

Board of Scientific Advisors

Meeting Minutes

March 23-24, 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 14th regular meeting at 10:00 a.m. on Thursday, March 23, 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 10:00 a.m. until adjournment for introductory remarks from the Chair; ongoing and new business; presentations and discussion on effective communications in the new millennium; Rapid Access to Intervention Development (RAID) program update; competitive planning for imaging probe development; preliminary review of the clinical trials restructuring initiative; an overview of the 5 A Day Program Evaluation Review Group; Request for Proposals (RFP) and Request for Applications (RFA) concepts.

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. Susan B. Horwitz

Dr. Kenneth W. Kinzler

Dr. Joseph V. Simone

Dr. Peter K. Vogt

Dr. Barbara L. Weber

Dr. Alice S. Whittemore

Dr. William C. Wood

Dr. Robert C. Young

Dr. Elias A. Zerhouni

Board Members absent:

Dr. Waun Ki Hong

Dr. E. Tyler Jacks

Ms. Amy S. Langer

Dr. Joan Massague

Dr. Herbert Y. Kressel
Dr. Caryn E. Lerman
Ms. Deborah K. Mayer
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Allen I. Oliff
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal

Dr. W. Gilles McKenna
Dr. Franklyn G. Prendergast
Dr. Louise C. Strong
Dr. Daniel Von Hoff

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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Division of Cancer Control and Population Sciences

- Population-Based Cancer Care and Outcomes Research Consortium (CanCOR); Dr. Arnold Potosky

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

Dr. Frederick Appelbaum called to order the 14th 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 8-9 NOVEMBER 1999 MEETING MINUTES - DR. FREDERICK APPELBAUM

Motion: The minutes of the 8-9 November 1999 BSA meeting were unanimously approved.

III. ONGOING AND NEW BUSINESS - DR. FREDERICK APPELBAUM

BSA at National Meetings: Dr. Appelbaum announced the BSA and staff representation at "NCI Listens" sessions at 2000 annual national meetings: American Association for Cancer Research (AACR), 1- 5 April, San Francisco, CA, Drs. Louise Strong (Chair), Marvin Kalt, Richard Klausner, Enrico Mihich, Nancy Mueller, Dinah Singer, and Alice Whittemore; Oncology Nursing Society's (ONS), 11-14 May, San Antonio, TX., Ms. Deborah Mayer (Chair), Ms. Mary McCabe, Drs. Elizabeth (Lisa) Begg, Paulette Gray, and Claudette Varrichio; Cold Spring Harbor Meeting (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 (ASTRO), 22-26 October, Boston, MA, Drs. W. Gilles McKenna (Chair), Paulette Gray, Richard Klausner, and Robert Wittes.

Other Issues. An "NCI Listens" session will be scheduled at the Society of Behavioral Medicine and the Society for Research on Nicotine and Tobacco meetings which will be held jointly in Seattle, WA, 21-24 March 2001. Members representing the BSA and NCI are Drs. Caryn Lerman (Chair), David Abrams, Robert Croyle, Paulette Gray, and Barbara Rimer.

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IV. MINI-SYMPOSIA: EFFECTIVE COMMUNICATIONS IN THE NEW MILLENNIUM-DRS. BARBARA RIMER, DAVID ABRAMS, DAVID GUSTAFSON, ROBERT CROYLE, KEVIN PATRICK, AND GARY KREPS

General Overview: Health Communications Challenges

Dr. Barbara Rimer, Director, Division of Cancer Control and Population Sciences (DCCPS), presented background information on NCI's mandate in the area of health communications, the importance and current state of health communications, and challenges for the future. Dr. Rimer characterized health communications as representing the intersection of practice and research and cited a report on quality cancer care in which the National Cancer Policy Board (NCPB) called communications a central and critical component of quality cancer care. In related activities, the Institute of Medicine (IOM) has constituted a committee to look at effective health communication for diverse populations. She reminded members that the National Cancer Act in 1971 addressed issues of communications and called for a plan and program to disseminate and interpret information for the public and other audiences. Moreover, cancer communications has been cited as an extraordinary opportunity for research in the 2001 Bypass Budget, with the goal of increasing the demand for access to and use of cancer communications for consumers, patients, the public, and health professionals. Dr. Rimer cited evidence from the literature that health communications, which has been defined as the research-based crafting of messages and strategies to promote the health of individuals and communities, can reduce cancer risk, incidence, morbidity, and mortality, and improve quality of life.

Dr. Rimer reviewed the strengths and weaknesses of the spectrum of communication modalities. The findings of the Science Panel on Interactive Communications and Health were cited. She told members that tailored approaches are increasingly part of the way medicine is practiced. Advantages of technology based communications include the ability to: (1) link individual characteristics and build in expert judgments in a way that makes it possible to reach more individuals; (2) produce tailored materials on desktop computers; (3) reach people where they live and work; and (4) acknowledge the heterogeneity of people. Dr. Rimer stated that new initiatives in collaboration with NCI's Cancer Information System (CIS) will be started over the next few months. She further stated that the new communication technologies: (1) should not replace interpersonal communications but should add to the menu of possibilities by providing access, reinforcing messages, and providing alternative ways of getting information; and (2) should be made available to multicultural populations.

