Board of Scientific Advisors

Meeting Minutes

June 24-25, 2002

Conference Room 10, C Wing, Building 31
Bethesda, Maryland 20892

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Meeting Minutes

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The Board of Scientific Advisors (BSA or Board), National Cancer Institute (NCI), convened for its 21st regular meeting on Monday, June 24, 2002, 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 5:30 p.m. on 24 June for opening remarks from the Chairman; the NCI Director's report; the NCI Congressional Relations report; ongoing and new business; award presentations; the Rapid Access to Intervention Development (RAID) Program progress report; the NIGMS/NCI Construction of New Beamlines for Macromolecular X-Ray Crystallography report; the Marketing of NCI Training and Career Development presentation; a Working Lunch; the Serum Proteomic Patterns report; Request for Applications (RFAs) and Cooperative Agreement (Coop. Agr.) concepts presentations; and from 9:00 a.m. on 25 June until adjournment for the Expansion of Biomedical Imaging Program report; the Public/Private Partnerships report; and the American College of Radiology Imaging Network (ACRIN) update.

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. Tyler Jacks
Dr. William G. Kaelin, Jr.
Dr. Herbert Y. Kressel
Ms. Amy S. Langer
Dr. Christine A. Miaskowski
Dr. Enrico Mihich
Dr. John D. Minna
Dr. Nancy E. Mueller
Dr. Richard L. Schilsky
Dr. Ellen V. Sigal
Dr. Louise C. Strong
Dr. Peter K. Vogt
Dr. Barbara L. Weber
Dr. William C. Wood
Dr. Robert C. Young

Board Members absent:
Dr. Waun Ki Hong
Dr. Susan B. Horwitz
Dr. Kenneth W. Kinzler
Dr. Caryn E. Lerman
Dr. W. Gillies McKenna
Dr. Franklyn G. Prendergast
Dr. Joseph V. Simone
Dr. Daniel D. Von Hoff
Dr. Alice S. Whittemore

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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XIII. Expansion of the Biomedical Imaging Program; Dr. Daniel Sullivan
XIV. Public/Private Partnerships: Overcoming the Barriers to Early Clinical Trials; Dr. Ellen Feigal
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I. CALL TO ORDER AND OPENING REMARKS - DR. FREDERICK APPELBAUM

Dr. Appelbaum called to order the 21st regular meeting of the BSA and welcomed members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Appelbaum reminded Board members of the conflict-of-interest regulations. Members were also reminded of future Board meeting dates. The 2004 meeting dates were confirmed.

II. CONSIDERATION OF THE 25 MARCH 2002 MEETING MINUTES - DR. FREDERICK APPELBAUM

Motion: The minutes of the 25 March 2002 meeting were unanimously approved.

BSA at National Meetings

III. REPORT OF THE DIRECTOR, NCI-DR. ANDREW von ESCHENBACH

Dr. von Eschenbach reported that emphasis, during his first few monthes, has been on creating relationships, establishing lines of communication, and reviewing the organizational structure of his office and the Institute's management team. He informed members that given the availability of talent and the current evolution of new knowledge, an opportunity exists to fundamentally change the paradigm of oncology based on integrating scientific discovery, development of interventions, and delivery of those interventions. The NCI's job, he noted, is to eliminate death and suffering from cancer.

National Lung Screening Trial (NLST). The Board was informed that the launching of the recently approved NLST had been postponed to ensure that: 1) there were no fatal flaws in the design; 2) partners to support financial and recruitment demands of the project could be found; and 3) the opportunity to capture information on the biology of lung cancer was appropriately integrated and coordinated with the study. He stated that administrative changes in the study design were made to accelerate accrual. Additionally, stringent principles are in place to ensure that interventions based on the detection of abnormal findings are followed uniformly, because those interventions will have a profound impact on the outcome of mortality. Dr. von Eschenbach reported that the American Cancer Society (ACS) is committed to providing $1M per year for 5 years and is also expected to aggressively promote the study to help reach accrual targets as rapidly as possible. The American Legacy Foundation may also make a financial contribution, and other partnerships are being explored.

Foundation for the National Institutes of Health (FNIH). Another area of potential partnering is working with pharmaceutical companies to examine barriers to clinical trials accession and create

an opportunity for supplements to Centers to increase accession. One potential avenue for supporting such a public-private partnership, i.e., contributions to the NCI Gift Fund, was not considered appropriate. Using the FNIH model, the NCI will allocate $1.5M per year for 2 years and five pharmaceutical firms will jointly contribute $1.5M per year. This will create a pool of $3M each year for supplemental awards to help Centers focus on barriers related to clinical research. Dr. von Eschenbach indicated that this useful partnership activity resulted from combined efforts of the BSA leadership and the NCI staff.

Ovarian Cancer Diagnostic Test. The development of a diagnostic test for ovarian cancer based on protein profiles has resulted from collaborations among the NCI intramural research program, the Food and Drug Administration (FDA), and Correlogic, a private software firm. Dr. von Eschenbach informed members that the FDA will provide regulatory guidance for the development of clinical applications, and NCI will be the reference laboratory that will collect specimens from around the country. He noted that this collaborative effort will reduce to 2 years the usual 5-year timeframe for bringing this type of technology to market.

NIH/DHHS Cofunded Activities. Members were told that, Dr. Elias Zerhouni, a former BSA member, had been appointed as the new NIH Director. Dr. von Eschenbach noted that Dr. Zerhouni brings a wealth of knowledge and insight to the NIH and will bring a new perspective to efforts to create partnerships and collaborations among NIH components. He noted that the NCI has 192 grants cofunded with other Institutes and, is collaborating with the National Institute of Allergy and Infectious Disease (NIAID) to create a vaccine facility at the Frederick campus. Plans are to work with the Army to rebuild and upgrade the Frederick facility. Dr. von Eschenbach said he continues to explore collaborations with the Human Genome Institute and the new National Institute for Biomedical Imaging and Biotechnology (NIBIB). Additionally, collaborations among the NCI, the Centers for Disease Control and Prevention (CDC), the ACS, and the National Governors Conference are to ensure that by 2003 cancer plans are established in each state's department of health.

Budget: Dr. von Eschenbach informed members that of the $4.2B in FY2002, nearly half will be obligated to Research Project Grants (RPGs). The anticipated 4,600 RPGs include approximately 1,200

new competing awards and represent an approximate 10 percent increase over the previous year. He stated that the payline had been increased from the 21st to the 22nd percentile. Of the estimated 816 R01 grants, 195 will be first-time R01 grantees.

