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 21, 2010

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its 23rd meeting on May 21, 2010, at the Bethesda Marriott Suites in Bethesda, Maryland. Dr. Roderic I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), presided as Council chairperson.

In accordance with Public Law 92–463, the meeting was open to the public from 8:45 a.m. to 12:45 p.m. for review and discussion of program development, needs, and policy. The meeting was closed to the public from 1:40 p.m. to 2:45 p.m. for consideration of individual grant applications.

Council members present:
Dr. Philip Alderson, Saint Louis University, St. Louis, MO
Ms. Rebecca M. Bergman, Medtronic, Inc., Mounds View, MN
Dr. Richard L. Ehman, Mayo Clinic, Rochester, MN
Dr. Katherine W. Ferrara, University of California, Davis, Davis, CA
Dr. Gary H. Glover, Stanford University, Stanford, CA
Dr. Mae C. Jemison, Biosentient Corporation, Houston, TX
Dr. Percival McCormack, University of Illinois at Chicago, Chicago, IL
Dr. Cherri Pancake, Oregon State University, Corvallis, OR
Dr. Buddy Ratner, University of Washington, Seattle, WA
Dr. David Satcher, Morehouse School of Medicine, Atlanta, GA
Dr. David Skorton, Cornell University, Ithaca, NY

Council member absent:
Dr. Hedvig Hricak, Memorial Sloan-Kettering Cancer Center, New York, NY

Ex officio members present:
Dr. Francis Collins, National Institutes of Health, Bethesda, MD
Dr. Anne Plant, National Institute of Standards and Technology, Gaithersburg, MD
Dr. James G. Smirniotopoulos, Uniformed Services University of the Health Sciences, Bethesda, MD
Dr. Andrew Watkins, Centers for Disease Control and Prevention, Atlanta, GA

Ex officio members absent:
Dr. John McGrath, National Science Foundation, Arlington, VA
Dr. P. Hunter Peckham, U.S. Department of Veterans Affairs, Cleveland, OH
Ms. Kathleen Sebelius, U.S. Department of Health and Human Services, Washington, DC

Executive Secretary:
Dr. Anthony Demsey

[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 conflict of interest may have occurred. This procedure only applies to applications that are discussed individually, not to "en bloc" actions.

Also present:
NIBIB staff present for portions of the meeting:

Mr. Angelos Bacas
Dr. Richard A. Baird
Ms. Angela Burks
Ms. Barbara Cantilena
Ms. Patty Clements
Dr. Zohara Cohen
Ms. Shirley Coney-Johnson
Dr. Richard Conroy
Ms. Nancy Curling
Ms. Chris Ann Darby
Ms. Keisha Dent
Dr. Emilios Dimitriadis
Mr. Jeff Domanski
Mr. Antoine Durham
Dr. Henry Eden
Ms. Angela Eldridge
Dr. Zeynep Erim
Ms. Carol Fitzpatrick
Ms. Pamela Galpin
Dr. David George
Ms. Marie Gill
Ms. Aubri Gillespie
Ms. Pam Glikman
Dr. Alexander Gorbach
Dr. Valery Gordon
Dr. Ruth Grossman
Ms. Jude Gustafson
Dr. John Haller
Ms. Rosslyn Hart
Dr. John Hayes
Ms. Eunica Haynes
Dr. William Heetderks
Dr. Lori Henderson
Mr. Shabriya Horton
Dr. Rosemarie Hunziker
Dr. Albert Jin
Dr. Heather Kalish
Mr. William Kane
Dr. Chris Kelley
Ms. Mary Beth Kester
Dr. Dale Kiesewetter
Dr. Peter Kirchner
Dr. Brenda Korte
Dr. Svetlana Kotova
Dr. Lixin Lang
Dr. Richard Leapman
Dr. Albert Lee
Dr. Guoying Liu
Dr. Hector Lopez
Dr. James Luo
Dr. Ying Ma
Mr. Allen Markowitz
Dr. Alan McLaughlin
Mr. Todd Merchak
Dr. Nicole Morgan
Mr. Larry Morton
Mr. Joe Mosimann
Dr. Peter Moy
Ms. Lisa Pang
Dr. George Patterson
Dr. Grace Peng
Dr. Karen Peterson
Dr. Roderic I. Pettigrew
Ms. Mary Pitonak
Ms. Diana Robinson
Dr. Mary Rodgers
Mr. Rolando Romero
Ms. Jessica Ryan
Ms. Stephanie Sabourin
Dr. Belinda P. Seto
Mr. Shaun Sims
Ms. Casey Stewart
Dr. Manana Sukhareva
Ms. Kawanna Taylor
Mr. Kwesi Wright
Ms. Li-Yin Xi
Dr. Guofeng Zhang
Dr. Yantian Zhang
Dr. Ruixia Zhou
Mr. Adnan Zubair

