Board of Scientific Advisors

Meeting Minutes

June 22, 1998

Conference Room 10, C Wing, Building 31
Bethesda, Maryland 20892

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The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 8th regular meeting at 8:00 a.m. on Monday, 22 June, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. David Livingston, Professor of Medicine, Dana-Farber Cancer Institute, presided as Chair.

The meeting was open to the public from 8:00 a.m. until adjournment on Tuesday, 23 June, for introductory remarks from the Chair; discussion of procedural matters and future meeting dates; ongoing and new business; and presentations and discussion on the status of the NCI budget and paylines, Request for Application (RFA) concepts, implementation of Program Review Group recommendations, guidelines for BSA review of extramural programs, metrics for evaluating the SPORE program, a strategic plan for NCI training programs, status of the Cancer Genetics Network, technology development initiatives, and the NCI informatics system.

BSA members present:

Dr. David Livingston (Chair)
Dr. Frederick R. Appelbaum
Dr. Mary Beryl Daly
Dr. Virginia Ernster
Dr. Eric R. Fearon
Dr. E. Robert Greenberg
Dr. Waun Ki Hong
Dr. Tyler Jacks

Ms. Amy S. Langer
Dr. Caryn E. Lerman
Dr. Joan Massague
Ms. Deborah Mayer
Dr. W. Gillies McKenna
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Sharon B. Murphy
Dr. Allen I. Oliff
Dr. Franklyn G. Prendergast
Dr. Stuart L Schreiber
Dr. Joseph V. Simone
Dr. Louise C. Strong
Dr. Barbara L. Weber
Dr. Alice S. Whittemore
Dr. Robert C. Young

BSA members absent:

Dr. Joan Brugge
Dr. Suzanne W. Fletcher
Dr. David D. Ho
Dr. Peter K. Vogt
Dr. Daniel D. Von Hoff
Dr. William C. Wood

NCAB liaison:

Dr. Philip A. Schein

Others present included: Members of NCI's Executive Committee (EC), NCI staff, members of the extramural community, and press representatives.

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CALL TO ORDER AND OPENING REMARKS - DR. DAVID LIVINGSTON

Dr. David Livingston called to order the 8th regular meeting of the Board of Scientific Advisors (BSA or Board) and welcomed members of the Board, National Institutes of Health (NIH) and National Cancer Institute (NCI) staff, guests, and members of the public. Dr. Livingston announced that the appointments of BSA members whose terms were scheduled to expire this month had been extended to June 30, 2000.

Dr. Livingston discussed upcoming BSA meeting dates, directing attention to the special meeting scheduled for Tuesday evening and Wednesday, September 22-23, 1998, to consider proposed new NCI initiatives that will require prompt action. BSA members were asked to report potential conflicts with the proposed dates as soon as possible.

CONSIDERATION OF MARCH 1998 MEETING MINUTES - DR. DAVID LIVINGSTON

A motion to approve the minutes of the 7th meeting of the Board of Scientific Advisors, which was held on 2-3 March 1998, was unanimously approved.

REPORT OF THE DIRECTOR, NCI - DR. RICHARD KLAUSNER

Dr. Klausner discussed NCI actions following several public announcements of cancer news, staff changes, progress in planning

the NCI FY 1999 budget and the FY 2000 Bypass Budget, and issues to be addressed during the special BSA meeting in September.

Cancer Statistics: Dr. Klausner announced that the nation's cancer statistics were reported in the spring in conjunction with the American Cancer Society, the Centers for Disease Control and Prevention (CDC), and the National Center for Health Statistics (NCHS). He reported that the Institute has initiated a process under the leadership of Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS), and Dr. Joseph Fraumeni, Director, Division of Cancer Epidemiology and Genetics (DCEG), for producing more in-depth analyses of these statistics annually. A series of intramural working groups have been organized to analyze, discuss, and model the data on a variety of cancers. The product of these trans-institute seminars and discussions will be a series of staff publications reporting on interesting trends in cancer.

Breast Cancer Prevention Trial (BCPT):NCI actions in response to the BCPT recommendation from the Data Safety Monitoring Board (DSMB) for the BCPT to the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the Institute was discussed. The results were announced to the public in conjunction with the launching of the Clinical Trials Web site and in the absence of a peer-review publication because of the necessity of alerting the participants. Dr. Klausner noted the challenge of communicating the early release of results of important clinical trials, especially in the developing field of chemoprevention, when the need for understanding individual risk and how to tailor decision making to individual risk must be communicated along with the promising results. With that challenge in mind, the NCI is planning a variety of approaches to provide useful information based on this important trial. The first approach, in addition to the new Clinical Trials Web site, is a BCPT workshop scheduled for early July to discuss the results of the trial and address the issue of breast cancer risk and the use of breast cancer risk models. Dr. Klausner announced that the NCI has approved the follow-up Phase II trial by the NSABP, which will compare tamoxifen directly with raloxifene. Dr. Klausner noted that the recent New York Times announcement of research results with angiostatin in animal models provided an opportunity for an open discussion of progress in cancer research, progress in science that makes possible

opportunities for intervention, and the long time frame and uncertainties inherent in moving discoveries from the laboratory to the clinic.

