Board of Scientific Advisors

Meeting Minutes

November 16-17, 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 16th regular meeting at 8:30 a.m. on Thursday, November 16, 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; ongoing and new business; reports on the NCI Center for Bioinformatics, and Informatics Issues Important to Cancer Centers; a report from the Director; presentations and discussion of Request for Applications (RFA)/Cooperative Agreement concepts; a presentation of the 5-A-Day for Better Health Program Evaluation Report; an update on the Office of Technology and Industrial Relations; and a report on the Molecular Signatures of Infectious Agents Workshop.

Board Members present:
Dr. Frederick R. Appelbaum (Chair)
Dr. David B. Abrams
Dr. David S. Alberts
Dr. Hoda Anton-Culver
Dr. Esther H. Chang
Dr. Neil J. Clendeninn
Dr. Thomas Curran
Dr. Mary Beryl Daly
Dr. Suzanne W. Fletcher
Dr. Waun Ki Hong
Dr. Susan B. Horwitz
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Franklyn G. Prendergast
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal
Dr. Joseph V. Simone
Dr. Peter K. Vogt
Dr. Alice S. Whittemore
Dr. Robert C. Young
Dr. Elias A. Zerhouni

Board Members absent:
Dr. Virginia Ernster

Dr. E. Tyler Jacks
Dr. William G. Kaelin, Jr.
Dr. Kenneth W. Kinzler
Dr. Herbert Y. Kressel
Ms. Amy S. Langer
Dr. Caryn E. Lerman
Dr. W. Gillies McKenna
Dr. Christine A. Miaskowski
Dr. Enrico Mihich
Dr. Louise C. Strong
Dr. Daniel Von Hoff
Dr. Barbara L. Weber
Dr. William C. Wood

NCAB Liaison:
TBN

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

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Division of Cancer Treatment and Diagnosis

- Tissue Resources for Cancer Research (Coop. Agr.)- Dr. Sheila Taube

- Shared Resources for Scientists without NCI-Funded Cancer Centers (RFA)- Dr. Roger Aamodt

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X. Informational Update: Office of Technology and Industrial Relations ; Dr. Carol Dahl

XI. Report on Molecular Signatures of Infectious Agents Workshop; Drs. Peter Greenwald and Paul Lambert

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

Dr. Frederick Appelbaum called to order the 16th regular meeting of the Board of Scientific Advisors (BSA or Board) and welcomed members of the Board, National Institutes of Health (NIH) and National Cancer Institute (NCI) staff, guests, and members of the public. Dr. Appelbaum introduced and welcomed new members to the Board: Dr. Neil Clendeninn, Corporate Vice President, Clinical Affairs Department, Agouron Pharmaceuticals, Inc. (Pfizer); Dr. Thomas Curran, Chairman and Member, Department of Developmental Neurobiology, St. Jude Children's Research Hospital; Dr. William Kaelin, Jr., Associate Professor, Department of Adult Oncology, Dana Farber Cancer Institute and Harvard Medical School; and Dr. Christine Miaskowski, Professor and

Chair, Department of Physiological Nursing, University of California at San Francisco.

II. CONSIDERATION OF 22 June 2000 MEETING MINUTES

Motion: The minutes of the 22 June 2000 BSA meeting were unanimously approved.

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

BSA at National Meetings

Cold Spring Harbor Laboratories (CSHL). Dr. Tyler Jacks reported good attendance and interactive discussions on a number of issues during the 18 August CSHL ANCI Listens@ session. Dr. Jacks informed members that questions related largely to funding opportunities for investigators in the transition from post-doctoral fellow to independent investigator, support of independent investigators in the early years, training experiences with first grants, and standard grant review issues. He explained that graduate, postdoctoral, and young investigators are very interested but not knowledgeable of the opportunities with respect to NCI training programs, i.e., eligibility and review criteria. Dr. Jacks emphasized the need to continue efforts to educate young investigators and their mentors about programs like the Howard Temin, K series and related awards.

Other major discussion points were calls for electronic grant submissions and for direct submission of grants to the NCI. The concern was that cancer-related research and, by extension, disease-related research might be undervalued by study sections that were not oriented properly towards the needs and issues in cancer. Dr. Jacks reported that there was more enthusiasm and increased participation in this second session and recommended that ANCI Listens@ sessions be continued at CSHL.

In subsequent discussion, the following point(s) was made:

- The difficulty that young investigators have in securing their first R01s is an issue that needs to be addressed.

American Society for Therapeutic Radiology and Oncology (ASTRO). Dr. Robert Wittes, Deputy Director for Extramural Science and Director, Division of Cancer Treatment and Diagnosis (DCTD), reported for Dr. Gillies McKenna, the session chair. Dr. Wittes informed members that the 25 October ASTRO ANCI Listens@ session was well attended by the general membership. He noted that it was a very interactive session and that questions centered on the impact of the redesign of NIH's Center for Scientific Review (CSR) study sections on funding to radiation biology; international involvement in NCI activities; training opportunities for radiation biologists to address the concern that a critical mass of young academic investigators does not exist; identifying targeted programs; and the potential combining radiation based diagnostics and therapeutics.