Non-NIBIB NIH Employees:
None

Non-NIH Federal Employees:
Dr. Charles Friedman, Office of the National Coordinator, DHHS

Members of the public present for portions of the meeting:
Ms. Jennifer Ayers, American Institute for Medical and Biological Engineering
Mr. Benjamin Corb, American Institute for Medical and Biological Engineering

Ms. Kelly Grossman, National Capital Captioning
Ms. Allyson Harkey, NOVA Research Company
Mr. Ricardo Henriques, Event Technology Solutions
Ms. Masako Kaufman, Correspondent Iri Sangyo Shinbun
Mr. Keith Kerneklian, Academy of Radiology Research
Mr. Vhic Mata, Event Technology Solutions
Mr. Michael Peters, American College of Radiology
Dr. Bernhard Weigl, Group Leader, Diagnostic Development Teams, PATH
Ms. Andrea C. Weiss, Pharmaceutical Product Development

I. Call to Order: Dr. Anthony Demsey

Dr. Demsey called to order the 23rd meeting of the National Advisory Council for Biomedical Imaging and Bioengineering. He reminded attendees that the morning session of the meeting was open to the public, welcomed attendees, and introduced Dr. Pettigrew, who formally welcomed all participants.

II. Director's Remarks: Dr. Roderic Pettigrew

A. Retiring Members

Dr. Pettigrew acknowledged Ms. Rebecca Bergman, Dr. Katherine Ferrara, and Dr. David Satcher, who are retiring from the NACBIB. Dr. Richard Ehman was scheduled to retire but has agreed to have his term extended until the end of February 2011; he will also serve as the NIBIB representative on the Council of Councils.

B. Rebecca Bergman

Dr. Pettigrew congratulated Ms. Bergman, who was elected to the National Academy of Engineering by her peers in the field of engineering. Ms. Bergman was cited for technical leadership in the development of interventional vascular devices and drug delivery systems.

C. Budget Update

The 2011 President's Budget requests a 3.2 percent increase over the 2010 budget, which totals just under $9 million. With a trend continuing of NIBIB applications scoring well, NIBIB expects to fund to approximately the 13th percentile this year.

D. NIH Update

The Patient Protection and Affordable Care Act has had several impacts on NIH, including the authority to establish the Cures Acceleration Network (CAN), the brainchild of Senator Arlen Specter. The goal of CAN is to accelerate the delivery of practical therapeutics to the public. Residing within the Office of the NIH Director, CAN would work to bridge the gap between basic research and its clinical use. The Act calls specifically for the delivery of high-need cures (drugs, devices, and biologics). There is currently no money appropriated for CAN, but the Act authorizes the eventual appropriation of $500 million.

E. New NIH-FDA Partnership

Dr. Pettigrew announced a new NIH-FDA Joint Leadership Council to improve translational research, make science "regulatory-review ready," and speed development of new medical products. A meeting on June 2 will be open to the public, specifically for public consultation, advice, and input on the activities and goals of this Council.

F. CT Dose Summit

The CT Dose Summit: Scan Parameter Optimization meeting was held recently and cosponsored by NIBIB with the American Association of Physicists in Medicine. The meeting focused on the problem of radiation dose in computed tomography (CT). More recent models of multidetector CTs have been successful in dramatically reducing dose levels. This meeting was an effort to educate the community

that uses CT on how to achieve the lowest dose possible while maintaining diagnostic image quality. Additional meetings will be held in the future.

