



DEPARTMENT OF HEALTH AND HUMAN SERVICES

**NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

**5th Regular Meeting
BOARD OF SCIENTIFIC ADVISORS**

**Minutes of Meeting
June 19, 1997
Building 31C, Conference Room 10
Bethesda, Maryland**

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 5th regular meeting at 8:00 a.m. on Thursday, June 19, 1997, 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 at 6:10 p.m. on Thursday, 19 June, for introductory remarks from the Chair; discussion of procedural matters and future meeting dates; ongoing and new business; presentations and discussions on the present status of paylines, the Prevention Program Review Report; Requests for Applications (RFAs) concepts, enhancing the Division of Cancer Biology (DCB) interactions with the scientific community, and proposed modifications of NIH review award policies.

BSA members present:

Dr. David Livingston (Chair)
Dr. Frederick R. Appelbaum
Dr. Joan Brugge
Dr. Mary Beryl Daly
Dr. Virginia Ernster
Dr. Eric R. Fearon

Dr. Suzanne W. Fletcher
Dr. David D. Ho
Dr. Waun Ki Hong
Dr. Tyler Jacks
Ms. Amy S. Langer
Dr. Caryn E. Lerman
Ms. Deborah Mayer
Dr. W. Gillies McKenna
Dr. Enrico Mihich
Dr. John D. Minna
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. Peter K. Vogt
Dr. Barbara L. Weber
Dr. Alice S. Whittemore
Dr. William C. Wood
Dr. Robert C. Young

BSA members absent:

Dr. E. Robert Greenberg
Dr. Joan Massague
Dr. Nancy E. Mueller
Dr. Daniel D. Von Hoff

NCAB lisison:

Ms. Zora Brown, (absent)

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 5th regular meeting of the Board of Scientific Advisors

(BSA) 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 discussed upcoming BSA meeting dates, noting a potential conflict with the meeting of the European Organization for Research on the Treatment of Cancer (EORTC) in June 1998. The extent of the conflict will be determined.

CONSIDERATION OF MARCH MEETING MINUTES - DR. LIVINGSTON

The minutes of the March 3-4, 1997, BSA meeting were approved.

REPORT OF THE DIRECTOR, NCI - DR. RICHARD KLAUSNER

Dr. Richard Klausner discussed aspects of the FY97 budget, progress in the development of the FY98 budget, and highlights in the Intramural Program.

Research Project Grants (RPG) Pool: Dr. Klausner stated that the paylines for R01s and R29s (FIRST Awards) were raised to the 23rd and 30th percentile, respectively, and the priority score for program project grants (P01s) was raised to 140, representing increases from those projected in the initial funding guidelines. A fraction of the RPG dollars will be used to fund investigator-initiated research through facilitating approaches such as: 1) exception funding (including Accelerated Executive Review [AER]), 2) supplements, and 3) internal funding and bridging mechanisms. In FY97, the success rate for grants reviewed through the AER mechanism is projected at 55 percent, up from 50 percent in FY96. Currently, about 10 percent of NCI dollars support grants received in response to RFAs. This year that percentage will decrease to 6 percent for new and competing RFAs.

Cooperative Groups: Cooperative groups were provided a cost of living increase and some restoration of funds based upon the recommended levels of funding. In addition to the base funding, about \$5.2M has been allocated to support tissue banks and the infrastructure associated with translational and correlative studies. An additional amount has been made available to help defray the costs of enhancing accrual to clinical trials through the agreements with the Veterans Administration (VA) and the Department of Defense (DoD). This money is also earmarked to support the electronics informatics infrastructure, in particular, to develop the capability for online clinical trials reporting to the NCI. A presentation is planned for a future BSA meeting on the National Cancer Informatics Infrastructure and the Scientific Information System.

Training: Pending final decision, the NCI projects that approximately seven awards will be made from an outstanding pool of applicants for the new Howard Temin Award for young investigators. Recently approved training initiatives include the AIDS Oncology Clinical Scientist Development Program and the NCI Scholars Program. The Division of Cancer Epidemiology and Genetics (DCEG) advertised a Program Announcement (PA) to stimulate the development of

comprehensive research training programs in the genetic epidemiology of cancer.