In discussion, the following point was made:

- The NCI, which has in the past worked primarily with the oncology community, must engage the primary care physician community if the focus is communication with patients who do not have cancer.

The Use of Proactive Health Communications to Improve the Public's Health

Dr. David Abrams, Professor and Director, Center for Behavioral and Preventive Medicine, Brown University School of Medicine, reviewed challenges and issues in making a public health impact using the new technologies, in particular, tailored communications; gave evidence-based examples of programs to indicate where the field is in terms of science and outcomes; and commented on research recommendations and opportunities for reducing the public health burden of cancer across the cancer continuum. Dr. Abrams defined tailored communications as credible information from a reliable source created for an individual based on unique information from that person, with the capability as technology advances for updating that information as the person changes. He stated that tailored communication can be combined with other interventions and it is now possible to produce what is called mass customization to reach larger audiences, but retain the essence of highly individualized and personal information. He expressed the view that individuals involved in developing health policy should look for ways tailored communications can introduce linkages between the three delivery systems (population/public health, primary care, health care specialists) to move a critical mass of people across the cancer continuum in ways that would save lives and reduce the cancer burden.

Examples of recently published research where tailored/targeted communications have been used were given. Those examples included: (1) a community-based smoking cessation program, which is successfully using tailored communications to reach rural, underserved, and disproportionately at-risk populations in North Carolina through a community health center; (2) a randomized trial studying the effect of tailored messages versus untailored messages versus no message in reducing total fat; short-term results showed a dramatic reduction in fat consumption in the tailored message arm;

and (3) a randomized screening mammography trial comparing the usual care, and tailored print communications and telephone counseling.

Dr. Abrams indicated that inter-disciplinary research challenges remain to be addressed for optimum use of the new technologies. He suggested that building the necessary infrastructure could require core research facilities in the clinical cancer centers for basic science and preclinical research, content analysis, and diagnostic variables and algorithm development. The need for an integrative, iterative process of design, empirical valuation, and evidence base building was emphasized.

He concluded that a strategic agenda should be developed, including both basic and applied research, across the cancer continuum to develop the evidence base to capitalize on advances being made in telecommunications, software, hardware design, and bandwidth to achieve real-time interactive communications tailoring.

In discussion, this point was made:

- There is a need to interdigitate the primary care provider in the overall schema because of significant human subject issues related to tailoring messages.

Computer-Mediated Health Support Systems for Diverse Audiences

Dr. David Gustafson, Professor of Industrial Engineering and Preventive Medicine, University of Wisconsin, presented an overview on the configuration and use of the Computer Health Enhancement Support System (CHESS), discussed ongoing research, and suggested key research issues to be addressed. Dr. Gustafson informed members that work on CHESS is based in the Center for Systems Research Analysis, University of Wisconsin, and involves a multidisciplinary faculty as well as people from a number of different organizations within the consortium. CHESS is an Internet-based computer system that is delivered to people in their homes. The example that Dr. Gustafson discussed is used by newly diagnosed patients for 3 months. By using the key elements of the system, patients can receive an overview of their disease,

track progress through a series of programs, keep a journal, receive help in making decisions using planning guides adapted to the individual learning styles, use the extensive resources of the reading room, ask questions and receive answers from an expert through a networking set of services, and join a discussion group or chat room.

Dr. Gustafson reported that three randomized trials and several field tests have been completed, and five additional randomized trials and two other types of research are in progress. He briefly reviewed the results of a preliminary analysis of data from the completed trials, that compared patients with access to CHES plus the Internet and patients given unguided access to the Internet. He emphasized that needs assessments are key to successful implementation of interactive health communications systems. Acceptance and use data were collected in a population study in which the goal was to install CHES in the homes of every woman over age 65 with breast cancer in a five-county area surrounding Madison. The findings were: about 75 percent of the women who were referred by participating physicians accepted the offer to go on CHES; the average use was once per day for the 3 months; 48 percent of the use occurred between 9 p.m. and 7 a.m.; and total use was not affected by age, education, race, computer experience, or gender. Data from studies measuring the impact of CHES on the quality-of-life outcome measures indicated significant improvement in patients' information competence and comfort in participation in health care, but no improvement in the level of social support. Research regarding the impact of CHES on the use of health services by a group of patients with Acquired Immune Deficiency Syndrome (AIDS) and a group of patients with heart disease showed similar trends away from higher cost care (physicians/specialists) to lower cost care (physical therapists, dieticians, rehabilitation counselors) and decreases in the number of hospital days. An analysis of use rates indicated that total use of CHES was identical in elderly Caucasians (>65 years old), younger Caucasians (<60 years old) and younger minority women, but there were differences in the use of the three services offered—analysis, information, communication—based on individual needs. Results from a study of the impact of CHES on underserved versus majority patients suggested that access to a system like CHES brings the underserved population up to the level of the adequately served in all outcomes measured.