G. The BIG Think

Recently, NIH Director Dr. Francis Collins invited 60 outside scientists and the 27 Institute and Center Directors to generate the most promising ideas to pursue through the Common Fund—an effort he termed "The BIG Think." On May 7, the group gathered to discuss the first three of Dr. Collins' five themes of key opportunities: the application of high-throughput technology; translation of basic research to diagnostics and treatments; and putting science to work for the benefit of health care reform.

H. Scientific Management Review Board

The Scientific Management Review Board (SMRB) was authorized by the NIH Reform Act of 2006 to advise the Department of Health and Human Services and NIH on use of its organizational authorities. The SMRB is considering two issues: (1) merging the National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse; and (2) enhancing the Clinical Center. The SMRB appears to favor a functional rather than structural merger, in which the two Institutes would retain their current organizational structures but collaborate more regularly to pursue initiatives of common interest.

The SMRB also discussed improving the vibrancy of the Clinical Center, particularly in enhancing collaboration with extramural scientists. The SMRB is also considering adding a line item to the Office of the Director's budget to cover the operating expenses for the Clinical Center.

Dr. Collins has charged the SMRB with formulating a plan to accelerate development and translation of practical therapeutics.

I. Research in the News

Dr. Pettigrew highlighted several advances from NIBIB grantees cited in recent news. Vscan, a pocket-sized, ultra-smart ultrasound, is the product of a grant provided to a General Electric investigator under the NIBIB Low-Cost Imaging RFA. This diagnostic ultrasound device was developed to provide physicians with noninvasive imaging capabilities at the point of care and costs only $8,000.

Another NIBIB grantee recently published in *Nature Materials* regarding nanotechnology in targeted therapeutics. When injected, a simple polypeptide therapeutic conjugated molecule self-assembles into a nanoparticle with a hydrophilic shield. This shield protects the patient from systemic toxicity. Upon entering the tumor cell, the shield is liberated, exposing the tumor to a hydrophobic chemotherapeutic agent.

A Johns Hopkins University investigator has developed a microsurgical assistant system that improves a surgeon's skill. A robot pinpoints small areas and works in small spaces, such as the eye, and corrects for the hand tremors of the surgeon.

A group at the University of California, Los Angeles, has published early results of work with radio genomics. This imaging approach shows promise for identifying imaging biomarkers of genetic variants involved in Alzheimer's disease, a potentially powerful advance.

III. A Science and Public Health Agenda for Health IT: Dr. Charles Friedman

Dr. William Heetderks introduced Dr. Friedman, Chief Scientific Officer in the Office of the National Coordinator for Health Information Technology (ONC), Department of Health and Human Services, who reviewed the national science and public health agenda for health information technology. Dr. Friedman emphasized that *population health* is a broad term describing public health, research of all kinds, quality improvement, and emergency preparedness.

The Health Information Technology for Economic and Clinical Health (HITECH) Act appropriated $2 billion to the ONC in support of progress in health information technology. HITECH allowed for national coordination through ONC by statute rather than executive order; payment of incentives through

Medicare or Medicaid to providers and hospitals that achieve meaningful use of certified electronic health records (EHRs), beginning 2011; supportive grants and contracts, including three mandatory grant programs (one to assist states in health information exchange, one to create a set of regional extension centers, and one to support development of the health information technology [IT] workforce) and other discretionary programs; and enhanced privacy and security provisions.

The Health Information Technology Policy Committee defined *meaningful use* as having five qualities: improving quality, safety, and efficiency and reducing disparities; engaging patients and families; improving care coordination; improving population and public health; and ensuring adequate privacy and security. This shifts the focus from health IT itself to how it would be utilized. Meaningful use is being conceived in three stages: Stage 1, which will be finalized in 2011, is being defined through a formal governmental rule-making process focusing on those uses that require data capture and sharing; Stage 2 (2013) will introduce more advanced clinical processes, such as more sophisticated decision support; and Stage 3 (2015) will add improved outcomes.