NCI Staffing Changes: Dr. Klausner announced the retirement of Mr. Philip D. Amoruso, Associate Director for Extramural Administrative Management, and the integration of the former Offices of Intramural and Extramural Administrative Management under the new Deputy Director for Management, Ms. MaryAnn Guerra. Other changes in NCI leadership were as follows: (1) Dr. George Vande Woude was appointed Director, Division of Basic Sciences (DBS); (2) Dr. Peter Greenwald was appointed Director, Division of Cancer Prevention (DCP); (3) Dr. Faye Austin, Director, Division of Cancer Biology (DCB), will be leaving the NCI to assume a position at the Dana-Farber Cancer Institute; and (4) Dr. Susan Sieber has been appointed Associate Director for Special Projects.

FY 1999 NCI Budget: Dr. Klausner reported that NCI distribution plans for the FY 1999 budget, if the 9 percent increase proposed in the President's budget is legislated, include: (1) a 13 percent increase for research projects grants (RPG), including a rise in the payline; (2) an increase in the training and career development line; and (3) an increase in funding for the clinical trials system. Issues related to raising the RPG payline include the average cost per grant, the cost of converting R29s to R01s, and the number of PO1 grant applications received. The increase in the training line includes a 25 percent increase in National Research Service Award (NRSA) stipends and an increased investment in multidisciplinary training, newly emerging areas, minority training, i.e., clinical investigators training and support. The funding for RFAs in the FY 1999 budget is expected to comprise between 10 percent and 11 percent of the RPG line, consistent with the planning processes in place to initiate the work outlined in the Bypass Budget. The number of grants funded through the RPG line will be reported to the BSA at the end of the fiscal year.

Bypass Budget for FY 2000: The draft of the FY 2000 Bypass Budget, *The Nation's Investment in Cancer Research: A Budget Proposal for Fiscal Year 2000*, will be completed and distributed to the BSA for review prior to the September meeting and will be available in a searchable format on the NCI Web site. Board members will have an opportunity at the September meeting to

discuss the extraordinary opportunities for investment and NCI's challenge included in the FY 2000 Bypass Budget and NCI's progress in meeting those goals. The four extraordinary opportunities identified in 1997 will be evaluated as part of the Bypass Budget for FY 2001 planning process which will begin in October. BSA members were invited to submit criteria for identifying new extraordinary opportunities or to suggest new opportunities for consideration.

September BSA Meeting: In addition to an update of initiatives stemming from the Bypass Budget, issues to be addressed: (1) the recommendations and deliberations of the Clinical Trials Implementation Group and an update on the NCI response to the report of the Clinical Trials Program Review Group (CTPRG); (2) the report of the Developmental Therapeutics Program Review Group (DTPRG); and (3) tobacco control initiatives to follow the American Stop Smoking Intervention Study (ASSIST), which is coming to an end.

In response to questions, the following points were made:

- Progress in the continuously evolving Cancer Genome Anatomy Project (CGAP) can be monitored daily on the CGAP Web site. Much technology development has been associated with CGAP, including the process for creating high-quality libraries from microdissected tumor and normal tissues. Over the next year, an increased emphasis will be placed on evaluating patterns of expression by other mechanisms (e.g., by incorporating the results of high throughput analysis with arrays into a Web-based system). As part of a future report on CGAP initiatives, Dr. Butow will present an update on the search for polymorphisms.

- An increase in the salary cap for clinical researchers has been discussed with great interest by NIH Directors but the general sense of the discussions in relation to the FY 1999 budget has been that time is needed to understand the budgetary implications.

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REPORT OF THE DEPUTY DIRECTOR FOR EXTRAMURAL SCIENCE - DR. ROBERT WITTES

Dr. Wittes related events of the past 4 months that reflect well on prospects for cancer research. He emphasized that the importance of communication and the obligation of the scientific community to communicate the results of basic research and clinical studies to the general public in an informative, but balanced and responsible manner. Updates were given on the following activities:

Clinical Trials Implementation Group: Dr. Wittes recalled for the Board that this diverse group of intra- and extramural scientists had been impaneled, with Drs. Michaele Christian and John Glick as co-chairs, to provide a blueprint for implementing the recommendations in the CTPRG report. Group discussions have focused on what constitutes an optimal clinical trials system, how such a system could be implemented, and how the excellences of the present system can be incorporated. The Implementation Group will integrate the results of all of their discussions and present its report for BSA consideration at the September meeting.

Report of the DTPRG: Members were told that implementation of the DTPRG recommendations appear to be less complicated and can probably be accomplished through a series of implementation proposals by the Developmental Therapeutics Program (DTP) staff. These proposals will presented for BSA review and discussion at a later meeting.

Progress of NIH/NCI and American Association of Health Plans (AAHP) Negotiations: The Board was reminded that the AAHP, representing about 1,200 managed care organizations, had approached the NIH with a proposal to craft an agreement in conjunction with the NIH regarding clinical trials activities in managed care organizations. An inter-institute group, chaired by Ms. Mary McCabe, Director, Office of Clinical Research Promotion, and Dr. Wittes, was convened to work with a delegation of health plan members toward that end. A draft document which describes the terms under which individual agreements between managed care organizations and individual investigator groups or institutes of the NIH has been crafted. The AAHP Board is reviewing the draft which will be reviewed at the

July NIH Directors' meeting.

