Board of Scientific Advisors

Meeting Minutes

June 22, 2000

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 15th regular meeting at 8:30 a.m. on Thursday, June 22, 2000, in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Frederick Appelbaum, Director, Clinical Research Division, Fred Hutchinson Cancer Research Center, presided as Chair.

The meeting was open to the public from 8:30 a.m. until adjournment for introductory remarks from the Chair; a report from the Director, NCI; ongoing and new business; an update on the Mouse Model Initiative; award presentations; presentations and discussions of Request for Applications (RFAs)/Cooperative Agreement concepts; a progress report on clinical trials restructuring; and a presentation on the initial experiences of small animal imaging resource programs.

Board Members present:
Dr. Frederick R. Appelbaum (Chair)
Dr. David B. Abrams
Dr. David S. Alberts
Dr. Hoda Anton-Culver
Dr. Joan Brugge
Dr. Esther H. Chang
Dr. Mary Beryl Daly
Dr. Virginia L. Ernster
Dr. Suzanne W. Fletcher
Dr. Waun Ki Hong
Dr. Susan B. Horwitz
Dr. E. Tyler Jacks
Dr. Richard L. Schilsky
Dr. Louise C. Strong
Dr. Peter K. Vogt
Dr. Daniel Von Hoff
Dr. Barbara L. Weber
Dr. Alice S. Whittemore
Dr. William C. Wood
Dr. Robert C. Young

Board Members absent:
Dr. Caryn E. Lerman
Dr. W. Gilles McKenna
Dr. Allen I. Oliff
Dr. Franklyn G. Prendergast

Dr. Kenneth W. Kinzler
Dr. Herbert Y. Kressel
Ms. Amy S. Langer
Dr. Joan Massague
Ms. Deborah K. Mayer
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Ellen V. Sigal
Dr. Joseph V. Simone
Dr. Barbara L. Weber
Dr. Elias A. Zerhouni

NCAB Liaison:
Dr. Philip S. Schein (absent)

Others present: Members of NCI's Executive Committee (EC), NCI Staff, Members of the Extramural Community, and Press Representatives.

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I. CALL TO ORDER AND OPENING REMARKS - DR. FREDERICK APPELBAUM

Dr. Frederick Appelbaum called to order the 15th 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.

II. CONSIDERATION OF 23-24 March 2000 MEETING MINUTES - DR. FREDERICK APPELBAUM

Motion: The minutes of the 23-24 March 2000 BSA meeting were unanimously approved.

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III. REPORT OF THE DIRECTOR, NCI - DR. RICHARD KALUSNER

Dr. Richard Klausner, Director, NCI, informed members of the status of the fiscal year (FY) 2001 budget. Dr. Klausner stated that the House and Senate had completed their markups of the 2001 request. The President's budget requests a $193M NCI increase, for a total budget of $3.5B or a 5.8 percent (%) increase.

RPG Pool: Dr. Klausner stated that the FY 2000 NCI budget was $3.31B, a $420M or 14.5% increase over FY 1999. The Research Project Grant (RPG) pool represents the largest part of the budget, i. e., greater than $1.5B, allowing for 260 more grants, a total of 4,320, to be funded in FY 2000. He stated that this was the first time in the NCI's history that the non-competing obligations were more than $1B, one-half of the total NIH increase. There has also been a significant increase in submitted applications, and the average requested cost is increasing faster than the growth of NCI's budget. A committee co-chaired by Drs. Klausner and Phillip Sharp, Chair of the National Cancer Advisory Board, will discuss RPG funding policy decisions. A report will be given to the BSA at its November 2000 meeting.

Funding Issues: Dr. Klausner told members that as a result of the increased average cost per grant, approximately 730 R01 grants will be funded. A success rate of 30%, down from 32% in FY99, was projected. He noted that there has been a 5-10% increase in applications and a 10% increase in average cost. Additionally, there has been an increase in program project (P01) grant submissions and the requested budgets are 50% greater than the previous year. Because P01s have been doing unexpectedly well, it has been necessary to pay 40 new and competing P01s at 15% below recommended levels. A 60% increase in funding for new and competing P01s is required. Dr. Klausner stated that of the new grant mechanisms that had been initiated, the most prominent is the R21/R33, the Phased Innovation Award. He reported that there was a 30% increase in funding for the K Award Program. Another major increase in the number of funded K Awards is projected, i.e., from 250 last year to approximately 370 this year.