Transcendent programs that fund research aimed at enhancing health IT will be necessary to bolster this work. For example, the Strategic Health IT Advanced Research Projects (SHARP) Program was established to spur development through targeted research projects to improve health IT in four specific areas where breakthrough improvements can greatly enhance the transformational effects of health IT: security of health IT; patient-centered cognitive support; health care application and network platform architectures development; and secondary use of EHR data. This $60 million program supports 4-year collaborative agreements aimed at tackling a problem through a multidisciplinary, multisite approach. Out of 75 applications, four were awarded: Harvard University (platform architectures development); Mayo Clinic (secondary use); University of Texas Health Science Center at Houston (cognitive support); and University of Illinois Champagne-Urbana (security). For each of these four, although only one institution is designated as the awardee, each award represents a collaboration of 20 to 25 institutions and 40 to 50 investigators from the public and private sectors.

The goals of meaningful use include improved individual and population health, increased transparency and efficiency, and improved ability to study and improve care delivery. Moving the nation toward meaningful use requires three elements: (1) adoption of certified EHR products; (2) exchange of health information from collection/storage point to where it is needed; and (3) capability of reporting quality measures from point of care to a data warehouse where those data could be aggregated and used to study and improve quality. Several integrated delivery systems are already in place at the National Cancer Institute, Kaiser Permanente, and Mayo Clinic, among others.

The last element will involve building a federated, integrated learning system for health care quality improvement and public health by 2015. The ONC and its new Nationwide Health Information Network are developing an interoperability framework to support this learning system. Dr. Friedman expects some pushback from stakeholders who currently enjoy a more lucrative system. ONC and the Institute of Medicine are planning a series of stakeholder meetings that will result in a report by the end of 2010.

Discussion

One Council member expressed concern that the success of this effort will be judged by such a broad, multifactorial outcome as "improved individual and population health." He suggested that it would be beneficial to develop appropriate criteria for judging success at a high level, such as in Dr. Friedman's office. Dr. Friedman responded that improvements in health that are directly attributable to health IT and meaningful use of EHRs are only one factor; for example, the Beacon Community Program focuses on improved health rather than technology by providing communities with funding to build and strengthen their health IT infrastructures and exchange capabilities. All applicants were required to articulate health improvement goals and propose a program to measure hypothesized improvement resulting from meaningful use and other activities in the community.

Another Council member noted that the government generally spends about 3 percent of the health budget on population health; as *population health* is defined by Dr. Friedman, 3 percent would be insufficient. Dr. Friedman stated that his definition of *population health* is somewhat techno-centric and includes all activities that require aggregation of data about individuals and appropriate analytics applied thereto. ONC will reevaluate its definition to ensure alignment with President Obama's health care reform agenda.

IV. Review of Council Procedures and Regulations

Dr. Demsey noted for the record that a quorum was present for this Council meeting. Council member Hedvig Hricak and *ex officio* members Drs. P. Hunter Peckham and John McGrath were unable to attend.

Dr. Demsey welcomed visitors, members of the science press, and members of scientific society constituencies. He thanked Ms. Carol Fitzpatrick and Ms. Pam Glikman for providing meeting logistics.

A. Council Regulations, Policies, and Procedures

Dr. Demsey summarized elements of the Government in the Sunshine Act and the Federal Advisory Committee Act that govern all Advisory Council meetings. These Acts require the U.S. Department of Health and Human Services to open Advisory Council meetings to the public except when proprietary or personal information is discussed. To comply with these regulations, the NACBIB meeting is open to the public for all but the review of individual grant applications. Dr. Demsey reviewed conflict of interest, confidentiality, and lobbying guidelines.

B. Future NACBIB Meeting Date

The next NACBIB meeting is scheduled for Monday, September 13, 2010, with the site to be determined. This meeting will test the move from Fridays to Mondays that Council members have been discussing. Dr. Demsey asked Council members to inform him about conflicts with upcoming meeting dates.