Cancer Survivorship Initiative: A request for competitive supplements has been released to identify potential cohorts of cancer survivors in which research studies can be performed. Letters advertising the initiative were addressed to cooperative groups; the Community Clinical Oncology Program (CCOP) research base; Surveillance, Epidemiology, and End Results (SEER) Program contractors; and any other group that has access to cohorts of long-term cancer survivors. A set-aside of \$2M is expected to fund up to 15 applications.

Department of Defense (DoD) Clinical Trials Agreement: The NCI/DoD Clinical Trials Agreement has completed its first year. To increase participation in sponsored and covered trials, the NCI and DoD have undertaken an extensive joint promotional campaign to inform the active-duty military community and the Civilian Health and Medical Plan of the Uniformed Services (CHAMPUS) beneficiaries of the agreement. Negotiations are under way to expand the agreement to include Phase I trials and a broad range of prevention and diagnostics trials. The NCI is also participating in meetings with the new TRICARE/CHAMPUS managed care contractors to ensure that the clinical trials option is a well-known and well-advertised part of the benefits package.

Veterans Administration (VA) Clinical Trials Agreement: Extensive changes in the VA medical system have resulted in the formation of the Veterans Integrated Service Networks (VISNs) for the administration and delivery of medical care. The NCI has been working with the VA to ensure continuation of the longstanding collaborations between the VA, cancer centers and cooperative groups. Discussions with VISN directors have been held to ensure that the regional health delivery system, as it undergoes reorganization, includes strong support for clinical research and a specific commitment to the joint NCI/VA clinical trials.

FY98 Budget: Dr. Klausner reported on multiple visits by the NIH leadership to Capitol Hill for the NIH FY98 appropriations hearings in both houses and to discuss how NIH sets priorities. A booklet about priority setting and decision-making at the NIH is being prepared by the Institutes for distribution to the advisory boards.

Dr. Klausner stated that the status of the NIH budget is not known. Although major increases for both the NCI and NIH have received much support in both houses, the balanced budget amendment creates uncertainty about the amount of money available to the Appropriation Subcommittee from which the NIH budget will be decided.

ByPass Budget: The latest Bypass Budget, which will be distributed when completed, supports the need for increased funding. Changes include the reevaluation of extraordinary opportunities on a 3-year cycle and expansion from two to three sections. The new section describes a 4-year plan to deal with the overarching infrastructures of discovery, clinical research, new epidemiologic bases, repositories, and training. As a planning document, the Bypass Budget has led to the establishment of Working Groups associated with each of the first four opportunities - Cancer Genetics, Preclinical Models, Developmental Diagnostics, and Detection Technologies. The

Cancer Genome Anatomy Project and Tumor Gene Index are successful initiatives that were based on recommendations of the Developmental Diagnostics Working Group.

Intramural Research Program (IRP): Dr. Klausner reported that the IRP continues to build and recruit even as its budget is decreasing, through the development of cost management principles and a rigorous review process. This year's focus has been on the integration of research programs within and across the three intramural divisions. Competitive grants, such as the Intramural Research and Advanced Technology Awards, have been instituted to fund collaborative intramural projects. The Advanced Technology Center was established to serve as a center for the development and exportation of technologies. The DCEG has taken the lead in integrating intramural projects relating to molecular epidemiology. A search has been initiated for a permanent director of the Division of Basic Sciences (DBS). Dr. Klausner concluded with an overview of important scientific discoveries by IRP investigators.

NCI AND THE CONGRESS - MS. DOROTHY TISEVICH

Ms. Dorothy Tisevich, Director, Office of Legislation and Congressional Activities (OLCA), gave a brief summary of the many recent hearings before the House and Senate Committees. In addition to appropriations, a major focus was biomedical research priorities and resource allocation issues.

Ms. Tisevich then presented an overview of the progress of the more than 100 bills being tracked by the OLCA in categories of particular interest to the BSA. BSA members were invited to provide suggestions of additional or alternative categories of legislation that they would like to have included in future updates.

ONGOING AND NEW BUSINESS - Dr. David Livingston

BSA at National Meetings: Status Report

BSA members and NCI staff reported on the "NCI Listens" sessions held at the national meetings of five professional societies.

American Society of Hematology (ASH)- Dr. Frederick Appelbaum reported that the major concerns of attendees were the difficulty of carrying out clinical research in the current private care environment and the limited access of minority patients to research trials. Other comments dealt with NCI support for educational programs, the difficulty in preparing and supporting individuals who are attempting to work between the laboratory and the clinic, and the difficulty cooperative groups have in connecting with pharmaceutical companies and contract research organizations because of cumbersome mechanisms.