In a summary of key findings from the above studies, he informed members that: (1) these tools have the potential to make a difference on cancer burden issues; (2) stereotypes about who will or will not use systems like CHESS do not hold, especially for the underserved and elderly; (3) systems impact data suggest an improvement in the use of health services; (4) the mechanism of effect is becoming more clear; and (5) development must be needs based. Key issues to be addressed include: a better understanding of the mechanism of effect to guide resource allocation for development of systems; the effect of using CHESS-like systems in combination with existing therapies; message tailoring to fit individual personalities while allowing users to be in control of the information they want to receive; exploiting the potential of the technology; and qualitative research to better understand the impact. In conclusion, Dr. Gustafson expressed the view that the Cancer Information Service has proven to be an excellent resource in applying earlier mechanisms of delivery to help people deal with their diagnoses and treatments and continues to work toward integrating the new information technologies in delivery systems of the future.

In discussion, the following points were made:

- Preliminary analysis of data indicates that the most intentional use of CHESS services produces the greatest improvement in outcome measures, not necessarily the longest use.
- Informed consent procedures approved by institutional review boards (IRB) have been used throughout the phases of CHESS development, and written informed consent is accompanied by an interview explaining the extent of information about the individual's online use that will be collected.

**Psychological Processes in Communications:
How Do Health Communications Work?**

Dr. Robert Croyle, Associate Director, Behavioral Research Program (BRP), DCCPS, stated that BRP's role is to ensure that NCI-supported behavioral research is fully informed by the basic behavioral sciences and advances in cognitive psychology and

neuroscience, social psychology, and medical anthropology. Research in the past tested different kinds of health communications but did not test underlying theory or provide fundamental answers to general principles of communication mechanisms. Dr. Croyle further stated that the NCI should play a major role in moving the behavioral science of communication forward so that future testing of health communication materials will be theoretically guided ensuring that the underlying processes are understood. The understanding of psychological processes (1) provide the basis for theoretically guided research and (2) accelerates progress by increasing the efficiency of research. Members were told that: (1) effecting behavior change involves more than rational decisionmaking; the interaction between cognitive and emotional processes is critical; (2) the role of the self in information processing and communication is critical because the processing mechanisms (cognitive and emotion coping) of individuals with and without cancer are different; (3) the psychological context of health communications is important because an individual's reaction to information is embedded in the context of family and cultural systems, neighborhoods, and environments of peers/health care providers.

In summary, Dr. Croyle stated that the convergence of the social and behavioral sciences with somatic science in terms of how information is processed is embodied in the principle known as parallel processing of health information. Parallel processing was described as an individual's response to information that occurs at both the conscious cognitive level and the emotional/somatic level, with the latter often driving behavior more than the former depending on the individual's position in the cancer continuum. One of the factors that underlies the effectiveness of mixed modality technologies, such as tailoring and targeting, is the ability to incorporate objective information with personal, emotionally involving information, which often drives critical decision-making. Dr. Croyle concluded with a demonstration of the parallel response model, which described the interplay between the mental representation of cancer in coping with a disease threat and the mental representation of self in coping with the threat to self that occurs in the processing of health information. He noted that, because research that decompartmentalizes the different processes underlying information processing can broadly and thoroughly inform health communication efforts, the NCI has the responsibility to try to engage cancer control and behavioral

science researchers in using the new tools and theories of basic behavioral science of communication to reduce the cancer burden through communication.

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Research Overview: Electronic Communications and Impact on the Health Care Environment

Dr. Kevin Patrick, Adjunct Professor of Public Health, San Diego State University, and Professor, University of California at San Diego, defined interactive health communication (IHC) as the interaction of an individual-consumer, patient, caregiver or professional-with or through an electronic device or communication technology to access or transmit health information or to receive guidance and support on a health-related issue (Robinson, Patrick, Eng, Gustafson; *JAMA*, 1998). Dr. Patrick stated that networked computers and the Internet are potentially the most important of the available communications technologies.

As summarized in the DHHS document *Wired for Health*, Dr. Patrick stated that health communication technologies function to relay information, promote healthy behaviors, peer information exchange and support, and self-care (to keep insurance premiums down), as well as manage the demand for health services. Benefits from the use of IHC include improved access to individualized and tailored information, broader choices for users, anonymity, immediate access to health information, social support, and the ability to scale to larger groups at minimal incremental cost. Risks include inappropriate treatment or delays in appropriate treatment, damage to patient-provider relationships, violations of privacy and confidentiality, wasted resources and delayed innovation, unintended errors, and widening gap between haves and have nots.

Dr. Patrick outlined four areas for consideration by investigators in which IHC has the potential to improve health care: (1) improved access and lower barriers, (2) cost, (3) qualitative assessments of individuals' perceptions of the health care system, and (4) objective measures of how healthy people are using IHC. In conclusion, he stated that recent research to predict the spectrum of IHC in the

future identified four categories of users-casual health seekers, worried well, newly diagnosed, and chronically ill. For these users, companies will be developing tools and technologies to serve customers representing the entire cancer spectrum.

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Implementation of the Extraordinary Communications Opportunity in Cancer

Dr. Gary Kreps, Chief, Health Communications and Informatics Research Branch, DCCPS, stated that the objective of the NCI's implementation plan for the communications extraordinary opportunity was to use health communication to reduce cancer risk, incidence, mortality, and morbidity to improve quality of life. It was designed to focus on the process of communication, new media, behavior change, and the evaluation/expansion/integration of NCI communication efforts. The goals are to accelerate reductions in the U.S. cancer burden through the use of cancer communication, integrate cancer communications into the cancer continuum, disseminate information about "best practices" to consumers and providers, and develop the infrastructure for rapid advances in knowledge about cancer communications, testing of strategies and tools, and dissemination of results to an array of audiences.