Because the NCI has significant commitments to Cancer Centers and Specialized Programs of Research Excellence (SPOREs), in that these programmatic areas are so critical to translational efforts, the Institute will invest appropriately in these mechanisms. Additionally, the intent is to coordinate relationships among Center and SPORE grantees, the grantees and the NCI, and the grantees, NCI, and community networks for cancer care delivery. To do that, a working group has been established to look at a number of issues related to Centers and SPOREs and to make recommendations for future growth.

Regarding grants transferred to the NIBIB, members were told that in FY2002, the NCI provided $21M (approximately 61 grants). In FY2003, an additional $60M will go to NIBIB (122 grants and $25M). NCI transfers represent 40 percent of the NIBIB portfolio. He noted that collaborating with the NIBIB is an exciting opportunity, but care is being taken to ensure that the transfers do not adversely affect the work of NCI principal investigators.

Although the NCI budget is expected to increase from $4.2B to $4.7B in FY2003, the NIH increase for FY2004 is anticipated to be at the 2.2 percent level. The NCI is working on models of various budget scenarios to evaluate the Institute's ability to protect its payline and continue to fund competing awards, especially those for new investigators and for innovative research.

Organization: Dr. von Eschenbach announced: 1) that Dr. Alan Rabson, Deputy Director, NCI, was chairing a search committee to select a new Director for the Division of Cancer Treatment and Diagnosis (DCTD); and 2) the retirement of Ms. Martha Fewell, secretary to the NCI Director. He acknowledged Ms. Fewell's gracious willingness to postpone retirement in order to help him make the transition into his position.

In discussion, the following point was made:

- The proposed Center for Translational Research mentioned

in the pending legislation introduced by Senator Feinstein to renew the National Cancer Act is separate and distinct from the current Cancer Centers and SPOREs programs. The current effort to reexamine these programs may parallel and enhance the new center mentioned in the legislation, but the working group was not convened as a response to that legislation.

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IV. NCI/CONGRESSIONAL RELATIONS-MS. DOROTHY FOELLMER

Ms. Dorothy Foellmer, Director, Office of Legislative and Congressional Activities, highlighted several bills: 1) reauthorization of an existing program on mammography quality standards; 2) a cancer survivorship bill to raise awareness of and expand research on cancer survivorship; 3) the Benign Brain Tumor Cancer Registries Act, which would require the CDC National Program of Cancer Registries to collect data on benign as well as malignant tumors; and 4) the Eliminate Colorectal Cancer Act of 2002 to require coverage for colorectal cancer screening by group health plans and individual insurers for those age 50 and over, as well as for those under 50 who are at high risk.

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V. ONGOING AND NEW BUSINESS-DR. FREDERICK APPELBAUM

BSA at National Meetings: Status Reports

American Association for Cancer Research (AACR). Dr. Enrico Mihich reported that attendance was good. Dr. Mihich stated that a number of issues were raised during the session. Specifically, 1) the lack of accessibility to certain reagents or drugs by academic institutions and researchers at universities, thus limiting their ability to get involved with developmental therapeutics; 2) the

"R01 squeeze," i.e., the extramural community is puzzled as to why NCI continues to apply administrative cuts to grants after peer-review approval. He suggested a public pronouncement to clarify this issue; 3) increased clinical trials insurance-related costs due to FDA and institutional review board (IRB) requirements and regulations. He noted that these costs become the principal investigator's and the institution's responsibility; 4) the need for cooperation among institutions to establish high-quality SPOREs; 5) insufficient support for pancreatic cancer research and treatment; 6) translational research and how to improve patient care; 7) how investigators can move from other research fields to cancer; 8) bioinformatics; and 9) the poor correlation data standards between the intramural and extramural communities.

American Society of Preventive Oncology (ASPO). Dr. Mary Daly reported that attendance was excellent. Dr. Daly stated that a major concern of ASPO members is the difficulty in incorporating behavioral projects into SPORE grants, i.e., unless those projects have a core biology laboratory component. Other issues raised by members were the recent caps on funding and career development and training opportunities. She noted that the training questions reflected a lack of knowledge of NCI's progress in recent years in developing new training grants. A suggestion was that since many new cancer prevention researchers are ASPO members, new NCI training grant mechanisms should be developed to support these researchers. In discussion, the following point was made:

- While NCI staff have implemented a redefinition of translational research for SPORE grants, the challenge remains at the review process level due to variations in the interpretation of the definition. Refocusing review staff, reviewers and closely monitoring the review process will be required.

Oncology Nursing Society (ONS). Dr. Christine Miaskowski reported participation at these sessions has been increasing and noted that a number of concerns expressed at the meeting were: 1) issues and challenges associated with the conduct of multisite biobehavioral research, particularly in the area of symptom management given the current budgetary cap on research grants. Participants recommended that NCI evaluate and recommend models that could facilitate multi-site research; 2) the benefits and limitations of establishing a multi-site IRB. A request was made to

present the results of the NCI pilot study on the multi-site IRB at the next ONS "NCI Listens" session; 3) prioritization of symptom and palliative care research at the NCI since a 1999 Institute of Medicine (IOM) indicated that the NCI spent less than 1 percent of its budget on research and training related to symptom management and palliative care. Further discussion of this issue is warranted at the next ONS "NCI Listens" session; 4) nurse researchers' difficulty in accessing Community Clinical Oncology Programs (CCOPs) in order to conduct NCI-funded research; 5) funding dissertation research; 6) nurse representation on the NCI PRGs; and 7) development of a Cooperative Group for symptom management and biobehavioral research. A list of research priority areas was also identified. A recommendation was to hold an "NCI Listens" session at the ACS/ONS meeting in February 2003.

Other Issues. Dr. Appelbaum presented an updated listing of "NCI Listens" sessions and participants for the remainder of 2002: Cold Spring Laboratory Symposium (CSHL), 16 August 2002, Cold Spring Harbor, NY, Drs. William Kaelin (Chair), Dinah Singer, and Paulette Gray; American Society for Therapeutic Radiology and Oncology (ASTRO), 7 October 2002, New Orleans, LA, Drs. Gillies McKenna (Chair), Norman Coleman, Daniel Sullivan, William Wood and Gray. An "NCI Listens" session will be held at the Society of Behavioral Medicine which will be held on 7 March 2002 in Salt Lake City, UT. Members representing the BSA and NCI are Drs. David Abrams (Chair), Robert Croyle, and Gray.