American Society of Preventive Oncology (ASPO) - Dr. Virginia Ernster stated that discussion

at the ASPO session focused on suggestions for improving the grant review process in general and the areas of epidemiology and cancer prevention and control in particular. Specific suggestions will be forwarded to the Division of Research Grants (DRG) for consideration as the peer review system is being revised. Other comments related to the need for support in the Cancer Center Support Grants (CCSGs) for shared resources such as a behavioral measurement resource or a molecular epidemiology laboratory; the need for NCI-supported mechanisms for training young investigators interested in preventive oncology; and the need to keep the field of preventive oncology strong at the cancer centers. This initial "NCI Listens" session was well received and productive, and the NCI was encouraged to continue these sessions on an annual basis.

American Association for Cancer Research (AACR) - Dr. John Minna reported that the AACR session was a well-attended and productive meeting. A major concern of the membership was the perception that NCI and NIH leaders believe that a 35 percent success rate would be adequate if the NCI budget were to be doubled. Other important issues included a concern about the grant review process, the perceived barrier between the intramural and extramural communities, and the need for access to informatics.

American Society of Clinical Oncology (ASCO) - Dr. Robert Young informed the Board that ASCO attendees touched on a wide array of issues of importance, including many already addressed in the previous reports. Specific areas of concern included: (1) translational research and the ability of clinically trained people to acquire enough basic science investigative experience; (2) questions about the next generation of clinical trial strategies with their huge informatics databases; and (3) questions by Community Clinical Oncology Program (CCOP) participants about the amounts of money being spent on monitoring clinical trials rather than clinical investigators.

Oncology Nursing Society (ONS) - Ms. Deborah Mayer reported that ONS members wanted an articulation of the NCI's process for setting priorities in the budget and research activities. Another major concern was that nursing research studies, such as quality of life and outcome studies or systems management, are viewed as peripheral and not given priority for statistical resources and support within cooperative groups. A third concern was the need for modification of training and fellowship opportunities so that nurses beginning a research career into a different career path than traditionally funded can apply and successfully compete.

A brief discussion resulted in the following points:

- A formal mechanism for logging, tracking, and responding to the input from discussions, letters, and comments to the NCI and the Board should be established. The response process that the NCI develops must deal with iterative comments and avoid duplication of effort.
- Suggestions of mechanisms for responding were: 1) a newsletter to the membership of each society visited; 2) reports of NCI responses to specific society concerns or

suggestions during the next "NCI Listens" session; 3) use of the Advisory Board World Wide Web (WWW) Page to communicate "NCI Listens" information and responses; 4) articles in the informational journals published by the societies, which are distributed to all members; and 5) consideration of meetings, such as the AACR Public Forum, as a venue for joint sessions (e.g., an "AACR/NCI Listens" session).

BSA members agreed to continue the "NCI Listens" sessions for another year at upcoming meetings of the same professional societies, pending clarification of a process for eliciting and communicating NCI response to comments from the first round.

PRESENT STATUS OF PAYLINES - MR. STEPHEN HAZEN

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch (EFDB), stated that the NCI has improved the paylines for RPGs funded within the budget: (1) traditional investigator-initiated grants (R01s) will be funded through the 23rd percentile; (2) program project grants (P01s) at the priority score of 140; and (3) FIRST Awards (R29) through the 30th percentile. In a new ruling, core grants (CCSGs) will be funded to recommended levels for priority scores up to 197 and on a sliding scale up to 212. Paylines will remain the same for clinical groups, fellowships, and institutional training awards.

PREVENTION PROGRAM REVIEW REPORT - DR. EDWARD BRESNICK

The Prevention Program Review Group (PPRG) Chair, Dr. Edward Bresnick, Vice Chancellor for Research, University of Massachusetts Medical Center, informed members that the key message of the PPRG Report is that discovery-driven cancer prevention research must be a key component in the National Cancer Program and must be appropriately funded. Prevention was defined as the development and evaluation of strategies for reducing cancer incidence aimed at preventing the initiation of the neoplastic process or at avoiding progression to malignancy of already initiated cells. The PPRG limited its focus to prevention, with the proviso that close interaction exist between prevention and control research regardless of the final organizational structure.

