DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

4th Regular Meeting
BOARD OF SCIENTIFIC ADVISORS

Minutes of Meeting
March 3-4, 1997
Building 31C, Conference Room 10
Bethesda, Maryland

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 4th regular meeting at 11:00 a. m. on March 3, 1997, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, Maryland. Dr. David Livingston, Professor of Medicine, Dana-Farber Cancer Institute, presided as Chair.

The meeting was open to the public from 11:00 a.m. to 6:30 p.m. on 3 March and 8:30 a.m. to 11:45 a.m., 4 March, for introductory remarks from the Chair, discussion of procedural matters, future BSA meeting dates, ongoing and new business, revised cancer center guidelines, present status of paylines,Program Review Group (RPG) report, and review of concepts.

BSA members present:
Dr. David M. Livingston (Chair)
Dr. Frederick R. Applebaum
Dr. Joan Brugge
Dr. Mary Beryl Daly
Dr. Virginia L. Ernster
Dr. Eric R. Fearon
Dr. E. Robert Greenberg
Dr. Waun Ki Hong
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. Sharon B. Murphy
Dr. Joseph V. Simone
Dr. Louise C. Strong
Dr. Peter K. Vogt
Dr. Daniel D. Von Hoff
Dr. Barbara L. Weber
Dr. Alice S. Whittemore
Dr. William C. Wood

BSA members absent:
Dr. Suzanne W. Fletcher
Dr. David D. Ho
Dr. Tyler Jacks
Dr. Nancy E. Mueller
Dr. Franklyn G. Prendergast
Dr. Stuart L. Schreiber
Dr. Robert C. Young

NCAB liaison:
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 4th 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 and clarified member's Request for Applications(RFAs) concept review assignments.

CONSIDERATION OF THE AUGUST MEETING MINUTES - DR. DAVID LIVINGSTON

The minutes of the November 21-22, 1996, BSA meeting were approved.

THE BSA AT SCIENTIFIC MEETINGS - BSA MEMBERS

Dr. Sharon Murphy informed the Board that the first BSA "NCI Listens" session had been held in December at the annual American Society of Hematology (ASH) meeting in Orlando, Florida. Dr.Murphy reported that the Board's discussions and interactions with ASH members were successful. Discussions dealt with funding, research opportunities, and questions on access to and support of clinical trials research in the community and institutions that are not recognized cancer centers or parts of the Community Clinical Oncology Program (CCOP).

Following a brief discussion, the following points were made:

- Issues raised during the discussion should be addressed within 30 days by the BSA subcommittee for this topic.

Results of the discussion should be provided to Board members. Primary issues include (1) clarifying the purpose of the sessions at national meetings to meeting attendees and (2) determining how to integrate information gathered at meetings for optimal dissemination to the BSA and the NCI.

- The BSA Executive Secretary should contact to BSA members to determine whether they plan to attend the upcoming American Society of Clinical Oncology (ASCO) and American Association for Cancer Research (AACR) annual meetings.

PRESENT STATUS OF PAYLINES ON NCI FUNDING POLICY - MR STEPHEN HAZEN

Mr. Stephen Hazen, Chief, Extramural Financial Data Branch, reported on changes in 1) the paylines for Research Program Grants (RPGs), 2) other major grant mechanisms, and 3) several funding polices. Mr. Hazen stated that the traditional investigator-initiated (R01) and program project (P01) grants paylines had not changed and were at the 22nd percentile and a payline of 135, respectfully. The First Award (R29) had increased from the 24th to the 27th percentile. While paylines had been established for the clinical groups and National Research Service Awards (NRSA) programs, paylines had not been set for Centers and CCOPs.

In a brief review of funding policies, he reported that there was a reduction of 13 to 11 percent from recommended levels for R01s, P01s, and initial MERIT (R37) awards. The reductions are very close to the average cost increase allowed by the National Institutes of Health's (NIH) cost management plan. Mr. Hazen informed the Board that the NIH is gradually reducing the future cost-of-living adjustments from 4 percent to 3 in 1997 and 2 in 1998. A review of efforts to consolidate K career awards was given.