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VI. AWARD PRESENTATIONS-DR. ANDREW von ESCHENBACH

Director's Service Award. Dr. von Eschenbach recognized Ms. Amy Langer, Drs. Suzanne Fletcher, Waun Ki Hong, Tyler Jacks, Caryn Lerman, Franklyn Prendergast, Joseph Simone, Louise Strong, Daniel Von Hoff, Barbara Weber, and Alice Whittemore, original Board members, for their many contributions and dedicated service to NCI and the Board from 1996-2002. He noted that this was "not a goodbye but, rather, a role change" and that he was looking forward to their continued support and participation in NCI's research efforts.

VII. RAPID ACCESS TO INTERVENTION DEVELOPMENT (RAID) PROGRAM PROGRESS REPORT- DR. EDWARD SAUSVILLE

Dr. Edward Sausville, Associate Director, Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD), explained that the RAID program was initiated as a means to change the pathway by which NCI provided assistance to the extramural cancer research community for the development of novel therapeutic ideas. RAID was initiated in 1998 to ensure that NCI-funded therapeutic concepts originated by extramural academic and small business scientists resulted in the issuance of an Investigational New Drug (IND) held by the investigator rather than by NCI. This mechanism would allow access to NCI's contract research and development resources and in-house expertise, while intellectual property would remain with the originating investigators. The original goal of the RAID program was to commit approximately $10M to $15M a year to contract-related research.

Review Process: Dr. Sausville described the RAID review process. He stated that a unique aspect of the RAID review process is that there is an interactive collaboration between NCI and the investigators and that the review is a modular process, i.e., the review committee can recommend that either all, or only some, developmental steps be pursued. In addition, since the review committee is decisional rather than advisory, a consensus opinion is not required. Individual members' advice is solicited. He discussed the role of the Biological Resources Branch Oversight Committee (BRB OC) in the RAID review process.

Projects: Of the 62 projects that have been approved through the RAID program, half of the projects investigate small molecules, while the remaining projects investigate biologics. About half of the proposals request only early preclinical tasks (pilot production and efficacy, pharmacology, and preliminary toxicology studies); a quarter of the proposals request assistance with late preclinical development (production of clinical-grade lot and IND-directed toxicology studies); and the remainder request assistance with all

stages of drug development. Presently, three RAID-supported products are in clinical trials, and others should be in the clinic by the end of the year. The average time for completion of a RAID project is 3 to 4 years. Dr. Sausville reviewed several RAID funded projects.

Dr. Sausville told members that of the176 applications submitted to RAID, 35 were approved for preclinical development and 13 of those have been completed. Eight of the 35 projects are suitable for advancement to further development. He informed members that the main focus, during the RAID program's first few years, was on non-Good Manufacturing Practice GMP) synthesis and analysis of products using animal models. Now that these steps have been fulfilled for many projects, there will be a shift over the next few years towards IND-directed toxicology studies and production of GMP-grade material. He noted that the program is not 1) a pipeline for NCI-held INDs; 2) an unconditional NCI commitment; 3) a funding mechanism for big pharmaceutical companies, nor 4) a grant program to fund particular laboratories.

Budget: The RAID program has remained within the $10M funding level with 1/3 invested in the production of biologics;1/3 towards toxicology and pharmacology studies; and the remainder allocated to non-GMP and GMP small molecules production.

RAID-like Projects: Dr. Sausville described several recently established initiatives that mimic RAID's structure: 1) the Development of Clinical Imaging Drugs and Enhancers (DCIDE) program (a biomedical imaging program that assists in the development of new diagnostic imaging agents); 2) Rapid Access to Preventive Intervention Development (RAPID) (a program that supports innovative prevention initiatives); and 3) Rapid Access to NCI Discovery (RAND) Resources (facilitates the production or synthesis of preclinical agents through the use of DTP's contract resources for drug discovery). The NIAID and NCI have started an inter-Institute program focused on the development of Acquired Immune Deficiency Syndrome (AIDS)-related therapeutics for both AIDS and AIDS-associated malignancies and opportunistic infections.

In closing, Dr. Sausville informed the Board of several of the issues the RAID program is currently trying to address, such as managing the increasing queue for biologics, improving efficiency of

development, defining the role of "Big Pharma."

In discussion, the following points were made:

- Currently, funding for the RAID program is sufficient to cover projects that have made it through the peer-review process. However, several applications for the development of biologics have been submitted, and at some point, more money will need to be appropriated to offset the increased need for the funding and manufacture of projects presently under review. BSA members expressed support for reconsidering an increase in the RAID budget.

- Due to conflict-of-interest issues, RAID has not asked investigators from biotechnology companies or big pharmaceutical companies to serve as RAID reviewers. However, several committee members are or were Small Business Innovation Research (SBIR) awardees or are associated with RAID funded researchers.

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VIII. NIGMS/NCI CONSTRUCTION OF NEW BEAMLINES FOR MACROMOLECULAR X-RAY CRYSTALLOGRAPHY-DR. JOHN SOGN

Dr. John Sogn, Deputy Director, Division of Cancer Biology, described the collaboration between the National Institute of General Medical Sciences (NIGMS) and NCI to construct a new set of beamlines for macromolecular x-ray crystallography. X-ray crystallography is used to complete the three-dimensional structure of proteins, nucleic acids, and macromolecular complexes, such as viral capsids and ribosomes. Dr. Sogn stated that this tool has recently been used at NCI for drug development, as well as for understanding molecular structure and function in basic cancer biology. These studies require a state-of-the-art, third-generation, synchrotron x-ray source, and construction of a facility along with the beamlines is presently underway. This project has been designed in such a way that it will not only undertake construction of the new facility but will facilitate advances in beamline design that will improve the throughput at existing x-ray crystallography

facilities.

Rather than build a new synchrotron, Dr. Sogn noted that, NIGMS/NCI is using the Department of Energy's (DOE) synchrotron. He explained that the synchrotron is divided into a number of sectors allocated to various research groups with different disciplines. While DOE's synchrotron provides the source of x rays, each group must provide the equipment and material to perform the actual structural studies. In order for NIGMS/NCI to gain access to an unused sector of the synchrotron, a collaborative access team was formed with the technical expertise and resources to perform the task. This team is known as the NIGMS/NCI Collaborative Access Team (GM/CA-CAT). Dr. Sogn described the floor plan of the sector and surrounding laboratory space assigned to GM/CA-CAT. He also explained that the GM/CA-CAT plans to use a dual undulator that will produce two beams of radiation originating from a single port. This system will double the number of experiments that can be performed in a single sector.