ByPass Budget: There are two new challenges in the ByPass Budget: (1) Quality Cancer Care and (2) Reducing Cancer-Related Health Disparities. He noted that the area of health disparities is gaining increasing emphasis all across the NIH. As part of the health disparities challenge and part of the need to create and

implement a strategic plan, one of the first goals has been to create a new and comprehensive plan to organize, coordinate and monitor NCI activities in health disparities research, education and health services support. He informed members that, Dr. Harold Freeman, President and CEO, Northern General Hospital in Harlem and Chair, President's Cancer Panel, has agreed to become the Associate Director of the newly created Center to Reduce Cancer Health Disparities within the Office of the Director, NCI. A draft of the 2002 ByPass Budget will be forwarded to Board members for comments.

NIH Statements: Dr. Klausner stated that the NIH had released new statements to highlight various issues. He reminded the Board that these statements were not necessarily new policies. One statement reiterates important questions regarding conflict of interest, particularly financial conflicts of interest for investigators, and potentially their institutions, relevant to clinical trials and the role of Institutional Review Boards (IRBs). Another statement addresses data safety and monitoring and the reminder that it is NIH policy that all Phase I, II, and III trials have monitoring plans that must be independent of the PI and are commensurate with risks. The plans should be submitted to the NIH and the IRB for review. A third issue is the new requirement relating to education for investigators involved in human subject studies. By 1 October 2000, all applicants and noncompeting continuations will be required to document their educational programs. He informed members that another activity relevant to clinical trials was President Clinton's announcement of the executive order stating that Medicare should pay the routine patient care costs associated with clinical trials.

Surveillance: Dr. Klausner reported that two program announcements have been made for funding opportunities linked to the 25-year mortality maps that were released last year. One of these relates to the development of methodologies and applications of geographic information systems to the study of cancer, the other calls for research in areas such as etiology and epidemiology based on hypotheses that can be raised from these maps. He stated further that he had signed a memorandum of understanding this past winter with the Centers for Disease Control and Prevention (CDC) to formally link the Surveillance Epidemiology and End Results (SEER) Program with the CDC's national monitoring system.

NIH Funding Initiatives: The NIH released several new funding initiative proposals, including a centers program, the National Programs of Excellence in Bio-computing, to create and support infrastructures at academic institutions to perform research at the interface of computer science and biomedical research. The NIH will now adopt the Phased Innovation Award mechanism for bio-computing and informatics. In addition, within the Office of the Director, NIH, a new office has been established to coordinate bioengineering, bio-imaging, and bioinformatics. A search is ongoing to find a director for this office.

NCI Center for Bioinformatics: Dr. Klausner informed members that the NCI had established a Center for Bioinformatics to address issues of funding and supporting major informatics needs. The Center is an experiment, with the principle of developing a modular structure that develops informatics tools and collects informatics expertise, reagents, and service. The Center is limited to investigators who have received funding from the following major initiatives: the Director's Challenge, the Cancer Genome Anatomy Project, the Mouse Models for Human Cancer Consortium, and the Clinical Trials System. Dr. Ken Buetow, Chief, Laboratory of Population Genetics, Division of Cancer Epidemiology and Genetics, has agreed to oversee this new Center. The Center will develop access portals allowing the nodes to: (1) communicate with each other, (2) allow the initiative cores to talk to each other and the Center, and (3) allow the cores function as access portals to the rest of the world. Module objectives will include: (1) establishing common data elements, (2) providing a data exchange infrastructure, and (3) developing electronic data interfaces so data can be shared or merged. Progress on the Center for Bioinformatics will be presented at the Board's November 2000 meeting.

In discussion, the following points were made:

- Concern was voiced that some of the new initiatives, expanded activities, and increased oversight might have a negative effect on the willingness of investigators and institutions to engage in clinical research. Larger risks now have to be assumed. Institutions are investing millions of dollars in compliance offices, clinical trials offices, and expanded IRB activities. IRBs are being asked to take increased roles in terms of monitoring, conflict of interest, and data monitoring plans.