In subsequent discussion, the following point(s) was made:

- "NCI Listens" session staff presentations should be expanded to include information on the availability of NCI funding mechanisms appropriate for subspecialties, in a format for possible publication in appropriate scientific journals.

- Young investigators are impacted by the tension created within their institutions by the differences in funding resources provided by the K awards versus the traditional R01.

An *ad hoc* BSA subcommittee (Drs. Robert Young (Chair), Alice Whittemore, and Hoda Anton-Culver) will discuss with NCI staff strategies for communicating NCI training opportunities to young investigators and their mentors. A report will be given at the March 2001 BSA meeting.

2001 "NCI Listens" Sessions: Dr. Appelbaum announced the BSA representation at the 2001 annual national meetings: **Society**

of Behavioral Medicine (SBM) , 21-24 March, Seattle, WA, Drs. David Abrams (Chair) and Caryn Lerman; **American Association of Cancer Research (AACR)**, 24-28 March, New Orleans, LA, Drs. Susan Horwitz (Chair), Hoda Anton-Culver, and Enrico Mihich; **American Society of Preventive Oncology (ASPO)**, 11-13 March, New York, NY, Drs. Mary Daly (Chair), David Alberts, Hoda Anton-Culver and Nancy Mueller.

(**Note:** *NCI participants at the 2001 sessions are:* **SBM** - Drs. Robert Croyle, Paulette Gray and Barbara Rimer; **AACR** - Drs. Dinah Singer, Marvin Kalt, Robert Wittes and Brian Kimes; **ASPO** - Drs. Paulette Gray, Peter Greenwald and Barbara Rimer.)

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IV. NCI CENTER FOR BIOINFORMATICS - DR. KENNETH BUETOW

Dr. Kenneth Buetow, Director, NCI Center for Bioinformatics (NCICB), reviewed the mission and goals of the newly constituted Center and outlined current initiatives. Dr. Buetow stated that the Center's mission is to provide bioinformatics support and integration of NCI-supported research initiatives, most of which are presented as extraordinary research opportunities in the 2001 Bypass Budget. Its goal is to provide a plan for systematically addressing, at the NCI level, the expanding research needs of large-scale initiatives, such as the Cancer Genome Anatomy Project (CGAP), Director's Challenge, Mouse Models for Human Cancer Consortium (MMHC), and clinical trials in treatment, prevention, and diagnostics. The Center will be the NCI point of contact with respect to information technology (IT). Informatics components in the context of the NCICB were defined as including the delivery of individual productivity tools, service as a communications vehicle, data management, data analysis, and information integration.

Dr. Buetow informed members that the NCICB is focusing infrastructure development on communities that are being formed around the individual NCI-supported research initiatives, rather than on individuals or given organizations. The challenge of meeting the IT needs of such diverse communities as those

working on the genome, clinical trials, mouse models, or molecular pathology will be met by deploying the infrastructure as a series of distributed efforts where each community develops informatics in support of its own activity. Advantages to distributed informatics development are the ability to capitalize on domain expertise, balance the IT development load, identify user priorities, and permit concurrent development exchange. Communication and information exchange will be facilitated through the development of a series of worldwide web- or internet-based portals. Modern software development techniques will be used to speed up the production of needed tools and infrastructure, and an open source model will be used in development and deployment so that codes, schemas, data definitions are widely available and redistributable, thereby increasing the number of people who can develop tools. A series of domain models will be developed so that raw collection of data and information specific to the individual domains can be extracted and IT tools built across all domains to link them. The three-tier architecture for systems of the future will consist of: (1) the local objects on desktop computers, (2) a middle tier to provide an abstract model of the business process and information and to encapsulate data for back-end physical storage, and (3) a level in which peer-to-peer communication takes place over the internet and allows applications to consume information from multiple domains independent of where it was generated. The key will be to focus on boundaries and interfaces and how things fit together, not on internal details of how the individual domains are built, assuming that they will be diverse and changing.

As the NCI bioinformatics infrastructure is envisioned, the NCICB would be the center core, and provide support for the deployment of a series of individual initiative cores (modules) within which individual grantees or participants in any research initiative would interact. The modules would be interoperable and interact with a center core, which would help develop and deploy the larger IT models and act as a conduit of information between all the individual initiatives. Individual modules would have the objectives of establishing common data elements, providing data exchange infrastructure, developing electronic data interfaces, distributing architecture models, and providing an application tool chest. The NCICB role would be to facilitate the hardening of nascent tools into production applications that can be shared across individual applications, and then define and develop information exchange portals that support both the individual communities and

the larger cancer research communities that would want to consume the resources of any of the individual nodes.

