DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL ADVISORY COUNCIL FOR
BIOMEDICAL IMAGING AND BIOENGINEERING

Summary of Meeting[1]
May 27, 2004

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its fifth meeting on May 27, 2004, in Natcher Conference Center, Building 45, Rooms F1 and F2, National Institutes of Health, Bethesda, Maryland. Dr. Roderic I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), served as Chairperson.

In accordance with Public Law 92-463, the meeting was open on May 27, 2004, from 8:00 a.m. until approximately 11:40 a.m. for the review and discussion of program development and policy, and closed to the public from 12:40 p.m. until 4:30 p.m. for discussion and consideration of individual grant applications.

Council members present:

Dr. Carlo De Luca
Dr. Janie Fouke
Dr. Robert Grossman
Dr. Linda Lucas
Dr. Barbara McNeil
Dr. Norbert Pelc
Dr. Rebecca Richards-Kortum
Dr. Stephen Williams
Dr. Frank Yin
Dr. James Zagzebski

Council members absent:

Dr. Shirley Jackson
Dr. C. Douglas Maynard

Ex officio members present:

Dr. James Smirniotopoulos
Dr. Andrew Watkins
Dr. Michael Weiner

Ex officio members absent:

Dr. Arden Bement
Dr. John Brighton

Members of the public present for portions of the open meeting:

Dr. Stephen Badylak, University of Pittsburgh
Mr. Michael Hamm, BMES
Ms. Joanne Hawana, The Blue Sheet
Ms. Marianne Marlowe, Capital Consulting Corporation
Ms. Nancy Moy, SRI International
Mr. Edward Nagy, Academy of Radiology Research
Ms. Andrea Smith, FASEB
Ms. Elaine Young, University of Florida

[1]For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a real or apparent conflict of interest might occur.

NIBIB employees present for portions of the meeting:

Ms. Lillian Ashley
Dr. Prabha Atreya
Ms. Pam Clatterbuck
Dr. Bonnie Dunn
Ms. Angela Eldridge
Ms. Cheryl Fee
Ms. Tinera Fobbs
Dr. David George
Dr. Gary Glover
Ms. Colleen Guay-Broder
Dr. John Haller
Dr. Joan Harmon
Dr. William Heetderks
Dr. Christine Kelley
Ms. Mary Beth Kester
Dr. Alan McLaughlin
Mr. Todd Merchak
Mr. Nicholas Mitrano
Dr. Peter Moy
Dr. Mary Pastel
Ms. Donna Pearman
Dr. Grace Peng
Dr. Roderic Pettigrew
Ms. Anna Retzke
Dr. Belinda Seto
Ms. Karen Shields
Ms. Theresa Smith
Dr. Patricia Sokolove
Dr. Richard Swaja
Ms. Sandra Talley
Dr. Meredith Temple-O'Connor
Ms. Florence Turska
Ms. Stacy Wallick
Dr. Fei Wang
Mr. Elijah Weisberg
Ms. Li-Yin Xi
Dr. Yantain Zhang

Other Federal employees present for portions of the meeting:

Mr. Pedro Del Corrid, National Institute of Child Health and Human Development
Mr. Peter Lentl, National Cancer Institute
Mr. Marc Rigas, Center for Scientific Review

I. Call to Order and Opening Remarks – Dr. Roderic I. Pettigrew

Dr. Pettigrew welcomed Council members, guests, and staff to the fifth Council meeting. He thanked Council for attending, noting that Dr. Jackson and Dr. Maynard were unable to attend.

Dr. Pettigrew drew attention to the calendar of future meeting dates. Council members should contact Dr. Harmon, if there are major conflicts with the following dates. Potential changes will be reviewed by e-mail, if necessary.

September 13-14, 2004
January 27-28, 2005
May 25-26, 2005
September 14-15, 2005
January 25-26, 2006
May 24-25, 2006
September 13-14, 2006

Council accepted the minutes of the January 2004 meeting without modification.

