

Dr. Lynch reported that concerns about insurance discrimination were a major impediment to an individual's coming forward for screening, and a significant number of those already screened had not come forward for counseling and information on their gene status.

Breast surveillance, which had included mammography, physician examination, and self breast examination, had been practiced by many of the women prior to counseling sessions and actual participation, and the percentages of women in both the gene-positive and gene-negative groups were similar. About 32 percent of those subsequently identified as having the BRCA1 gene had already had mastectomies for cancer prior to the counseling session compared with 6 percent in what was later found to be the gene-negative group. An equal number in both groups had already undergone prophylactic mastectomies, and a few had mastectomies for other medical indications. Of the women in the counseled group who had not had prior mastectomies for either prophylactic or cancer treatment purposes, many in both the gene-positive and -negative group had considered prophylactic mastectomy before being counseled. After receiving their screening results, only one additional BRCA1-positive woman considered prophylactic mastectomy; and no one in the BRCA1-negative group considered the surgery, although 20 percent in that group had considered it prior to counseling.

Dr. Lynch noted that with regard to ovarian surveillance, a minority in both the positive and negative groups had already undergone CA125 and ultrasound evaluations prior to the counseling session. Percentages of women in the BRCA1-positive group who had bilateral oophorectomies prior to the counseling session were as follows: about 7 percent for carcinoma of the ovary (compared with none in the negative group); about 19 percent for prophylaxis; and a small percent for other medical reasons. Dr. Lynch noted that the number of women considering prophylactic oophorectomy before receiving the testing results was 73 percent in the group that was ultimately positive and 40 percent in the negative group. After counseling, one patient was added to the positive group who were already strongly considering that option, and one patient in the negative group did undergo prophylactic oophorectomy, citing the large number of ovarian cancer deaths in her family as the reason.

In summary, Dr. Lynch reiterated the two primary reasons patients sought their risk assessment: to inform other family members of potential risk and to make informed decisions about their own future surveillance. Other study highlights included the findings about the percentages of women who considered prophylactic surgery and who expressed concern for insurance discrimination, as noted above.

Dr. Lynch reviewed the recommendations on gene testing promulgated by ASCO and noted that they reflect actual practice in his institution. Factors to be considered and recognized are the magnitude of the public health problem with respect to hereditary cancer of all types; the limited number of genetic counselors; physician responsibility; and patients' right to know.

Dr. Lynch highlighted some of the principles and recommendations endorsed by ASCO in its May 1996 statement on genetic testing for cancer susceptibility: ASCO affirms the role of clinical oncologists in documenting family history of cancer in their patients and then providing genetic counseling; oncologists must assure that informed consent has been

given and that the patient understands the informed consent; to the greatest extent possible, genetic testing for cancer susceptibility should be performed where there is an opportunity for long-term outcome studies; and ASCO endorses all efforts including legislation to prohibit discrimination by insurance companies or employers based on an individual's inherited susceptibility to cancer.

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## TESTING SHOULD BE RESTRICTED

In her introduction, Dr. Rimer commended Dr. Collins for his efforts in promoting the responsible use of this type of genetic information and serving as a model of how that could be accomplished. Dr. Collins stated that Dr. Lynch's charge for this presentation was to present the favorable side of moving cancer genetic testing into the general practice of medicine and his own charge was to present the contrary view that cancer genetic testing still belongs in the research arena because benefits and risks are not well defined. Dr. Collins pointed out that because the protocol for

Dr. Lynch's study has received IRB approval, their positions are actually similar but he would still make the counterpoint case as strongly as possible.

Dr. Collins reported that the National Action Plan on Breast Cancer (NAPBC) had issued a statement in response to the ASCO statement, both of which were presented in the May issue of the *Journal of Clinical Oncology*. The NAPBC statement differed from the ASCO statement only in its assertion that it is not yet appropriate to perform testing for BRCA1, BRCA2, and hereditary nonpolyposis colon cancer (HNPCC) outside of an IRB-approved protocol. Dr. Collins noted that this point of difference is an important one because of the possibility that less experienced physicians could be pressured into offering the test to their patients outside of the research environment; in this case, all of the safeguards described by Dr. Lynch might be maintained less confidently. Dr. Collins applauded the data on reactions of the 181 counseled members of the BRCA1 families as reported by Dr. Lynch and noted that more data are needed to determine exactly how patients absorb this information and what behavioral and medical changes occur as a consequence.

Dr. Collins announced that he would focus almost completely on BRCA1. He added that the marketing of a test for the Ashkenazi Jewish mutation has, in effect, already opened the door to testing outside research protocols.

Dr. Collins reported that mutations in BRCA1 on chromosome 17 account for 5 percent of breast cancer cases. The penetrance curve—derived from studies of families that were ascertained due to a high frequency of breast and ovarian cancer—suggests that individuals with this mutation have a 85 to 90 percent life-long chance of developing breast cancer. Dr. Collins pointed out, however, that many scientists are unwilling to accept the fact that this penetrance curve will hold up in a general population ascertainment of BRCA1 mutation carriers. The 80 to 90 percent penetrance may be an overestimation because of the ascertainment bias inherent in the families studied in the development of the curve. Resolution of this uncertainty is needed before families can be counseled adequately.

Dr. Collins indicated that mutational heterogeneity in the BRCA1 gene is another problem that presents a challenge both in the laboratory and for counseling purposes. Dr. Collins referred to a slide presented by Dr. Lynch listing more than 100 mutations identified in specific individuals as of January 1996 and noted that the number had increased since then; most of these germ-line mutations had been identified in only one family. The notable exceptions were the Ashkenazi Jewish mutation (185delAG), which appears to be present in about 1 percent of Jewish individuals, and the 5382 insertion C mutation, which had a high frequency relative to other germ-line mutations but still accounted for only a very small fraction of total BRCA1 mutations. Dr. Collins stated that a very robust laboratory test is needed in most populations to avoid missing mutations that have not yet been identified and could lead to false-negative results. He observed that no laboratory has yet demonstrated that it has adequate sensitivity and specificity for testing for BRCA1.

Scientists attempting to interpret the meaning of BRCA1 sequence changes have benefitted to some degree by the fact that BRCA1 mutations seem to be frameshifts, splice alterations, or nonsense mutations, none of which are likely to be benign polymorphisms. Dr. Collins noted however, that some mutations alter a single amino acid and raise questions as to whether they are the cause of disease or a benign variant. For counseling purposes, this distinction is difficult to make with these so-called missense mutations unless a functional test is also performed, which is not currently

available. Dr. Collins observed that although false-positive results for BRCA1 will not be frequent, the number will not be negligible, especially if large numbers of people are screened.

Dr. Collins stated that the issue of genetic discrimination in health insurance has a very high priority because of its public health implications. He noted that most people carry DNA anomalies and could eventually be the objects of such discrimination. He characterized the current health insurance situation—which allows the use of this information to deny coverage or charge exorbitant premiums—as both unjust and unworkable. He called attention to the bills being considered in both houses of Congress that include genetic information on the list of items health insurers may not use to deny coverage. Dr. Collins expressed the view that significant change would not occur time soon and physicians will have to continue taking this situation into account when counseling patients.

Dr. Collins summarized the barriers to rapid introduction of presymptomatic testing for BRCA1 mutations in high-risk individuals: technical complexity; the lack of genotype and phenotype correlation information; complexity of large-scale genetic counseling; potential for genetic discrimination; and uncertainty of best medical management of mutation carriers. Dr. Collins concluded that for all of these reasons, the National Breast Cancer Coalition (NBCC), NAPBC, and several other organizations have consistently stated the view that the risks and benefits of BRCA1 testing were insufficiently well defined at present to offer testing outside of IRB-approved research protocols.