In summarizing NCICB implementation progress to date, Dr. Buetow stated that achievements include (1) the deployment of an NCI-specific CGAP portal, (2) the first prototype of a MMHC consortium web site, and (3) a portal in support of the Molecular Analysis of Cancer Working Group, a component of the Director's Challenge consortium. He demonstrated how the Molecular Analysis of Cancer Web Site can be accessed to obtain information on analytic tools, reagents used in micro array experiments, protocols, and other governance and logistics information within this community. Site features that enable the research community to submit their own tools, data, and protocols, as well as for downloading the data analysis tools from the repository of information on the site were described. He noted that a tool registration form is provided and a working list of tools, data, and protocols that have been submitted by individual groups is maintained. The site also provides investigators the capacity to develop ongoing discussions associated with any one of the tools, i. e., an internet white board. Examples of component redistribution and recycling that has already begun were shown. In conclusion, Dr. Buetow emphasized that the NCICB is attempting to deploy infrastructure and integration that will be useful in support of the individual research communities.

In discussion, the following points were made:

- The Director's Challenge consortium is sponsoring a series of Gene Expression Analysis Workshops, which will include comprehensive efforts associated with evaluating tools and approaches to micro array experiments. NCICB is providing IT support and plans to utilize this type of consensus-building conference within research communities to be the curatorial forces for externally submitted tools.

- Recognizing that there is no one set of common data elements (CDEs) across all of the domains that NCI will be supporting, the Center=s goal is to facilitate the building of CDEs needed by each group to cross communicate within their initiative, then find the proper subset of elements that are critical to communicating across the units or build the interfaces that inter-translate information between the

individual domains.

- Governance will be provided through weekly meetings of Center staff and directed leaders of the initiative modules who will identify the specific requirements and needs of their individual communities.

V. REPORT OF THE DIRECTOR, NCI - DR. RICHARD KLAUSNER

Dr. Richard Klausner, Director, NCI, briefed the Board on the uncertain status of the budget and NIH's efforts to set funding policies while operating under the continuing budget resolution, pending enactment of the full appropriation. Dr. Klausner stated that the continuing resolution would provide exactly the same level of funding for FY 2001 as allocated in FY 2000. Principles and policies developed by the NIH will affect how the Institutes and Centers (ICs) begin payment of grants and contracts, as well as the level of funding for internal operations. NIH's interim funding policy permits prudent spending immediately and restoration of full funding if the full appropriation supports that level of growth. Dr. Klausner summarized NCI funding decisions as follows:

Non-competing continuation grant (Type 5) awards will be at the current level of funding, without the projected 3 percent cost management increase. New (Type 1) and competitive renewal (Type 2) grant awards will be made with the expectation that the mix will be the same as in the past. Research project grant (RPG) pool funds will be provided to maintain an average cost of award at a level no greater than the FY 2000 average. This would establish a preliminary FY 2001 competing R01 payline at the 18th percentile. The amount of funding for exceptions will be reduced to reach this level of competing support. Funding by accelerated executive review (AER) will be suspended until further notice. Sufficient funds will be assured to pay Astar@ R01 awards, i.e., first time grantees, to a success rate equivalent to the overall success rate. No specific payline for Program Project grants (P01s) is being set, and total dollars committed to P01s will be held proportional with FY 2000. Since the total number of P01 applications for FY 2001 is less than FY 2000 (110 vs. 89), the number of P01 awards projected for FY 2001 will be reduced should the terms of the current budget remain. This would equate to a success rate of

approximately 25 percent for the full fiscal year. The NCI will honor the published set aside for all RPG RFAs in effect for FY 2001. The total number of dollars allocated across all RFA competitions in FY 2001 will be equal to or less than FY 2000 levels and will not exceed 6.4 percent of the competing RPG pool.

Dr. Klausner stated that the above policies are projected to result in 640 new and competing RPG awards within the pay line and an overall RPG success rate of approximately 23 percent for FY 2001, compared with approximately 30 percent for FY 2000. The total number of grants in the RPG pool is projected to be 4,532 compared with 4,558 for FY 2000. He indicated that the NCI remains hopeful, that when the final budget is appropriated, these numbers will improve substantially. In keeping with the freeze on levels of external funds, funding for internal NCI activities will remain at FY 2000 levels. Dr. Klausner stated that decisions will be made soon about funding plans for non-RPG items, such as Cancer Centers, Special Programs of Research Excellence (SPOREs), and training. Members were assured that policy changes arising from the enactment of full appropriations will be announced and broadly disseminated.

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VI. SPECIAL TOPIC: INFORMATICS ISSUES IMPORTANT TO CANCER CENTERS - DRS. BRIAN KIMES AND MARGARET HOLMES

Dr. Brian Kimes, Director, Office of Centers, Training and Resources, Office of the Deputy Director for Extramural Science (DDES), briefly discussed the importance of framing the most appropriate, effective, and affordable role of the NCI in the development of bioinformatics in many areas of biomedical research. Dr. Kimes stated that there is the possibility for cancer centers to partner with the NCI.