Rapid Access to Intervention Development (RAID): The RAID program has been announced through NCI publication channels. This program opens up to academic investigators the development capabilities of the NCI to aid in the transition from the laboratory to the clinic of promising discoveries that would not otherwise have a direct pathway to the clinic. Members were told that the NCI is simultaneously reorganizing the intramural decision making process for obligating NCI preclinical or clinical development of drugs and biologics resources, which is presently the responsibility of the Decision Network Committee. The goals of the reorganization are to: (1) speed up the decision making process; (2) to take into account the diversity of the new compounds of interest; and (3) to integrate NCI contract resources decision making.

Complementary and Alternative Medicine (CAM): In response to public interest, Congress established the NIH Office of Alternative Medicine (OAM). Over the years the NCI has selectively evaluated CAM modalities as dictated by public health needs. The NCI is working with the OAM to set up a process for evaluating data from the CAM community to determine whether claims of efficacy are supported by evidence in the public domain. A committee of extramural individuals to assist in the process is being organized. The Office of Cancer Information, Communication and Education (OCICE) has recently integrated the evaluation of CAM claims into the editorial board processes for the Physicians' Data Query (PDQ) database.

In the discussion and in response to questions, the following points were made:

- One member commented that new mechanisms and resources may be needed to rapidly validate the breadth of scientific discoveries expected over the next few years, including an extension of the RAID program to the biotechnology industry. Staff responded that the NCI already has mechanisms in place to address the industry's needs in this area, although an effort may be required to ensure that industry is aware of the mechanisms.

- An NIH plan to address the issue of medical privacy and the

impact of informed consent requirements on the availability of samples clinical translational research will be issued shortly.

- When asked about maintaining the balance between the expected increase in opportunities for clinical verification of new ideas and treatments and avoiding too great a degree of centralization, staff responded that the restructuring of the Decision Network Committee is expected to evolve toward a decision making process that involves a group of extra- and intramural experts with the necessary expertise to deal with critical decisions about what compounds the NCI should develop.

- One member asked how the NCI evaluation of CAM modalities of interest to the public will be balanced with opportunities presented by other new agents. Staff indicated that the decision as to whether a formal trial is merited for any CAM modality will rest on the solidity of the evidence supporting the claim.

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NCI/CONGRESSIONAL RELATIONS - MS. DOROTHY FOELLMER

Ms. Dorothy Foellmer, Director, Office of Legislation and Congressional Activities (OLCA), reported that the OLCA Web site has been activated and the home page can be reached directly at http://www.nci.nih.gov/legis.index.html or through the NCI home page by clicking on Legislative. Text versions of the legislation, NCI testimony, selected NIH testimony, legislative histories for the NCI, and a list of committees of interest to the cancer community will be available at the Web site. The OLCA home page also provides a link to THOMAS, the Web site maintained by the Library of Congress for legislation. An overview of the OLCA responsibilities and how the NCI communicates with Congress.

ONGOING AND NEW BUSINESS - DR. DAVID LIVINGSTON

BSA at National Meetings: Status Reports

American Society of Preventive Oncology (ASPO) - Dr. Mary Daly reported that there was good attendance and many questions at the ASPO "NCI Listens" session. Key issues of interest were: (1) the involvement of primary care practitioners in cancer prevention and control activities; (2) how to implement research projects at the clinical level; and (3) the status of community-based research. The BSA consensus was that the sessions should be continued at ASPO meetings.

American Association for Cancer Research (AACR) - Dr. W. Gillies McKenna reported very good attendance and participation in the AACR "NCI Listens" session. Questions addressed by NCI staff largely pertained to grant funding, projected funding levels for coming years, and the impact of increased numbers of training slots, new initiatives such as the unmentored transitional training awards, and the involvement of consumers in the peer-review process. AACR leadership called for the NCI's continued interaction with various elements within the AACR (e.g., the Young Associates Group and Women in Cancer Research).

Oncology Nursing Society (ONS) - Ms. Deborah Mayer reported that although attendance was low because of scheduling conflicts, an in-depth discussion by the members in attendance focused on how to stimulate the nursing profession's awareness of the opportunities presented by the NIH K awards and on methods for increasing participation in the peer-review process. A list of recommendations was drawn up that will be implemented over the coming year to address these issues within the ONS membership. The consensus was that the "NCI Listens" sessions should be continued, with attention to identifying a better time slot on the agenda.

American Society of Clinical Oncology (ASCO) - Dr. Frederick Appelbaum reported poor attendance and impassive discussion at the ASCO "NCI Listens" session. Topics of greatest interest were the activities of the Clinical Trials Implementation Group and the need to market clinical trials to the public before cancer occurred. The consensus of BSA members was that an attempt should be made to generate greater interest in these sessions among ASCO members. An *ad hoc* subcommittee was formed, consisting of Drs. Barbara Weber (chair), Appelbaum, and Ms. Amy Langer, to meet with the ASCO Board to identify members concerns and plan a format for the "NCI Listens" session at the 1999 meeting that will address those issues. The subcommittee will report the outcome of these meetings at the September or November meeting of the BSA.

Reports on "NCI Listens" sessions at the Cold Spring Harbor Laboratories Symposium to be held in August 1998 and the American Society of Hematologists (ASH) to be held in December 1998 will be presented at subsequent BSA meetings. Board members will coordinate their attendance at the ASH meeting at the September BSA meeting.