Dr. Bresnick summarized the basic recommendations made in the areas of modifiable risk factors, animal models and extrapolation to human cancer prevention, genetic predisposition to cancer and detection of precursor lesions, chemoprevention trials in human populations, behavioral research and behavioral intervention trials in cancer prevention, training of health professionals with expertise in prevention research, and organization and infrastructure of the NCI Prevention Division. The recommendations called for establishing subcommittees of the BSA: a Cancer Prevention Advisory Board, but supplemented by other experts, and a Cancer Prevention Clinical Trials Group patterned after the Oncology Therapy Trials Groups.

In response to questions from Board members, the following points were made:

- Because of the potential for significant overlap between the Prevention and Cancer Control Program Review Reports, the BSA should either allocate enough time in the regular meeting to consider the cancer control and prevention reports in an integrative way or consider appointing a subcommittee to do so.
- When asked to identify the top recommendations that would most impact structurally or operationally on programmatic development, Dr. Bresnick listed the following: 1) recruitment of outstanding leaders in the fields listed in the report, 2) a new training paradigm, 3) changing the chemoprevention elements in the prevention program to include development or adoption of models with greater utility in the preclinical and chemopreventive drug development program, and (4) development of a prevention trials group.
- One member noted that large-scale dissemination efforts are necessary for the Nation's public health and should probably be done in partnership with organizations such as the American Cancer Society (ACS) and the Centers for Disease Control and Prevention (CDC). The role of the NCI would be to conduct the vanguard research, share leadership in public education, and conduct the research evaluation.
- When asked if a less costly model, such as that used by the National Heart, Lung, and Blood Institute (NHLBI), for prevention trials had been considered as an alternative, members were told that the NHLBI model would also have applicability.
- A steering committee should be formed to work with the Prevention Division on the development, analysis, and validation of animal models.

BSA WORKING LUNCH

The Board of Scientific Advisors lunch period was devoted to a consideration of opportunities and issues of interest to the Board as representatives of the extramural community acting in an advisory capacity to the leadership of the NCI. One topic suggested for discussion by several members was the review of NCI R01 grants by the Division of Research Grants (DRG), National Institutes of Health (NIH). Another issue suggested was a discussion of clinical data monitoring committee procedures and the consequences of the 5-year old rule change.

NCI R01 Grant Review Concept

The Chair, Dr. Livingston, presented a draft concept entitled "Revised Method for Reviewing NCI R01 Grants". In framing the discussion, he summarized the steps in and problems with the process as currently executed in the DRG, NIH. The concept proposed: (1) that the system for organizing the study section be changed as it relates to cancer grants to specify study sections for NCI grants composed primarily or solely of cancer research scientists; (2) that cancer grants be segmented on

the basis of generic categories, such as basic science, clinical investigation, or population science, with corresponding study sections; (3) that a process be developed whereby the Institute and the DRG share the responsibility for the study section appointments; and (4) that investigators receiving a higher than average amount of R01 or P01 support be requested to serve for a fraction of time on study sections, during the time they are exceptionally well funded.

A discussion of the topic resulted in the following points:

- There are distinct advantages in having study sections that are not solely cancer focused. For example, the three standing cancer committee members on the Behavioral Study Section provide continuity in cancer expertise; experts from other areas contribute significantly in terms of conceptual models, mechanisms, and interventions; and cancer ad hoc members are invited to participate, as needed.
- While there appears to be a real strength in behavioral and population based research areas of having people on the review committee working in various scientific areas, a member queried whether this was the case in other areas, for example epidemiology. It was noted that there is a problem in that one of the two study sections in disease control and epidemiology is heavily constituted with cancer reviewers. One of the difficulties is that service on the study section precludes a member's grant from going to that study section. The grant application instead goes to the study section where members have no knowledge of cancer.
- An unintended consequence of the proposed concept is the possibility that other institutes or centers (ICs) may take a similar attitude, with a serious risk for fragmentation at the level of the DRG and an inability to properly implement NIH study sections. Moreover, a large fraction of the total review responsibility for NCI grants (e.g., RFAs, program project grants [P01s], and cancer center support grants [CCSGs]) is already consigned to chartered study sections for the NCI. The proposed concept, however, has merit for clinical research grants.
- Experimental Therapeutics -2 (ET-2) was created to address clinical R01s in the area of therapeutics, but it evolved over time to become more like ET-1 in makeup due to an insufficient number of good applications. However, the quality of clinical investigation has improved, and preclinical cancer therapeutic study competes in study sections with the current emphasis on molecular biology, creating the need for a forum as proposed in the concept.
- Many investigators over the years have advocated for a clinical study section to no avail. Clinical research is very important and expensive. It is also very hard to do, get peer reviewed, and funded. This only adds to the endangerment of the clinical investigators, particularly now in times of severe strain on academic health centers. There is the potential to make the clinical investigator and investigation extinct without some change. The