II. Review of Regulations and Review of Operating Procedures – Dr. Joan T. Harmon

Dr. Harmon summarized the requirements under the Government in the Sunshine Act and the Federal Advisory Committee Act. These Acts require the Department of Health and Human Services (DHHS) to open to public observation as many advisory committee meetings as

possible, including the meetings of the National Advisory Councils. The Council meeting, therefore, would be open to public observation except during grant application review, scheduled to begin at 12:40 p.m. and concluding by the end of the day. Notice of the Council meeting was published in the *Federal Register* 30 days prior to the meeting.

Dr. Harmon also reviewed regulations concerning conflict of interest, and Council members were reminded that materials furnished for review purposes and discussion during the closed portions of the meeting are considered privileged information. All Council members present signed a statement certifying that they did not participate in the discussion of, or vote on, an application from any organization, institution, or any part of a university system, except for those which have multi-campus institution waivers or are specifically designated as separate organizations under 18 U.S.C. 208(a), of which they are an employee, consultant, officer, director or trustee, or in which they have a financial interest.

Dr. Harmon asked Council to consider two changes to current Council Operating Procedures. Council approved by unanimous vote the following:

- Applications denoted as select pay are outside the program plan and are recommended by staff for support with funds as available. These applications will not be automatically assigned to council members for discussion, but members are encouraged to raise any for discussion that they deem appropriate.

- A communication is a letter or other written document from an applicant received after the scientific review group meeting and prior to a council meeting that, as judged by NIBIB staff, to simply provide additional information or data and does not trigger the appeal process. Communications are often post-review pre-council requests for restoration of project dollars, time, or for select pay. Communications are included for Council information purposes and may or may not be acted upon by Council and need not be brought up for special discussion.

III. Director's Report – Dr. Roderic I. Pettigrew

Dr. Pettigrew began his remarks by recognizing two Council members. Dr. Shirley Jackson was elected President of the American Association for the Advancement of Science. Dr. Rebecca Richards-Kortum is collaborating on design of a fiber optic device to improve diagnosis of cervical cancer. This research was discussed in a recent "L.A. Times" article.

Dr. Pettigrew provided an update on the FY 2005 appropriations and other legislative activity, recent and upcoming workshops and meetings, the scientific portfolio and new initiatives, and future directions for the NIH and the NIBIB.

Appropriations and Legislative Update
The NIBIB received an appropriation of $288,900,000 in FY 2004 which represented approximately a 3 percent increase over FY 2003. The President's Budget request for FY 2005 is $297,647,000, an increase of 3.1 percent over FY 2004. Dr. Pettigrew participated in both the

Senate and the House Appropriations Hearings held on April 1 and April 21, respectively. Members of Congress were interested in a progress report on the Institute.

Dr. Pettigrew, along with Dr. Seto, Dr. Heetderks, and Ms. Guay-Broder, met with staff of the House Energy and Commerce Committee and the Senate Committee on Health, Education, Labor, and Pensions – the committees responsible for preparing re-authorization legislation for the NIH. The discussions focused on the mission of the Institute, priority-setting, overlap between the other Institutes and Centers, the role of the NIBIB in the NIH Roadmap activities, and challenges for the Institute.

Conferences and Workshops
Since the February Advisory Council meeting, the NIBIB has participated in seven workshops with multiple other Institutes and Centers and eight additional workshops are planned through September 2004. On May 10, 2004, the NIBIB, along with NIGMS, NIDCR, and the NSF, held an Interagency Conference on Research at the Interface of the Life Sciences and Physical Sciences in response to FY 2004 House appropriations report language. Ten agencies, including NIH, DOE, NIST, NSF, EPA, FDA, USDA, NOAA, NASA, and DoD, were represented at the conference. The goals of the conference were to demonstrate that there are current successful collaborative interagency efforts and activities; identify opportunities and barriers for interagency collaborations aimed at applying methods and principles from the physical sciences to address biomedical problems; and develop courses of action to validate the barriers and opportunities and to address those identified during the workshop. A follow-up meeting is planned for the fall of 2004, in which researchers from the extramural community will specifically identify key areas of opportunity and associated barriers to realizing these opportunities.