Dr. Kreps briefly described the 13 actions being undertaken to implement the NCI's Cancer Communications Plan and reported on the status of each. (1) A large-scale longitudinal survey to achieve an understanding of the American public's information-seeking practice, needs, expectancies, and problems is in the planning stage. (2) Efforts to expand interdisciplinary research are under way. (3) A concept for Centers for Excellence in Cancer Communications Research (CECCR) is being developed. (4) New strategies are being developed for integrating knowledge and packaging information. (5) Practical tool kits for the dissemination of cancer information are being developed. (6) A variety of partnerships with academia and industry are being developed. (7) Partnerships with the Centers for Disease Control and Prevention

(CDC) and other agencies and institutes are being strengthened, and jointly sponsored programs and projects are developing. (8) Work is ongoing with the academic community to develop better health communication educational programs and innovative delivery strategies for training the next generation of health communication scientists. (9) The Eleanor Nealon Extraordinary Communicators' Lecture Series has been established. (10) A wide range of new technologies are being developed to adapt cancer communications to a variety of audiences. (11) Joining Opportunities for Leading Technologies (J-O-L-T), the organization of cancer information providers and new technology companies, is being expanded. (12) In support of the DHHS Secretary's "Quality of Care" initiative, a Request for Applications (RFA) entitled "Making Quality Count for Consumers" is being jointly sponsored with the Agency for Healthcare Research and Quality (AHRQ). And (13) a new program called Pilot Research to Overcome the Digital Divide (PRODD) has been initiated with the CIS to work towards developing strategies for delivering cancer information to underserved populations.

In discussion, the following points were made:

- The development of a training program for medical students and new residents in interactive health communication should be considered by the NCI or in partnership with other federal agencies.
- One of the most important aspects of the NCI's research and service delivery in communications is the assurance of quality. Because the demand for what the NCI can produce will probably outstrip its ability to supply, future efforts may require partnerships, and the issue to address will be determining the kinds of partnerships that are acceptable.
- The transdisciplinary focus of evolving technologies may create the need for new and faster mechanisms for processing and reviewing applications and new models for reviewing the science coming from the Centers of Excellence and disseminating it to the public.
- The field of cancer communications has attracted many Small Business Innovation Research (SBIR) grants.

Disseminating and making available products already developed is an issue to be addressed; current efforts include developing an on-line catalogue as part of the DCCPS web site. Other issues are: (1) specifically marketing areas where new development is needed and (2) finding ways to expedite review and award of SBIRs.

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V. UPDATE: RAPID ACCESS TO INTERVENTION DEVELOPMENT (RAID) - Dr. EDWARD SAUSVILLE

Dr. Edward Sausville, Associate Director, Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD), presented a progress report on implementation of the RAID program, which was initiated after concept approval by the BSA in February 1998. The approved commitment was approximately \$10M/year. Dr. Sausville described RAID as a contract-research assisted pathway for the development of agents which provides extramural investigators the opportunity to participate in the preclinical drug development process. Under the RAID program, decisions to bring forward a candidate for development are vested with academic and small business community investigators. NCI preclinical contract research resources are provided to bridge the gap between a lead discovery and a drug. RAID also allows studies to occur under investigator or academic center sponsorship. Unique features of the program include: the nature of the review process, which is accomplished within 3 months of application receipt; second level review of biologicals for technical production feasibility; criteria for review (strength of hypothesis, scientific novelty, cost/benefit value); the fact that the review committee can recommend all or any of the proposed steps; and the interactive collaboration of NCI with RAID participants.

Dr. Sausville reported that, in each of the three grant cycles, between 30 and 40 applications were received and reviewed. Between 5 and 6 agents per round were approved for complete development leading to a clinical trial product, and an additional number in each round were approved for partial development. Dr.

Sausville noted that interactions with investigators and tracking of these projects has been accomplished by DTP staff through various initiatives and tools developed specifically for this purpose, including the new Web-based project tracker. He briefly discussed progress made on specific agents approved for development in RAID I (August 1998 cycle) and RAID II (February 1999). He emphasized the detailed nature of the interactions between staff, investigators, and potential contractor sites, from acceptance of applications through generation of projects and plans to coordinate the projects. Dr. Sausville also emphasized that review of proposed projects is vested with the extramural community, in line with the philosophy espoused by the 1998 DTP review regarding greater extramural involvement in the prioritization of drug development decisions. He pointed out that reviewers for RAID I and RAID II represented a range of expertise and academic institutions for both small molecules and biologicals, and that SBIR grant recipients were used as reviewers beginning with RAID III (September 1999). Preparations are under way for conducting the review of RAID IV (February 2000) applications.

Dr. Sausville then reported on actual expenditures for fiscal year (FY) 1999 and projected expenditures for FYs 2000 and 2001, informing members that the projection of \$12M in contract resources committed for FY 2000 activities is on target. In conclusion, Dr. Sausville raised the following questions for BSA consideration: (1) Should RAID continue in its current configuration? (2) How can the problems of distinguishing between "Rapid" versus research and development (R&D) projects, communication, and "backsourcing" versus "outsourcing" be addressed? (3) What are the best metrics for evaluating RAID? (4) Is the current level of industry involvement appropriate? (5) How efficient is project tracking and coordination? (6) What should the "stopping rule" be for projects? He informed members that formal review of the program and funding will occur at the next DTP program review.