Dr. Collins cited two reasons why he personally advocates keeping genetic testing in the research arena: (1) genetic information has risks as well as benefits and should be subjected to the same strategy accorded new drugs in clinical trials prior to adoption into health care practices; and (2) an opportunity now exists to gain knowledge needed to answer questions related to options for prevention. He noted that premature release of this kind of testing essentially guarantees that most information will not be collected in a readily usable format.

Dr. Collins acknowledged that the view that genetic testing should not yet move outside of research protocols has been questioned. Dr. Collins deplored the polarization that has resulted, and offered a program that has been initiated by the NCI as a solution to the problem. The program involves development of the National Cancer Genetics Network (NCGN), which will expand access but maintain the research environment to collect information needed to answer pressing questions. The Network will likely be organized much like the NCI's Clinical Cooperative Groups, except that the clinical trials will look at the testing process instead of the drugs. Participation will be open to physicians interested in offering testing within this research network, who may apply to be co-investigators. Educational materials will be supplied to prepare the physicians and will educate a cadre of physicians to begin to achieve competency in genetics and the delivery of medical genetic services. Patients will have access to the testing through their own physicians and at the same time will be participating in an IRB-approved protocol that ensures protection of human subjects and promotes the collection of important data. Dr. Collins reviewed the types of data that could be collected and noted that a registry of mutation-positive and -negative individuals could thus be available for followup intervention trials. Dr. Collins identified confidentiality of data in such a registry as a high priority in the planning process. The Network Steering Committee and its three subcommittees have been working to implement the Network on a fast-turnaround basis so that the demand for access to genetic testing can be determined. Dr. Collins emphasized the importance of proceeding with genetic testing through a program that protects the rights of human subjects and furthers the collection of research information. He cautioned that omitting this step dedicated to answering questions and learning how best to implement genetic testing would cause regret in the future. Dr. Collins commended the leadership position assumed by Dr. Klausner and the NCI in committing the time, effort, and resources to this important research.

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## **GENETIC TESTING FOR SUSCEPTIBILITY ISSUES IN GENETIC TESTING**

Dr. Lerman described her charge in the debate as discussing the essential elements of genetic testing and counseling for cancer susceptibility.

Dr. Lerman listed the essential elements that she would review: extensive family history and cancer risk assessment; pretest education and informed consent; post-test genetic counseling and discussion of prevention and surveillance options; long-term followup to assess adverse effects; and safeguards to protect privacy. Dr. Lerman began the discussion with pretest education and informed consent. To date, there are no controlled studies that examined the effects of pretest education for genetic testing for cancer susceptibility. To fill this gap, the Lombardi Cancer Center is

conducting a randomized trial, funded by NCHGR and NIMH, which is studying the impact of pretest education on women who have at least one first-degree relative with breast or ovarian cancer. The study aims to observe the effects of education on their knowledge, awareness of the limitations and risks of testing, and subsequent testing plans and behavior.

Study subjects are randomized to one of two education arms or a waiting-list control arm. Those in the first education arm receive standard pretest education; those in the second education arm receive more extensive genetic counseling including in-depth discussion of psychosocial issues. Dr. Lerman stated that these groups were equivalent at baseline; for the purpose of this presentation the two education arms were combined. At 1-month followup, the education group compared with the control group demonstrated significantly greater knowledge of key pieces of information such as paternal transmission of BRCA1, proportion of cases attributable to BRCA1, and incomplete protection with surgery. However, approximately half of the women in the education group failed to grasp critical information, even after spending 1 1/2 hours going over the issues with an oncology nurse.

Dr. Lerman presented preliminary data compiled when the education and control groups were asked to rate the importance of the following limitations and risks: confidentiality of the information in medical records; concern about insurance discrimination; and concern about stigmatization. The education group rated these limitations and risks from 10 percent to 20 percent higher than the control group. Dr. Lerman pointed out, however, that a substantial proportion of women did not rate these issues as highly important, suggesting a divergence of perception between researchers and some of those seeking genetic testing.

Dr. Lerman highlighted the conclusions to be drawn from the incomplete analysis of these preliminary data: pretest education may improve knowledge, and it may improve awareness of the limitations and risks, but it may not influence women's decisions. She observed that this finding is somewhat consistent with information she has received from genetics counseling colleagues, namely, that some women seek genetic counseling to validate decisions they have already made and not necessarily for help in decisionmaking.

Dr. Lerman next addressed the issue of post-test counseling and its component topics, which include disclosure and interpretation of test results, implications for family, limitations of options for surveillance, and psychosocial support. To describe what is known about the effects of disclosure of results in post-test counseling, Dr. Lerman presented preliminary data from an observational study funded by DoD, conducted in collaboration with Dr. Lynch and the Creighton Hereditary Cancer Institute. The study includes a 2-year followup of members of hereditary breast and ovarian cancer families who are and are not seeking BRCA1 testing. Dr. Lerman presented two slides with information that focused on the impact of testing and disclosure of information on three groups—those identified as carriers, those identified as noncarriers, and those who declined testing. In the extensive hereditary breast/ovarian cancer families described by Dr. Lynch, only 43 percent of the individuals offered testing decided to be tested, even after multiple interviews. The first slide compared changes in depressive symptoms exhibited by the three groups. Changes were measured from prior to pretest education and counseling in the study to 1 month after disclosure of test results. In the group identified as noncarriers, a significant decrease in depressive symptoms was seen from baseline to 1 month after disclosure. In the carrier group—those who received the news that they had an 80 percent to 90 percent risk of developing cancer—no increase in depressive symptoms was seen. Neither was there a change in depressive symptoms in those who declined testing. Dr. Lerman pointed out that a similar pattern was seen when impairments in functional health status—that is, in daily living activities and productivity—were compared in the three groups.

In terms of interpreting these data, caveats included in the manuscript describing this study noted that the individuals were part of a registry, had been extensively counseled in ideal circumstances (by Dr. Lynch and colleagues), and were tested in the context of a research protocol. Additional analysis is planned to identify subgroups of individuals who may be more vulnerable psychologically to the effects of testing. A 2-year followup is in progress for this observational study.

Dr. Lerman addressed the next essential element of genetic testing and counseling for cancer susceptibility—long-term followup to assess adverse effects. Because data are not yet available for genetic testing for cancer susceptibility, she used data derived from a Huntington's disease study published by Wiggins and colleagues in the *New England Journal of Medicine*. Study groups included those who declined to be tested for the Huntington's gene mutation or whose

results were ambiguous, those informed they were carriers and at high risk, and those informed they were not carriers and at decreased risk. Dr. Lerman reported that differences were seen in the short term similar to those in her observational study—a statistically significant difference in distress between the family members who were told they carried the gene versus those who were told they did not. When these groups were followed for 12 months, no differences were found in any of the measures of psychological well being among the three groups. Dr. Lerman observed that long-term followup can identify both positive and adverse effects that may not be apparent in the short term.

Noting that safeguards to protect privacy had already been addressed by the earlier speakers, Dr. Lerman concluded with a list of six areas where information is needed to meet future challenges in testing for cancer susceptibility genes: (1) identity of all mutations and their associated risks; (2) data on the efficacy of prevention and surveillance strategies to assist individuals in making informed decisions; (3) details on the potential for adverse effects in a variety of populations, including those who are more naive than the populations already tested; (4) strategies to ensure protection against the risk of discrimination; (5) consensus as to the propriety of prenatal testing and testing of children; and (6) data on costs and benefits to inform public health decisionmaking.