Dr. Pettigrew also discussed the upcoming BECON/BISTIC symposium entitled, "Biomedical Informatics for Clinical Decision Supports: A Vision for the 21st Century." The goal of this symposium is to examine software tools and approaches that combine gene expression, medical history, and image data that will ultimately deliver patient-specific information at a time and place where clinical decisions are made regarding risk, diagnosis, treatment, and follow-up. Specifically, this meeting will provide a scientific vision of the future where health care information technologies may be more fully deployed in the clinical workflow to improve efficiency and outcomes.

Funding Strategy for New Investigators
Dr. Pettigrew presented a new funding strategy for new investigators. In an effort to increase the number of new investigators, the NIBIB will fund applications scoring within 5 percentile points of the established pay line. This policy will apply only to investigator-initiated applications (R01s) and those received in response to program announcements. It is anticipated that this funding strategy will improve the success rates of new applicants in investigator-initiated research.

NIH Roadmap for Medical Research
The NIBIB staff continues to participate in the NIH Roadmap activities with representation on six Roadmap Implementation Groups. The first applications in response to the high-sensitivity,

high-specificity molecular imaging probe development Roadmap initiative will be considered during this council round.

FY 2005 Initiatives
The Institute did not issue any Requests for Applications during FY 2004 due to the overwhelming response in FY 2003 and the limited resources available for new initiatives. For FY 2005, the NIBIB may, depending upon the availability of funds, issue Program Announcements focusing on tissue-engineered human model systems; nanotechnology-based diagnosis and therapy; multi-scale modeling in biomedical systems; computer-assisted, image-guided surgery; chemistry of imaging agents and molecular probes; micro-imaging of pancreatic islets; and the NIH Physiome Project. The Institute is also planning several training initiatives for FY 2005, as well as the launch of the quantum projects, discussed at a previous Advisory Council meeting.

Research Highlights
- Dr. H. Harry Asada, Massachusetts Institute of Technology, is developing a combination of sensors and computational algorithms to non-invasively measure circulatory and cardiovascular hemodynamics.
- Dr. Jeremy Mao, University of Illinois at Chicago, has had remarkable success in tissue engineering a mandibular condyle from mouse mesenchymal stem cells.
- Dr. Watt Webb and his colleagues at Cornell University have been developing an imaging technique capable of producing histology-like images using auto-fluorescence rather than staining. This results in much higher resolution when compared to conventional histological methods.
- Dr. Richard Robb, Mayo Clinic, is using image analysis and bioinformatics to address the treatment of cardiac arrhythmias, particularly atrial fibrillation. His approach uses images of the heart in combination with electrophysiological mapping data to help interventional cardiologists identify a target area for treatment.

Future Directions
The NIBIB intramural research program received funding in the FY 2004 budget, and plans are underway. The Institute is convening a September meeting of a Blue Ribbon Panel to make recommendations to the Advisory Council on the scope and direction of the intramural program. An interagency agreement was signed in February to form a joint laboratory between the NIBIB and the FDA Center for Radiological Devices and Health to assess medical imaging systems. In addition, the Institute is pursuing training opportunities within the intramural program.

In FY 2005, the NIBIB will begin supporting the Bioengineering Summer Internship Program, formerly supported by the Whitaker Foundation. Also in FY 2005, the Institute will support an NIH NIST fellowship program – a 2-year program for graduate students who wish to pursue research in both the physical sciences and the health sciences. They will spend 1 year at NIST engaged in physical science research and 1 year at NIH doing health science research. The NIBIB will also participate in the Stetten Fellowship program which seeks to encourage historical research and writing about biomedical research and technology. The first NIBIB-supported participant will begin the program this summer.