In discussion, the following points were made:

- Important metrics for evaluating the program would be investigational new drug (IND) filings and the amount of science that was generated as a result of the program.
- Filing for INDs is expected to be the responsibility of the

investigator; however, Cancer Therapy Evaluation Program (CTEP) consultation and resources could be available to facilitate the process.

- RAID has succeeded in bringing the academic community and the NIH together in a unique way and could provide an opportunity for expansion to a clinical trial mechanism.
- The outcome of BSA-approved major initiatives, such as RAID and the clinical trials restructuring effort, will be discussed at a future Board meeting.

Following the Board's endorsement of continuing the Rapid Access to Intervention Development project, a committee comprised of Drs. Barbara Weber, William Wood, and Robert Young was formed to suggest to the NCI an approach to use in presenting generic funding allocations, i.e., the characterization and clustering of budgetary information, for future staff presentations to the BSA.

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VI. IMAGING UPDATE: A COMPETITIVE PROGRAM FOR IMAGING PROBE DEVELOPMENT - DRS. ELLEN FEIGAL AND DANIEL SULLIVAN

Dr. Ellen Feigal, Deputy Director, DCTD, stated that the imaging update would include an overview of: (1) NCI's goals and plans in biomedical imaging, (2) how NCI imaging initiatives fit in the context of past events and future directions, and (3) how they interact with other high-priority research. Imaging was identified as an area of extraordinary opportunity in 1997 when it was recognized that the ability to detect the molecular changes associated with a tumor cell would improve the ability to detect and stage tumors, select appropriate treatments, monitor the effectiveness of a treatment, and determine prognosis. Since then, the Biomedical Imaging Program was created and a series of imaging initiatives were conceived, developed, and implemented. An Imaging Sciences Working Group was established to advise on how to move the field forward, and subsequent interactions through

a variety of workshops, symposia, and conferences have helped define research needs and opportunities.

Dr. Feigal informed members that NCI's broad objectives in biomedical imaging, as outlined in the Bypass Budget, are being implemented through initiatives covering the spectrum of imaging in cancer. Current imaging initiatives specific to the NCI include the Mouse Models of Human Cancer Consortium, Molecular Target Drug Discovery, Interdisciplinary Research Teams for Molecular Target Assessment, the Early Detection Research Network, Cancer Genetics Network, Breast Cancer Surveillance Consortium, and an assortment of clinical trials in the cooperative groups, cancer centers, and Special Programs of Research Excellence (SPOREs). In addition, the Biomedical Imaging Program has been the center of activity for imaging initiatives across the entire NIH and jointly sponsors programs with three other Institutes and the National Library of Medicine (NLM). As a result of a 1999 forum and workshop conducted jointly with the National Electrical Manufacturing Association, the Biomedical Imaging Program has established ties with the Food and Drug Administration (FDA), Health Care Financing Administration (HCFA), and a variety of professional societies and industries to help lead the way for emerging imaging technologies to get into the marketplace.

Dr. Daniel Sullivan, Associate Director, Biomedical Imaging Program (BIP), DCTD, presented an overview of recent BIP programs in the priority areas of molecular imaging, morphologic imaging, image-guided procedures/therapies, informatics, and image interpretation. Dr. Sullivan reported on: (1) the status of BSA-approved initiatives that were solicited through RFAs, Program Announcement (PAs), and Requests for Proposals (RFPs); (2) activities like the establishment of the NCI-Industry forum as a mechanism for facilitating device development; (3) imaging research that was part of trans-NCI initiatives (CTEP feasibility trials and cooperative group confirmatory trials, CISNet, ACRIN) or are being conducted in collaborations with other federal agencies (National Science Foundation/NCI Optical Imaging RFA, NLM Visible Human Project). Members were told that areas needing future programs or expansion of current scope include feasibility trials for morphologic/molecular imaging devices; all stages of image-guided procedures/therapy devices development; informatics (informatics processing, artificial intelligence); and

image interpretation (psychophysics, outcomes assessments).

Dr. Sullivan identified imaging probe development as an area of primary interest and reported on the status of the RFAs issued for: (1) Imaging in Therapeutics (9 awards, 1 year of funding), (2) Small Animal Imaging Research Programs (SAIRP) (5 awards, 7 months of funding), and (3) Molecular Imaging Centers RFA will be reissued. An approach is being considered for integrating imaging into a DTP-sponsored PA for Molecular Target Drug Discovery. Additionally, applications in response to the small animal and molecular imaging center RFA have come in essentially equal numbers from radiology and non-radiology departments, indicating that the programs have generated interactions across departments and have brought different modalities into the field. Multidisciplinary workshops held recently have been favorably received. Dr. Sullivan emphasized the importance of multidisciplinary programs to develop the field of molecular imaging.