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## QUESTIONS AND ANSWERS

### **Forum: Should Genetic Susceptibility Testing Be Limited to Research Protocols or Be Made Generally Available**

Dr. Rimer asked Board members to begin thinking of actions that can be taken to close these information gaps and advice for the Institute in this regard.

Dr. Bishop asked whether the insufficiency of genetic counselors could be attributed to inadequate interest, opportunity for training, or employment opportunity. Dr. Collins responded that the insufficiency could probably be explained as a combination of all those reasons.

Dr. Schein asked Dr. Klausner to describe what the NCI hopes to accomplish in implementing the Network and to estimate the timeframe in which substantive new information can be provided that could affect how this new technology is used. Dr. Klausner explained that a network is envisioned that will provide an infrastructure to answer questions relating to the range of issues raised by the three speakers and represents an attempt to solve the problem of polarization.

This extensive network will be tied together with an informatics system. The Network is conceptualized as a very simple research base that will feed into, but not compete with nor replace, the standard approach to hypothesis-driven research protocols for surveillance, prevention, detection, and treatment. The research base will be a confidential, encrypted, and protected long-term epidemiologic observational study. It will provide an opportunity to follow the natural history of individuals who seek testing and are tested. Physicians and patients will have access through the Network to information on available studies for participation.

Dr. Klausner stated that the NCI is attempting to complete plans as quickly as is consistent with creating a workable structure with informatics that are completely encrypted, protected, and secured.

Dr. Sigal asked Dr. Lynch why the number of women who considered prophylactic surgery prior to confirmation that they had the BRCA1 gene mutation did not increase significantly after confirmation. She also asked whether statistics were available on those in the positive group who did not consider surgery. Dr. Lynch stated that, except for one addition, the number of women in the positive group who decided to have prophylactic surgery before confirmation remained unchanged. The effect of confirmation in the negative group was dramatic; only one woman who considered surgery prior to confirmation did not change her mind later. Dr. Lynch noted that the long-term study with Dr. Lerman should provide more definitive answers.

Dr. Freeman asked if risks could be calculated based on data from the BRCA1 research. For example, could risk be estimated for his patient with lobular carcinoma in situ (LCIS) if she were tested and found to have the BRCA1 gene? Dr. Lynch replied that these are important questions without answers at this time. Dr. Lynch stated that he would not

ordinarily perform a lumpectomy on a woman who is BRCA1 positive.

Dr. Freeman asked Dr. Lerman if she acquires patients who have complex risk factors other than BRCA. Dr. Lerman replied that very little is known about risk factors that may affect the age of onset in carriers and that may modify the risk of penetrance. She suggested that some of the studies that will be undertaken through the Network will help answer these questions. Dr. Klausner affirmed that part of the reason for gathering data in the Network is to address what is known by all but may be forgotten, namely, that identification of genetic susceptibility genes does not mean that attention to environmental and other issues is not also extremely important. To the contrary, identification of genetic predispositions clarifies one aspect of risk and makes it easier to interpret other aspects of risk.

Dr. Freeman suggested that the point he raised deserves consideration. Because many more people in the country are going to have the other usual risk factors, both sets of circumstances should be taken into account in formulating future policies.

Dr. Day asked Dr. Collins if there is a plan in the Genome Project or elsewhere to calculate these frequencies in a random sample of the population. Dr. Collins responded that, just in terms of allele frequencies, the task would be difficult because of the need to obtain informed consent. He described the dilemma: Can one obtain a random sample of the population, preserve enough clinical information, and then do genotyping without having a fully informed consent from those participants—because the consequences to their health might be considerable? He pointed out that this problem has been widely discussed in the past few years. The National Health and Nutrition Examination Survey (NHANES) that the CDC has been carrying out—with 18,000 to 20,000 individuals surveyed—has been suggested by many to be an ideal sample because of the amount of clinical information that has resulted. But those individuals did not consent to DNA testing. Dr. Collins expressed the view that it would be very valuable to backtrack and obtain that consent, although the cost would be high. Potentially, genotype frequencies could be obtained in the context of some credible clinical information. If obtaining consent is not possible, the alternative would be to obtain samples that have been rendered anonymous by stripping them of all identifiers.

Mrs. Brown asked if it is known how long it will be before gene testing becomes beneficial to the public as a whole, and whether the public will eventually see the gene manipulated so that a cure for disease might be found. Dr. Collins responded that the gene discovery has more immediate consequences for diagnostic capability; other benefits are still rather unclear. He envisioned that patients would, in 3 to 5 years, have a much better idea of the value of knowing if they are BRCA1 mutation carriers and a clearer understanding of what options provide what benefits. At this time, it is impossible to determine the point at which odds will be predicted and disease cured.

Dr. Chan asked if Dr. Lynch's data could be made available to the Board after the ASCO meeting. He expressed concern, considering the protection of confidentiality, about whether it would be possible for an individual to obtain all necessary information from relatives and then estimate from genetic tracking data some kind of risk factors. He wondered whether coverage could be denied only to the individual. Dr. Collins confirmed Dr. Chan's concern, and pointed out that one reason the NCHGR and NCI had worked hard to ensure that the bills currently in the Congress use the words "genetic information" rather than "genetic testing" was to cover family history, because that itself could be sufficient to deny insurance coverage.

Dr. Ghosh asked how he could advise his patients who had survived either breast or ovarian cancer and asked to have the test done before considering prophylactic surgery—either oophorectomy or mastectomy. Dr. Collins agreed that this is another group of individuals looking for access to information. He expressed the view that, ideally, access should be provided by a rapid expansion of the number of research protocols available through the Network and other mechanisms. Individuals asking about tests could then be immediately enrolled in studies that would involve the series of steps outlined by Dr. Lynch and Dr. Lerman. Dr. Collins observed that although it is difficult to document the demand for testing, there is the sense that access to existing research protocols is not keeping up with the interest. He expressed the view that addressing this problem is the responsibility of all scientists in the research community.

Dr. Ghosh asked for advice on handling requests for prophylactic surgery from patients who are cancer survivors and are subsequently found to be positive for the BRCA1 mutation. Dr. Collins replied that no solid data exist about the value of mastectomy and oophorectomy for reducing risk in mutation carriers with regard to whether or not they have

previously had a cancer of the breast or ovary.

Dr. Lynch agreed that research is needed, but he noted that prophylactic surgery to reduce risk has a certain amount of logic that appeals to many. First, studies performed 20 years ago have shown that the contralateral breast is at 46 percent risk over 20 years. The risk increases at about year 9, and goes up extremely high at years 17, 18, and 19, at a little over 5 percent per year. Dr. Lynch pointed out that early carcinomas have been detected in individuals who had contralateral prophylactic mastectomy and bilateral mastectomies. He added that his institution has been very conservative in performing bilateral mastectomies for gene-positive individuals and, previously, women who were at 50 percent risk, based on the pedigree. Dr. Lynch described a category of women, however, who could be candidates for prophylactic surgery—those at high risk whose quality-of-life is absolutely destroyed, whose fear of possible discovery during breast examination and mammograms leads to noncompliance, or who have proliferative disease with atypia or multiple biopsies so that there is distortion on physical examination and on the mammogram. Dr. Lynch acknowledged the possibility of residual breast tissue and the consequent risk of recurrent or primary disease, but noted that statistics show this risk is only 0.6 to 5 percent.