Dr. Margaret Holmes, Chief, Cancer Centers Branch, DDES, presented an idea for developing informatics in NCI funded Cancer Centers. Dr. Holmes stated that there continues to be a need for a broader effort to develop informatics in the cancer centers, even

with the growth in bioinformatics research on a broad level and major ongoing NCI initiatives in cancer informatics. This would be accomplished through the cooperative effort of NCI and the centers. She informed members that Cancer Centers integrate research activities across a broad spectrum of cancer research. The Cancer Centers already have some momentum in the development of cancer research informatics and are thus in a very good position to define cancer research informatics needs and priorities. The advantages in focusing on Cancer Centers and the current uneven and, in many cases, inadequate state of informatics in the Centers were reviewed. She stated that priorities would be to develop clinical trials management systems, continue to develop Cancer Centers' role in ongoing NCI bioinformatics initiatives, and initiate population-based research informatics. An NCI-Cancer Centers Cooperative Informatics Group will be formed to define common needs, share problems and solutions, outline the parameters of an ideal clinical trials information system, and define the functions of an ideal system, i.e. set standards, specifications, and develop data models. Benefits from the cooperative effort that would accrue to the clinical trials program, cancer centers, and NCI were identified. Dr. Holmes stated that participants in a September 2000 workshop were enthusiastic about the proposal and supportive of NCI=s coordinating the activity. She informed members that a web-based discussion is planned and that NCI will work to link the Cancer Centers and the Food and Drug Administration (FDA), and other major components.

In subsequent discussion, the following point(s) was made:

- Biotech and established pharmaceutical companies, together with the FDA, should be represented in the cooperative initiative to address the needs of all groups involved in clinical trials. Commercial vendors in the information systems industry, particularly individuals from their software development departments, should be included as partners early in the discussion for their knowledge beyond the Cancer Centers.

- Informatics support for clinical trials is critical in the cancer prevention area, where there are quality control issues across the board for all Cancer Centers that could be addressed.

- The proposed initiative should be coordinated with all other NCI informatics activities, particularly those of the Cancer Therapy Evaluation Program (CTEP) and NCICB.

- If the cooperative group initiative goes forward, preliminary steps should include obtaining a cost estimate for developing an integrated informatics system in Cancer Centers and conducting a survey of the basic operating systems that already exist in the centers and their interfaces.

A concept for a cooperative NCI-Cancer Centers informatics initiative will be presented at the March 2001 meeting.

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VII. WORKING LUNCH

Request for Application (RFA)/Request for Proposal (RFP) Concepts Annual Report

Dr. Paulette Gray, Deputy Director, Division of Extramural Activities (DEA), presented a brief overview of the BSA's RFA/ RFP Concepts Annual Report, which had been compiled at the request of the Board. Dr. Gray indicated that the report summarizes BSA actions on all RFA and RFP concepts reviewed from November 1996 (the first meeting of the newly instituted BSA) to June 2000, together with the outcome of concepts that were approved and issued. Detailed information on numbers of applications received in response to solicitations, numbers and recipients of the resulting awards, project periods, funding, and dates and outcomes of RFAs that were re-released is included. She explained the organization of the report and discussed the data. A list of NCI related acronyms will be distributed at the next meeting.

After much discussion, members requested that future RFA concept presentations include: (1) a discussion of other existing RFAs or grant areas related to the proposed RFA; (2) indicate the

percentage of overall RPG activity represented by the RFA; BSA reviewers will determine the appropriate denominator for each concept; (3) include criteria or a mechanism to evaluate success, and (4) if possible, demonstrate how funded individuals have fared. Additionally, members indicated that a report of re-issued RFAs should be given during future BSA meetings.

NCAB *Ad Hoc* Working Group on Research Project Grant Pool Policies Report

Dr. Klausner explained that the NCI now has an *ad hoc* working group under the auspices of the National Cancer Advisory Board (NCAB), which meets to discuss fiscal policy issues related to the RPG pool. The group includes NCAB, BSA, and Board of Scientific Counselors (BSC) Chairs and members of the NCI Executive Committee (EC). In the ongoing forum, mathematical models of projections using many types of parameters (number of applications, size of grants, current year, and out year implications) are discussed. He stated that these discussions help the Institute set some of its fiscal policies. The group's recommendations will be presented to the BSA after a final FY 2001 budget is enacted.

Dr. Klausner commented that the working group has also been discussing the creation of a annual report that would describe how NCI funding is being distributed in the context of historic trends. He stated that the working group had recommended that the Director=s discretionary reserve be increased from its current level of 1.5 percent to 2 per cent of the NCI budget.

Board members requested a detailed presentation on the deliberations of the NCAB Working Group on RPG Pool Policies related to the FY 2001 policy agreements. The presentation should be given at the March 2001 meeting. A report of the RPG pool should be given annually to the BSA.