- The central function of the Center for Bioinformatics is to adequately support the informatics needs of a limited number of initiatives as a test that this can be done successfully. The Center will be evaluated on a continual basis.
- Minimal standards for establishing criteria for accreditation of clinical research staff or faculty are needed.

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IV. ONGOING AND NEW BUSINESS - DR. FREDERICK APPELBAUM

BSA at National Meetings and Status Reports

Dr. Appelbaum announced the BSA and staff representation at ANCI Listens' sessions at 2000 annual national meetings: Cold Spring Harbor Laboratory (CSH), 16-20 August, Cold Spring Harbor, NY, Drs. Tyler Jacks (Chair), Joan Brugge, Paulette Gray, Dinah Singer, and Louise Strong, and American Society for Therapeutic Radiology and Oncology, 22-26 October, Boston, MA, Drs. W. Gilles McKenna (Chair), Richard Klausner, Herbert Kressel, Robert Wittes, and Paulette Gray. (Note: Dr. C. Norman Coleman was also a participant.)

American Association for Cancer Research (AACR). Dr. Louise Strong, Professor, Department of Experimental Pediatrics and Medical Genetics, University of Texas M.D. Anderson Cancer Center, reported that the meeting was well attended. Dr. Strong indicated that there was a general shift in the focus of questions from those more general in nature in previous years to questions related more to individual needs this year. She stated that it appears that the NCI has been doing a very effective job in communicating, particularly with new investigators and with relaying information about new award mechanisms.

Oncology Nursing Society (ONS). Ms. Deborah Mayer, Chief Medical Officer, Cancer Source.com, reported that the meeting was well-attended. She noted that problems with IRBs concerning multi-

site, multi-institutional outcome studies were becoming significant barriers to moving forward some of the research that was ongoing within and outside the ONS.

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V. UPDATE: MOUSE MODEL INITIATIVE - DR. CHERYL MARKS

Dr. Cheryl Marks, Associate Director, Office of the Director, Division of Cancer Biology (DCB), reminded Board members that the concept for the Mouse Model Initiative was approved by the BSA in March of 1998. Dr. Marks reported that the RFA was advertised in July of that year, and of the 31 applications received 18 were funded; eight of those were cooperative agreements (U01s) and one was a large intramural project on breast cancer. As of July 1, 2000, the Mouse Models of Human Cancer Consortium will be completed with the addition of a Department of Defense-funded project to model neurofibromatosis I and II in the mouse. Members were told that the Mouse Models of Human Cancer Consortium structure includes eight disease site-specific committees, which serve as bridges to other cancer research community components. Six standing committees provide resources and address issues that span all of the disease sites.

Dr. Marks stated that of the original consortium goals, the most important is to develop and implement a flexible community-based infrastructure to allow: (1) continuing validation of models, (2) setting the standards for this continuing validation, and (3) reaching out to the community so the needs for various applications of these models can be met and can be integrated with the rest of the cancer research community. Dr. Marks described the ongoing activities of the various groups and committees in the consortium, such as the Central Nervous System (CNS) Tumors Group, the Hematopoietic Malignancies Group, the Breast Cancer Models Group, the Technologies Committee, and the Preclinical Trials Committee. She noted that a mouse engineering workshop will be held at one of the AACR meetings, and a hands-on modeling laboratory will be held at Jackson Laboratories in the fall for colon cancer models.

Following a presentation of the Mouse Models of Human Cancer Consortium to the imaging community, Dr. Marks stated that the imaging community expressed interest in learning the biology of the mouse to ensure that new mouse models incorporate the kinds of tags and markers that would allow them to image these models as soon as possible. Dr. Marks noted that although the consortium includes 20 groups and about 60 or 70 collaborators, input from the rest of the community is needed. Input is gained through: (1) consensus workshops sponsored by the Consortium; (2) a recently established repository at the NCI Frederick facility; and (3) several databases that are being formulated. The Consortium also is going to link to a database at the Jackson Laboratories and is establishing links with the American Society for Hematology and the Leukemia and the Lymphoma Society. The intent is to use these Web sites for a leukemia and lymphoma vocabulary project, which the Consortium's Hematopoietic Malignancies Group is developing. A Mouse Implementation Group, which has members from the various NCI Divisions, has been established.