Dr. Sogn described the GM/CA-CAT organization, composition and functions of the Science Advisory Board, and CAT staffing efforts. He reported that the cost of construction of the dual undulator beamlines is expected to reach $18M, with the cost shared equally between NCI and NIGMS; any amount over budget will be paid by NIGMS. Once the beamlines are fully operational, the yearly operating cost is expected to be $4M, with NCI providing $1M and NIGMS covering the remainder. DOE requires that the public have access to the sector at least 25 percent of the time. As such, the sector will be available to the public 50 percent of the time; the other 50 percent will be set aside for development of the facility, use by the research staff, and special use by NCI and NIGMS. Following a brief overview of the timeline for this project. Dr. Sogn informed members that preliminary designs have been reviewed this year and the first usable x-rays are expected in 2 years. The facility should be fully operational by 2005.

In discussion, the following points were made:

- A fully operational facility should be able to process one complete three-dimensional structure per beamline per day, as long as the crystals can provide useful data. With the ability to process crystal structures at this rate, a library of structures could be completed within several years.

- There is a supplement program available for grantees to provide additional funding when grantees collaborate with x-ray crystallographers to generate crystals.

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IX. MARKETING OF NCI TRAINING AND CAREER DEVELOPMENT OPPORTUNITIES-DR. CAROLYN STRETE

Dr. Carolyn Strete, Chief, Cancer Training Branch, Office of Centers, Training, and Resources (OCTR), described the NCI Training and Career Development Opportunities program, which was initiated in 1998 in response to BSA and the National Cancer Advisory Board (NCAB) recommendations. Dr. Strete informed members that the main programmatic goals are to: 1) stabilize endangered disciplines (e.g., clinical sciences and populations sciences); 2) address the future needs of more multidisciplinary, team, and translational research approaches; 3) provide the flexibility needed to attract new scientific disciplines into cancer research; and 4) develop strategies for increasing the involvement of minorities in cancer research. The program announcements are listed through the NIH/NCI omnibus mechanisms, and career development grants are awarded to mentored and unmentored individuals as well as to institutions. Dr. Strete stated that the task of marketing the program only began in the fall of 2001 in response to BSA recommendations. To address the Board's concerns and working with the BSA executive secretary, an information packet was developed that included a letter of introduction to scientists, a breakdown of the 14 funding mechanisms, targeted career stages, eligibility and review criteria, application deadlines, and contact information. Dr. Strete described the distribution of the packet to academic and cancer-related institutions nationwide. The packet has been posted on the Cancer Training Branch Web site. Dr. Strete concluded by describing other marketing strategies, for example, 1) a contact database will be developed; 2) a massive marketing campaign will be conducted every 3 years; and 3) the Web site (www.cancertraining.nci.nih.gov) will be enhanced as needed. In discussion, the following points were made: . Agendas and meeting summaries of NCI Cancer Training Grant Writing sessions should be placed on the training Web site (www.cancertraining.nci.nih.

gov) for those individuals who are unable to attend the sessions. . An outreach program targeting young investigators through cooperative clinical trials groups should be developed. . The NCI training Web site should be appropriately indexed (i.e., meta tag) by standard Internet search engines (Yahoo, Google, etc.).

- Postdoctoral fellowship stipends and career development awards often fall below the benchmark salary set by an institution. Since the Principal Investigator often does not have access to non-Federal funds to compensate for the salary difference, it becomes difficult to have a participant accept one of these fellowships. Further discussion on how to address this salary difference should be scheduled at a future BSA meeting.

- Young investigators should be made aware of any loan-forgiveness programs that are applicable upon acceptance of a training grant.

- The full BSA or a subcommittee should review NCI's overall training portfolio to determine other areas that should be targeted for funding once population and clinical sciences show an increase in awarded training grants.

- To increase basic scientists' interest in clinical research, cross-disciplinary training should be emphasized. While K25 awards are specifically used for transdisciplinary science, the response to this funding mechanism has not been successful. More aggressive strategies to disseminate the availability of this funding mechanism must be sought.

- The peer-review process should be evaluated to ensure that the applications are being properly assessed, especially since the career training program is the first grant review experience for many young investigators. During the review, a greater emphasis should be placed on the applicant's research environment rather than on details in the scientific plan; constructive feedback should be provided in the summary statements.

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X. WORKING LUNCH

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

Dr. Marvin Kalt, Director, Division of Extramural Activities (DEA), stated that the NCAB *ad hoc* Research Project Grants (RPGs) Working Group was established to: 1) educate NCAB members on the impact of academic and clinical research settings on the budget, and thus, the consequences on funding policies; and 2) assist the extramural research community in understanding NCI's funding constraints. Members were told that NCI has committed to an R01 payline of the 22nd percentile. With a 4-year average length of award, three-quarters of the awards are noncompeting continuations. For FY2002, about 3,389 of the 4,700 grants are noncompeting, so approximately 1,280 new RPGs will be awarded, a projected success rate of about 28.5 percent. To attain this success rate with a 22nd percentile payline, policy reductions from peer-reviewed recommendations would need to be made. For new T1 R01s, those reductions would average 10 percent; T2 renewals, approximately a 6 percent reduction. With the projections, the number of total RPG awards is expected to increase in FY2003; but this increase will be due to an increase in the number of noncompeting awards. The success rate for competing awards is expected to drop because of an increase in the number of applications without a concomitant increase in the number of awards. The R01 payline is also expected to decline approximately 1 percentile point.

Dr. Kalt indicated that after reviewing different budget scenarios and projections, the *ad hoc* Working Group created six principles to guide the allocation of FY2003 funds: 1) continue to give special consideration to supporting new investigators; 2) identify and initiate special one-shot supplement initiatives, such as equipment awards or other infrastructural items; 3) implement a more restrictive cap on competing renewal requests; 4) continue the accelerated executive review process for R01s; 5) engage in a review of budgets within the Institute in order to establish the relative values of different initiatives that are ongoing; and 6) oppose any proposed change in the modular grant ceiling.