Following a brief discussion, the following points were made:

- Further discussion with Drs. Klausner and Elvera Ehrenfeld, Director, Division of Research Grants, about the options available to applicants when submitting and adjusting grant applications for the reduction in cost-of-living adjustments is needed.

- A member suggested that a breakdown of extramural funding be presented to the Board at its next meeting.

REVISED CANCER CENTER PROGRAM GUIDELINES - DR ROBERT WITTES

Dr. Robert Wittes, Director, Division of Cancer Treatment, Diagnosis, and Centers, (DCTDC)presented NCI's response to the Cancer Centers Program Review Group (CCPRG) report. Dr. Wittes informed the Board that the National Cancer Advisory Board (NCAB) had approved the Institute's interim guidelines which will serve as a two year test document. At the end of the two years, the results would be presented to both the NCAB and the BSA for their assessment.

He stated that most of the CCPRG recommendations were implemented, with a few modifications to allow Centers and NCI more flexibility. For example, the NCI will follow the CCPRG's recommendation that the Cancer Center Support Grant be a science-oriented infrastructure, while continuing to provide support for outreach, education, and information dissemination to professional and lay audiences. Dr. Wittes noted that the comprehensiveness designation will be contingent on the centers achieving a fundable priority score during peer review and on the centers' willingness to list their outreach, education, and information activities in an NCI-structured and supported database. Planning grant initiatives and reasonable criteria for funding were briefly discussed. Members were informed that evaluation is focusing on the science rather than the process. It will be easier for peer review to reconcile funding recommendations with the quality of the science.

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

- Industrial support is not peer reviewed and is not included when determining research base size or the constitution of individual programs; the research base must meet certain scientific standards and be peer reviewed. The use of core resources for industry studies is reasonable if the investigators in the center have a major role. It was thought that this would promote industry/center interactions as well as emphasize the scientific contributions of the center. Members were informed that the industry relationship would be re-evaluated.

- When asked to clarify the comprehensiveness designation, members were told that the peer-review criteria for comprehensiveness, which indicates minimum research bases in three areas and interaction among them, can be assessed through the peer-review process without additional supporting information.

- The budget assessment justification will be a part of the peer-review process.

- A cap for first-time Cancer Center Support Grants (CCSG) was strongly supported by the CCPRG. Institutes should demonstrate up-front commitment to the center, that is, financial support and participation of the scientific and clinical community.

- The review would consist of three sessions each year, with a center's proposed funding plan based on the priority scores. The unknown factor in the peer-review process is the ability to attract excellent individuals to participate as reviewers, i.e., on site visits and serving on the parent committee.

INTEGRATION OF BSA AND EXTRAMURAL DIVISIONAL INTERESTS - BSA MEMBERS

Dr. Livingston and Board members discussed opportunities and possibilities for advising the Institute's leadership on extramural policy matters and for receiving and reviewing NCI information.

The following action and agenda items were identified:

- A 1-day retreat will be held at the NIH in early summer to determine how best to carry out quadrennial reviews.

- A newly formed BSA subcommittee, Drs. Joan Brugge, Caryn Lerman, Enrico Mihich, Joseph Simone and Ms. Deborah Mayer, will consider how best to carry out quadrennial reviews and will send relevant information to Dr. Livingston in advance of the June meeting.

- Board members were requested to identify major topics for discussion one month in advance of the June meeting and to provide agenda topics for a two hour lunch meeting that will be held as part of the June meeting. The lunch meeting will allow for informal discussion on topics of interest that might later be included as agenda topics for full BSA meetings. Suggested topics should be sent to Dr. Gray. Designated NCI staff would be invited to attend and provide information relevant to the topic under discussion.

- Members will receive information on Executive Committee (EC) actions relative to the Board.

- The Board discussed the need to review grant portfolios prior to concept reviews. Members emphasized the difficulty in reviewing specific portfolio topics when historical information and the amount of funds allocated by the NCI to that specific topic is not available. Portfolio analysis is needed to determine the gaps and weaknesses in new and specific research areas; to assist the NCI in providing basic and translational observations that have a clinical impact; to review what the NCI perceives as opportunities; and to determine where the portfolio stands in relationship to those opportunities.