C. Approval of the January 22, 2010, NACBIB Meeting Minutes

A motion to approve minutes of the January 22, 2010, NACBIB meeting was made, seconded, and approved unanimously.

D. Early Expedited En Bloc Council Concurrence

At the September Council meeting, the Early Expedited En Bloc Council concurrence process will be used. Dr. Pettigrew will identify three Council Members to review and approve a subset of applications so that those projects can be funded well in advance of the end of the fiscal year.

V. Report of the Strategic Plan Workgroup: Dr. Richard Ehman

During its meeting on May 20, the Strategic Plan Workgroup was joined by a number of NIBIB program staff and senior leadership. Five topics were discussed: the Multi-Scale Modeling Initiative; success rates of women investigators; the nanotechnology program; the Biomedical Informatics program planning retreat; and the current draft of the revised strategic plan.

Dr. Grace Peng proposed revisions to the Multi-Scale Modeling Initiative, which involves multiple NIH institutes and federal agencies. Now in its third year, the Initiative has funded 13 projects. The main revision under consideration is a change from R01 to U01 (Cooperative Agreement). The Workgroup concurred with this proposal and suggested beginning to assess the impact of the Initiative.

Dr. Katherine Ferrara reported on the success rates of women investigators in obtaining grants from NIBIB and the NIH. The major issue identified that affects the relative amount of grant funding received by women is the low number of applications by women. Also, at each stage in the career pathway, women are leaving at a higher rate than men. She suggested that the Strategic Plan should reflect this important issue.

Dr. Peter Moy gave an in-depth progress review of the nanotechnology program. The Workgroup's feedback focused on employing understandable terminology that reflects an emphasis on technology

development and science, rather than purely operational activity. The Workgroup commended NIBIB leadership for conducting this self-evaluation. The Workgroup also discussed whether NIBIB should create a formal nanobiotechnology program.

Dr. Chris Kelley reported on a recent NIBIB Biomedical Informatics program retreat.

In addition to hearing these reports, the Workgroup also discussed the revised Strategic Plan.

VI. NIH Director's Report: Dr. Francis Collins

Dr. Pettigrew introduced Dr. Collins, Director of the NIH. In January, Dr. Collins published a paper in *Science Magazine* that outlined five themes that bring together opportunities in medical research. NIH also has been called upon to play a role in health care reform through areas such as comparative effectiveness research, personalized medicine, and pharmacogenetics. Many of these areas will rely on innovative approaches to technology.

NIH's mission statement comprises two parts: (1) "science in pursuit of fundamental knowledge about the nature and behavior of living systems" and (2) "the application of that knowledge to extend healthy life and reduce the burdens of illness and disability." The first part is largely driven by investigator-initiated R01s; NIH has supported 131 Nobel Prize winners, including 5 of the 6 from 2009. Dr. Collins gave several examples of projects that NIH has supported in the basic science arena, including the Voxelwise Genome-Wide Association Study. This study aims to determine gene variants that influence brain structure/function, particularly in Alzheimer's disease, using a whole-brain concept, a complete genome-wide association data set, and fully automated analysis. The opportunities in applied science are improving as more technologies, targets, and research directions are developed.

The public may not be aware of how well NIH investments have improved human health. For instance, deaths from coronary artery disease have decreased by 60 percent in the last 40 years and chronic disability in people over age 65 has decreased substantially in the last 30 years. Dr. Collins gave several examples of NIBIB- and NIH-supported projects that have a high likelihood of directly improving human health, including a microchip to isolate circulating tumor cells.

NIH investigators have the opportunity to play a more significant role in the development of therapeutics than in the past. Rather than competing with the pharmaceutical industry in drug development, NIH investigators should be in the position to take on projects previously considered unattractive to private sector investment. NIH investigators would move these projects past the risks and, ideally, hand them off in partnership with a private company. Throughout this process, the investigators must communicate with FDA to ensure approval. To that end, Drs. Collins and FDA Commissioner Peggy Hamburg have formed the NIH-FDA Joint Leadership Council to improve translational research, make NIH science "regulatory review ready," and speed development of new medical products.