STATUS OF PAYLINES ON NCI FUNDING POLICY - MR. STEPHEN M. HAZEN

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch, reported that the paylines remain unchanged since the March meeting at the 24th percentile for R01 grants, the 30th for FIRST (R29) awards, and a 135 priority score for program project grants (P01s). The decision on whether paylines for NRSAs will change is pending.

INTERIM REPORTS FROM SELECTED PROGRAM REVIEW IMPLEMENTATION GROUPS - DRS. BARBARA RIMER, BRENDA EDWARDS, AND MARK MANLEY

Surveillance Implementation Group (SIG): Dr. Brenda Edwards, Associate Director, Cancer Surveillance Research Program (CSRP), DCCPS, reviewed the membership of the SIG, and summarized the questions to be addressed. SIG activities focus on three major recommendations that were included in the Cancer

Control Program Review Group (CCPRG) report: (1) expand surveillance activity; (2) produce a "cancer report card;" and (3) maintain strong support of the Biometry and Applied Research Branches. Dr. Edwards reported that the purpose of the SIG is to develop a plan that enhances the NCI CSRP, helps establish priorities, and sets research directions. SIG subcommittees are addressing five main topics: (1) expansion of the Surveillance, Epidemiology, and End Results (SEER) database; (2) data and data systems for risk factors and screening linked to outcomes; (3) surveillance methodologic research; (4) partnerships and collaboration; and (5) evaluation and report card. Current activities in each topic area and the timeline for deliberations and production of the final report were summarized.

In subsequent discussion, the following points were made:

- The SEER Expansion Committee should consider using the SEER infrastructure to obtain therapeutic and intermediate outcome information to provide an ongoing data sample of how cancer medicine is practiced.

- When the SIG report is presented, the BSA will have the responsibility of evaluating the cost-benefit ratio for the broad spectrum of potential new surveillance mechanisms that the SIG is considering. The report optimally should attach a rough estimate of cost to each proposed mechanism and include a prioritization of critical issues.

- The committee should consider building on NCI-funded cohorts that are already in place in terms of following groups with certain risk profiles for outcomes.

- One member commended the CSRP vision of promoting the widest possible data collection in the general United States population but questioned the feasibility of expecting data collection to occur at the individual level in an institution or in practice. Staff explained that the problems of infrastructure for the registry-based population component, data cost and quality are priority topic areas for the CSRP. Board members were informed that the current surveillance budget extends beyond the SEER program, and an initiative to add a cancer control supplement to the National Health

Interview Survey in the year 2000 is in the planning stages.

Members were invited to submit comments to DCCPS on any aspect of the process outlined for the SIG or on any of the topics that already have been submitted.

Tobacco Research Implementation Plan (TRIP): Dr. Mark Manley, Chief, Tobacco Control Research Branch, DCCPS, reported on the current status of tobacco research at the NCI and the process being used to develop the NCI's Tobacco Research Implementation Plan (TRIP). Recommendations to be implemented in the TRIP have come from the CCPRG, the National Cancer Policy Board (NCPB), and other organizations and individuals. The TRIP's immediate objective is to develop a research plan to marshal NCI resources and to work with other NIH institutes, other federal entities, and private organizations to determine the role each is to play and to leverage the resources of all. Areas needing further study in basic sciences and epidemiology include the process of tobacco-related carcinogenesis, changing histopathology of lung cancer, early-onset lung cancer and its interaction with genetic predisposition, and the effect of hormones on people with mutations in cancer susceptibility genes.

Tobacco Research Implementation Group (TRIG): The TRIG was formed to examine the NCI's research portfolio and determine priorities for tobacco-related research for the next five to seven. To establish a historical context for the work of the group, Dr. Manley briefly summarized the patterns of tobacco use in the United States since 1980, which showed that although tobacco use is leveling off among adults, it is increasing among high school youth, both boys and girls, and that tobacco use is responsible for one in six deaths and about 30 percent of all cancer deaths. A report based on progress made in monthly meetings from May through August will be presented at the fall meetings of the BSA and the National Cancer Advisory Board (NCAB).

In discussion, the following points were made:

- Increases in promotional spending on tobacco products in the 1980s and 1990s were shown to be followed by an uptake in youth smoking.

- The role of the NCI, as states begin receiving money to initiate ASSIST-like programs, will likely be to coordinate across state and nationally based programs, being prepared to deal with states already funding extensive intervention research and those that are not.

WORKING LUNCH - DR. DAVID LIVINGSTON

Interim Report: Sexennial Reviews - Dr. Wittes discussed NCI staff progress in incorporating the changes to the draft "Guidelines for BSA Review of Extramural Programs" requested by members at the March meeting. The Guidelines will be presented for final approval at the November meeting.

Status Report: Metrics for the SPORE Program - Dr. Robert C. Young presented the report of the *ad hoc* subcommittee that was appointed to develop evaluation criteria for the SPORE grant program. After briefly reviewing the deliberative process, Dr. Young summarized what the subcommittee considered to be the five important areas for evaluation: (1) significant scientific advances toward diagnosis, prevention, or treatment of cancer, (2) translational research,(3) novel research programs, (4) unique research interactions, and (5) creative use of flexibility. The subcommittee also suggested that the first evaluation be conducted in the year 2000 and proposed a structure for conducting the evaluation. After extensive discussion, the subcommittee concluded that it could make no specific recommendations as to size, spectrum of diseases, or future expansions of the SPORE program at this time. The subcommittee believed it appropriate to continue the current policy of presenting new or expanded SPORE grant initiatives to the BSA.