- An agenda item at the June BSA meeting will be a discussion of determining a practical approach for gaining

familiarity with the NCI's research portfolios, particularly with regard to what information is needed to facilitate quadrennial reviews and evaluation of concepts.

- Proposed agenda items for the June meeting are 1) a review of the AIDS Malignancy Program; 2) a discussion of how the NCI manages program project grants; 3) a general discussion about creating infrastructures; 4) an update on the progress of the Cancer Control Program Review Group; and 5) the Prevention Program Review Group report.

STATUS REPORT: CANCER CONTROL PROGRAM REVIEW GROUP - DR. DAVID ABRAMS

Dr. David Abrams, Chair, Cancer Control Program Review Group, reported on the Review Group's mission, activities to date, and organization of its report. Dr. Abrams stated that the Group had heard presentations from the leadership of the Division of Cancer Prevention and Control (DCPC), as well as reports from the Division of Cancer Biology (DCB), the Division of Cancer Epidemiology and Genetics (DCEG), and DCTDC on their respective views of cancer prevention and control. Additional information had been presented by former and current NCI staff and other organizations.

Dr. Abrams asked Board members to send him any questions or topic suggestions that they felt the Program Review Group should address.

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

- Because of the shared topics between the Cancer Control Program Review Group and the Prevention Program Review Group, each report will contain some redundant and/or complementary recommendations. The Cancer Control Program Review Group will address the more behavioral social science opportunities; the more biomedically-driven opportunities will be addressed by the Prevention Program Review Group. It is estimated that the Cancer Control report will be ready sometime between midsummer and the fall.

- The Prevention and Cancer Control Program Review Groups should draft a concise definition of cancer control. The draft definition should be forwarded to the NCI leadership.

RFA CONCEPTS: PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Treatment, Diagnosis and Centers

Innovative Approaches to Diversity Generation and Smart Assay Development for Cancer Drug Discovery (RFA) - Dr. Edward Sausville, Associate Director, Developmental Therapeutics Program (DTP), in a series of slides, provided background information on the reformatted concept that had been presented originally to the BSA in November 1996. Dr. Sausville stated that the restructured RFA, a P01 grant, would be used to catalyze the formation of chemistry-biology collaborations that could generate novel structures resulting from synthetic or biosynthetic approaches in which producer organisms are actually engineered. The RFA would include a biology component capable of devising or implementing a novel assay strategy and expanding the potential diversity available to chemists and biologists. Presently, DTP manages a portfolio of approximately $80M, which includes biochemistry and pharmacology grants that are primarily devoted to standard agents or analogs and address standard therapies.

This would be a one-time RFA, costing $3.75M per year, with 5 awards for 5 years, at a total projected cost of $18.75M.

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

- Funds would be derived from the RPG pool.

- When queried about the "smart assay" aspects of the RFA, staff stated that the goal is to generate numerous structures through a variety of technologies, to act as a catalyst for the interaction of biologists and chemists, and to find drugs or molecules that can interact with significant targets.

- In response to a member's suggestion that this effort could be accomplished through private industry or the market place, staff indicated that development of linkages and liaisons between academic and corporate partners are expected. The potential for interactions between assay developers and chemists was discussed.

- In response to questions concerning the need for the NCI to bring together different groups to ensure the exchange of assays and compounds, Dr. Sausville stated that the RFA mechanism was chosen over the Cooperative Agreement mechanism to allow for more individual investigator initiatives and to allay concerns from private industry about government oversight. He noted that data would be exchanged during the 5 years.

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

Pediatric Brain Tumor Clinical Trials Consortium (Cooperative Agreement) - Dr. Malcolm Smith, Head, Pediatric Section, stated that childhood brain tumors are increasing. Dr. Smith informed the Board that the RFA would be used to establish a Pediatric Brain Tumor Clinical Trials Consortium to stimulate collaborative efforts; foster infrastructures that would conduct pilot studies and develop more effective and innovative therapies for childhood brain tumors; and take advantage of molecular tools that allow for improved diagnosis and prognosis assessment for brain tumors. The consortium would consist of 8 to 10 clinical trial member institutions. New therapies evaluated by the consortium could be integrated with future trials to be conducted in the cooperative groups. While the cooperative groups focus primarily on Phase III clinical trials, the consortium will focus on Phase I and possibly Phase II trials.