Dr. Sullivan informed members that the new Development of Clinical Imaging Drugs and Enhancers (DCIDE) program's objectives are to facilitate the development of promising imaging agents and provide the resources needed for successful IND application. He indicated that the lack of resources for routine studies (biodistribution, toxicology) had been identified as a barrier by academic and small or large industry investigators with ideas or actual product to develop. The process for solicitation and review of the proposed program would be similar to that for RAID. Contracts already in use for the various developmental steps in RAID would be used for DCIDE, with the addition of contract resources for steps specific to imaging agent development, such as feasibility, radiolabeling, and a translational probe library. DCIDE, however, would differ slightly from RAID in that the development and provision of agents that are useful only in animals would be considered because of their potential value to research elucidating molecular pathways. In addition, oversight would be provided by an expert committee; commitment for development of an individual agent would not be unconditional; and the program would be scalable and flexible. Estimated administrative costs (\$348,000) and program costs for approximately 7 compounds for two rounds (\$9.5M) would total \$9.848M over a 2-3 year period. The amount of money available to initiate the program would be determined in the FY 2001 budget distribution process. In

summary, Dr. Sullivan noted that imaging agents and enhancers successfully evaluated in the two-stage review would be submitted either to DCIDE for pretrial development to IND filing or, if they are ready for clinical trials, to an imaging probe library where they would be available for use in a variety of NCI programs.

In discussion the following points were made:

- The range of options for using the new imaging technologies should be expanded to include cancer prevention by combining images of early precancerous changes with tailored feedback. Novel precancerous model systems should be used.
- Expansion of the Biomedical Imaging Program should be presented at a future meeting. Data on all expenditures, including solicited and unsolicited dollars should be explained.
- Future overviews should include the financial implications of individual BSA-approved initiatives in comparison with the overall investment in broad areas.

Motions:

- A motion to request a report two years after initiation of the Development of Clinical Imaging Drugs and Enhancers (DCIDE) initiative being undertaken in the Biomedical Imaging Program was unanimously approved.
- A motion to form an ad hoc oversight committee for the DCIDE program was unanimously approved. Committee members are Drs. Herbert Kressel, John Minna, and Elias Zerhouni. The Board requested that a report be given in 2 years on agents similar to that given for the RAID program.

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PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Early Clinical Trials (Phase I or Phase II of Promising Agents (RFP). Dr. Sullivan described the concept as a follow-on to the DCIDE program. The overall purpose is to establish a contract mechanism for conducting safety and efficacy clinical trials of imaging agents, analogous to Phase I and Phase II trials for therapeutic agents. The need for this RFP is justified in that existing grant mechanisms (R21, R01) for preclinical development of imaging agents are investigator initiated and not avenues to develop compounds of specific interest. The objectives are to characterize the molecular interactions of candidate agents and validate the clinical value of the image information produced. The size of the trials will depend on the scientific question to be answered and FDA data requirements. Estimates for the concept were based on safety trials requiring approximately 10 patients, preferably at two institutions, and efficacy trials with 25 to 75 patients depending on the information needed to validate a particular biochemical or physiological endpoint, also preferably at two institutions. It was estimated that 8 safety trials might be conducted the first year, 12 or 16 safety or efficacy trials in the second and third years, and 20 efficacy trials in years 4 and 5.

A competitive application process to establish about five standing sites qualified for conducting these kinds of trials was proposed. Trials would then be assigned on a task order basis under already executed contracts, and sites would be paid on a work-delivered basis. Ad hoc sites as needed to address unique situations could be procured through either a sole source or competitive process (or a combination of both for multi-site trials). Total costs were estimated at \$1,694M in year 1, \$3,284M in year 2, \$4,873 in year 3, and \$6,091M in years 4 and 5.

In discussion, the following points were made:

- An attempt should be made to avoid funding imaging agents that other sources would fund; therefore, the language in the RFP narrative should clarify what characteristics would make an agent eligible for support. In addition, intellectual property issues should be spelled out in the RFP; and one

criterion in the RFP should be that the proposed research adds resources to the molecule candidate, which could potentially raise the net value of the project.

- Agents are needed that adequately image precancerous lesions as well as established cancers, and this mechanism for clinical trials is an outstanding opportunity in that area.

Motion: A motion to approve the RFP concept entitled "Early Clinical Trials (Phase I or Phase II) of Promising Imaging Agents" with the proviso that "Phase II efficacy trials" be renamed "Phase II accuracy trials" in the narrative was approved unanimously. Also, the text should be clarified to: (1) ask specifically for agents not likely to be developed in other venues; (2) address intellectual property issues; and (3) ask for agents that would be useful in detecting preclinical lesions.

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VIII. STATUS REPORT: PRELIMINARY REVIEW OF CLINICAL TRIALS RESTRUCTURING INITIATIVE - DR. MICHAELE CHRISTIAN

Dr. Michaele Christian, Associate Director, CTEP, DCTD, reported on the status of NCI's clinical trials restructuring plan, which had been developed by the Implementation Committee in accordance with the Armitage Committee recommendations. Dr. Christian indicated that the goal is to strengthen the clinical trials system's capacity to conduct translational research, bring the best ideas from the laboratory to clinical application, and support and strengthen the cooperative groups ability to do more developmental research. Board members were reminded that NCI's approach to restructuring was to devise pilot projects of key components of the clinical trials system to demonstrate the feasibility and effectiveness of these approaches before they were implemented on a larger scale. Major pilots for the large clinical trials program are: state-of-the-science meetings, concept evaluation panels, a Clinical Trials Support Unit (to facilitate the administration of large clinical trials), and a national network of treatment trialists. Dr. Christian

emphasized that the initial projects are part of one overall pilot approach that is limited to genito-urinary (GU) and lung cancer, and she described activities undertaken in each pilot project since the presentation of the plan.