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VIII. PROPOSED RFA/COOPERATIVE AGREEMENT CONCEPTS - PRESENTED BY NCI PROGRAM STAFF

Division of Cancer Control and Population Sciences

Centers of Excellence in Cancer Communications Research (CECCRs) (RFA). Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS), stated that the proposed cancer communications centers were key to achieving communications objectives articulated in the FY 2002 Bypass Budget (Extraordinary Opportunity in Cancer Communication). Goals of the RFA are to (1) conduct research in the proposed centers that will lead to scientific advances in knowledge about cancer communications and their translation into practice; (2) increase the number of investigators from relevant disciplines who focus on the study of cancer communications as part of interdisciplinary teams; (3) increase the number of peer-reviewed publications in the area of communication processes; (4) generate basic research evidence to improve understanding of the processes underlying effective cancer communication; (5) produce evidence-based cancer communication tools; (6) support novel interdisciplinary research to inform medical and public health practitioners about how best to communicate; (7) increase the number of evidence-based interventions in understudied areas; and (8) train interdisciplinary investigators capable of conducting cutting-edge communications research. The proposed research would use new communications and informatics technologies to reduce cancer burden by changing behaviors of individuals, health professionals and, ultimately, communities.

Dr. Robert Croyle, Associate Director, Behavioral Research Program, DCCPS, stated that the rationale for establishing CECCRs is to: (1) ensure that evidence-based content and interventions are being developed in both traditional and new media; (2) meet the challenges imposed by the new emphasis on informed patient decision-making; (3) work in interdisciplinary teams to bring relevant old and new evidence to bear on cancer prevention, control, treatment, and survivorship; (4) apply emerging technologies to the task of tailoring and targeting communications at the individual level; (5) achieve a better understanding of basic mechanisms in health communications research to address unanswered questions across the cancer continuum; and (6) provide evidence to inform the communication-related goals of many of the extraordinary opportunities. The intent

is to use the SPORE grant mechanism (P50) to address the complexity of cancer communications; deficiencies in past research; and the need for interdisciplinary research, application of research results, and training. The centers would also accelerate the pace of discovery and application, increase the focus on communication with diverse audiences, and stimulate research in understudied communication areas. NCI's communications research portfolio currently funds only a small number of grants to study communications as a process. [Extraordinary Opportunity in Cancer Communications]

The proposed length of award for this one-time solicitation is 5 years with a first year set-aside of $10M and a total cost of $45M for an estimated 4-5 awards.

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

- The RFA concept should be modified to (1) compress the list of topics; (2) make the call for an integrative theme more explicit in terms of what sort of components might demonstrate a linkage among the ten areas; (3) incorporate the stated goals of the RFA in the final narrative; (4) expand the list of possible outcomes of applied research to include evaluation of hazards of communication and costs of the new health interventions; (5) use the phrase Ahypothesis driven@ as a modifier to distinguish the communications research proposed in the RFA from the broader term, which often refers to outreach and communication activities; (6) emphasize the interdisciplinary nature of the requirements; (7) encourage multi-institutional activities and collaborations; (8) include the ethics underlying communications and participation in clinical trials as additional research areas.

Motion. The RFA/Cooperative Agreement concept entitled "Centers of Excellence in Cancer Communications Research (CECCRs)" was approved, 25 in favor, 5 opposed and 3 abstentions, with the proviso that the goals are delineated in the RFA and other outcomes are included, such as hazards, costs, etc..

Consortium for Colorectal Cancer Screening Surveillance (COLORS) (Coop. Agr.). Dr. Carrie Klabunde, Epidemiologist, Applied Research Branch, DCCPS, stated that the proposed initiative would address the demonstrated need for a research focus on colorectal cancer (CRC) screening. The RFA would establish a COLORS consortium with four main objectives: (1) build an observational database to assess performance and practice patterns for CRC screening and diagnostic follow-up across diverse health care settings; (2) evaluate outcomes of different CRC screening approaches; (3) foster collaborative research to assess different approaches to delivering CRC screening and follow-up in community practice; and (4) develop standardized definitions, data collection instruments, and methodologies to facilitate collaborative research. The proposed consortium would be modeled after the successful Breast Cancer Surveillance Consortium, although more complex. The complexity of the CRC initiative relates to data collection from multiple screening modalities (fecal occult blood testing [FOBT], sigmoidoscopy, colonoscopy) and multiple types of providers and locations. As structured, the consortium would address a set of primary questions with core, pooled data and secondary questions through site-specific special research projects. Similar to the breast cancer consortium, the CRC consortium would provide an infrastructure to evaluate new screening technologies that are emerging.

The proposed COLORS initiative would be funded as a cooperative agreement (U01) and would be issued in two phases. In the 2-year first phase, the consortium infrastructure would be developed at 2-3 sites and a data/statistical coordinating center. The second submission, beginning in year 3, would broaden practitioners, practice sites (7-8) and patient populations represented in the consortium for the collection and analysis of data to address the research questions. [NCI's Challenge in Studying Emerging Trends in Cancer]

The estimated set-aside for the first year is $2.6M, and the estimated total for the 7-year (Phase I - 2 yrs.; Phase II - 5 yrs.) project period is $33M. An estimated 3-9 awards are anticipated.