With respect to ovarian carcinoma, Dr. Lynch stated, the risk for significant sequelae—peritoneal cystadenocarcinoma—occurring as long as 20 years after normal ovaries have been removed, is only 3 to 5 percent; the risk for ovarian carcinoma in some of these families ranges from 40 to 66 percent.

Dr. Collins asked about the origin and certainty of the risk estimate of 3 to 5 percent for ovarian cancer sequelae. Dr. Lynch agreed that research is needed on that score. He noted that his patients often ask whether having a prophylactic oophorectomy will predispose them to peritoneal cystadenocarcinoma; and said there is no basis for that predisposition.

Ms. Malek asked Dr. Lynch if he had any data indicating how much higher the risk of prostate cancer is in males who carry the BRCA1. Dr. Lynch replied that he had no data on that risk, but data from the international collaborative group, estimate a three- to fourfold relative risk increase for prostate cancer and about a fourfold relative risk increase for colon cancer.

Dr. Calabresi asked what can be done to translate the gene research to clinical practice. He referred to a report several months ago by a group in Texas that the BRCA1 gene encodes a protein that has an effect on the cell nucleus. A group in Vanderbilt seemingly held the contradictory view that the protein comes outside the cell and then acts on the cell surface. Dr. Calabresi asked Dr. Klausner and Dr. Collins which of these views they believed to be correct, and what the NCI was doing to resolve this seeming controversy. Dr. Klausner acknowledged that the problem is interesting but complicated. He reported that he has invited all of the researchers to bring their unpublished data and join him for a private discussion. Dr. Calabresi expressed satisfaction at this action for an issue that could be very controversial and could add to the confusion.

Dr. Goldson expressed the hope that the language of the RFA on the Network will specify some type of preferential priority for those groups that do collaborative work so that the largest cross section of the American population is included. He suggested that the skills of these various groups would grow in tandem.

Dr. Correa observed that, in his experience, the steps taken early in a program have an amplified effect later. He advised that attention should therefore be directed to the fact that cancer susceptibility means susceptibility to other things, mostly carcinogens; this has widespread implications because these people are more susceptible to diet- and smoking-related cancers. Dr. Correa emphasized the need for more research on alternative prevention strategies, such as hormonal strategies to prevent cancer, and for the development of intermediate endpoints. He concluded with a plea that there is a need to remember that individuals are exposed to carcinogens; this will interact with the research on the other forces that drive cells to become malignant. Dr. Rimer agreed with Dr. Correa's point that some of the information could be used to encourage people with these genotypes to make appropriate behavioral changes.

Dr. Schein asked Dr. Klausner whether there would be any significant material or rationale that might allow this new and very important information to be applied, perhaps more effectively, in a reasonable period. Dr. Schein acknowledged that the options that can be defined with absolute certainty may be very limited at this time, but pointed out that clinical oncology often does not have absolute answers. He suggested that clinicians now may have a real opportunity, if they react to it. He suggested that a database of bilateral prophylactic mastectomies should be

developed on a national basis. The data existing in institutions like Columbia Presbyterian Hospital could be collected very quickly and evaluated for their effectiveness in situations where the calculated risk was enormous. He stated that this information should be made available, because other therapeutic options are going to be limited and physicians are going to have to use the information available today.

Dr. Schein agreed that for the long-term goal of understanding the science as effectively as possible, the NCI should gather all information, enroll individuals into the Network, and address questions as quickly as possible with the best minds that can be assembled.

Dr. Klausner agreed with the position articulated by Dr. Schein. He cautioned against misunderstanding the function of the Network. For example, a woman would not need to go to Dr. Lynch and make a decision to have a oophorectomy; she could simply call the 1-800 number and find out that Dr. Lynch exists, and that the information she needs is available. If women choose to have an oophorectomy or mastectomy—not only for BRCA1 but for any possible cancer predisposition—they will have a database to follow.

Dr. Rimer observed that many hospital-based registries are not able to identify a patient who has had a prophylactic mastectomy as a carrier of the gene because informed consent had not been obtained from the patient for research purposes. The Network provides an opportunity to study people prospectively. She commended the speakers for their excellent presentations and the discussion for outlining some of the issues that will have relevance for patients.

Dr. Rimer conceded that the NCI has an important responsibility with regard to genetics, and she concluded with an enumeration of genetics-related topics for future NCAB meeting agendas: (1) basic biological questions related to prevention; (2) too much reliance on case reports and anecdotal data; (3) lack of knowledge on which to base recommendations to patients for screening or treatment; and (4) minority issues such as emerging data showing that African-American women are much less informed about genetic discoveries and about their options. Dr. Rimer expressed the view that the Board shares the responsibility for ensuring that these problems are dealt with appropriately. She thanked the speakers, particularly Dr. Collins for his willingness to accept the role he was asked to play, and all who shared unpublished data to help in the learning process.

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## ADMINISTRATIVE STREAMLINING INITIATIVES

Dr. Rimer introduced Ms. MaryAnn Guerra, Associate Director, Office of Intramural Management, to present a progress report on the NCI administrative reorganization.

Ms. Guerra pointed out the difficulty of following the breast cancer stamp and genetic testing presentations with a topic like administration, but looked forward to describing what had already been accomplished.

Ms. Guerra outlined the administrative reorganization that has taken place, steps taken to streamline processes, and initiatives that are being implemented to ensure that these improvements are not just temporary in nature, but permanently ingrained in the culture of the Institute.

Five recommendations emanated from the Bishop-Calabresi Report that related to administration: (1) streamline to eliminate redundancy; (2) promote coordination of administration through the elimination of division fragmentation; (3) recognize that different skills and abilities are required to manage intramural versus extramural programs; (4) provide flexible rather than rigid application of rules; and (5) provide ongoing informal review of the administration. Ms. Guerra noted that these five recommendations were translated into three operating principles that are driving the NCI's administrative streamlining plan: (1) improving coordination and eliminating fragmentation in the divisions; (2) establishing customer-oriented ARCs; and (3) delegating the authorities necessary to establish a permanent change in the NCI's business operation.

The first major area addressed was the elimination of the fragmented division structure and provision of the specialized skill necessary to manage an active intramural research program. In the previous organization, the Office of Administration Management (OAM) was a single entity that supported both intramural and extramural science. Additionally, each of the five divisions had a separate administrative management branch, and each of those

administrative management branches reported to the individual division directors. Dr. Klausner approved a reorganized structure that created and established two separate management groups to oversee the NCI operations—the OIM and the OEM. Functional areas previously in OAM were realigned within OIM and OEM, based on an assessment of where the major emphasis, workload, and/or impact on operations and staff requirements existed. Human Resources Management and Consulting, Information Resources Management, and Information Systems and Technology Branches, as well as all of the administrative staff supporting intramural operations were realigned to the OIM. The OEM under the leadership of Mr. Philip Amoruso continued to have all of the extramural functions, as well as the administrative staff that formerly supported the extramural divisions.

Ms. Guerra noted that the second major issue to be addressed was the creation of a new administrative model. The new model was necessary to address problems identified by the Bishop-Calabresi Report such as the need to modify entrenched administrative behaviors and administrative requirements that impede rather than facilitate support to scientific operations. The principles of the new administration model are: responsiveness and resourcefulness in carrying out duties; improved service through the elimination of unnecessary requirements, streamlining of procedures, and development of user-friendly information systems; persistence in accomplishing tasks that continuously question the value and need for standing requirements; creativity in the development of methods to conduct business; creation of a work environment that provides challenges and encourages reasonable risk-taking in accomplishing tasks; hiring and maintenance of a qualified, competent, and diverse workforce that is vested with the authority, accountability, and autonomy to do their jobs; continuous development of staff through mentoring, training, work challenges, and trained supervisors; recognition of staff through effective performance management (i.e., appropriate, rigorous, and effective performance evaluation reviews), provision of career development opportunities, awards, and promotions; and effective leadership that provides open channels of communication and supports ongoing interaction among ARCs, management, and scientific staff.