The establishment of the Cures Acceleration Network (CAN), part of the Patient Protection and Affordable Care Act, also will aid in accelerating therapeutics development. CAN's goal is to dramatically advance development of new treatments and cures for debilitating and life-threatening diseases by reducing barriers between laboratory discoveries and clinical trials. With a budget of $500 million (authorized but not appropriated), this program gives NIH the opportunity to pursue therapeutics in an open atmosphere.

NIH has also made contributions to comparative effectiveness research. The new Patient-Centered Outcomes Research Institute (PCORI), authorized in the Patient Protection and Affordable Care Act, will identify areas that are in particular need of comparative effectiveness research attention and ask entities such as NIH to focus on them.

NIH has continued interest in supporting innovation and growing a rich workforce, acknowledging that advancing science requires more than success in basic and applied activities. Approximately one-third of the Common Fund goes to Transformative R01s, NIH Director's Pioneer Awards, and New Innovator

Awards, illustrating NIH's commitment to innovation even in difficult budgetary times. Likewise, the new Pathfinder Awards are intended to identify new ideas for diversifying the scientific workforce.

NIH has benefited greatly from American Recovery and Reinvestment Act (ARRA) funding. Unfortunately, as that extra funding ends, NIH faces a budget drop of $4 billion, and ARRA-funded projects may lose momentum. Dr. Collins suggested granting reasonable no-cost extensions for an additional year, recognizing that many projects were not funded until well into the first year of ARRA funds availability. Regardless, success rates—already declining—will likely suffer. Early-stage investigators, who are prone to leaving biomedical research, should receive particular attention.

One way to increase NIH's prominence is to educate people about the importance of biomedical research and inspire passion for science in the next generation. National Lab Day encourages NIH-supported scientists to interact with the next generation through spending time in high school biology classes. By participating himself, Dr. Collins endorses connecting with teachers and students to show that science is exciting and a great career choice. He hopes that scientists will begin to consider this kind of interaction part of the job.

Discussion

A Council member suggested that NIH consider using digital screen data feed subscriptions to spread the word about NIH accomplishments. The feeds can be targeted to the audience (students, scientists, etc.).

Dr. Collins responded that he has been attempting to reach the public in non-headline-oriented ways as well. This weekend's *Parade* magazine includes one of three articles Dr. Collins has written.

Another Council member suggested appealing to the private manufacturing and high-tech sectors for help with scientific research funding and addressing pipeline issues; this helped during the recession of the 1990s. Several national organizations connect higher education and business. He also noted that, because of his background and publicly stated beliefs about the juxtaposition of religion and science, Dr. Collins is uniquely positioned among scientists to use his bully pulpit to focus on ethical issues, such as stem cell research.

Another Council member inquired about NIH's role in eliminating health disparities. Dr. Collins responded that NIH research provides evidence to explain the basis of disparities and to test interventions. No true progress in advancing the health of the nation can be made until significant progress has been made in eliminating disparities. The recently passed health care reform legislation will help obtain health insurance for many people, thus improving access. Dr. Collins would also like to mount a prospective, longitudinal, scientifically designed study of health and disease in one million people, with over-representation in under-represented groups, sampling everything possible about environment, genetics, and medical experiences. The United Kingdom is currently accruing participants for a study of this kind. The Council member expressed his hope that all of NIH will increasingly articulate the importance of eliminating disparities, which also will help attract minorities into research.

Another Council member noted that the lack of industry involvement in the Clinical and Translational Science Awards (CTSAs) impedes progress of technologies. Dr. Collins agreed and remarked that the National Center for Research Resources (NCRR) held a workshop in February that focused on better connecting industry and CTSAs. NCRR is working out how best to exhort CTSAs to strengthen these connections without being heavy-handed.