In subsequent discussion, the following points were made:

- Smaller, more focused projects were suggested on topics such as new molecular modalities of screening, novel

technologies and imaging opportunities, or hypothesis-driven communications research.

- The lack of transition between the two phases, absence of an alternative plan if the first phase is not successful, and lack of coordination with the Division of Cancer Prevention were noted.

- The value added in the concept does not appear to justify the size of the proposed project.

- The RFA in its present form does not appear to address the problems that exist in complying with screening recommendations.

- The RFA should indicate how the proposed initiative would relate to or be integrated with research in the Prostate, Lung, Colorectal Oncology (PLCO) trial, Cancer Genetics Network, Early Detection Research Network, or other chemoprevention studies.

The concept entitled "Consortium for Colorectal Cancer Screening Surveillance (COLORS)" was withdrawn by staff. A BSA subcommittee (Drs. Suzanne Fletcher, Hoda Anton-Culver, Mary Daly, Waun Ki Hong and William Kaelin, Jr.) will work with staff to address concerns that were expressed during the discussion. The concept will be revisited at the March 2001 meeting.

Division of Cancer Treatment and Diagnosis

Tissue Resources for Cancer Research (Coop. Agr.). Dr. Sheila Taube, Associate Director, Cancer Diagnosis Program (CDP), DCTD, stated that the proposed initiative is intended to develop human tumor resources to meet critical scientific needs articulated in the 2001 Bypass Budget and identified by various NCI Program Review Groups (PRGs) and other working groups. In addition, the Specimen Resources Committee, a BSA subcommittee composed of academics and NCI scientists, at its August meeting, recommended the rapid and rational creation of resources to meet anticipated needs for the next 5-10 years. The proposed initiative

would request applications from pre-formed consortia composed of two to five cooperating institutions and would be open to the clinical cooperative groups. Collections of specimens with clinical and outcome data from all organ systems not adequately represented in existing resources, as well as specimens focused on high-incidence and high mortality tumors, would be provided by the new tissue resource.. Targeted organ sites would be lung, colorectal, lymphoma, pancreas, bladder, stomach, kidney, head and neck, brain, liver, and esophagus. Applicants would be encouraged to include fresh/frozen specimens and pre-neoplastic specimens in their plans. Information must be provided on data and specimen quality, and provisions must be made for equitable access to the resource by the research community. Individual grants would be administered by the appropriate program. [Extraordinary Opportunity in Defining the Signatures of Cancer Cells]

The estimated cost for the 5-year project period is $62.5M for 5 (R24) awards, with a first year set aside of $12.5M. Two award dates are anticipated.

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

- Consideration should be given to creating a centralized resource for the collected materials.

- Incentives to encourage participation of institutions should be included in the concept.

- Larger supplements should also be considered for the cooperative groups that already have repository informatics as well as procurement and ascertainment processes in place.

Motion. A motion to approve the RFA/Cooperative Agreement concept entitled "Tissue Resources for Cancer Research" was approved, 18 in favor, 3 opposed, and 5 abstentions.

Shared Resources for Scientists without NCI Funded Cancer Centers (RFA). Dr. Roger Aamodt, Chief, Resources Development Branch, CDP, DCTD, stated that the goal of the

proposed initiative is to provide a mechanism to support core resources for R01 investigators without NCI-funded cancer centers. The initiative continues trans-NCI efforts begun with program announcements (PARs) issued in FY 1998 and FY 1999 to grant access to specialized expertise, equipment, technologies, model systems, databases and other kinds of core resources that are provided in Cancer Center Support Grants, P01s, and SPOREs. There is no way to establish those kinds of resources in the direct budget of an R01. Applicants would be able to propose a new resource, add a new component to an existing resource, or expand an existing resource to increase its usefulness. The resources must serve scientists at the applicant institution and can support others beyond that. Applicants must obtain letters from at least six NCI-funded investigators indicating that they have plans to use the resource. Program management for the solicitation would be in the CDP in coordination with NCI programs, as appropriate. Oversight and scientific administration would reside with the appropriate program.

The estimated first year set aside is $3M for 10-15 (R24s) awards, and the estimated total for the 5 year initiative is $18 M.

Motion. A motion to approve the RFA concept entitled "Shared Resources for Scientists Without NCI-Funded Cancer Centers"was unanimously approved.