Another innovation in the NCI reorganization was the creation of full-service ARCs. This was accomplished by delegating all responsibilities associated with serving the divisional laboratories and branches to these centers, including Personnel Management, Procurement, Ethics, Budget, Facilities, and Information Management. These ARCs replace the division administrative offices and are located in each building housing the NCI laboratories and branches. They provide the varied skills and expertise needed to support the building and the understand the unique issues that confront scientists in that building. The IAB has also been established and has provided assistance in areas such as core facilities and administrative issues.

Dr. Bishop noted that Dr. Klausner had made an important point in his remarks concerning the elimination of the parallel structure in management that existed before reorganization. He asked for clarification. Using a slide comparing the former and new administrative processing flow charts, Ms. Guerra reviewed the former flow of administrative requests. Laboratory or branch personnel submitted requests to a program administrative office. In the new scheme, laboratories, branches, and division offices submit requests directly to the ARC for action in most day-to-day operations. Ms. Guerra noted that the delegations mentioned by Dr. Klausner reflected the transfer of authorities to the new organizational components. She added that some delegations of authority to laboratories and branches have been delayed because the moves were considered too dramatic to implement immediately or because information management systems were not yet in place. Ms. Guerra pointed out that the changes have resulted in a flatter organization, and have reduced the time required for moving requests through the system.

The third objective of the NCI administrative reorganization was to delegate authorities within the new streamlined structure. First, management authorities were delegated to division directors and to the laboratories, including the ability to approve recruitment, retention, relocation bonuses, cash awards, training, fellowships, and detailing of staff. Second, administrative authorities have been delegated to the ARCs. Adverse actions, classification of jobs, and special pays above the minimum are other types of actions that have been delegated. Third, two procurement authorities have been delegated. Fourth, authorities to approve travel, special expenses, and contracts have been delegated to a lower level. Fifth, in the area of technology transfer, the authority to approve Material Transfer Agreements and Confidentiality Agreements has been transferred to the principal investigator level.

Ms. Guerra stated that the Human Resources Management and Consulting Branch provides training for many more people now that authority to act has been delegated to the local levels. Ms. Guerra reported the Center for Work Force

Excellence has been developed in OIM, which is establishing an infrastructure to ensure that the NCI's recruitment strategies, training programs, and career development efforts are competency based.

Ms. Guerra reported that the Support Staff Training and Retention (SSTAR) Program is another innovation, established because the shortage of clerical staff was a common complaint heard in her meetings with laboratory and branch staff. Through this program, the best support staff that can be found will be recruited, hired, and trained, eliminating the complex administrative hurdles for scientific staff. When a vacancy occurs, scientific staff will be able to choose from a group of people already hired and trained in the competencies identified previously by then, and around which the OIM organized the training program.

Ms. Guerra described the third innovation of the streamlining activities as the establishment of a new position—the Administrative Laboratory Manager. The HRMCB has developed the position as a career ladder in the laboratories that is equivalent to the administrative career ladder and is designed so that good staff can be developed and kept in the laboratory rather than being lost to the administrative career ladder.

Ms. Guerra reported that the information technology structure was reorganized to form the Information Systems and Technology Branch (ISTB) and the Information Resources Management Branch (IRMB). These new information technology branches are working to establish a single NCI-wide networking system. The goals in this system are: (1) to provide a set of core services that all NCI staff can have access to; and (2) to improve the information management systems and support currently provided to staff.

Ms. Guerra stated that her last item of information related to the CRADA established between the NIH and Applied Research and Technology, Inc. She noted that this CRADA is being sponsored by the NIH Intramural Reinvention Working Group, which she and Dr. Michael Gottesman co-chair. Ms. Guerra explained that the initiative was undertaken to improve the procurement process throughout the NIH, and that NCI involvement was important because the procurement process was a major complaint to the Working Group as well as NCI scientific staff..

The objectives of this CRADA are to: (1) develop and implement an NIH "Intra-Mall" for the scientific and administrative communities; (2) provide access to scientific supply vendors and products through the WWW; (3) provide a mechanism for NIH staff to purchase directly through the "Intra-Mall"; (4) integrate acquisition regulations, standards, order and budget tracking systems, and an interface to existing NIH administrative systems into the "Mall" automated process; and (5) provide simplified shopping, customized product catalogs, order processing, and tracking via the "Mall."

Ms. Guerra concluded that through the reorganization, the NCI has developed a new model to provide streamlined, efficient, and responsible administrative service to the scientific community; established local service centers; restructured core functional areas, such as human resources and information technology; and created a structure that will provide flexibility for the future to meet the evolving needs of the communities.

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### **QUESTIONS AND ANSWERS**

#### **Administrative Streamlining Initiatives**

Dr. Yodaiken, Dr. Calabresi, and Dr. Sigal commended Ms. Guerra for her presentation and for the accomplishments it represented.

Dr. Klausner commented that he long ago recognized the need in the NIH for delegated authorities that would enable the NIH staff to do many of these things. He pointed out that the reorganization reflects his expectation that the NCI administration should be as creative as the science is expected to be. Dr. Klausner observed that administrative streamlining is making real changes, and he commended the innovative approaches adopted by Ms. Guerra and her staff and the amount of effort expended.

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### **SUBCOMMITTEE ON PLANNING AND BUDGET**

Dr. Sigal reported that comments received from outside organizations attested to their satisfaction with and support of

the FY 1997/98 Bypass Budget. The Subcommittee plans to monitor the progress of the Bypass Budget and to determine the results. The Subcommittee also discussed the budget for the next fiscal year, the budget development process and the need to address this issue at the NCAB retreat.

Another focus of the discussion was the issue of important scientific opportunities and how the Subcommittee would react if funding were not appropriated. No plans or resolution of the issue resulted from the discussion because members believed funding would be forthcoming.

The Board passed a motion to approve the Subcommittee minutes.

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### **SUBCOMMITTEE ON CANCER CENTERS**

Dr. Day reminded the Board that the decision had been made not to recompute or compete for the first time any applications for comprehensiveness, because that issue is under review by the Cancer Centers Working Group. Dr. Margaret Holmes, Chief, Cancer Centers Branch (CCB) presented an update on the cancer center planning grants. Since 1992, planning grants to about 17 institutions have been funded, and most of these institutions are submitting applications for Cancer Center Support Grants (CCSG); Dr. Day noted the estimated result will probably be four new centers. The Subcommittee reviewed some of the issues surrounding planning and cancer center grant applications and the length of time it often takes an institution to compete for a successful core grant.

Dr. Brian Kimes, Associate Director, Centers, Training, and Resources Program, reviewed the prior deliberations of the Subcommittee about budget caps in cancer centers and about a proportionate cap that was recommended but not implemented in 1992. The proportionate cap would relate the size of the core grant to the amount of the NCI support and this issue has been referred to the Working Group; however, the Subcommittee found the history to be informative and valuable.