Prioritization of the clinical research agenda will be determined by a steering committee of the institutional principal investigators. A total of 80 to 100 patients per year are anticipated to be entered into 3 to 4 clinical trials. The consortium will focus on a restricted number of institutions that are multidisciplinary and have the necessary laboratory resources. Ten 5-year awards are anticipated, with a first-year funding of $3M and a total projected cost over the 5 years of $15M.

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

- In response to a member's concern regarding the funding source, Dr. Smith stated that the funds would come from the RPG pool.

- When queried whether the 1) infrastructure created through the RFA already existed in centers and was currently being used by the Pediatric Oncology Group (POG) and the Children's Cancer Group (CCG), 2) probability that the necessary organizational research expertise already exist, and 3) possibility that this RFA may result in duplication and in a loss of patient accrual to these groups, staff stated that a nationally focused effort did not exist and that the RFA would provide the necessary infrastructure for that effort.

- Several members felt that because the infrastructure was already in place, the funds might be channeled to the pediatric and cooperative groups directly, rather than issuing a new RFA. A separate mechanism might be developed to stimulate the needed research.

- A Board member questioned whether the amount requested was too small to generate interest from most major institutions and suggested funding only 4 or 5 institutions instead of 10.

- In response to a request for further clarification on what the infrastructure would support, members were told that innovative pediatric brain tumor research cannot be conducted at just one or two institutions. The infrastructure

would provide support for innovative treatment approaches at numerous institutions and is needed to evaluate the research expeditiously.

- While a member acknowledged the importance of the peer-review process for the RFA, a concern was expressed that those individuals who would provide the best review might not be eligible to participate because of conflicts.

- A member agreed that the research intent of the RFA was very important since there are very few new effective therapies. However, a different approach, with an expanded funding level, was needed for novel and innovative science and research, but not for existing lines of research that are based on past efforts.

- In response to a question concerning tissue banking, it was indicated that funds were included to set up a tissue banking infrastructure for the system.

- Pediatric oncology should be conducted through a consortium, as single institutions do not have the necessary resources and the number of patients is frequently limited. Although pediatric oncology approaches have been conservative, the gain over time has been significant. This research is important, and the RFA should be restructured.

Dr. Wittes reviewed what the Board considered to be the main concerns with the RFA: (1) There may be existing infrastructures in place and, if so, are they adequate? Will they bring groups together or is another infrastructure needed? (2) Are there new and innovative ideas out there? If ideas are lacking, will this RFA encourage and facilitate new ideas? As a result of the discussion, he suggested that the RFA concept be tabled for reconsideration and reformulation by the staff.

Motion: A motion was made to temporarily table the concept to allow reconsideration by DCTDC staff. The motion was seconded and unanimously approved.

Cooperative Trials in Diagnostic Imaging (Cooperative Agreement) - Dr. Wittes, Director, DCTDC, presented the concept, which proposes the creation of a standing cooperative group for the systematic study and facilitation of the development of technologies relevant to diagnostic imaging for cancer. Current medical, marketing, and regulatory needs justify the establishment of a more systematic and rigorous technology assessment program applied to imaging. This enterprise will consider methodologic development issues and conduct expeditious, reliable, and comprehensive evaluations of new imaging modalities. Translational research in imaging by providing a clinical evaluation infrastructure for the testing of new discoveries will be facilitated.

Historically, the NCI has been involved in this enterprise in the form of a series of studies called the Radiation Diagnostic Oncology Group (RTOG). Rather than setting up a standing group, these studies have been funded on a trial-by-trial basis, either according to the question that has been asked or what is most pressing at the time. They have accomplished the goal of providing the imaging community with a basis for doing rigorous technology assessments in the particular designated area has been accomplished. Because the current pace of progress in imaging is sufficiently substantial and anticipated to intensify in the future, it is now appropriate to consider a model that creates an infrastructure with the flexibility to go where the scientific questions are.