disadvantage, however, of instituting too many special review committees or ad hoc reviews is the elimination of any corporate memory and the inability to relate a particular grant to the overall effort, field, or portfolio for ongoing research. In any process revision, the quality of P01 reviews must be ensured. As a point of clarification, NCI staff noted that P01 review takes place within the NCI and is not relevant to the proposed concept. Program project grant (P01) review was proposed as a future BSA agenda item.

- Members were told that the type of review proposed in the concept is needed for translational and clinical research because both deal more with cancer-specific issues. The review of basic cancer research benefits from the outside perspective. Specifically, basic research cancer grants in the area of chemistry would benefit from a change in the current study section makeup to include chemists who could integrate chemistry with modern findings of cancer biology.
- The review problem is particularly acute for cancer prevention and control protocols where multidisciplinary input is essential. A weakness in the current process is the lack of appropriate expertise to evaluate the protocols that are to be reviewed at any given time. A possible solution is to find the needed experts for a particular study section and assign them as ad hoc members. Another suggestion for improving the quality of study sections was to have experienced reviewers serve as mentors to younger reviewers.
- Staff pointed out that because many applications are dually assigned, some applicants would risk the opportunity to compete in multiple arenas if their applications were assigned to a cancer-specific study section. Neither the total number of applications received nor the total number of grants awarded would change, so the success rate would be identical. Only the mix of awards would be different.
- Even though a member stated there is a real need to support the proposed concept, one member suggested that the BSA should separate DRG and NCI functions and work on mechanisms of assuring meaningful dual assignment possibilities. The BSA can function most effectively by making recommendations regarding the review processes, selection of reviewers, and mechanisms for grants reviewed, etc.
- It was noted that even though dedicated AIDS study sections review the majority of AIDS R01s, many of the similar types of problems are encountered, reflecting the quality of the people who sit in the study sections. The suggested requirement to have investigators with substantial funding serve for a greater fraction of time has the potential for solving the problem of achieving accuracy and fairness in the review without drastic changes to the DRG process.
- Members were reminded that while there is always a great deal of scientific expertise in the membership of the study section, there may not be sufficient scientific wisdom. The cross fertilization can really be important, particularly if senior people are on the study section.

Members were informed that the National Cancer Advisory Board's (NCAB) Subcommittee on Cancer Centers, in its revision of the centers' review process, is considering strategies such as extending the known lead time for senior reviewers and expanding the concept of service on the committee to allow service for shorter periods of time and/or not for every meeting of the year. In addition, Institute senior staff and NCAB members will be helping to recruit, on the premise that service would be of value to the whole enterprise.

In concluding the consideration of this topic, there was disagreement on how far members wanted to go towards implementing the proposed concept, but there was support to work with DRG to see improved quality reviews. Dr. Livingston noted that the results of the discussion would be forwarded to Drs. Klausner and Rabson for reply. Any proposals would involve the BSA.

Clinical Data Monitoring Committee Procedures

The consequences of the 5-year-old rule change for clinical data monitoring committees for clinical cooperative groups was discussed. It was noted that anyone directly involved with designing or performing a trial cannot receive any information about the results of that trial. Consequently, investigators have no access to accrual information that would influence the design of subsequent trials. Attempts to change the situation have not been successful. The only recourse at present is to have the cooperative group's petition the data monitoring committee for permission to look at the data after accrual has been completed, and most of the treatment was given. The response time for such requests is considerable and tends to slow the process. BSA members from the clinical cooperative groups discussed their experience with the procedures.