The final item for discussion was the consortium cancer center concept. Dr. Kimes reviewed the history since implementation of the guidelines in 1987; three consortium center grants were awarded but only one grant is active at this time. The Subcommittee discussed the possibility of cancer centers evolving in areas where there are needs for cancer control and how that might be done as an adjunct or as part of the cancer centers program; this issue is to be reviewed by the Cancer Centers Working Group.

The Board passed a motion to approve the Subcommittee minutes.

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### **SUBCOMMITTEE ON SPECIAL PRIORITIES**

Mrs. Brown reported that the meeting began with a recap of the January Conference on the Recruitment and Retention of Minority Participants in Clinical Research. Dr. Paulette Gray informed the Subcommittee that the RFA resulting from the conference was approved by the Board at a previous meeting and will be announced in the NIH Guide to Grants and Contracts; awards are projected to be made by the end of FY 1996, and the monies spent in the next fiscal year. Seven awards of about \$50,000 each are expected, and they will support regional conferences throughout the country where clinical researchers and organizations that carry out community outreach and education can discuss strategies for recruiting and retaining minorities in clinical trials. Dr. Gray also reported that the transcript from the January conference will be available by mid-July, and will serve as a guide for the upcoming regional conferences.

Suggestions for new Subcommittee initiatives were requested. Dr. Goldson proposed that data from the recently published SEER Monograph Racial/Ethnic Patterns of Cancer in the United States: 1988-1992 be melded with the findings from the conferences to enable the Subcommittee to formulate and prioritize strategies to improve survival in minority populations. Mrs. Brown noted that this would help promote clinical trials involvement by helping special populations to understand the risks and mortality rates for the various types of cancers. Another suggestion was to find ways to increase awareness about cancer control in special populations, for example, by identifying actions the NCI could take to deliver information about cancer to special populations. Mrs. Brown referred to the earlier presentation on BRCA1 susceptibility testing and suggested this is the type of area where there is a lack of awareness on the part of minority populations. Dr. Goldson also suggested the development of courses to instruct minority oncologists,

internists, and general practitioners in the conduct of clinical research. Mrs. Brown reported that these suggestions for Subcommittee initiatives, with the goal of increasing the number of minority participants in clinical trials, will be discussed during the September meeting.

The Board passed a motion to approve the Subcommittee minutes.

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### **SUBCOMMITTEE ON INFORMATION AND CANCER CONTROL**

Dr. Rimer thanked Mrs. Malek, whose term of office ended with the February meeting, for agreeing to return to report on the Subcommittee's cancer control activities. In lieu of a Subcommittee meeting report, Mrs. Malek presented an update on the Healthy Women 2000 Conference on Smoking and Young Women's Health. This conference is being sponsored by the U.S. Public Health Service Office on Women's Health and co-sponsored by the NCI, the CDC, and the Robert Wood Johnson Foundation.

The purpose of the conference is to raise awareness of the health effects of smoking, focusing on girls and young women. An objective of the conference is to provide and disseminate information to policymakers, health care professionals, voluntary health organizations, consumer groups, educators, parents, and the media.

The conference is scheduled to be held in Washington on September 12, 1996.

Because of the strong Administration commitment to the prevention of smoking among the nation's most susceptible population—girls and adolescents, the Office of Research on Women's Health (ORWH) has been working with Girl Scouts U.S.A. to develop a smoking prevention program, which will feature the award of merit badges to Girl Scouts who earn them by completing the requirements.

Next, Mrs. Malek reported on the April 11-12 meeting of the Working Group convened to address issues related to behavioral research. She briefly reviewed the events leading to the meeting, noting that the NCI, through the Division of Cancer Prevention and Control (DCPC), has made a commitment to provide greater focus on behavioral research in its efforts to reduce cancer morbidity and mortality. On July 6-7, 1995, the NCI held a 2-day workshop in Washington to identify behavioral needs in cancer prevention and control. One outgrowth of the workshop was the establishment of a formal Working Group to continue the work begun in the 1995 workshop.

Mrs. Malek reported that participants in the April meeting presented the Working Group with specific research recommendations to address cancer prevention in the behavioral areas identified during the 1995 workshop, together with suggestions for implementation. On behalf of the Working Group, Mrs. Malek thanked Dr. Klausner for attending the meeting and providing insight into the problem, which helped guide the discussions over the course of the meeting. Mrs. Malek noted that the final report has been drafted and will be circulated to Board members upon completion.

Mrs. Malek concluded with a review of the ultimate aim of the Working Group: to contribute to cancer prevention and control by determining the most valuable behavioral research worthy of support by the NCI and then to see that this research is conducted. She reported that the April meeting made progress in that direction.

Dr. Rimer thanked Mrs. Malek for her support of the September conference.

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### **MEETING OF THE REPRESENTATIVES FROM THE NIH ADVISORY COUNCILS**

Dr. Rimer reported that she and Dr. Sigal attended a meeting convened by Dr. Harold Varmus and Dr. Ruth Kirschstein, which brought together the representatives of all the NIH advisory councils. She commented that the experience had been valuable for learning how other advisory councils function. Dr. Varmus's charge to the attendees was to look at how responsibilities are discharged by the various councils including: the second-level review of grants; participation of council members in strategic planning; the role of council members in setting policies and priorities; the role of council members in the streamlining process; and ways to improve the selection of council and board members. She stated that she will be attending a followup meeting in June.

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## CONTINUING AND NEW BUSINESS—SESSION II

Dr. Rimer called attention to the letter received from the Center for the Advancement of Health, asking the NCAB to support two tobacco-related performance indicators as part of the Health Plan Employer Data and Information Set (HEDIS). Dr. Rimer explained that the move toward managed care has resulted in the development of HEDIS as a type of report card that lists certain indicators that are identified as quality measures for managed care. In the past, this report card has listed certain kinds of immunizations and mammography as indicators of quality measures and has the effect of applying pressure within the managed care organizations to deliver those services. Many believe that if tobacco counseling were a HEDIS indicator, there would be more emphasis within managed care organizations on tobacco counseling, and surveillance for tobacco counseling would be built into the encounter and tracking systems. Dr. Rimer suggested that the time has come when an emphasis on tobacco counseling can be translated into increased delivery of smoking cessation programs within managed care organizations. Dr. Rimer asked the Board to consider supporting the inclusion of two tobacco-related performance indicators in HEDIS. A motion to that effect was seconded and approved by the Board.

Dr. Rimer announced her intention to include a followup discussion of genetics susceptibility testing in the September meeting agenda. She noted that one topic for discussion at the retreat will be how the Board can follow up on important topics such as this when discussions cannot be adequately concluded during the Board meeting.

Mrs. Brown asked for details concerning a mammography seminar mentioned earlier as being scheduled for the fall and asked whether it would be possible to take part in the planning. Dr. Rimer noted that the NCI is sponsoring the seminar, to be chaired by Dr. Barnett Kramer, to revisit the issue of how frequently women above age 40 should be screened based on emerging data from the Swedish trials. Dr. Greenwald explained that the NCI is attempting to gather all information from the investigators, including promised followup data, on the trials presented at a recent meeting in Sweden and make the information available to the American public. An attempt will be made to resolve questions about interpretation of results and other issues. Dr. Rimer suggested that Mrs. Brown should be involved in the planning process that is in progress.

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### FORMAT OF PROGRAM REVIEW MEETING AND PREVIEW OF JUNE RETREAT

Dr. Rimer announced that the NCAB working group retreat to consider the restructuring of NCAB subcommittees is scheduled for June 11-12 at a hotel in the vicinity of Dulles Airport. Issues to be addressed are: mission and role of the Board; priorities for the next few years; subcommittees needed for the Board to function effectively; and format and timing of information from Dr. Kalt and the NCI staff for developing priorities, carrying out program reviews which are an important responsibility of the Board, and conducting the second-level review of grants.