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IX. 5-A-DAY FOR BETTER HEALTH PROGRAM EVALUATION: PROGRAM REVIEW GROUP REPORT - DRS. ROBERT CROYLE AND JOHN POTTER

Dr. Robert Croyle, Associate Director, Behavioral Research Program (BRP), DCCPS, informed members that the 5-A-Day program evaluation was one of the initiatives undertaken in the newly reorganized and expanded BRP to identify gaps in the behavioral research portfolio, look at current programs, and develop priorities. Dr. Croyle stated that the other initiatives were: (1) the Tobacco Research Implementation Group, which issued the

Tobacco Research Implementation Plan; (2) an evidence report in the area of dietary intervention and behavior change, which was commissioned from the Agency for Health Care Research and Quality (AHRQ); (3) a meeting of funded principal investigators; and (4) new recruitments in the area of dietary intervention.

Dr. John Potter, Head, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, and Chair, 5-A-Day Program Evaluation Group, reminded members that the 5-A-Day for Better Health Program was initiated in 1991 as a partnership between the vegetable and fruit (V&F) industry and the NCI. The message to Americans was 'eat five or more servings of V&F daily for better health.' The multi-component program was carried out through the media, community coalitions, research, and point-of purchase initiatives. In 1999, the Program Review Group (PRG) was established to (1) evaluate the science, (2) review the implementation process and accomplishments, and (3) evaluate the degree to which the program had achieved its goals. Dr. Potter stated that the PRG was also charged with making future recommendations about the conduct of the program and articulating possible NCI roles in the overall activity. He informed members that the group evaluated the program based on implementation, process (message communication), dietary change and mediators of change, and controlled trials that were part of the Program. Conclusions based on the Group's evaluation were summarized.

The PRG's recommendations were that the NCI should: (1) continue its 5 A Day Program as a multi-faceted program to support research and increased V&F consumption; (2) continue to coordinate the Program, and ensure that the Program's director has the scientific credibility and appropriate expertise; (3) partner more closely with the U.S. Department of Agriculture (USDA) to better focus dietary guidelines and to promote research that will encourage V&F consumption; (4) partner with the Centers for Disease Control and Prevention (CDC) to develop and manage state-level 5-A-Day programs; and (5) partner with other NIH Institutes and Centers to promote research on the role of specific V&F components in lowering disease risk, promote methodologic and applied behavioral research, expand awareness of other V&F benefits, and partner with CDC and FDA to develop a surveillance plan to monitor V&F consumption. Specific recommendations in the areas of program implementation, research, and surveillance

were also presented.

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

- Biobehavioral, biological, and population research are needed to tailor effective messages and to develop a more focused approach to the various U.S. populations.

- Partnerships with weight loss groups and the restaurant industry should be considered.

- Small and carefully selected large scientific studies are needed, per the Greenwald-Cullen model. A major focus should be on mechanisms that accelerate large-scale population change.

- Report cards are needed that assess the state of progress. A SEER-type surveillance system that focuses on the mechanisms and mediators of community-level change is also needed.

- DCCPS's report card will be available in early 2001. This first-generation report card will assess penetrance of diffusion and dissemination initiatives that attempt behavioral change, based on national and community level surveillance data.

A review of the Institute's discussion at its annual planning retreat of diffusion, dissemination, application, and how that relates to NCI's research program should be presented at the March 2001 BSA meeting.

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X. INFORMATIONAL UPDATE: OFFICE OF TECHNOLOGY AND INDUSTRIAL RELATIONS - DR. CAROL DAHL

Dr. Carol Dahl, Director, Office of Technology and Industrial Relations (OTIR), described OTIR's dual mission as promoting and enabling the development of new technologies, and promoting and facilitating scientific collaborations between the NCI and the private sector. Dr. Dahl presented updates on the Industrial Relations and Technology web sites, the Innovative Molecular Analysis Technologies (IMAT) Program, the Unconventional Innovations Program (UIP), and collaborations with the National Aeronautics and Space Administration (NASA).

Industrial Relations and Technology Web Sites. The OTIR's Industrial Relations web site includes information about research resources, scientific collaboration opportunities for industry with the NCI and extramurally funded investigators, NCI-industry forums, technology transfer mechanisms, and establishing vendor relationships. The Technology web site includes information on funding opportunities, ongoing NCI programs in technology development, opportunities for bioengineering research, small business opportunities, complementary resources and programs, and NCI's Strategic Technologies Seminar Series. One popular feature of the Technology web site is the listing of all opportunities and technology development support organized in the context of Bypass Budget priorities. Both sites include information on funding and small business opportunities.

IMAT Program. The IMAT program solicits technologies that can support the analysis of the genome and the effect of environmental factors on the genome. IMAT needs throughout the NCI are addressed through support of technologies suitable for in vitro, in situ, or in vivo analysis of alterations and instabilities in genomic DNA, gene expression and gene products, proteins and their processes and interactions, and major signal transduction networks involved in cancer to identify potential targets for therapeutic and preventive interventions. The program currently consists of four Program Announcement with special Review (PARs) solicitations for developing innovative technologies for the molecular analysis of cancer and for transitioning those technologies into early validation. Funding mechanisms being used are the Phased Innovation Award and the Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) awards. There have been five rounds of funded applications, 61 Phased Innovation Awards (R21/R33) and 43 SBIRs/STTRs, which have

elicited positive feedback from the technology development communities. Award information (including abstracts) and updates on IMAT principle investigators meeting updates are on the Technology web site. The web site and meetings contribute to the overall effort to foster collaborations between technology developers to integrate complementary technologies that accelerate systems development and enhance the utility of the technological tools. Efforts are also directed toward fostering collaborations between IMAT investigators and basic and clinical cancer researchers to enhance the utility of tools for cancer research and speed the maturation and exportation of technologies into applications. Other strategies to promote collaborations are enhancing access to tissue resources, providing administrative supplements, and assisting in the identification of collaborators.