In subsequent discussions, the following points were made:

- The SPORE review should be done as part of the entire sexennial review process.

- A committee without conflicting interests and a broad knowledge of the field will do the review which should be

conducted with a view towards the best use of future NCI funds on behalf of clinical translational research.

- Another criterion should be added to the five, namely, that the SPORE grant mechanism be compared with clinical translational mechanisms and all other NCI funded research. Consideration must be given to what science the same money would produce under other mechanisms.

Motion: A motion to adopt the report of the BSA SPORE Grant Evaluation Subcommittee unanimously approved. The proposals of the Subcommittee were approved as the basis on which the NCI can formulate a review process for the SPOREs that will be part of the sexennial review of the Organ Systems Program, to occur in the year 1999 or 2000.

Status Report: Data Safety Monitoring Boards (DSMB) for NCI-Sponsored Clinical Trials - Dr. Michaele Christian informed members that an BSA ad hoc task force convened a follow-up workshop to address issues of concern related to DSMBs for NCI-sponsored clinical trials, to be preceded by a survey of some operational characteristics. The survey results and written report of the 11 June workshop, which featured representation from 14 data monitoring committees, the National Cancer Institute of Canada, and the International Breast Cancer Study Group, as well as the chairs of most of the cooperative groups was presented. Relevant NIH policies were reviewed, and discussions addressed the variability in DSMB operations and procedures related to handling data requests and other matters. Following a brief discussion, the Board concluded that appropriate systems are in place for disease committee chairs to obtain interim clinical trial data promptly and that no further action is needed.

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STRATEGIC PLAN FOR NCI TRAINING PROGRAMS - DR. BRIAN KIMES

Dr. Brian Kimes, Associate Director, Office of Centers, Training

and Resources, presented the NCI Strategic Plan for Research Training and Career Development. Major goals of the strategic plan were to stabilize the number of clinical and population scientists; address future needs for multidisciplinary team science and translational research approaches; provide the flexibility to attract new scientific disciplines into cancer research; and more effectively engage underserved populations. Fundamental operating principles of the plan are to focus on investigator-initiated grants; ensure equal opportunity of different disciplines through effective management of the peer-review process; phase in new activities based on priorities and the availability of adequate resources to sustain them; provide an uninterrupted continuum of training, career development and career stabilization opportunities where needed; and improve communication of opportunities to scientists.

Dr. Kimes reviewed for the Board the research tracks as outlined in the plan and the types of awards already in effect or planned for each track for basic scientists, clinical scientists, prevention, control, behavioral, population and underserved scientists. Negotiations with NIH are underway to institute the transition grant mechanisms. Barriers to immediate implementation of proposed training activities relate to increased costs, necessary policy changes, and logistics of completing the preliminary work in time for FY 1999 funding.

Points made in answer to questions and in the discussion:

- Training programs to reach the underserved populations are the responsibility of a much broader constituency and should begin earlier than high school and may require a separate program that leads up to the proposed new supplemental awards.

- The issue of indirect costs related to mentoring time by full faculty must be addressed. Members strongly supported Increases in salary caps, greater flexibility in using supplemental NIH funds, support for clinical investigators, and the translational scientist career award.

Motion: The NCI Strategic Plan for Research Training and Career Development was approved as presented. The NCI will work with

the division directors as PAs for the awards are being developed and will report the results of the implementation plan to the BSA at the November meeting. Follow-up reports will include information on the types of people applying for awards.

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DIVISION OF CANCER CONTROL AND POPULATION SCIENCES (DCCPS) UPDATE ON THE CANCER GENETICS NETWORK - DRS. BARBARA RIMER AND SUSAN NAYFIELD

Dr. Rimer stated that the Cancer Genetics Network (CGN) is envisioned as a dynamic infrastructure for collaborative research on the genetic basis of human cancer susceptibility, designed to drive the science as it evolves. The network will be composed of a multidisciplinary group of scientists linked by a state-of-the-art informatics infrastructure to answer the most pressing practical questions in human genetics.

Dr. Susan Nayfield, Program Director, Epidemiology and Genetics Program, presented an introduction to the network and information on how the informatics components will link with the research component. Dr. Nayfield stated that the RFAs for the participating centers and for the informatics group were announced the previous summer. Applications received in the fall were reviewed in December and January, and the funding plan has been approved. Announcement of awards is pending completion of the final details.

Dr. Nayfield briefly summarized how potential research participants would be recruited for the main registry, how the registry would interact with the Network centers, and the roles of participants, investigators, and the registry in subsequent research projects. The CGN research agenda will focus on studies related to the translation of genetics into medical practice, public health issues in genetic susceptibility, and the genetics of cancer susceptibility. Another update of progress in developing the Network will be presented to the BSA next year.