IV. Report on AIMBE 13th Annual Event – "Public Policy Issues Related to Imaging" - Dr. Barbara J. McNeil

Dr. McNeil presented summary of the American Institute for Medical and Biological Engineering (AIMBE) 13th Annual Event. The focus of this event was to discuss new frontiers of imaging and bioengineering as well as best practices for translating discoveries from the laboratory to industry and the clinic. Dr. Zerhouni was the keynote speaker. Dr. McNeil focused her report on a session, entitled "Public Policy Issues Related to Imaging." The theme of the session was the interplay between research conducted by basic science laboratories in the areas of devices and drugs and the evidence demands of the medical and reimbursement communities prior to use of these devices or drugs. Basic scientists came away with a better understanding of what is required to translate discoveries into useful patient therapies that will ultimately be reimbursed by insurance. The Council members discussed examples of valuable diagnostic tools that are not fully utilized because they are not eligible for reimbursement by insurance.

V. Report on NIBIB Tissue Engineering Program – Dr. Christine A. Kelley

Dr. Kelley reported on the tissue engineering program at the NIBIB, including an overview of tissue engineering and regenerative medicine and a snapshot of the grant portfolio.

The terms "tissue engineering" and "regenerative medicine" are sometimes used interchangeably. However, the NIBIB portfolio includes the engineering of tissues *in vitro* as well as the regeneration of tissues *in vivo* to repair, replace, maintain, or enhance organ function. Tissue engineering involves combining cells and scaffolds in a bioreactor to engineer or "grow" the tissue *in vitro* and subsequently implanting these tissues *in vivo*. In contrast, regenerative medicine involves using the body as the "bioreactor" to actually regenerate the tissue *in vivo*.

The NIBIB tissue engineering portfolio currently includes approximately 46 grants encompassing a variety of research areas. Approximately one-half of the funded tissue engineering grants were received in response to the Request for Applications entitled "Research Opportunities in Tissue Engineering," issued in December 2002. The remainder of the portfolio is comprised of investigator-initiated research followed by exploratory applications from new investigators.

Dr. Kelley presented examples of NIBIB-supported research in tissue engineering and regenerative medicine. As an example of tissue engineering applications for replacement tissues, researchers have developed a mandibular condyle joint that may eventually replace defective jawbones. In the area of tissue engineering for repair, scientists have developed tissue engineered cartilage capable of integrating with native cartilage resulting in improved joint implant assimilation. For drug discovery applications, researchers are working to engineer a three-dimensional human liver that would mimic the liver function *in vivo* and could be used in high-throughput assessment of drug candidates to evaluate metabolism, excretion, and toxicity.

The Institute will host its' first tissue engineering grantees meeting in October 2004. This meeting will bring together grantees supported through several initiatives including the

development of novel biomaterials, tissue engineering, biosensors, and drug and gene delivery systems with the goal of encouraging collaborative relationships. The meeting will also include opportunities for the principal investigators to interact with industry representatives, technology transfer specialists, venture capitalists, and patent lawyers. The fostering of these interactions is important to move discoveries more quickly from the bench to the bedside.

Dr. Kelley continued by delineating future challenges in tissue engineering and some of the efforts to address those challenges. Current research needs include: (1) improved sources of cells; (2) innovative strategies for vascularizing 3-D constructs; (3) further understanding of basic cellular molecular biology, as well as the biomechanics of native and engineered tissues; (4) optimization of scaffolds; (5) development of bioreactors; (6) improved preservation methods for engineered tissues; (7) modulation of the immune response; (8) development of high-resolution real time nondestructive imaging. Future areas of opportunity include tissue engineering approaches to the development of biosensors which could be useful for biodefense applications. To meet these current and future challenges, the NIBIB is a member of the Multi-Agency Tissue Engineering Science Working Group (MATES). MATES is a trans-agency group charged with coordinating tissue engineering research across Federal agencies and to improve communication between agencies. In addition, numerous Federal agencies have developed a Federal Initiative for Regenerative Medicine (FIRM) led by the Department of Health and Human Services.