In discussion, the following points were made:

- The Consortium was instrumental in helping the NIH, NCI, and DuPont come to an agreement regarding the onco-mouse patent. Other pharmaceutical companies have approached the Consortium to collaborate in the development of therapeutics.
- Board members were asked to suggest effective ways to inform the community about the activities of the Mouse Models of Human Cancer Consortium. Suggestions should be sent to Dr. Cheryl Marks, DCB, NCI.

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VI. PROPOSED RFA/COOPERATIVE AGREEMENT CONCEPT - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Control and Population Sciences

Population-Based Cancer Care and Outcomes Research and Surveillance Consortium (CanCOR) (RFA/Coop.Agr.) Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS), stated that this initiative is central to a number of the challenges and opportunities that are in the ByPass Budget. The initiative will examine the dissemination of cancer treatment across different kinds of treatment settings, situations, and cancers. It will also look for ways to study health disparities in cancer care and is tied to the continuing challenge of identifying and tracking emerging cancer trends. CanCOR will be focusing on lung cancer and colorectal cancer. Studies of these cancers are particularly helpful when examining health disparities. Dr. Rimer noted that being able to compare the treatments that men and women receive is another appealing aspect.

Dr. Rachel Ballard-Barbash, Associate Director, Applied Research Program, DCCPS informed members that staff had addressed Board members concerns from the last Board meeting by: (1) clarifying the goals, (2) assuring data standardization, (3) addressing quality control and feasibility, and (4) clarifying what will comprise the core research effort. She referred to the SEER patterns of care effort to illustrate that feasibility and standardization are possible for large-scope efforts across diverse practices.

Dr. Arnold Potosky, Senior Investigator, Health Services and Economics Branch, DCCPS, further reviewed several ways in which the concept had been modified in response to concerns and suggestions raised at the previous Board meeting. Dr. Potosky stated that the concept goals had been changed to more clearly reflect the broad areas of investigations that are going to be pursued. He reviewed amendments and clarifications in the following areas: (1) prospective measurements of processes of care in newly diagnosed cancer patients, (2) the necessity of linking these processes of care to best identify what constitutes good quality of care, and (3) investigating health disparities as an NIH challenge area. Members were told that the overall aim of the CanCOR Consortium is to support innovative research to move beyond the description or the identification of disparities in treatment and care. The intent is to understand the causal factors, which may be related to variations in care, and the extent to which such variations may be contributing to poorer outcomes in vulnerable populations. To demonstrate the feasibility of this effort

and its implementation possibilities, a staged approach with two types of cancer, lung and colorectal, was adopted. Another major change is encouraging applicants to consider factors beyond cancer patient barriers to care, such as the clinical or nonclinical characteristics of patients, and to focus on provider knowledge, attitudes, practices, and health system factors that also may be importantly related to who receives high quality cancer care.

Dr. Potosky stated that CanCOR will support large prospective studies in cohorts of approximately 6,000 lung and colon cancer patients. To help ensure the standardization of data collected by this Consortium: (1) each of the five to seven research teams will collaborate with one another and will identify core measures to be collected by all the research teams; (2) a single statistical coordinating center (SCC) will cover both lung and colorectal cancer; (3) the SCC will develop data dictionaries, informatics, and software that will be used by all the research centers; and (4) a data standards committee, chaired by the PI of the SCC and including representatives from each of the research centers, will establish quality control procedures to be used in the collection of abstract medical record and survey data.

The estimated cost of CanCOR over its 5-year period is $40M . At the BSA meeting next March, plans are to propose a second RFA concept for breast and prostate cancer, which will probably have more emphasis on the study of prognostic factors beyond treatment.

In discussion, the following points were made:

- Applicants to this RFA could include academic institutions, cancer centers, state agencies, professional managed care organizations, collaborative groups, Community Clinical Oncology Programs, large health care delivery organizations, and professional societies. The concept encourages partnerships with population-based tumor registries.
- A cohort of a population is not necessarily population-based, and even if the demographics are balanced, it is not population-based if it requires hospital, patient, and physician consent for participation. One of the ways to provide population based analyses is to define in the RFA that applicants are sought who could accrue patients from

diverse socioeconomic backgrounds and minorities.
- A health disparities presentation will be given at a future Board meeting.