The core of this infrastructure will be within academic imaging departments that, based on peer-review criteria, represent the finest and most innovative departments in the country. Other institutions that have substantial accrual potential will be added. The structure of the group, made up of coordinating committees, scientific committees, and various participant institutions, will emphasize flexibility. The central core will include an operations office, a statistics and data management office, and a quality-assurance function.

The total projected cost over 5 years is $22M. One award is anticipated.

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

- In response to a concern that it may not be in the NCI's best interest to put money into the commercialization of new imaging technologies rather than into research for their development, Dr. Wittes clarified that the concept will create a structure that will enable the country to move through the regulatory process more effectively. The purpose is not commercialization as such, but to put the imaging industry on the same footing that the pharmaceutical and the biotechnology industries have had for years through agreements and other relationships with the NCI.

- When asked if there is a shortfall of translational research through these kinds of opportunities, staff explained that the liaison with industry is something that is entirely parallel with what the NCI has done with therapeutics. This cooperative agreement will substantially lower the need for industry to commit prematurely to positive development decisions in early- to mid-development cycle, before the technology is ready for the clinic. Knowledge that NCI support will be there when the product is ready to be tested clinically will encourage product development.

- When queried as to the plan for coordination of all the resources required, members were told that the group will need to be integrated with the treatment agenda for many reasons, one being that some of the outcome studies for new imaging modalities may well involve long follow-up. Ultimately, the committee and the decision making structure will incorporate the major cooperative groups.

- When asked to differentiate between the RDOG and this concept, Dr. Wittes observed that although the RDOG mechanism worked well, it had to be reinvented and recompeted every time a new study was needed. The RDOG had no lasting impact. This RFA is intended to completely replace the RDOG.

- For a new institution to become a core member, staff explained that a group will need to be established and funded from 3 to 5 years, depending on peer review. At some intermediate point, this concept will again be brought to the Board for review, and, if it is approved for recompetition, new institutions will then come into the group.

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

Division of Cancer Prevention and Control

Health Maintenance Organization Cancer Research Network (Cooperative Agreement) - Dr. Martin Brown, Applied Research Branch, Cancer Control Research Program (CCRP), informed the Board that the purpose of the concept is to expand and enhance cancer research by supporting the development of a Health Maintenance Organization (HMO) Cancer Research Network through a cooperative agreement. The goal of the concept is to formulate and implement a joint HMO/ cancer research agenda by developing standardized research methods, instruments, data formats, and systems across numerous HMOs. Dr. Brown stated that this will accomplished through establishing ongoing meetings and communication between the clinical practice and research personnel within individual HMOs, between HMOs, and between the HMO network and NCI personnel. HMO research capacity can be built and increased by sharing specific experiences and resources across the HMO members in the network. Potential research areas include a variety of psychosocial, medical, epidemiologic, and economic subjects.

The concept includes two components. One is an infrastructure component that will provide organization and structure to facilitate research across the network of HMOs. The second is a research component that would comprise a number of research projects to be conducted by collaborative multicenter HMO networks.

The proposed budget is a total of $16.4M, with two rounds of applications. The first round would begin in 1998 with a $2M budget and a 5 percent yearly inflation factor, ending in 2002. The second round would begin in 1999 with $1M, have a similar yearly inflation rate, and end in 2003. It is anticipated that there will be one to three awards.

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

- A Board member suggested that because HMOs generally have a patient turnover that approaches 25 percent per year, longitudinal follow-up of patients in a study may be problematic. In response, staff cited cancer patient turnover studies that found little turnover in large staff model, not-for-profit HMOs.

- Reimbursement in a particular HMO network would be on a flat fee basis.

- When asked to clarify the statement "sharing of specific expertise and resources" as defined in the goal of the concept, staff explained that large HMOs have a substantial autonomous research capacity. Six HMOs maintain their own research institutes as part of their HMO structure, and some have been the lead researchers on R01 and other NCI research mechanisms. Discussions with HMOs indicated that research capacity of these HMOs would be enhanced through more integrated discussions between researchers and practicing oncologists. Also, the research capacity of other HMOs with little or lesser capacity would be increased through collaborative meetings, joint work on research projects, methods, and data development.