Subsequent discussion resulted in the following points:

- One member suggested that, prior to taking any action, members of the Board should hear from a representative, preferably the statistician, of one cooperative group's data monitoring committee to fully appreciate the issues. Historically, the reasons for secrecy have been to avoid compromising the quality of the output and the whole trial.
- One concern of the data monitoring committee is that by showing data before total accrual is accomplished, continued accrual under those studies will be compromised. Another concern is that the study investigator might conclude one arm is the better arm and, without solid evidence, make it the control group on the subsequent study.
- Cooperative group investigators are asking only that a limited group of individuals, sworn to secrecy, have access to data as the trial is in progress.
- The subset of trials that have completed accrual and finished delivering treatment should be made available for interim analysis. The level of accrual needed before data entry would

be compromised by interim access is a separate issue.

- An experienced clinical investigator looking at the many layers of data as they are accrued can observe many more issues than the single issue taken into account in a statistical decision. Additionally, many of the issues could have a profound influence on how to think about the next trial.
- A member suggested that the genesis of the current policies regarding the makeup of data monitoring committees and the rule mandating that investigators are to be blinded to data until the end of studies should be ascertained.

Discussion on this topic will continue at the fall BSA meeting. In the interim, a committee, Drs. William C. Wood (Chair), Frederick Appelbaum, Sharon Murphy, and Ms. Amy Langer, was asked to propose a set of rules for consideration by the Board together with, but not limited to, Drs. Klausner, Rabson, and Wittes. A representative from the data safety monitoring community should also be invited.

RFA CONCEPTS: PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Prevention and Control

Cancer Research Networks (CRN) Across Health Care Systems (Cooperative Agreement) - Dr. Martin Brown, Applied Research Branch, Cancer Control Research Program (CCRP), Division of Cancer Prevention and Control (DCPC), informed the Board that the research goals of the revised concept are to support translational research on cancer prevention control in large and diverse populations. Changes from the original concept include: 1) a focus on research goals; 2) broader criteria; 3) an emphasis on collaboration between researchers at academic medical centers and health care provider organizations; and 4) only one round of applications.

The cooperative agreement mechanism was chosen to facilitate coordination of complementary research resources and data systems across health care systems, which is necessary for research requiring large and diverse population-based data and interdisciplinary research methods. A budget of \$4M is proposed for the first year, and \$16.5M is the anticipated cost for the project period. One or two awards are anticipated. Renewal of this one-time solicitation would be contingent on successful performance in the first round.

In the discussion of the concept, the following points were made:

- Health care provider organizations represent a large potential resource for information that should be developed, and this concept is a step in that direction. The 25 organizations that have a research component will be particularly useful for cancer prevention now and cancer treatment research in the future. These organizations are good settings for risk

studies, studies of behavioral change in large populations, studies of secondary prevention, and genetic testing because of the large denominator of patients and good databases.

- One concern expressed in the previous presentation of this concept was a turnover rate that may be too high for longitudinal follow-up of patients. However, the high turnover has been seen mainly among young people. Research expertise is lacking in all but a few of the health care provider organizations, and a clinical research environment has not evolved throughout these organizations as it exists in academic medical centers.
- The proposed budget may be insufficient to fund the research and an infrastructure comprising networks of research units and covering several million people.
- When asked to clarify whether the funding was intended largely for putting the network together and/or the conduct of the research, staff explained that a balance of both components is expected.
- In response to the concern that the solicitation would be, in effect, a sole-source contract because of the limited number of organizations that could respond, staff stated that the eligibility criteria had been broadened to address institutional diversity.
- When asked about the anticipated number of awards and the pools from which the ad hoc review committee would be drawn, staff explained that both would be contingent on the applications that are received.
- A Board discussion of the overarching issue of infrastructure development and informatics is needed because both are a part of every RFA concept proposal. Questions that require clarification are: (1) how the cancer research networks can span health care systems if only one award results from the solicitation; (2) how the aim of common database development would be accomplished; (3) whether the time is adequate for preparation of outstanding one-time submissions that would bring forth a good pool of applicants; and 4) what the guidelines would be for review of both the infrastructure and the research.
- The cooperative agreement mechanism is justified because of the public nature of medical research and the research proactivity that could result from such a collaboration.
- When asked for clarification as to whether cancer center involvement in network development would be required, staff explained that the RFA would be written such that during the review process a high value would be placed on appropriate collaborations with academic medical center researchers, including cancer centers.
- When queried whether other organizations are interested in the research capabilities of health care provider organizations, staff stated that multiple groups are moving toward

collaboration, but that the availability of funding is a key component. Plans are to provide support to actually undertake research and build an infrastructure.