He explained that the February/March 2002 grant application receipt deadline resulted in the receipt of approximately1,400 R01 grant applications, an increase of about 300 more than the October 2001 round. The success rate will decrease, because a fixed number of awards will be funded. As far as exception dollars, members were told that $8M is for accelerated executive review; $7M is for new investigators; and $20M is for high-priority P01s, R01s, and other research project grants outside those paylines. Special consideration this year will be given to pancreatic cancer R01 applications, i.e., up to the 33rd percentile. Dr. Kalt asked the Board to consider effective ways of communicating funding policies with respect to RPGs so that extramural researchers can understand application policies, their chances for success, and NCI's budgetary constraints leading to current policy decisions.

In discussion, the following points were made:

- A payline for R01s should be maintained at or near the 20th percentile.

- Measures and methods to assess impact and address the question of accountability should be developed.

RFA Reissuance Working Group Report

Dr. Appelbaum provided an overview of the formation of the RFA Reissuance Working Group (Drs. Anton-Culver, Appelbaum, Gray, McKenna, Mihich, Rimer, Singer, and Young). He stated that while the BSA is responsible for the concept review of new RFAs, the Board is not involved with the reissuance of RFAs. Members were reminded that a summary of all approved concepts is given at each November meeting, but that the summary does not include RFA outcomes. During the March 2002 BSA meeting, the question was raised as to whether the Board might provide better advice to the NCI by reviewing the outcome of RFAs. He presented the Working Groups recommendations and stated that if the Board approves them, the review would begin at the November 2002 meeting. Following NCI executive committee (EC) approval, the Division Director would provide a three-person subcommittee (selected by the BSA chair and executive secretary) with a short

statement rating overall enthusiasm for the reissuance and noting any particular issues with the RFA concept on which specific BSA input would be desired. The subcommittee will report its recommendation to the full Board at a subsequent meeting. The subcommittee may recommend reissuance, request more information from NCI staff, or request a more in-depth BSA discussion at a future meeting. If the Division Director or the EC decides not to reissue an RFA, either because the RFA has been successful and has met its goal or because the RFA has been unsuccessful, the BSA will request from the Division a brief statement sharing that opinion with the Board. Dr. Appelbaum indicated that with this plan, the BSA could be kept up to date on the outcome of RFAs without unduly burdening NCI staff or the RFA review process.

Motion: A motion to approve new procedures for BSA review of RFAs proposed for reissuance was unanimous. Beginning in November 2002, RFAs approved for reissuance by the NCI executive committee will be submitted to a three-person BSA subcommittee (selected by the BSA Executive Secretary and the Chair); reviewers (i.e., current Board members) of the original RFA will be included on the subcommittee. The subcommittee's recommendations (concur, request detailed information from NCI staff for educational purposes, or place the reissuance on the Board's agenda for further discussion) will be reported to the full Board.

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XI. SERUM PROTEOMIC PATTERNS: A NEW PARADIGM FOR EARLY CANCER DETECTION-DRS. LANCE LIOTTA AND EMANUEL PETRICOIN

Dr. Lance Liotta, Chief, Laboratory of Pathology, Center for Cancer Research (CCR), outlined the development of the NCI-FDA Clinical Proteomics Program. Dr. Liotta described the serum proteome as containing thousands of proteins and peptides from every tissue in the body and reflected that changes in the physiologic state of a tissue would add, subtract, cleave, or enzymatically modify proteins in the serum proteome. He hypothesized that protein patterns could develop into a diagnostic

tool, even without prior identification of the proteins.

Technology. The technology to analyze serum proteomic patterns was developed from the use of the Ciphergen Biosystems' Surface Enhanced Laser Deabsorption and Ionization (SELDI) system. A subset of proteins from a drop of unprocessed serum sticks to the surface of an aluminum bar that, when hit with a laser beam in a vacuum tube, results in the proteins flying off. The size of the proteins determines their time of flight. Dr. Liotta explained that compilation of these data generates a barcode-type readout that can distinguish among different serum samples. A collaboration with Correlogic Systems, Inc., has resulted in the development of an artifical intelligence (AI) system to analyze the complex patterns. The AI system combines a genetic algorithm with a self-organizing cluster analysis to discriminate between two training sets: healthy and cancerous serum.

Detection Paradigm. To field-test their new detection paradigm, Drs. Liotta and Co-Director Emanuel Petricoin, Laboratory of Immunology, Division of Therapeutic Proteins, Office of Therapeutics Research and Review, Center for Biologics and Research (CBER), FDA, processed serum samples from patients from a high-risk ovarian cancer clinic. Recently, samples were unblinded and correlated with data from a 5-year follow-up. A paper describing the results was published in the Lancet. The categorizations made by the Proteomics Program were found to be 99 percent specific, with a sensitivity of 99 percent. Importantly, the technology diagnosed, with 100 percent sensitivity, stage 1 disease. Patients treated at this early stage show increased 5-year survival rates, emphasizing the great clinical importance of detection at this stage.

Dr. Liotta reported that the testing has been extended to prostate cancer screening. He cited 94 percent specificity and 96 percent sensitivity as the result of a blinded test series. Of the samples with nondiscriminatory prostate-specific antigen (PSA) values between 4 and 10, benign disease could be identified in 71 percent of the cases. Ultimately, this new screening paradigm could help a physician decide whether or not to perform a biopsy, thus providing a better indication of the patients disease status.

Screening Paradigm. An exciting aspect of this screening paradigm is that the system can learn and become more accurate depending

on the feedback it is provided and the number of samples entered into the training set. Moreover, Dr. Liotta envisions the accumulation of spectra through a central computer, allowing a diagnosis to be relayed to the treating physician. Not only will this diagnosis have the highest level of sensitivity, but its availability also levels the playing field for physicians regardless of their access to analytical software or the large database of samples. The challenge now is to speed development of this technology to benefit the public while ensuring its evaluation with the highest levels of scientific rigor.

Plans to make the test publicly available consist of offering the proteomics system out of NCI's IRP, using as a reference laboratory the Laboratory of Pathology, which is Clinical Laboratory Improvement Act and College of American Pathology (CLIA/CAP)-certified. The NCI IRP will be the lead institute for performing clinical trials. The four phases of the clinical trial to test and validate the new paradigm were presented.