- Concern was voiced that the funding mechanism would (1) be a disservice to the CCOPs that are working outside of HMOs; (2) provide an unintentional competitive market advantage to HMOs; and (3) put academic medical centers at a serious disadvantage. Another concern was the broadness of the research possibilities, with little focus on a specific need.

- A Board member pointed out that there are people in HMOs who were trained in academic centers and who would be interested in doing more research if the infrastructure support existed. Because university-based HMOs are becoming more common, it is important to consider whether to use nonacademic HMOs specifically. A number of applications would come from academic centers that would use their own HMOs for their study population and this may or may not accomplish the goals of the concept.

- It was suggested that this concept would encourage the standardization of data collection, variables collected, and ability to link population-based cancer registries across medical practice groups. Also, this may be regarded as more of a medical outcomes network using existing data and therefore may be less threatening to CCOPs.

- Specific guidelines must be developed to safe guard data, such as genetic findings and subsequent use in the medical marketplace or by insurance companies. Information and examples of the methods for maintaining confidentiality of data used in the Breast Cancer Surveillance Consortium, usually through individual research institutions with separate, encrypted databases for sensitive research data, were given. A series of observations including issues of legality, practicality, equity in funding, and financial resources of some HMOs were discussed.

- The use of a demonstration project was suggested, which, if successful, could escalate to a higher level of commitment in an expanded program.

- A Board member suggested that if this concept has some particular HMO model in mind, perhaps one with strong academic ties, the model needs to be better defined before the concept is approved.

Dr. Klausner summarized the purpose of the concept by explaining that it was a vehicle to begin to bring managed care into the research system. The concept would provide an opportunity not only to learn about HMOs but also to connect with them in a useful partnership.

Motion: A motion was made that Drs. Gillies McKenna, Virginia Ernster, Alice Whittemore, and Daniel Von Hoff serve as an advisory group to the DCPC Director and his staff. The objective is to modify the concept for presentation and reconsideration in June. The motion was seconded and unanimously approved.

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

Cancer Survivorship (RFA): Dr. Claudette Varricchio, Program Director, Community Oncology and Rehabilitation Branch (CORB), began the presentation by providing some background information. Dr. Varricchio stated that the concept originated from the Office of Cancer Survivorship, which was established to provide a focus for the articulation of opportunities and challenges of survivorship research and represents the collaboration of three NCI divisions, DCTDC, DCEG, and DCPC. The timeliness of this concept, to look at long-term survivorship issues, is supported by Surveillance, Epidemiology, and End Results (SEER) data that demonstrate significant improvement in the 5-year relative survival rates for many cancers. The purpose of the concept is to fund research leading to a decrease in the physiologic and psychological morbidity associated with long-term cancer survival. Programmatic responsibilities will be determined by the area of science represented in the peer-reviewed grants that are approved for funding by both R01 and R03 vehicles.

The RFA funding mechanism was chosen because the current research portfolio is limited in terms of long-term cancer survivor issues and because of the multidisciplinary aspect of such a concept. The proposed cost is $2.25M per year for 2-5 years, with a total projected cost of $10.5M. Five to six R01 awards, at an average of $300,000 per year, and five to six R03 awards, limited to 2 years and $50,000 per year are anticipated. Both the National Institute for Nursing Research (NINR) and the National Institute on Aging (NIA) have expressed an interest in collaboration on this RFA and are awaiting decisions from their respective boards concerning funding contributions. The National Institute of Mental Health (NIMH) also has been approached to determine any collaborative interest.

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

- Staff indicated that as with previous RFAs in this area, applicants will be required to budget money for annual travel to Bethesda to meet as a group, for the purpose of building up a community of survivor research investigators who can serve as a long-term source of information and peer support.

- When asked to clarify the difference between an existing RFA and this new concept, staff explained that the previous RFA only looked at adult cancer survivors and the proposed RFA will include both pediatric and adult long-term survivors, as well as survivors over 5 years beyond the end of their treatment. The previous RFA did not produce successful applications that looked at long-term survivors.