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RFA/RFP CONCEPTS: PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Control and Population Sciences (DCCPS)

Preventing Adult Cancer by Promoting Cancer Prevention Behavior During Childhood (RFA) - Dr. Roselyn P. Epps, Medical Officer, Behavioral Research Program, DCCPS, presented a concept whose key features would be: (1) a focus on children 11 years of age or younger, (2) promotion of research relevant to developmental stage, (3) inclusion of social context, psychosocial, and cultural factors of family and environment, and (4) a focus on interventions with one or more of the following cancer risk behaviors: tobacco use, dietary practices, or sun exposure. Because fewer than 10 grants in the NCI portfolio address or even include children 11 years of age or younger and research is needed on innovative, developmentally appropriate interventions, this initiative would seek to stimulate investigators to focus on this age group.

A total of $12M is requested for a 4-year period to fund 16 to 20 grants. Amount of set aside for year 01 is $3M.

In discussion or in answer to questions, the following points were made:

- Suggestions for framing the RFA were: (1) begin with a discussion of specific levels of risk factors in the three behavioral areas; (2) include more information on how this proposed research might stimulate a change in the environment; (3) address the difficulties related to the whole area of research in children and informed consent; (4) provide information on how the interventions would be made appropriate for every population group; and (5) encourage respondents to propose ways to engage either

professional or youth organizations and their resources. The need for long-term follow-up was suggested to evaluate the durability of behavioral changes that are effected as a result of interventions.

- Suggestions for stimulating a large number of applications was to: (1) hold a preapplication meeting for interested investigators before announcing the RFA; and (2) to develop a research agenda with the help of experts in developmental and behavioral pediatrics.

- A concerted effort across the entire NIH will be needed to address the issue of how to influence childhood behavior in a broad, rather than narrowly focused, manner. The RFA should be scaled down to include only the preintervention aspects at this time.

On the basis of the discussion, the proposed concept was withdrawn so that DCCPS staff could give the concept further consideration and consult with experts in the field and staff in other divisions and institutes.

Division of Cancer Treatment and Diagnosis (DCTD)

Small Animal Imaging Resource Program (SAIRP) (RFA) - Dr. Daniel Sullivan, Associate Director, Diagnostic Imaging Program, DCTD, stated that the purpose of the RFA is to provide an imaging resource to oncology researchers and a laboratory for research and small-animal imaging technologies research and development to expand the possibilities for noninvasive, quantitative, *in vivo* imaging. Technologies would include positron emission tomography (PET) and magnetic resonance (MR) scanners and optical imaging equipment. The SAIRP would be expected to foster multidisciplinary interactions beneficial to the growth of both the oncology and imaging research fields. Applicants would be expected to describe their own plans for governance and protocol selection, and a midpoint review by program staff would be conducted to confirm that both imaging services and research are provided. Cofunding commitments have been received from the National Center for Research Resources (NCRR) and the Department of Energy for equipment acquisition and technology

research.

The estimated set aside is $7.5M for four-six awards in year 01 and $3.5M for each year, for a 5-year total of $22M.

In discussion, the following points were made:

- Members suggested that: (1) the funding for equipment should be based on what resources an applicant already has and not be built into every grant; (2) a competitive basis for making the awards be assured; (3) the narrative makes clear that the RFA applies to modeling for a variety of small animals, not just mouse or rat; (4) more extensive collaborations be encouraged to provide greater opportunities for access to the technologies; and (5) exportability of technologies dealing with small animals be encouraged.

- The number of awards estimated for this RFA may be too low to accomplish the original goal of developing facilities that would allow access to the mouse and cancer communities as a whole. Much practical planning would be needed on how the experiments would be performed and what the imaging facilities will require, for example, in the form of mouse house maintenance.

Motion: A motion to approve the DCTD RFA entitled "Small Animal Imaging Resource Programs", was unanimously approved.

Development and Application of Imaging in Therapeutic Studies (RFA) - Dr. Daniel Sullivan proposed an RFA to encourage investigators to apply imaging technologies in the assessment of investigational cancer therapeutic agents. This initiative would stimulate multidisciplinary research bringing together oncologists, imaging scientists, and basic scientists to develop imaging techniques that would noninvasively or nondestructively determine the biodistribution and/or mechanism of action of a variety of administered therapeutic agents. Both clinical and preclinical studies would be allowed. Few projects within the Diagnostic Imaging Program portfolio use imaging agents within the context of new drug assessment, and very few of the more than 2,000 papers on drug development identified in a

MedLine search incorporated techniques such as MR spectroscopy or PET scanning.

This initiative would fund six-eight R01s at an approximate level of $350K per year per award. The estimated cost for the 4-year project period is $11.2M, with an estimated set aside of $2.8M in year 01.

Motion: A motion to approve the DCTD RFA entitled "Development and Application of Imaging in Therapeutic Studies." The motion was seconded and unanimously approved.

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TECHNOLOGY DEVELOPMENT INITIATIVES - DRS. RICHARD KLAUSNER, ROBERT HAMMOND, AND CAROL DAHL

To introduce the presentation on these initiatives, Dr. Klausner described two major pathways for making advances in research: one related to conceptual advances based on asking questions and posing hypotheses; the other related to the creation of usable and functional tools for asking questions (e.g., analytic approaches to the development of data). He noted that technology development demands different sets of approaches in terms of review criteria, evaluation, and milestones. In response to the need expressed by the scientific community for science-enabling technologies, the NCI has developed two proposals for consideration by the BSA. The first proposal would create a new funding mechanism to deal with near-term opportunities for technology development and for discovery based on the development, evaluation and validation of the technology; the second proposal would deal with high-impact, long-range opportunities to create revolutionary technologies.