V. Cells, Scaffolds and Biomolecules for Tissue Engineering; from Benchtop to Beside– Dr. Stephen F. Badylak

Dr. Stephen Badylak is a research professor in the Department of Surgery and director of the Center for Pre-Clinical Tissue Engineering within the McGowan Institute for Regenerative Medicine at the University of Pittsburgh.

Dr. Badylak began by presenting examples of tissue engineering successes that have been extended to patients. He described the use of a porcine-derived resorbable biologic scaffold that can be engineered in a variety of thicknesses and with different growth factors depending on the architecture of the tissue in need of repair. When implanted in a patient, the cells of the surrounding tissue (e.g., tendons, the urinary bladder, or the heart) attach to this surface and grow into it, eventually replacing the scaffold. By providing a favorable environment for the growth of new tissue, the scaffold essentially alters the normal wound repair mechanisms of the body. Approximately 250,000 patients have been treated over the past four years with this scaffold. For example, the scaffold has been used to repair the lower urinary tract in women with post-menopausal urinary incontinence and to replace large portions of the bladder in individuals with cancer. The scaffold has also been used to heal not only traumatic superficial skin wounds, but also diabetic ulcers of the lower extremities. Dr. Badylak discussed successful use of the scaffold for tissue repair in veterinary medicine and its relevance to reconstructive surgery of the human face.

Dr. Badylak discussed ongoing tissue engineering efforts in industry. He discussed partnerships to move tissue engineering advances more quickly from the bench to the bedside. Dr. Badylak attributes some of his success to excellent partnerships with industry from the early stages of his

research. However, license agreements between academia and industry continue to be a barrier to the development of effective partnerships. Additionally, academic and Federal researchers not only have to educate industry about how tissue engineering is meant to be used in a patient, but also need to listen to industry about issues such as manufacturing and marketing costs, and third-party reimbursement. Early partnership with the Food and Drug Administration is essential to develop a regulatory strategy during the research and development stage to speed products to commercialization. Dr. Badylak finished his presentation by pointing out the inter-disciplinary nature of tissue engineering research.

VI. Training and Career Development Report – Dr. Linda C. Lucas

On behalf of Dr. D. Charles Maynard, Chair of the Training and Career Development Subcommittee, Dr. Linda C. Lucas provided a summary of a meeting held on May 26, 2004, at the Natcher Conference Center. Minutes of this meeting may be found here (INSERT LINK TO MEETING MINUTES).

Dr. Lucas presented an update on the training portfolio, ongoing planning in the Division of Inter-disciplinary Training, the Bioengineering and Bioinformatics Summer Institute, the NIH Roadmap, and a new partnership with the Howard Hughes Medical Institute.

Currently, the majority of training awards in the NIBIB portfolio are supported through fellowships and institutional training grants. Training constitutes approximately 2.6 percent, or approximately $7.8 million, of the NIBIB budget. New initiatives focus on pre-doctoral fellowships and dissertation level trainees. The NIH is supporting a Medical Residency Research Program to attract residents to research as well as a Post-doctoral Faculty Transition Award to assist junior investigators to transition from a post-doctoral fellow position to a faculty position. The NIBIB will hold a training grantee meeting in June. There will be a workshop in the winter of 2005 to further discuss future training plans for the NIBIB. The NIBIB continues to be involved in the planning and implementation of training through the NIH Roadmap.

The NIBIB, along with the National Science Foundation, is again co-sponsoring the Bioengineering and Bioinformatics Summer Institute (BBSI). The aim of this program is to provide students majoring in the biological sciences, computer sciences, engineering, mathematics, and physical sciences with inter-disciplinary bioengineering or bioinformatics research and education experiences. The Summer Institutes target undergraduates, juniors, and seniors, as well as new graduate students. The NIBIB and NSF supported nine Summer Institutes across the country with 128 students participating. The faculty/student ratio was 1:1 and women comprised 40 percent of the participants. Approximately 35 percent of the students will be returning to the program this summer. It is anticipated that the BBSI will begin a second 2-year cycle in the summer of 2005. The BBSI held their first grantee meeting in November 2003. A number of successes, such as strong interaction across career levels and high enthusiasm by the students and the mentors, were identified. In addition, some challenges were recognized – finding a balance between the quantitative and the biological scientific background and between didactic teaching and laboratory training.