- The issue of informed consent should be addressed when the full text RFA is written.

Motion: A motion was made to approve the concept with the recommendation that informed consent be addressed in the final cooperative agreement. The motion was seconded and approved, with 14 for, 8 opposed, and 2 abstentions.

Division of Cancer Prevention and Control & Division of Cancer Treatment, Diagnosis, and Centers

Long-Term Survivors: Research Initiatives (RFA) - Dr. Claudette Varricchio, Program Director, Community Oncology and Rehabilitation Branch (CORB), stated that the concept originated from the NCI Office of Cancer Survivorship (OCS) in collaboration with representatives from DCPC, Division of Cancer Treatment, Diagnosis, and Centers (DCTDC), and Division of Cancer Epidemiology and Genetics (DCEG). The purpose of the Cancer Survivorship RFA is to support research leading to a decrease in the physiologic and psychologic morbidity associated with long-term survival. Modifications to the original concept include: 1) the requirement for a multidisciplinary approach to the topic; 2) multiple endpoints; 3) collaboration across the NCI; 4) a detailed portfolio analysis; and 5) increased funding. Specific areas of interest to NCI Divisions will be delineated in the RFA as suggestions only.

The proposed budget is \$3M per year for the 5 year project period. The award mechanisms will be the R01, R29, and R03 (small grants). Investigators will select the mechanism most appropriate for the type and scope of research proposed. Totals for each mechanism will not be specified to permit the funding of the best grants over the total pool of applications.

In response to questions from Board members, the following points were made:

- Funding either too few large grants or too many small projects with insufficient budgets to make an impact should be avoided. Corrective suggestions included: (1) de-emphasizing funding projects concerned with the cost of medical care delivery as it affects survivorship; and (2) adding language in the RFA to encourage the submission of projects that educate survivors about the resources currently available to them.
- One member commented that the change from encouraging to requiring a multidisciplinary approach essentially excludes single discipline projects that might answer specific and important questions. It was noted also that the RFA should address the cooperative groups' need for a small amount of money that would enable them to maintain contact with long-term survivors of controlled clinical trials as a worthwhile investment for future research.

- When queried about opportunities for investigators to share methodologies and findings, staff explained that all RFAs are written with the requirement that applicants include in their applications funds for an annual trip to Bethesda to meet with NCI staff and other investigators funded on the same RFA.

Motion: A motion was made to approve the concept as presented. The motion was seconded and unanimously approved.

Division of Cancer Epidemiology and Genetics

Informatics Support for Breast and Colon Cancer Cooperative Family Registries (RFA/ Cooperative Agreement) - Dr. Iris Ostrom, Chief, Extramural Epidemiology and Genetics Program, DCEG, described the organization and progress to date of the Cooperative Family Registry for Breast Cancer Studies (CFRBCS) that is operating at seven sites in the United States, Canada, and Australia. Similar to the CFRBCS and due to its successful implementation, the DCEG is now funding six sites for a Cooperative Family Registry for Colon Cancer Studies (CFRCCS), for a total of 13 sites for both registries. Dr. Ostrom explained that the proposed concept was developed in response to an urgent need to provide for coordination of the central database for the Breast Cancer Registry now and for the Colon Cancer Registry in the future.

Information management functions of the proposed informatics center will include: 1) coordinating activities, 2) providing data and updates to the NCI, 3) conducting cross-site analyses, and 4) developing novel methods for capturing diverse types of necessary data such as family pedigrees. The informatics center will coordinate the provision of data and specimens to registry investigators and those outside investigators whose proposals are approved by the advisory committee and supported by the steering committees of the registries. The center will also be asked to work on the development of informatics in support of novel initiatives proposed by the registries that could be translated to the other NCI family initiatives. The NCI and DCEG will provide coordination and linkage between these activities, scrutinize confidentiality safeguards, and ensure implementation of the center with the least disruption of registry activities.

This proposed budget is \$850K for year 01. A total cost of \$4.6M is needed to support one group to develop the informatics infrastructure.