Dr. Rimer asked for discussion about the suggestion that some subcommittees, notably Cancer Centers and Budget, be structured as subcommittees of the whole Board, and that discussion of the issues under their purview be built into the structure of the plenary session of the Board rather than in separate meetings. She reasoned that these subcommittee meetings are currently attended by almost every Board member because the issues are so important.

Dr. Day, Chair of the NCAB Subcommittee on Cancer Centers, agreed that scheduling a review of the Cancer Centers Working Group report, expected to be completed in July, as an agenda item for the September NCAB meeting was reasonable, particularly because the new members should be in attendance by then. Consideration of the proposed changes and new guidelines will be the responsibility of the full Board. He suggested that the subcommittee would have little business except for regular reporting on the budget and progress of the Cancer Centers Program, and that separate meetings need not be scheduled for a while because they would duplicate what is going to happen in the full Board meeting. Dr. Rimer explained that considering Cancer Centers a subcommittee of the Board as a whole would enable Dr. Day to lead the discussion.

Dr. Rimer asked Dr. Sigal to comment as Chair of the Planning and Budget Subcommittee. Dr. Sigal agreed with the idea of considering this a subcommittee of the Board as a whole because of the importance of the issues and widespread interest that has been demonstrated. She expressed concern about the possibility that adequate time for subcommittee deliberations cannot be built into the regular Board agenda and that discussion of the issues might

become superficial and unsubstantive. She emphasized the need for adequate time and for redefinition of the role of the subcommittees.

Dr. Rimer gave assurances that she and Dr. Kalt would work with the Chairs of the two subcommittees to determine the amount of time needed in the agenda. She asked Dr. Kalt to comment.

Dr. Kalt agreed with Dr. Rimer's central point, namely, that some things lend themselves to full Board discussion all the time, particularly if they are Board priorities. He emphasized that the opportunity can be provided for additional and separate meetings of the subcommittees if and when they are necessary.

Dr. Day pointed out the need for discussion during the retreat of providing for regular reporting back and forth with the BSA and BSC. Dr. Rimer gave assurance that this was on the agenda.

Dr. Rimer asked Dr. Kalt to describe the types of information that can be provided by the DEA to Board members in preparation for program review meetings. Dr. Kalt reminded members that, by statute, it is the responsibility of the NCAB to do an overall program review of the Institute, although the procedure and the depth of the review done is not prescribed in detail. The Board is required to meet at least four times a year. Dr. Kalt noted that the 2-year rotating model used in recent years lends itself to some rethinking.

A second consideration is how the Board wishes to conduct the program reviews. Dr. Kalt noted that the chairs of the BSA and the BSC could be invited to report annually, and the Board could decide how the information presented could be integrated most appropriately for its own consideration.

Dr. Kalt briefly reviewed the types of information that can be provided prior to program meetings: (1) issues related to the fiscal and scientific priorities of the Institute that have been raised in past reviews of applications and in overall discussion of major portions of the budget and the portfolio; (2) items that had been requested by the Board for past program reviews, which the Board might wish to have periodically for all programs, possibly presented in a tabular form that would serve as an ongoing report card; and (3) the NCI's priority areas as defined by virtue of previously expressed interest of the Board, by the percentage of the NCI budget allocated to the area, or by being highlighted in documents such as the Bypass Budget. Dr. Kalt noted that an attempt could be made to integrate such issues as these into a plan for an overall program review.

Dr. Day suggested that the format of the information is of paramount importance. He expressed interest in being able to review the scientific strategy and evaluate how it is reflected in the grant portfolio and the intramural program. In his experience, program review materials tended to be encyclopedic and the underlying strategy was difficult to discern. He welcomed the opportunity to review some of the background materials before a Board meeting. Dr. Day also expressed the view that priorities for the presentation and discussion should be issues such as major new developments in informatics that are going to have much scientific impact, rather than details that can be reviewed in other ways. Dr. Rimer agreed with the need to absorb some types of detailed information before the meeting. She asked Board members to consider this issue and provide Dr. Kalt with guidance as to the types of information to include as soon as possible.

Dr. Day expressed interest in seeing the distribution of funding for various topics in the grant portfolio and in knowing whether the NCI has the flexibility to move additional funding to important emerging research areas such as genetic susceptibility testing and counseling. Dr. Rimer indicated that the NCI should be able to provide this information on desired topics, within the limits of the CRISP system and other data systems.

In this regard, Dr. Klausner commented that he is frequently confronted with requests for information on what is done in the Institute, but the reality is that CRISP usually provides lists in response to queries. He stated that one major issue to be addressed by the new Associate Director for Planning will be to rethink how the CRISP system can be queried about the NCI operations so that information is provided in a useful format. Dr. Klausner noted that CRISP and other systems do not readily answer the types of queries that people actually ask. For example: What are the important questions in cancer research? How is the NCI addressing these questions?

Dr. Klausner stated that he would like a discussion at the retreat about how issues can be addressed when there is a

need for input and decision by the Board—such as what NCI priorities should be and how progress can be monitored—so that the Board's input may be of value to the Institute. Dr. Klausner reported that NCI staff have been exploring ways to create a query system that is question-based rather than list-based as is the current case.

Dr. Rimer concluded the discussion of program review format and the June retreat with a request that Board members review and comment on the revised statement on the role of the Board. She acknowledged help from Dr. Day in making the revisions.

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## REVIEW OF TRAINING AND CAREER DEVELOPMENT MECHANISMS

Dr. Kimes introduced Dr. Cairoli, Chief, Cancer Training Branch (CTB).

Dr. Cairoli briefly described the activities of the CTB with regard to training, career development, and education and discuss some key issues. Using a slide, he presented an overview of the training grants awarded by the Branch in 1995 in the three program areas that compose the formal NCI training grants budget. The National Research Service Awards (NRSA) account for about 60 percent of the training budget with the Career Awards and Cancer Education at 25 percent and 16 percent, respectively. Dr. Cairoli pointed out that NRSA is a line item in the NCI budget, and Careers and Cancer Education are included in the "Other Research" budget line.

Dr. Cairoli reviewed the characteristics of each type of training program with respect to the NCI's authority to control funding, noting that the NRSA allows the least flexibility. Because these awards are embedded in congressional legislation appropriation, the NIH ensures that all Institutes follow the same formula for stipends and tuition. The Career Awards provide more flexibility, because the NIH has created six generic Career Awards and each Institute is free to adapt these generic awards to its particular mission. The NCI's ability to institute the Temin Award is an example of that authority. With respect to the Cancer Education Awards (R25s), the National Cancer Act provides the Director, NCI, with broad authorities that cover the entire spectrum of health professionals, students, and lay people. The cancer education awards, therefore, are not only the most flexible but also the most heterogeneous NCI program.

Dr. Cairoli reported that the NCI awarded 242 individual NRSA fellowships to the three categories: predoctoral (F31), postdoctoral (F32), and senior (F33). He noted that the number of applications per year received by the NCI has steadily increased from 200 in past years to 310 in FY 1995; the first cycle of FY 1997 (the October round) has 152 applications, for a possible total for the year of 400 applications, if that trend continues for the remaining cycles.