State-of-the-Science (SOS) Meetings. The meetings were planned as national forums to identify new research opportunities in specific cancers or important gaps in the research portfolio, with multidisciplinary participation to stimulate integrated research opportunities. Lung and GU meetings were held in 1999, in line with the goal of two meetings per year in target diseases, and two more are scheduled for 2000. In addition, group chairs held two meetings in February to focus on the state of the science in acute leukemia and unanswered treatment questions in colorectal cancer. As an example of outcomes, Dr. Christian noted that as a result of the small cell lung cancer meeting, a national tumor bank has been created by collaborative efforts of the lung cancer SPOREs, Armed Forces Institute of Pathology, and CTEP; discussions are under way with interested investigators to move neuropeptide receptor antagonists into clinical trials as quickly as possible. Significant promotional activities are planned to disseminate the research opportunities and needs identified at the SOS meetings, using the Web site (<http://www.webtie.org>), direct mail, *Journal of the National Cancer Institute (JNCI)* articles, cooperative group newsletters, e-mail notices, meeting exhibits, and web-based links. implementation challenges include: (1) effectively integrating basic scientists and clinicians and keeping them focused on research opportunities rather than administrative and process questions; and (2) the logistics of coordinating frequent meetings.

Concept Evaluation Panels (CEPs). With the goal of strengthening the review of Phase III trials and increasing access of other physicians and scientists to clinical trial determinations, the panels, which have already begun to meet monthly, are composed of clinical and basic scientists, statisticians and patient advocates from the cooperative groups, cancer centers, SPOREs, Community Cancer Oncology Programs (CCOPs), and the Institute. Lung cancer CEPs have reviewed four concepts since December 1999 (one returned for revisions, and disapproved three). GU cancer CEPs have reviewed three concepts since October 1999 (two returned for revisions, and converted the third to a pilot study, which is currently under way). The monthly meetings are perceived as proceeding efficiently with help from the Internet-assisted

conference call, which makes frequent meetings possible and facilitates online reviews and scoring of concept proposals. Challenges to implementation are: (1) the need for panel members to gain experience with scoring and prioritizing processes; (2) the lack of familiarity with the new tool; and (3) software and hardware incompatibilities.

Cancer Trials Support Unit (CTSU). The contract for establishing the CTSU was awarded in September 1999 to WESTAT (subcontractors - Coalition of National Cancer Cooperative Groups, Oracle Corporation). The CTSU was designed to consolidate many of the duplicative administrative functions now carried out by the nine adult cooperative groups in the areas of protocol registration, transfer of study data, training and education, investigator credentialing and IRB databases, disbursement of funds/accounting, and auditing management. The CTSU also provides a single point of access for cross-group participation in large clinical trials and a common informatics approach. The scope of the pilot project includes: (1) participation of all adult cooperative groups from the outset; (2) cross-group enrollment beginning July 2000 in a menu of 17 clinical trials in breast, lung, prostate and GU cancers and leukemia; and (3) extension to nongroup members in years 2 and 3, with the goal of having approximately 750 sites by year 3, i.e., if the initial experience is successful. Challenges to implementation have been: (1) the coordination effort involved in integrating nine different infrastructures, policies, and procedures; and (2) the need for the CTSU to integrate its informatics systems with multiple cooperative group and CTEP systems.

Dr. Christian briefly described progress in addressing perceived obstacles and impediments associated with clinical trial participation. For example, members were told that the NCI has been involved in discussions with the NIH Office of Protection from Research Risk (OPRR) and the FDA to develop a pilot project for a central IRB, working with 30 institutions in the Cancer and Leukemia Group B (CALGB). The CTSU will provide the infrastructure to support the pilot project. She stated that in response to strong concerns expressed by the Armitage Committee and recommendations of the Implementation Group, cooperative group funding will be increased to full funding over the next several years. Dr. Christian concluded with a description of other high-priority initiatives and a review of promotional activities for

the new clinical trials initiatives, which are being planned and implemented in conjunction with the Office of Clinical Research Promotion and the Office of Cancer Communication.

In discussion, the following points were made:

- In future evaluation of the pilot CEPs, focus should be on:
(1) the opportunities available for young clinical investigators to present ideas, carry them through to publication, and get the exposure needed to succeed; (2) possible effects of the pilot projects on the relationship between cancer centers and community/regional physicians; (3) data quality from the EPP and adequate training of nongroup participants at the outset, including a certification process; (4) whether there has been a shift in type of questions that can be answered, and whether the program has given up some types of high science questions with major corroborative studies; (5) motivation of physicians for participation; and (6) using the infrastructure to reach primary care physicians for cancer prevention and control studies.
- Funding issues to be addressed are: (1) the lack of funding for behavioral science research; (2) the fact that the supplemental funding awarded to groups in recent years is very directed, with no allowances for discretionary use of the funds by group leadership; (3) adequate and stable support for pathology coordinating offices in the groups; and (4) overall adequacy of per patient reimbursement as a means to increase accrual.
- The pilot projects provide an opportunity to introduce behavioral/social science into the process of enhancing and improving clinical trials, beginning with the initial design phase.
- An update on the Interdisciplinary Research Teams for Molecular Target Assessment, formerly called Centers of Excellence, should be given at the June 2000 BSA meeting.