Motion: A motion to accept the Cooperative Agreement concept entitled "Population-Based Cancer Care Outcomes and Surveillance Consortium (CanCOR)" as written, taking into consideration the comments of the Board, was approved with one member opposed and four abstentions. Specifically, pilot projects should be included during the first year to assess feasibility; hypotheses driven research should be emphasized; study populations must be diverse; additional funds should be directed toward the statistical center; and input should be sought from patients, advocacy groups, and people at the community level.

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VII. PROGRESS REPORT: CLINICAL TRIALS RESTRUCTURING - DR. JEFFREY ABRAMS

Dr. Jeffrey Abrams, Senior Investigator, Clinical Investigations Branch, Clinical Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis, informed BSA members that some of the large projects underway in clinical trials restructuring involve redoing some of the Phase III or larger trials and developing ideas for these trials. Dr. Abrams stated that instead of the traditional cooperative group strategy meetings, state-of-the-science meetings, which are open to a broader audience, are now being held. Once ideas for Phase III trials surface, they can be submitted for a concept review. After concepts are approved and become protocols, they move into the Cancer Trials Support Unit (CTSU). It is hoped that this process will be expanded to include investigators from outside the cooperative groups who would use the CTSU as a "one-stop shop" for the management of clinical trials. An investigator participating in four or five trials led by different groups would not have to deal with the mechanisms of each group. There would be a common mechanism and, hopefully, this will reduce some of the barriers to participation. In the next step of this process, concepts are forwarded to Concept Evaluation Panels (CEPs). Traditionally these kinds of NCI reviews have been

conducted in-house within the CTEP; however, in this program the CEPs are composed of one-third NCI members and two-thirds outside members from cooperative groups, cancer centers, basic researchers, and patient advocates. Dr. Abrams noted the pilot nature of this effort and described the online review tool and scoring system that has been developed. Once the concepts are approved, and if there are available protocols, they go into the CTSU.

The state-of-the-science meetings that have been held and are planned were described. Dr. Abrams indicated that a Web site had been developed to ensure that the results and ideas from these meetings are disseminated. As of April 2000, the site has progressed from 100 to 200 hits per day to nearly 10,000 hits per day.

Dr. Abrams indicated that $31M of the approximately $60M was being used to support leadership activities, cooperative groups to help them modernize their systems, and patient reimbursements. The remainder is being used to fund a subcontract to support centralization of the databases for all cooperative groups, IRB databases, audit management, and establish uniform training and education as well as promote the trials.

In discussion, the following points were made:

- Cost per patient associated with this program is expected to be $15,000. Once this program enters a maintenance phase and the startup costs are minimized, the cost per patient will be reduced.
- New policies related to the conduct of clinical trials and clinical trial research will be presented to the Board at a future BSA meeting. Specifically, staff should address safety and data monitoring, the role of IRBs, and education/ training of principal investigators regarding adherence to clinical trial protocols.

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VIII. PROPOSED RFA CONCEPT - PRESENTED BY NCI PROGRAM STAFF

Office of the Deputy Director for Extramural Science

Innovative Cancer Complementary and Alternative Medicine (CAM) Initiative in Cancer Centers (RFA): Dr. Jeffrey White, Director, Office of Cancer Complementary and Alternative Medicine, stated that the purpose of this initiative is to encourage and support therapeutic, basic , epidemiologic, clinical prevention, palliative, and population-based cancer research within NCI-supported cancer centers. The intent is to: (1) facilitate communication and collaboration between CAM practitioners and the conventional cancer research communities; (2) support pilot projects that have the highest likelihood of being developed into successful R01 investigator-initiated applications; and (3) to assist NCI's designated Cancer Centers in building their CAM research capabilities. Dr. White informed Board members that there is a paucity of data available to indicate whether many CAM practices are efficacious or safe; despite this, there is large-scale use of many of these approaches throughout the United States, and there is every indication that use of these practices is growing among cancer patients.