Dr. Cairoli described the F31 predoctoral as unique in that the NIH rarely supports an individual fellow at the predoctoral level. The NCI had supported nurse-oncologists seeking doctoral degrees for several years prior to the establishment of the National Institute for Nursing Research (NINR); NCI support has decreased because NINR now receives these applications for review and funding. However, the NCI has an arrangement that nurse-oncology applications ineligible for funding through the NINR are transferred to the NCI for possible funding. Dr. Cairoli pointed out that the new program for minorities and disabled students is growing; of the 14 applications received in FY 1995, 10 were funded. He suggested that this award, which provides support for up to 5 years, should be more widely publicized.

The classical postdoctoral fellowship (F32) provides support for up to 3 years by legislative decree. Postdoctoral NRSA fellowships have a success rate of about 40 percent because the NCI specifically promotes the area, and also because of the 15 percent requirement for individual NRSA fellowship awards. In addition, the NCI promotes this type of award because the data confirm that those individuals who undergo their own peer review by DRG study sections have a higher success rate in future research applications than trainees on the large institutional training grants.

Dr. Cairoli noted that the third type of individual NRSA, the Senior Fellowship (F33), is a program for senior scientists seeking to make a mid-career change, move into the cancer area, or retrain in areas such as molecular biology. The funding, which can be obtained for up to 2 years, is used as additional support—during a sabbatical, for example. The NCI normally receives 3 or 4 applications per year; currently 3, senior awards are being funded.

Dr. Cairoli pointed out that the large institutional training grants (T32) in the NRSA program can be predoctoral,

postdoctoral, or a combination. They provide up to 5 years of support for research in any area that is relevant to cancer.

Dr. Cairoli noted that currently, there is no pay-back requirement for predoctoral fellows and a greatly modified one for postdoctoral fellows in that the second year of training pays back the first year. Financial payback for the first year is required only from those postdoctoral fellows who are on the training grant for 1 year and then leave the area of research and teaching.

The NCI currently has 184 T32 grants in force. Of these, 20 percent of the trainees and about 19 percent of the fellows are clinicians; 40 percent of the total are women; and 6 percent of the grants have women as principal investigators.

Dr. Cairoli stated that the supply and demand factor—as it relates to Ph.D.s—is a recurrent issue. He pointed out that for almost 2 decades, the number of fulltime training positions on the NRSAs for the NCI has been consistently below the peak years of 1979 and 1980, although a peak of between 1,540 and 1,550 is expected in 1996. Dr. Cairoli cited other data indicating that the NIH component accounts for only 15 percent of all new Ph.D.s entering the market. He expressed the view that the NIH is supporting the cream of the crop, and noted that the National Academy of Science's quadrennial review of the nation's biomedical research needs supports this view.

Dr. Cairoli turned next to a review of the NCI's Career Awards, which are intended to support the investigator during the transition from the postdoctoral fellowship to full status as an independent investigator able to apply for and receive a research grant. In FY 1995, the NCI had a portfolio of 181 positions awarded through the following mechanisms: K07 for prevention awards; K08 for individual clinical awards; and K12 for institutional clinical awards. Dr. Cairoli provided additional information about the purpose, eligibility requirements, and program of the K08 individual career award. Dr. Cairoli reported a success rate varying from 30 to 45 percent and credited this success to the efforts made by CTB program directors to identify high-priority projects below the payline and successfully compete for end-of-year monies in the NCI's internal competition.

The K12 clinical oncology career award is awarded to institutions which, in turn, recruit clinicians for the grant. Announcement of this award was issued as an RFA to emphasize clinical research training and translational research. Dr. Cairoli reported that the RFA announcing this program for training clinical oncology scientists resulted in 17 K12 awards and 39 trainees, but the program was considered to have started off in a diluted fashion. The peer review-recommended trainees for these 17 awards would have totaled 80, but only 39 out of 80—two or three at the most per application—are being funded. The Branch is therefore undertaking an evaluation of the progress being made in these programs in preparation for a meeting with the NCI EC to determine whether to once again announce this RFA.

Dr. Cairoli turned next to a description of the preventive oncology academic award (K07), which focusses very specifically on cancer prevention and control. Dr. Cairoli noted that the program requires only 2 years of postdoctoral experience and provides 5 years of support. Curriculum development and leadership skills are a particular emphasis, reflecting the attempt to build cancer prevention curricula within academic institutions. Dr. Cairoli noted that the program has always been small, having graduated only 23 prevention researchers. Because of this, the CTB was able to track the careers of every one of the graduates, which has been impressive. Dr. Cairoli concluded that, by every measure, this investment has been a good one.

The Temin Award was established as a means to stabilize the transition from a mentored to an unmentored situation and, at the same time, identify those who have high potential. An important feature of the Temin award is the provision for an appropriate mentor for a limited period of time. The length of the mentoring is expected to vary greatly, but the awardee must move to independence in the laboratory by the end of year 3 to receive the remaining years of funding. Another feature is portability, which will allow an investigator to move to another school, carrying along the salary and \$50,000. The goal is to help sustain the awardees while they focus their research and collect the preliminary data needed to be competitive for an R01 grant. The salary has been increased above the other Career Awards to \$75,000 plus fringe benefits. When the awardee moves from a mentored to an unmentored situation, the allocation for expenses increases from \$20,000 to \$50,000; 10 awards per year are expected.

Finally, Dr. Cairoli reviewed the history of the Cancer Education Program since its inception, more than a decade ago, as a clinical education program primarily for medical oncologists. The transition to a cancer education focus occurred in 1987, when it was determined that there were sufficient medical oncologists. However, at that time, applications

could only be made in response to an RFA or a PA in the NIH Guide to Grants and Contracts. The program was converted in 1993 to a regular investigator-initiated program targeting biomedical researchers, health professionals, students, and lay communities. A variety of cancer education programs are supported, including cancer prevention training, curriculum, breast cancer outreach, pain education and hospice workshops, nutrition curriculum, and student assistants. Dr. Cairoli reported that the NCI has encouraged and succeeded in getting schools of public health to collaborate with cancer centers and departments of preventive and family medicine. In these arrangements, one institution provides the cancer expertise and the other side provides prevention expertise; the prevention training awards are funded with cancer control monies. Currently, the NCI has 15 grants supporting the 80 pre- and postdoctoral trainees. Dr. Cairoli noted that it had become necessary to increase the incentives, particularly to recruit oncologists into preventive oncology, so career-type salaries are being paid.

Dr. Cairoli reported that the student assistantship program supports 500 students for 2 to 3 months during the summers in research laboratories; of these 500 students, 20 percent are from underrepresented minorities.

Currently, three workshops are being supported by the R25 program. The first trains graduate students in the histopathobiology of cancer and is located at Keystone, Colorado. The course and laboratories are designed as an orientation in cancer pathology, which enables the graduate students to communicate with clinicians and have a disease orientation to their research. Dr. Cairoli noted that a great number of students in this class have never had a course in either histology or pathology.

Dr. Cairoli reported that the NCI is considering a course for minority oncologists in the area of clinical research and clinical trial design. He concluded by pointing out that the NCI training awards encompass a spectrum of disciplines: biology, diagnosis, etiology, treatment, and prevention. He called attention to the increase in prevention funding from 6 percent to almost 18 percent. Dr. Cairoli invited Board members to contact any of the branch staff for additional information or for a copy of the guidelines.

Dr. Rimer noted that cancer education and training is an important part of the NCI portfolio, and she thanked Dr. Cairoli for his presentation. There being no further questions or comments, Dr. Rimer adjourned the 98th meeting of the National Cancer Advisory Board at 1:04 p.m.

Dr. Barbara Rimer, Chairperson



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