IX. OVERVIEW: 5 A DAY PROGRAM EVALUATION REVIEW GROUP - DR. ROBERT CROYLE

Dr. Robert Croyle, Associate Director, Behavioral Research Program, DCCPS, reviewed the history of the 5 A Day-for Better Health program and outlined the review process that has been initiated to assess the status of the program, future directions, and the NCI's role. The 5 A Day program was established through a memorandum of understanding between the NCI and the Produce for Better Health (PBH) Foundation with the goal of increasing the U.S. public's consumption of fruits and vegetables to an average of five or more servings daily. Although 5 A Day was conceived primarily as a public health education promotion campaign, it connects with NCI's research program in nutrition and behavioral sciences and is conducted jointly by the DCCPS and the Office of Cancer Communication. As the program moves from a demonstration model to a wider diffusion and dissemination model, this broad-based review group has been convened to examine the complex national partnership program and make recommendations about the NCI's future scientific contributions and role in translating behavioral interventions to public health promotion programs. The 5 A Day for Better Health Program Evaluation Review Group has been meeting since January 2000 to consider its charge to evaluate whether the original goal has been achieved, evaluate the science base, consider and advise on NCI's role in this kind of broad, nationally coordinated program, and consider implications for NCI's behavioral research priorities and future directions. A report to the BSA will be presented at the November meeting.

In discussion, the following points were made:

- The 5 A Day for Better Health Program Evaluation Program Review Group report will be presented at the November 2000 BSA meeting.
- Additional questions regarding the 5 A Day for Better Health Program Evaluation review should be submitted to the Program Review Group Co-Chairs, Drs. John Potter (BSC member) or Dr. Franklyn Prendergast (BSA member).

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

Division of Cancer Control and Population Sciences

Population-Based Cancer Care and Outcomes Research Consortium (CanCOR) (RFA/Coop. Agr.): Dr. Arnold Potosky, Senior Investigator, Health Services and Economics Branch, DCCPS, stated that the proposed RFA Cooperative Agreement would support large, longitudinal observational cohort studies conducted by a newly formed consortium on cancer treatments and outcomes in community settings. Under the joint sponsorship of the Health Services and Economics Branch and Outcomes Research Branch, DCCPS, the CanCOR infrastructure would consist of 5-7 research teams for breast and colorectal cancer. Each team would consist of a research organization partnering with a data collection organization (primarily population-based cancer registries). Dr. Potosky noted that this project would begin to address one of four objectives in NCI's quality of care research plan by strengthening the methodological and empirical research base for quality assessment in cancer. The proposed project also responds to the need for research to identify components of high-quality cancer care indicated in reports of the National Cancer Policy Board, President's Cancer Panel, and Surveillance Implementation Group. CanCOR study objectives are to: assess dissemination and effectiveness of state-of-the-art interventions; describe reasons for variations in care, with a focus on vulnerable subgroups; longitudinally assess clinical and patient-oriented health outcomes; assess contributions of patients, providers, and health systems to processes and outcomes; and evaluate new methods for assessing outcomes, data collection, and analysis.

The estimated set aside for approximately 10-14 awards (5-7 research teams) is \$9M per year, for a total of \$45M over the proposed 5-year project period.

In discussion, the following points were made:

- The RFA should include a requirement for gathering data on patient awareness of and access to clinical trials, and how patients make the decision to enter clinical trials, with the additional purpose of assessing the impact of programs like CancerNet to get some indication of utilization of that resource.
- The proposed program is important because it addresses the question of how quality care is distributed nationwide, a weak area in the cancer program. Concerns relate to structure, i.e., how to create a detailed, broad scope in-depth infrastructure (national-level cancer data system) and at the same time address hypothesis-driven research questions. A 5-year funding period is unlikely to be long enough to establish the needed infrastructure to answer prospective, long-term questions. Another concern is the feasibility of some of the proposed research. Much groundwork is needed to identify how the research is to be done.
- Issues to be addressed include: (1) attrition over the 5-year period, (2) why separate groups for each cancer site; (3) the possibility of making use of consortia already in existence (Breast Cancer Consortium, Cancer Research Network); (4) adequacy of the proposed funding; (5) the balance between investigators ideas and NCI directives; (6) getting enough information to understand the reasons why disparities exist; and (7) direction and governance in relation to data access.

Motion: A motion to withdraw the RFA concept entitled "Population-based Cancer Care and Outcomes Research Consortium (CanCOR)" was approved unanimously. A BSA subcommittee (Drs. Hoda Anton-Culver, Mary Daly, Virginia Ernster, Suzanne Fletcher and Caryn Lerman) will work with program staff to address concerns expressed during the discussion. The concept will be revisited at the June 2000 BSA meeting.

Adjournment: The meeting was adjourned at 12:01 p.m. on Friday, March 24, 2000.