The proposed RFA will fund supplements to clinical and comprehensive P30 cancer center grants. A competitive peer review will be conducted by an NCI special emphasis panel with input from the National Center for Complementary and Alternative Medicine (NCCAM). The proposed length of award is 3 years with a first year set-aside of $2M and a total cost of $6M. The projected budget will be shared equally by the NCI and NCCAM. Each application will contain up to three pilot projects, and each award would provide up to $300,000 in total costs. The initiative is limited to the clinical and comprehensive cancer centers to allow for the efficient facilitation of the establishment of collaborations between research-intensive organizations and the practitioner and academic CAM communities.

In discussion, the following points were made:

- Between one-half and two-thirds of cancer patients use complementary medicine as part of their treatment, much of

which is unregulated, untested, and of unknown benefit and risk.

- The definition of CAM needs to be clearly articulated and the initiative may be more successful if two projects, rather than three, are funded.
- In addition to a focus on CAM's safety and efficacy, applicants should be encouraged to address research in the following areas: (1) integrating CAM with conventional cancer therapy; (2) delivering CAM; (3) educating and communicating CAM therapies and their optimal use to cancer patients, survivors, and the public; (4) elucidating special approaches to psychosocial and practical aspects of CAM therapies; and (5) credentialing CAM research.

Motion: A motion to approve the letter RFA concept entitled "Innovative Cancer Complementary and Alternative Medicine Initiative in Cancer Centers" was unanimous. The concept, however, should be revised to: (1) more clearly define complementary and alternative medicine (CAM); (2) more clearly define the research questions; (3) emphasize the need for rigorous study design; (4) encourage collaborations among Cancer Centers; (5) allow two projects, rather than three; (6) clarify that NCI will submit any required investigational new drug (IND) applications; (7) emphasize integrating CAM with conventional medicine; (8) address oversight and quality control; and (9) highlight efficacy and the pathophysiology of comp

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lementary approaches to pain management.

IX. PROPOSED COOPERATIVE AGREEMENT CONCEPT - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Prevention

Collaborations on Nutritional Modulation of Genetic Pathways Leading to Cancer (Coop. Agr.): Dr. John Milner, Acting Chief, Nutritional Sciences Research Group, stated that this concept, developed by the Nutrition Science Research Group, is aimed at

establishing interdisciplinary collaboration to expand and facilitate research dealing with the precise role that diet has in the cancer process. Dr. Milner explained that the concept builds on a wealth of information from a variety of sources suggesting that diet can be a key factor regulating overall cancer risk. Data arising from epidemiological and animal studies suggest that a variety of nutrients may modify one or more phases of the cancer process. Certain nutrients may increase cancer risk in some cases, but in other circumstances, these same nutrients may decrease cancer risk. This concept is an effort to move the science of nutrition from observation to probing studies that will identify those individuals who would benefit from nutritional intervention and those individuals who might be placed at risk by dietary intervention. Genetic pathways play a key role in deciding the overall response to a nutrient. This concept will also capitalize on the special expertise and talents of the investigators and allow them to embody the newest and most innovative techniques to address the role of diet in gene regulation and genetic pathways. Four broad areas that might be appropriate to address are: (1) methylation patterns as they relate to phenotype; (2) the nutrients that modify the balance between differentiation, growth, and apoptosis; (3) antioxidants or oxidative stress; and (4) folates.

The proposed two-phased approach is a six month planning period (Phase I) and a four year collaborative project (Phase II). The P20 planning grant mechanism will be used for Phase I and the U54 grant mechanism will be used for Phase II. The intent is to fund twelve 6-month Phase I studies at $100,000 per year. The number of projects would be reduced to six during Phase II, with approximately $1.75 million awarded to each of the six projects per year. The estimated first year set-aside is $1.2 M and a total cost of $45.1M over 5 years is anticipated.

In discussion, the following points were made:

- The project might be more successful if it began on a smaller scale, i.e., build a pool of investigators who have a proven track record in the combination of necessary skills.
- The mechanism by which these investigators come together for these collaborative projects, the nature of the collaboration, and whether these grants will be P01s or R01s should be made clearer.

Motion: A motion to approve the Cooperative Agreement concept entitled "Collaborations on Nutritional Modulation of Genetic Pathways Leading to Cancer" was amended to specify that the concept be funded at half the requested amount. Approval of additional funding would be dependent on the evaluated success of the initial projects. The amendment was passed unanimously. The motion to accept the concept, as amended, was approved with one abstention.