Phased Innovation Award: Dr. Robert Hammond, Chief, Office of Advisory Activities, DEA, stated that this award was developed as a support mechanism for the rapid review and funding of large-scale technology development research. A key element in the

award is that the new R33 grant mechanism, will provide a second phase for the support of innovative exploratory and development research initiated under the R21 mechanism. Technology research would be supported from the evolution of innovative concepts through feasibility testing (R21 phase) to full-scale development (R33).

Innovative Technologies for the Molecular Analysis of Cancer: Phased Innovation Award (PA) - As an example of how the new grant mechanism has been applied, Dr. Carol Dahl, Director, Office of Technology and Industrial Relations (OTIR), ODDES provided a brief overview of the development of the PA which is being sponsored jointly as a Phased Innovation Award by the extramural divisions and several offices of the NCI. Technologies of interest to the program are: (1) detecting alterations and instabilities in genomic DNA; (2) monitoring the expression of genes and gene products; (3) analyzing and detecting the cellular localization, post-translational modification, and function proteins; and (4) monitoring major signal transduction networks involved in cancer in support of basic, clinical, and epidemiological research. Dr. Dahl informed the Board that an identical PA has been released as a Small Business Innovation and Technology Transfer Award (SBIR/ STTR) to take advantage of the funding available for the SBIR and STTR mechanisms. Only the format for preparing applications differs between the two PAs.

In the brief discussion that followed, the following suggestion was made:

A workshop should be sponsored at the end of the R21 phase so that grantees can discuss new technologies and/or results that were not known prior to the PA.

Motion: A motion to endorse the identical PAs entitled "Innovative Technologies for Molecular Analysis of Cancer" that were released as a Phased Innovation Award and an SBIR/STTR Initiative was seconded and unanimously approved.

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Unconventional Innovation Program: Dr. Dahl requested Board approval of a new program to support unconventional innovation in technology discovery for cancer research applications. Current challenges to the success of this type of application relate to the conventional NIH and NCI review and management processes. The NCI's approach to implementing the new program would be to target quantum improvements in existing technologies or entirely novel approaches; recruit the involvement of investigators from disciplines that have not traditionally received support from the NCI; foster broadly multidisciplinary teams; provide ongoing interactive program management; and utilize the broad agency announcement contract mechanism. The next step, would be soliciting ideas (white papers) on technology opportunities from the research community to aid in defining an appropriate scope for the first solicitation. A broad agency announcement solicitation would be issued in early fall, which would result in an investment of up to $4M in quality projects. Updates to the BSA would be provided annually or as appropriate in a first round contract solicitation in FY 1999 and $6M in each of the next 2 years.

In discussion and in response to questions, the following points were made:

- The proposals would be peer reviewed by a DEA committee.
- The challenge will be to distinguish the ideas that are truly revolutionary from those that are only slightly less conventional than normal.
- The material science and applied mathematics communities would be good sources for research collaborations, as well as the physics and engineering communities.

Motion: A motion to approve the Unconventional Innovation Program and the concept for the PA. The motion was seconded and unanimously approved. NCI staff will submit an external oversight plan for the expert technical evaluations that will be necessary. The plan will include budget and levels of risk management.

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INFORMATICS AND THE NCI: REDESIGN OF PDQ - MS. DEBORAH COLLYAR, DR. ROBERT WITTES, AND MS. SUSAN HUBBARD

Ms. Deborah Collyar, President, Patient Advocates in Research (PAIR), and Chair, Clinical Trials Information System (CTIS) Steering Committee, presented for Board consideration the Committee's Report to the Director entitled "Recommendations for the New Clinical Trials Information System." A new model for information for the CTIS was developed, with the patient community as the main user focus together with health care, information, and support providers and health care systems. At the May 1998 design meeting, representatives of these user groups outlined their expectations for the new CTIS and the NCI's four pivotal roles, which were to: (1) produce useful clinical trial information; (2) provide access to cancer-related information; (3) deliver information in multiple ways; and (4) continually evaluate and update. Specific recommendations for carrying out each of these roles were included in the Report to the Director. The challenge to the NCI will be to integrate all of the channels used to transmit cancer information to the general public into a single, comprehensive message that contains objective information for public and professional decision making regarding clinical trial participation or directions.

Dr. Wittes reported that the NCI is creating an implementation plan based on the specific recommendations included in the CTIS Steering Committee report and will set up project teams to address each broad areas covered in the recommendations. The teams will prioritize the recommendations and develop timelines for fulfillment over a period of time consistent with funding requirements. The proposed implementation plan will be presented for BSA consideration at the November meeting.

Ms. Susan Hubbard, Associate Director, OCICE, reported that the redesign of the PDQ, including the recommended name change, is being integrated into the formal CTIS implementation plan. Ms. Hubbard explained how the NCI is already linking the PDQ to the Food and Drug Administration (FDA) Web site list of

mammography facilities and plans to use similar criteria to identify other good sites that have information the NCI would not need to duplicate. Future protocols will be submitted by the principal investigator to the Cancer Therapy Evaluation Program (CTEP) and ultimately linked to the information system. Negotiations are underway with the pharmaceutical biotechnology industries to develop a Web-based interface for electronic submission of their protocols to the CTIS.