Expedited Review. In a unique arrangement, the FDA has agreed to allow the FDA-NCI Proteomics Program to obtain an expedited review of the Premarket Application (PMA). The PMA is an FDA application request for clearance to market a class III medical device. The criteria for an expedited review include evidence that: 1) the device, i.e., the test, can be classified as breakthrough technology since no approved alternative exists; 2) offers significant advantages over existing approved alternatives; 3) availability of the test is in the best interest of the patients and provides a specific public health benefit; and 4) a number of cooperative groups are willing to provide samples. The expedited review will decrease a new diagnostic test approval time from 3-6 years to1-2 years. A PMA clinical trial may be initiated as early as the fall of 2002. The expectation is that after the FDA sanctions the test, it will be coupled with current diagnostic screening modalities for breast, prostate, and pancreatic cancers.

Licensing Issues. Dr. Liotta explained the approach being taken regarding licensing issues. As a reference laboratory, the Laboratory of Pathology can offer the test under the PMA. Other reference laboratories such as Quest can: 1) license the technology; 2) license the patent from the Government and Correlogic Systems, Inc., with whom the Proteomics Program has a Cooperative Research And Development Agreement (CRADA); or 3) cross-

license the PMA. Drs. Petricoin and Liotta are currently in discussions with the American Medical Association to determine the test's reimbursement code. The goal, Dr. Liotta reiterated, is to make the test available with the greatest speed to obtain the greatest public benefit.

In discussion, the following points were made:

- Currently, and for the duration of the PMA approval process, the test will be used as a diagnostic tool in people already suspected of having cancer. General population screening cannot be considered at this point due to FDA regulations.

- PLCO study samples have been banked and will be available when the code is broken in 2 years. These samples of patients with known clinical outcomes provide a phenomenal opportunity to validate the proteomics test as a screen for the general population.

- FDA assessment of a project jointly sponsored by the Agency may appear inappropriate. Drs. Liotta and Petricoin assured the Board that the FDA review process of the proteomics test is being done according to the strictest criteria and under public scrutiny.

- Until larger populations of samples are obtained, the proteomics test can not discriminate different histologic types of cancer.

- Advocacy and outreach groups, such as the Ovarian Cancer National Alliance and the Lynn Cohen Foundation, are instrumental in helping the Proteomics Program identify high-risk
- clinics with large patient populations as sources of patient samples.

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XII. RFA AND COOPERATIVE AGREEMENT CONCEPTS-PRESENTED BY NCI PROGRAM STAFF

Office of the Deputy Director for Extramural Science

NCI Predoctoral Research Training Partnership Award (Coop. Agr.). Dr. Brian Kimes, Director, OCTR, stated that the purpose of this initiative is to pilot new formal predoctoral training programs that are partnerships between scientists in extramural institutions and specific groups of intramural scientists, either in the CCR or the Division of Cancer Epidemiology and Genetics (DCEG). Dr. Kimes noted potential benefits of this new program are to: 1) expand training opportunities in areas of high interest to both the extramural community and the Intramural Research Program (IRP); 2) expand and stabilize long-term scientific collaborations; 3) maximum access to intramural resources by the extramural community; 4) expanded and stabilized access to high-quality candidates by the intramural program; 5) enrich the intramural research environment; and 5) expand training in areas of national need.

Staff of CCR will serve as intramural Deans to facilitate extramural programs and match them with intramural mentors. The pilot program also requires the appointment of Intramural and Extramural Research Training Program Directors, as well as a Steering Committee to implement and evaluate the program. Funds will be allocated for program advertising to aid in recruiting high-quality candidates and for travel to facilitate mentor interactions. Two functional methods for paying a predoctoral candidate will be used, i.e., via the standard National Research Service Awards (NRSA) rules and the Cancer Research Training Award (CRTA). A new Cooperative Agreement grant mechanism, the TU2, will be utilized. An NIH requirement is that there be a Cooperative Agreement any time there is intramural involvement.

The proposed length of award for this one-time solicitation is 5 years, with a first-year set-aside of $1M and a total cost of $3M for an estimated four to seven TU2s. Intramural funds will be used to support CRTAs.

In discussion, the following points were made:

- Course work in the training program would be conducted at

the extramural institution. The thesis work, however, could be done partly at the extramural institution and partly at NIH.

- Selection of a thesis advisor should not be a problem. IRP researchers involved in the training program will likely have faculty appointments within the participating institution.

Motion: A motion to approve the Cooperative Agreement RFA concept entitled "NCI Predoctoral Research Training Partnership" was unanimous. Issues discussed by the BSA will be incorporated into the RFA.

Division of Cancer Prevention (DCP)

DNA Methylation, Diet and Cancer Prevention (RFA). Dr. Sharon Ross, Program Director, Nutritional Science Research Group, stated that the purpose of the concept is to promote novel research on the role of bioactive food components in DNA methylation processes involved with cell vulnerability to cancer and/or cellular responsiveness to cancer prevention. Dr. Ross stated that this concept was designed to encourage collaboration between nutrition and DNA methylation experts to study bioactive food components with cancer-preventive components and to establish linkages between methylation patterns and tumor incidence and behavior.

NCI's investment in DNA methylation research is $22M. Approximately $5M is allocated for nutrition projects related to DNA methylation. However, most of these studies are population-based and do not address the relationship between diet and DNA methylation. Through the use of R01s, R21s, and supplements to existing grants, NCI's intent is to double the number of grants that are funded in this research area. This concept is consistent with the 1999 NCI Nutrition Implementation Report and the 2001 "Diet, DNA Methylation Processes, and Health" workshop recommendations.

The proposed award length for this one-time solicitation is 4 years, with a first-year set-aside of $2.5M and a total cost of $10.3M for

an estimated 7 to10 R01, R21, and supplemental awards.

In discussion, the following point was made:

- Although there is little evidence that diet is involved in processes other than DNA methylation, other epigenetic processes should be included.

Motion: A motion to approve the RFA concept entitled "DNA Methylation, Diet, and Cancer Prevention" was 23 votes in favor and 1 opposed. Members suggested that the RFA be broadened to encourage collaboration between nutrition scientists and scientists studying epigenetics in general. The focus should not be limited to DNA methylation.