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X. PROPOSED RFA CONCEPT - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Technologies for Comprehensive, Quantitative Protein Analysis in Human Tumors (RFA): Dr. James Jacobson, Chief, Technology Development Branch, Cancer Diagnosis Program, stated that the goal of this initiative is to stimulate the development of novel innovative technologies for the quantitation of the spectrum of proteins that are expressed in human tissues. It is anticipated that the technologies developed would provide both the identity and the relative abundance of each protein detected and analyzed. Dr. Jacobson explained that the protein technologies available for comprehensive analysis are not very quantitative and there is a real need to promote quantitative technology development. Comprehensive data about the ribonucleic acid (RNA) and protein expression are needed to determine what is happening at the functional level, particularly when trying to take these comprehensive protein analyses and organize them into cellular pathways and understand how those pathways are functioning in tumors. It is hoped that this concept will challenge the community to propose novel approaches to developing these technologies, going beyond the incremental improvements in technologies to facilitate some new approaches that may be high risk but have the potential for moving the field forward substantially.

The proposed length of award is 5 years with a first year set-aside

is $1.5M and a total cost of $6.5M for an estimated 5 R21/R33 awards.

In discussion, the following point was made:

- The issue of adequate sensitivity must be considered.

Motion: A motion to accept the RFA entitled "Technologies for Comprehensive, Quantitative Protein Analysis in Human Tumors" was unanimously approved. To pick-up the differences in proteins that are likely regulatory enzymes, sensitivity should be included.

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XI. SMALL ANIMAL IMAGING RESOURCE PROGRAMS: INITIAL EXPERIENCE C DR. DANIEL SULLIVAN

Dr. Daniel Sullivan, Associate Director, Biomedical Imaging Program, presented an update on the Small Animal Imaging Programs, noting that the results after less than one year of existence have been impressive. The purpose of the RFA was to provide: (1) an imaging resource to oncology researchers, and (2) a laboratory for the research and development of small animal imaging technologies. Dr. Sullivan said there was initial skepticism as to whether imaging researchers would be willing to devote half of their time to providing this resource to other researchers when they have to worry about their own careers and academic advancement; however, initial results suggest that this is not a major concern. In the original RFA, applicants had to have experience with small animal imaging and an existing imaging resource. It was required that they add one additional resource because the prevailing mature technology was magnetic resonance imaging (MRI) and the intent was to have other imaging technologies involved. Investigators had to provide imaging services to three oncology collaborators by the end of the first year and six by the start of the third year. Dr. Sullivan reported that a total of five MRI programs were funded from that first RFA. All are providing an aspect of radionucleid imaging, and four of the five are providing derivatives of optical technologies, including

bioluminescent imaging. The five programs are currently collaborating.

Dr. Sullivan provided Board members with examples of the work completed to date. He discussed how tumor growth data derived from these programs have been useful to certain research projects. He also noted that the imaging techniques and technologies being developed and/or perfected can detect tumors that are a submillimeter in size. These imaging technologies also allow researchers to follow tumors back to earlier time points when it is almost invisible, calculate the growth rate for all individual tumors, and acquire data that are not possible to acquire by sacrificing the animal at individual time points. Dr. Sullivan noted that the animals in these studies have to be anesthetized and ventilated, cardiac rates and respiratory rates have to be monitored, and they must IVs. He stated that there are not enough people experienced and trained in these issues, and that future workshops and training opportunities could come under the auspices of this program if it expands in the future.

Dr. Sullivan explained that the optical techniques used in this program are very effective tools, particularly in mice. It is less clear how effective they would be in humans. The RFA will be reissued next fiscal year and a requirement for training, both for professional and technical staff will be added.

In discussion, the following points were made:

- There is much interest in scaling up the MRI and positron emission tomography methodologies and making them feasible in human patients. For optical technologies, it is less clear as to whether they can be used effectively in human tumor research, diagnosis, and treatment. Additional programs to help facilitate the interaction between engineers who are working on the technologies and clinicians who could see the potential applications may be planned.
- If this program is successful, it may be expanded and modified by adding training and other components without the consent of the BSA.

Adjournment: The meeting was adjourned at 4:18 p.m. on Thursday, June 22, 2000.