Unconventional Innovations Program (UIP). Objectives of the UIP are to support unconventional innovation in technology discovery for cancer research applications and target high-risk investments in novel technologies or quantum improvements in existing technologies. The subject area chosen for this program is how can cancerous cells be identified at the earliest stages of transformation to prevent full-blown disease. The goal is to develop technology platforms that measure, analyze, and manipulate molecular processes at an appropriate scale and in the context of the body. The UIP was approved in concept by the Board and issued as a Broad Agency Announcement in February and December 1999 and September 2000. In FY 1999, about $12M was invested in five awards for a 3-year project period; in FY 2000, approximately $8.9M was invested in four awards over 3 years. The plan is to invest up to $48M through FY 2003, depending on budget appropriations. Dr. Dahl noted that the funded projects are different, high-risk, and are anticipated to add to biological understanding, make technological improvements, lead to near-term offshoots, or evolve in terms of creating new strategies and approaches. Dr. Dahl briefly described the funded awards and noted that the information is on the UIP web site.

NASA Collaboration on Biomolecular Sensors. This initiative evolved from discussions between NASA and the NCI about the possibilities of working together to expand cancer technologies into domains where NASA may have additional expertise. As a result of a June 1999 workshop, co-sponsored by the NCI and NASA, a memorandum of understanding was executed, and the first

planning meeting of the Working Group on Biomolecular Systems and Technology was held in April 2000. In accordance with recommendations of the Working Group, a jointly supported NCI and NASA activity was initiated. A Broad Agency Announcement will be issued within the next few weeks. The projected joint investment is approximately $12M for FY 2001 for 3-year awards. The goal is to issue a second solicitation and to capitalize on the value of the program by using supplements as a tool to foster collaborations and cooperation between groups that may have complementary approaches and tools. Dr. Dahl noted that the UIP is considered complementary to this project in terms of goals and objectives and much interaction is anticipated.

In discussion, the following points were made:

- The IMAT PIs meetings should be posted on the web site as is done with the Cancer Therapy Evaluation Program's state of the science meetings.

- NCI's advanced technology programs should be disseminated throughout the cancer research community as well as to those communities not usually connected with the NCI.

- Partnerships should be sought with pharmaceutical companies so that they can run their screens with the NCI compound libraries.

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XI. REPORT ON MOLECULAR SIGNATURES OF INFECTIOUS AGENTS WORKSHOP - DRS. PETER GREENWALD AND PAUL LAMBERT

Dr. Peter Greenwald, Director, Division of Cancer Prevention (DCP), stated that sponsorship of the Workshop on Molecular Signatures of Infectious Agents (September 7-8, 2000) reflects the NCI=s strong interest in this research area because of the potential for interventions to lower cancer risk and prevent cancer.

Dr. Paul Lambert, Professor of Oncology, University of Wisconsin Medical School, and Workshop Chair, related the goal of the Workshop, defined what is meant by identifying molecular signature of infectious disease and why that is valuable, and discussed the three main Workshop findings. Dr. Lambert stated that the charge to Workshop participants was to suggest areas of future research, especially in the field of cancer screening and detection and identification of biomarkers for disease. Molecular signatures were defined as a set of biological markers that identify stage of disease (cancer), induced by an infectious agent. The value is their potential as diagnostic markers for clinical screening and targets for intervention strategies, and for understanding the basic mechanisms by which virally induced cancers arise. The major Workshop findings were: (1) molecular signatures might provide a new diagnostic tool to identify the subpopulation of exposed individuals who are likely to develop cancer as a consequence of the initial exposure to an infectious agent; (2) effective animal models will be required, specifically validated models; and (3) molecular signatures could help identify other human cancers with viral etiology.

In discussion, the following points were made:

- Additional focuses for molecular signatures research should be the role of clonality in a tissue, gene expression, viral load as a predictor, and the development of functional biomarkers of immune response (TH1/TH2). The natural history of viruses is best studied in the human host. Multi-disciplinary follow-up initiatives are needed. There is a need to address informatics challenges for both animal and human populations studies and tissue procurement needs for studying natural history and progression of disease and gene-environment interaction in a human tissue model.

- Finding immunological differences very early in viral infection could lead to finding a less toxic compound to destroy the virus than would be needed later.

Adjournment. The meeting was adjourned at 11:37 a.m. on Friday, 17 November 2000.