Office of the Deputy Director for Extramural Science

Aging/Cancer Research Program Development in NCI Cancer Centers (RFA). Dr. Kimes, Chief, OCTR, stated that the purpose of this concept is to promote the development of interdisciplinary programs or other equally effective models in NCI-designated Cancer Centers in order to conduct and build a competitive research base in collaborative and translational research at the aging and cancer interface. Its focus will be on three areas: 1) biology of aging and cancer; 2) treatment efficacy and tolerance; and 3) effects of comorbidity on cancer. Currently, there are no programs in Cancer Centers dedicated to integrating aging and cancer research. Many institutions, however, have both National Institute on Aging (NIA) Research Centers and NCI-designated Cancer Centers; therefore, there are real and feasible opportunities to establish these types of programs. The proposed grant mechanism for the concept is a P20 planning grant to give Cancer Centers more flexibility in how they address aging/cancer research questions. Funds would be used for paying leaders and co-leaders, reimbursing administrative costs, creating a dialogue for setting priorities, recruiting new scientists, and supporting pilot projects. Flexible funds for developing feasibility data would also be available.

The proposed length of the award for this one-time solicitation is 5

years, with a first-year set-aside of $5M ($3M from NCI and $2M from NIA) and a total cost of $25M ($15M from NCI and $10M from NIA) for an estimated five awards.

In discussion, the following points were made:

- Approximately 70 percent of mortality in cancer patients occurs in patients over the age of 65, yet there is little research in this area.

- The focus of the concept should not be limited to the three research areas suggested. Applicants should be allowed to define the type of collaborative opportunity they would like to pursue along the cancer/aging research interface.

- The end product of the P20 grant is the establishment of an aging/cancer program to conduct and build a competitive research base that will be sustained through R01s and P01s. Renewal and possibly, expansion options should be considered.

- The concept should clearly state that the support of the Aging and Cancer Program would be through P01s or R01s.

Motion: A motion to approve the RFA concept entitled "Aging/ Cancer Research Program Development in NCI Cancer Centers" was 23 votes in favor and 1 abstention. The RFA should clearly state that its purpose is to encourage the establishment of collaborative aging and cancer programs within NCI Cancer Centers, using either P01or R01 grants. Consideration should be given to increasing the number of research questions. This concept should be brought back to the Board in 3 to 4 years so that the Board can determine whether the RFA should be reissued.

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XIII. EXPANSION OF THE BIOMEDICAL IMAGING PROGRAM - DR. DANIEL SULLIVAN

Dr. Daniel Sullivan, Associate Director, Biomedical Imaging Program (BIP), provided an overview of the future challenges and

opportunities for the BIP with respect to in vivo imaging in oncology. Dr. Sullivan stated that the two major areas that BIP is interested in developing are: 1) clinical imaging methodologies, which are associated with cancer diagnosis, treatment, monitoring, and therapy delivery; and 2) laboratory methodologies, specifically drug development and in vivo genomics and proteomics.

Funding: The BIP was established in FY1996, and funding over the past 5 years has doubled to $120M as of 2001. The majority of grants funded through BIP are investigator-initiated, with RFAs composing the next largest percentage of funding and the remainder of the money is allocated to program projects and technology development. Dr. Sullivan briefly described a number of single-investigator or consortium RFAs that fund studies on image-guided therapy, a lung image database, magnetic resonance (MR) spectroscopy of head-and-neck lymphoma, and MR breast cancer imaging. He noted that several of the RFAs will not be reissued due to lack of funding for groups working on different modalities or disease-targeted applications.

Future Opportunities: In focusing on future diagnostics imaging opportunities, Dr. Sullivan stated that while ACRIN has made great strides in this area, other mechanisms (e.g., R33s and R01s for multi-institutional trials) must be made available to support these studies. Additionally, there is a need to integrate imaging studies in the Cancer Therapy Evaluation Program's (CTEP) therapy trials. He noted that there are a number of Cooperative Groups forming imaging committees and that BIP plans to facilitate the formation and integration of these committees into an intergroup imaging council to work with CTEP staff. There is also a need to establish imaging cores in Cancer Centers, and that Cooperative Groups and research groups need to increase access to imaging resources that are presently overwhelmed by a diagnostic workload.

Detection: Dr. Sullivan described how spectroscopy is being used to detect molecular changes in response to therapy. He noted that these studies have been so reliable that spectroscopy will soon be evaluated in a multi-institutional prostate cancer trial organized by ACRIN. He also briefly described potential improvements in MR imaging. He noted that there is a debate in the research community as to whether the use of molecular imaging in therapy monitoring should focus on generic pathway events or on indicators specific to particular molecular signatures or drug interactions. Clinical trials

are being designed to evaluate the use of PET scanning as a prognostic indicator of how a patient is responding to a therapy. Dr. Sullivan also discussed the use of targeted molecular probes capable of fluorescing after cleavage by a tumor-specific protease or nano-particles that can deliver imaging agents or drugs to a tumor through interactions with tumor-specific ligands or receptors. While the effectiveness of these types of imaging agents should be analyzed in clinical trials, Dr. Sullivan explained that the present challenge is to determine whether the correct patient populations are being selected and evaluated in the clinical trials. Molecularly targeted agents have generally been used in patients with late-stage cancer, and at that stage of the disease, it is difficult to measure the cytostatic effects of these drugs, as the tumors are not likely to respond to a single drug treatment or even a combination treatment. Thus, future studies must be performed selecting the most appropriate patient population with early-stage disease, ensuring that the drug is being given at the correct time point, and appropriately assessing the biological endpoint.

Novel Approaches: Novel approaches presently being undertaken by BIP funded investigators were discussed. Dr. Sullivan informed members that several image-guided interventions are being investigated in the United States and other countries. He noted that the success of the CT/PET scanning system has led to the recent development by one of NCI's imaging centers of an MRI system combined with the optical technique referred to as fluorescence-mediated tomography.

Screening: Whole-body screening has become widely used worldwide. In the United States, some major problems with whole-body screening include over-diagnosis and false positives. Dr. Sullivan described a technique that combines focused ultrasound with MRI as a noninvasive therapy that can be used as an inexpensive, yet functional cancer treatment. Members were told that this type of integrated platform falls under the Unconventional Innovations Programs and not under NCI's imaging program. A video of how some of the technologies discussed might be used in an unexpected manner sometime in the future was shown.

In discussion, the following points were made:

- Some large-device companies have created organizational units, such as molecular imaging divisions, that are working

with NCI in an effort to integrate new molecular-targeted agents with their devices, thus developing partnerships with both drug and contrast agent companies. This is a new way of doing business

- A concept should be developed for the establishment of imaging cores within comprehensive Cancer Centers to ensure that clinicians are aware of the available imaging capabilities.

- In an effort to reduce variability in reporting, there should be a method to standardize how tumor volumetrics are defined.