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RFA CONCEPTS: PRESENTED BY NCI PROGRAM STAFF (cont'd)

Division of Cancer Prevention

Specialized Education Conferences: Application of Genomic Technologies to Nutrition and Cancer Prevention (RFA/Coop. Agr.) - Dr. Carolyn Clifford, Acting Associate Director, Cancer Prevention Research Program, DCP, requested BSA approval of the concept for a cooperative agreement to fund specialized education conferences. The objectives of the conferences and workshops would be to stimulate innovative research about applications of genomic techniques to nutrition and cancer prevention research, enhance the knowledge and skills of nutrition scientists, and encourage interdisciplinary collaboration for the application of these techniques and knowledge to diet, nutrition, and cancer prevention research.

The estimated cost for the 3-year project period is $1.5M, with a set aside of $500K in year 01. Five awards per year are estimated.

Based on the BSA discussion, the concept for a cooperative agreement on "Specialized Education Conferences: Application of Genomic Technologies to Nutrition and Cancer Prevention" was withdrawn. DCP staff will consult with BSA members and refine the concept for possible consideration in November.

SPORE in Ovarian Cancer (RFA) - Dr. Andrew Chiarodo, Chief, Organ Systems Coordinating Branch, ODDES, presented an RFA to establish a SPORE in ovarian cancer. The intent is to capitalize on the expanding scientific base for an investigator interest in ovarian cancer and encourage translational research that would require interdependence between basic and clinical investigators to focus on the human disease. It was envisioned that the SPORE in ovarian cancer would have an opportunity to collaborate with breast cancer SPOREs in terms of consortial types of research and at the annual SPORE workshop.

Costs for the one 5-year award is $12M, with a year 01 set aside of $2.5M.

Motion: A motion to approve the concept for a RFA entitled "SPORE in Ovarian Cancer", was approved unanimously. Dr. Chiarodo will provide information on how cancer control efforts will be interpreted in the narrative text of the RFA.

Following approval of the concept, BSA members discussed the suggestion that the timetable for evaluating the SPORE program be accelerated as a basis for discussions about how the mechanism can be opened to the general scientific and clinical community without the need for the NCI to broadcast an initiative. It was decided that the BSA members who attend the July 12-14 SPORE meeting in Rockville will submit a report at the September BSA meeting.

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Supplementation of Cancer Research in General Clinical Research Centers (GCRC) of the National Center for Research Resources (NCRR) (RFA) - Dr. Margaret Holmes, Chief, Cancer Centers Branch, ODDES, stated that the intent of this concept is to provide competitive supplements for GCRCs located in NCI-designated cancer centers. The supplements would provide cancer center investigators with greater access to the GCRC resources and

facilities for the conduct of early-phase clinical trials by expanding cancer research beyond the GCRC policy limit of 25 percent to 33 percent for any disease entity. Another benefit would be the strengthened collaborative partnership between the GCRCs and cancer centers.

The anticipated cost for the 3-year project period is $6M for an estimated five awards, with a set aside in year 01 of $2M.

In subsequent discussion, the following points were made:

- The idea of unique effects of initial investigation of clinical cancer trial research is addressing a significant need and certainly all of NCI cancer centers have that need for things like nursing support, biostatistics costs, computerized data bases, and core laboratories. Those needs are not unique to just 29 institutions that have clinical research centers (CRCs). The concept should be designed such that both CRC containing institutions and non-CRC containing institutions can respond.

- Coverage of routine patient care costs may not be a good idea since (1) true patient care costs could consume the dollars with as few as three or four patients; (2) an unwise precedent may be set; and (3) institutional support structures may be altered. If the concept causes these institutions to alter their percentage on a permanent basis, for instance, then it would be of long-term significance.

- A few members indicated that GCRC's are under-utilized in some institutions and the cap on GCRCs limits cancer clinical trials participation in them. Data which show how fully utilized GCRC's are is needed. Staff responded that NCRR policies are designed to protect the GCRC from domination by any one disease entity and, in fact, it is their mission to provide access to GCRC's in an equitable way to as many diseases as possible, which explains their limit. The GCRC cap has been explored before and the National Center for Research Resources (NCRR) continues with its policy because of its mandate.

- NCRR staff indicated that GCRC budgets are allotted for

inpatient and outpatient activity depending upon the previous year's activity. A facility may be larger than what NCRR actually is funding; for example, there may be a ten-bed unit but NCRR only funds four beds. Another example, is that occupancy is also leveraged by having non-research patients on the ward for which NCRR gets money back. NCRR supports a very complex system. Its core mission is to support clinical research for funded investigators no matter where it is within the hospital, thus the whole concept of having one unit with an occupancy is evolving to performing research wherever the patients are, being careful to maintain a mix of diseases.

Motion: A motion to disapprove the RFA entitled "Supplementation of Cancer Research in General Clinical Research Centers (GCRCs)" of the National Center for Research Resources was disapproved. The vote was 11 yeas, 4 nays, and 4 abstentions. If the proposed concept is resubmitted, modifications should include: occupancy and utilization information and data; potential for program to be open to organizations other than GCRCs; and a review of patient care costs.

Adjournment: The 8th regular meeting of the Board of Scientific Advisors was adjourned at 12:41 p.m. on Tuesday, 23 June 1998.

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