In response to questions, the following points were made:

- The definition of informatics, as used in this concept, should be clarified to avoid potential problems in implementation. Specific questions that should be addressed in writing the RFA include: 1) Is the RFA intended primarily for algorithm and software development? If so, it must be sufficiently generic and hardware and platform-independent to satisfy the requirements for NIH-funded proposals. 2) To what extent will the successful institution and their informatics development interact with some of the initiatives that are being funded? 3) What will be the accessibility of the databases? and 4) Will the other applicants

be encouraged to participate and contribute data from their registries that were not funded under this RFA? Staff responded that data standardization has been a large part of the work of the past 2 years and that a core to make data at all sites accessible is needed.

- When queried about peer review, staff explained that applications will be reviewed by an ad hoc committee convened by the Division of Extramural Activities (DEA). DCEG will not limit the ability to apply only to registry sites. Other potential applicants will receive the information needed to develop an application.
- In response to questions concerning overlap or redundancy between this initiative and the recently approved cancer genetics network, staff explained that the two are parallel and complementary efforts. The target populations and the research questions are different.
- One member expressed concern that obtaining this service through the RFA would be too slow to be useful and too costly and suggested contracting for it. Staff responded that DCEG plans to work with the registries to begin the effort within the registry system, with the help of supplemental funding. The option of contracting out an informatics support center was considered and rejected because of the difficulty of specifying in detail what the deliverables would be at this stage of development and because of the cost compared with universities and other organizations that apply.
- The RFA should have a clear statement of deliverables. An effort should be made to coordinate work on this informatics infrastructure with that of other registries and networks to identify areas of commonality that can be carried over from one project to another.

Motion: The motion was made to approve the concept for an informatics support RFA. The motion was seconded and approved, with 17 in favor, 1 opposed, and 6 abstentions.

ENHANCING DCB INTERACTIONS WITH THE SCIENTIFIC COMMUNITY - DR. FAYE AUSTIN

Dr. Faye Austin, Director, DCB, reminded members that during the DCB program review in the fall, enhancing interactions with the scientific community and encouraging feedback was identified as an issue to be addressed in 1997. Dr. Austin stated that the DCB is planning a series of activities to obtain more direct feedback from the community in terms of how program staff can best address their needs and facilitate their progress. Those activities include: 1) visits by the DCB Director to a series of regional grantee institutions to give presentations on basic research programs and opportunities and to hold small-group discussions at all levels; 2) discussions with basic research professional societies; and 3) increased electronic communication with the scientific community. The Board was asked for suggestions of other opportunities to facilitate communication and suggestions to make any of the planned or ongoing activities more effective and useful.

PROPOSED MODIFICATIONS OF NIH REVIEW AWARD POLICIES - DR. MARVIN KALT

Criteria for Peer Review of RPG Awards: Dr. Marvin Kalt, Director, Division of Extramural Activities, informed the Board that the new Research Project Grant (RPG) review criteria recommended by the Peer Review Oversight Group (PROG) are: significance, approach, innovation, investigator, and scientific environment. The new criteria will be in place for the peer review of RPG awards as of the October 1 receipt date. The criteria will not be weighted individually. The scoring will be related to the perspective of the reviewer in relation to overall integration and impact of the research in advancing the field or producing novel insights. The changes will be publicized in the NIH Guide for Grants and Contracts and on the NIH Home Page. These new approaches will be modified to apply to program project grants and other grants that are reviewed within the DEA.

Modular Awards and Applications: Dr. Kalt informed members that the proposed modular awards and applications represent a new paradigm for applicants, sponsored research administrators, grants management staff, and reviewers as part of the NIH administrative streamlining effort. Modular awards would offer applicants the option to choose from among five total direct cost grants of \$50K, \$75K, \$100K, \$125K, and \$150K. Modular applications would provide the streamlined On-Time application procedures for project applications up to \$500K. Objectives of the modular award mechanism are: (1) to offer investigators and institutions a mechanism of project support that facilitates science and simplifies administration; and (2) to offer NIH staff the opportunity to focus professional expertise on essential management requirements. Dr. Kalt briefly summarized the positive and negative aspects of implementation and noted that the question before the BSA and other groups is whether this type of competition would be useful to the applicant community.

Dr. Kalt agreed to keep the Board informed on the outcome of proposed modifications to the NIH review award policies as they are implemented.

Adjournment: The meeting was adjourned at 6:10 p.m., June 19, 1997.