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XIV. PUBLIC/PRIVATE PARTNERSHIPS: OVERCOMING THE BARRIERS TO EARLY CLINICAL TRIALS - DR. ELLEN FEIGAL

Dr. Ellen Feigal, Acting Director, Division of Cancer Treatment and Diagnosis (DCTD), described a new NCI public/private partnership pilot initiative designed to overcome the barriers that prevent new therapeutics from being tested in early clinical trials. Dr. Feigal informed members that the NCI invests both money and time into the science involved in the development of innovative therapeutic treatments; however, it also needs to focus efforts on developing the infrastructure and resources to get these products tested expeditiously and rigorously in clinical trials. Members were told that the initiative was established after the Friends of Cancer Research Foundation and the Association of American Cancer Institutes approached NCI with a proposal for partnering with pharmaceutical companies and Cancer Centers to address ways to enhance the nation's capacity to evaluate new therapeutic and preventive agents in the clinical setting. Dr. Feigal noted that while no intellectual property or clinical trials with proprietary agents was planned to be involved in the initiative, the issue remained of how to involve pharmaceutical companies while avoiding any real or perceived conflict of interest. Thus, the NCI and the FNIH established a partnership to meet the goals of this initiative. Commercial partners presently working through the Foundation

are: Aventis, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, and Novartis.

Objectives: The initiative's objectives are to utilize the expertise, experience, resources, and dollars of pubic and private partners to address the critical barriers in the clinical trial pathway and to identify better treatments for cancer patients. Whereas, the goal is to develop a spectrum of models that NCI Cancer Centers and other organizations could use to increase and sustain patient accrual rates to clinical trials. The pilot initiative will focus on NCI-funded Cancer Centers since they already have the infrastructure, experience, and networks to conduct early-phase clinical trials. A main issue of the initiative will be to address the accrual of underrepresented individuals. Barriers that contribute to this suboptimal accrual rate are: 1) lack of knowledge by the general public, health care professionals, cancer patients, and health plan providers of the importance of identifying better treatments through clinical trials; 2) inadequate clinical trials compensation; 3) increasing Federal oversight and regulatory requirements; and 4) lack of understanding by overburdened IRBs. Others barriers were presented.

Funding: The exploratory/ developmental award mechanism, the R21 grant, through a Program Announcement, will support this initiative. The application submission deadline is 23 August 2002. Approximately 5 to 8 nonrenewable applications will be awarded, for a total cost of $6M over 2 years. Half of the funding will be provided by NCI, and the remainder will be provided by partners represented in the FNIH. A reserve of $100,000 will be used by coordinating groups, selected by the funded grantees, to manage the logistics and reporting requirements of the workshops. Awardees must agree to: 1) disclose all information and models that are developed; and 2) include an evaluation plan to measure the success of each approach to overcoming a barrier. NCI can be authorized by the awardees to share certain grant-related documents with FNIH and its pharmaceutical partners.

In closing, Dr. Feigal asked the Board a number of questions to consider regarding the relevance of establishing partnerships with the private sector and the potential areas of concern generated by the establishment of such partnerships.

In discussion, the following points were made:

- The relevance of the industrial partners in this initiative is unclear beyond their limited financial contribution. The value of creating a new structure and process to address barriers to recruiting patients into early clinical trials is doubtful.

- This initiative will provide the infrastructure to Cancer Centers that are presently attempting to set up core services on their own without any funding.

- The NIH partner companies are legally bound to remain involved for 2 years.

- Consideration should be given to including individuals from medical professional and nonprofit organizations on the initiative's review panel.

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XV. THE AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK (ACRIN): UPDATE AND FUTURE PLANS - DR. EDWARD STAAB

Dr. Edward Staab, Acting Branch Chief, Diagnostic Imaging Branch, explained that ACRIN is a multicenter network to rigorously assess and develop new and standard technologies relevant to the diagnostic imaging of cancer. ACRIN is funded through two 5-year U01s, which provide a total budget of $23M. There are two supplements, one for the digital mammography trial and the second for the NLST. The mammography trial, a parallel trial comparing digital versus screen-film mammography, involves 4 manufacturers and 50,000 women. The NLST is a randomized trial involving 50,000 high-risk patients to determine whether cancer-specific mortality is reduced when patients are screened by spiral CT versus standard chest radiographs. One of ACRIN's roles in NLST will be to evaluate the quality-of-life issues and the impact of screening on smoking cessation, as well as to provide a biorepository of fluid and tissue samples for future biomarker research.

Goals and Protocols: Dr. Staab emphasized that the goals of ACRIN were early assessment of emerging technologies relevant to cancer and evaluation of the efficacy of established imaging technologies and patterns of practice in radiology. ACRIN meets these goals by providing imaging trials with such infrastructure components as informatics, statistical support, and data management, among others. Participation in ACRIN is open to both individuals and sites. Dr. Staab reviewed the number of participating institutions, protocols, and patients accrued in 2002. He noted that there are 41 participating institutions, 15 protocols, and more than 6,000 patients. The protocols are under development, under review, approved awaiting activation, already opened, or closed, and include studies on screening, diagnosis and staging, imaging as a biomarker, and image-guided therapy. ACRIN has developed relationships with NCI Cooperative Groups as well as with industry groups, which mainly supply equipment and provide equipment support rather than any direct funding.

Reviews and Accomplishments: ACRIN has undergone 3 reviews over the past 3 years. All reviews concluded that the program has been properly developed and has been efficient and effective in decision making, prioritization, and generation of protocols. The reviews also noted that ACRIN has a number of unique policies that promote trial participation and data evaluation. ACRIN accomplishments over the past 4 years include: 1) a Web-based paperless operation; 2) conducting a clinical trial from beginning to completion; 3) preparing a report on the findings; 4) initiating a training program for young investigators; and 5) implementing innovative approaches to imaging research methods. New improvement efforts consist of developing new imaging methods and processes to generate a focused scientific agenda, providing data to other researchers, and establishing new cooperative groups and industry relationships as well as improving existing relationships. Specifics of the proposed Letter RFA to which ACRIN will be applying in the near future were reviewed.

In discussion, the following point was made:

- ACRIN is responsible for recruiting half of the 50,000 patients involved in the NLST and making adjustments for the accrual rate after the first year.

Adjournment: The meeting was adjourned at 11:20 a.m. on

Tuesday, 25 June 2002.

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