It is important to follow trainees as they move to independent careers. The Institute is

developing tracking mechanisms to analyze the usefulness of the training programs. The NIBIB is currently exploring existing models of training assessment.

The Howard Hughes Medical Institute and the NIBIB are exploring a partnership to support the development of novel inter-disciplinary pre-doctoral training programs emphasizing the integration of quantitative and life sciences. The Howard Hughes Medical Institute will lead the first phase over 3 years, focusing on program development, curriculum development, faculty recruitment, and pilot support of trainees. NIBIB will lead the second phase over 5 years, focusing on the support of trainees and on the program director. It is anticipated that, after 5 years of support, awardees would be better positioned to receive support through the standard NIH institutional training award process. It is hoped that this joint venture will increase training opportunities two- to three-fold. Discussions will continue throughout the summer and the Council will be provided an update in September.

VII. Strategic Plan Development Report – Dr. Frank C. Yin

Dr. Frank Yin, Chair of the Strategic Plan Development Subcommittee provided a summary of a meeting held on May 26, 2004, at the Natcher Conference Center. Minutes of this meeting may be found here (INSERT LINK TO MEETING MINUTES).

Dr. Yin provided summaries of Dr. Janie Fouke's and Dr. Barbara McNeil's presentations on May 26, 2004, and the ensuing discussion (further details can be found in the minutes)

On a strategic level, the Institute is working to find the right balance between focused support areas and broad research areas in response to the legislative mandate creating the NIBIB. Overall, the Subcommittee feels that the Institute has succeeded in this endeavor. The issuance of ten Requests for Applications allowed the NIBIB to focus the attention of the external community on important or emerging research areas.

Since the January 14, 2004 meeting of the Strategic Planning Subcommittee, the NIBIB senior staff have attended two multi-day retreats with a third scheduled for June. The strategic planning website (http://www.nibib1.nih.gov/about/SP/strategicplan.htm) provides a "Message from the Director" and an opportunity for public comment. Thus far, the NIBIB has received approximately 20 comments through the website. It is expected that additional comments will be forthcoming once the draft strategic plan is posted on the website following the September 2004 Advisory Council meeting. Dr. Yin encouraged the Advisory Council members to make their constituents aware of the opportunity to provide comments on the strategic planning process and, after September, on the draft strategic plan.

Dr. Yin announced that Dr. Nobert Pelc will chair the Strategic Planning Subcommittee for the next year.

VIII. Closing Remarks – Dr. Roderic Pettigrew

Dr. Pettigrew thanked everyone for their participation. The meeting closed for lunch and then the review of applications at approximately 11:40 P.M.

IX. Closed Session

This portion of the meeting, involving specific grant review, was closed to the public in accordance with the provisions set forth in Section 552b (c) (4) and 552b (c) (6) Title 5, U.S. Code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).

X. Adjournment

The Council adjourned at 3:30 pm.

We certify that, to the best of our knowledge, the foregoing minutes and attachments are accurate and complete.

/s/
Joan T. Harmon, Ph.D.
Executive Secretary
National Advisory Council for Biomedical Imaging and Bioengineering
Director, Office of Extramural Policy
National Institute of Biomedical Imaging and Bioengineering

/s/
Roderic I. Pettigrew, Ph. D., M.D.
Chairperson,
National Advisory Council for Biomedical Imaging and Bioengineering
Director
National Institute of Biomedical Imaging and Bioengineering

The Council will consider these minutes at its next meeting. Corrections or notations will be incorporated in the minutes of that meeting.