- When queried as to how the EC determined the funding level for the two mechanisms, that is, the R01 and R03, staff stated that the data and the scientific development warranted some small grants for methodological issues. The funding amount requested was based on a pragmatic approach of what would be approved.

- A P01 mechanism for funding was suggested, as it mandates a multidisciplinary nature, including questions in basic science and etiology as well as psychosocial issues. Population based registries should be encouraged. Staff replied that the P01 mechanism could be explored and explainedthat the use of that mechanism would have an impact on the approved budget.

- Following the suggestion that a program announcement (PA) mechanism should be used, the limiting features of a PA were discussed. It was noted that in this instance a PA would not meet the proposed objectives. A member pointed out that the inclusion of multiple endpoints, using multidisciplinary studies, are not normally part of a PA.

- Staff was asked to consider inviting supplements from the cooperative groups instead of creating a whole new apparatus.

- A member added that the budget appeared to be inadequate to meet the long-term endeavors required of such a

study and asked if it would be better to add the funding to existing studies.

- In response to a member's suggestion that the Division of Cancer Biology be listed as a collaborator on the RFA, staff responded that including basic biology questions in the concept is premature. The immediate concern is that the addition of basic research questions could skew the reviewers' scores and long-term survivorship questions may appear to have less merit.

- The BSA felt that sites should be looking at multiple endpoints, because so much of the cost goes into identifying and following the cohort. A request was that multiple endpoints should not only be integrated within the response to the RFA, but within the specific applications that are submitted.

- Staff was encouraged to actively involve the other Institutes because there will be multiple endpoints that effect many aspects of health; the support of other ICs would perhaps increase resources to broaden the base of this research program.

- A member indicated that this might be a good opportunity to pull together the principal investigators funded through the proposed RFA into a consortium so that a community of people involved in survivorship research can be established. This could provide a long-term source of information and peer support.

- The very large ongoing U01 to follow-up childhood cancer survivors that includes some 20,000 survivors was not included in the portfolio listing. Staff indicated that since it was funded as an investigator-initiated grant with multiple institutions, almost a consortium, it might serve as a model.

- The enormous diversity of grant applications, from molecular mechanisms of late effects to psychological impact of impotence in prostate cancer patients, was questioned. It was thought that it will be very difficult to put a panel together that can really balance and weigh the applications against one another.

- A member indicated support was needed to carry out protocol-specified, long-term follow-up. Another member stated that there were conflicting objectives about the concept. The BSA has the responsibility to defer the concept and that perhaps two concepts should be brought forward.

Subsequent discussions resulted in the following points:

- The concept should be broad-based to bring together several investigators doing molecular biology, as well as psychosocial analyses.

- Members requested that staff rework the concept into perhaps two separate proposals or rework the concept and present as one concept.

- Members would like to see some balance about where the dollars are going so that they aren't feeling like they are putting all of the money into new initiatives and short-changing those already existing, very effective mechanisms where there are disciplinary groups following the patients.

- Staff was asked to incorporate ideas from the meeting and to bring the concept back for approval in June. At that time, staff should provide an analysis of the portfolio, not only the number of grants, but the overall investment in this area of research in terms of dollars, and how this would relate to enhancing the importance of the concept, including all mechanisms.

Motion: A motion was made and seconded, based on staff's addressing the balance in emphasis and including multiple endpoints, to approve the concept. The motion was defeated with a vote of seven in favor and nine against.

In response to additional comments from the Board, the following points were made:

- It was suggested that a more global description of the different methods currently used by the NCI to fund long-term survivors is needed. This would provide a broader point-of- reference, as opposed to focusing on this specific RFA.

- It was observed that, when previous RFAs were presented and found to have problems, a subcommittee was appointed to work with the NCI staff. The point was raised that if this is done routinely, there will be a splintering of the Board as a whole. Also, this would raise the issue of micromanagement by the Board.

Motion: A motion was made that NCI staff modify the concept based on issues raised during discussion and present the concept for reconsideration in June. An analysis of the portfolio should also be given. The motion was seconded and unanimously approved.