The Patient Protection and Affordable Care Act attempts to provide relief to the biotechnology industry by setting aside $1 billion to be distributed by the Department of the Treasury to companies that have recently invested in projects that could lead to therapeutic or diagnostic products to benefit the public. These companies, which must employ 250 people or fewer, can apply to the program for a grant or a tax break if they are not yet profitable. Awardees are reimbursed for up to 50 percent of expenditures in 2009 and 2010, up to $5 million. Dr. Collins expects many of the applicants will be Small Business Innovation Research (SBIR) awardees.

VII. Point-of-Care Diagnostics for Global Health: Dr. Bernhard Weigl

Dr. John Haller introduced Dr. Weigl, group leader of the Program for Appropriate Technology in Health (PATH) Diagnostics Group and principal investigator of the NIBIB-supported Center for Point-of-Care Diagnostics for Global Health. PATH is an international nonprofit organization with 900 employees worldwide that focuses on appropriate technologies for health, particularly in developing countries.

Despite much investment and many years of work in this area, global health is not greatly improving. Although life expectancy is increasing overall, it is decreasing in 16 countries. Infant mortality is 10 times worse in developing countries, on average, than in developed countries. Mortality for children under 5 years of age is decreasing, but 27 percent of these children are underweight and malnourished.

Funded primarily by the Gates Foundation and the government, PATH focuses on developing technology specifically for low-resource settings. PATH aims to form product development partnerships between private and public entities to reduce the risk for companies and increase viability of product development. PATH works on many kinds of technologies, from command and control interventions (e.g., vaccines) to provider-directed interventions (diagnostics) to consumer-directed interventions (e.g., over-the-counter health products, and safe water).

Diagnostics laboratories in developing countries often have limited instrumentation, no clean running water, intermittent electricity, no refrigeration, and little product support or quality control. Successful diagnostics must work in these kinds of settings. Likewise, transportation is uncontrollable; a multicountry PATH study found that over 70 percent of diagnostics were officially out of specification before they arrived at the laboratory due to age, exposure to heat, etc. Usage of point-of-care diagnostics is difficult to control, making quality control impossible.

A common misconception is that people's time in developing countries is not worth as much as people's time in developed countries, when in fact the opposite is true. Few people in developing countries have paid time off, transportation, or savings. Spending 4 hours in a clinic means losing 4 hours' pay, which could mean less food for their families.

Point-of-care (POC) testing is defined as diagnostic testing that is performed near to or at the site of patient care, with the result leading to possible change in the care of the patient. In developed countries, POC testing is an adjunct to central laboratory testing, not a replacement. With one exception (glucose testing for diabetes), POC testing has not yet been transformational for many patients or caregivers. Dr. Weigl outlined four ideas that could be transformational in developed countries: (1) a POC trauma or emergency EMT suite that focuses on assays where speed truly affects emergency care; (2) tests that bridge the health access gap, for use in public clinics, house calls, etc.; (3) a disaster laboratory in a box (disaster POC testing); and (4) a universal home health interface.

There are many challenges to employing POC testing in developing countries*:* higher costs per test, quality control risk, lack of trained health workers, test procurement and distribution issues, limits of performance, the risk that telemedicine might disempower local capacity, and lack of a POC test for every situation. However, POC testing offers many advantages: lower startup cost, more flexible innovation, customizable solutions, empowerment of local health care providers, minimal infrastructure requirements, rapid turnaround of test results and start of treatment, and the absolute need for POC in situations where access to a central laboratory is slow or limited. Another POC transformational opportunity lies in creating a POC-based health system in developing countries that do not have a central laboratory infrastructure. It may be more efficient not to build such an infrastructure and focus efforts on telemedicine.

PATH works to remove risks for its partners, resulting in viable, low-resource diagnostic products with lower profit margins. For example, PATH developed a strip test to increase access to diagnosis and care of Chagas disease, a regional disease in Central America. The existing diagnostic requires a laboratory. By performing much of the research and testing for this strip test, PATH reduced the company's risk and

created a viable product that sells for $2, far below what the company would have charged had it taken on all of the research and development risk.

PATH has also developed lateral flow strip tests for use in hepatitis B, malaria, HIV, and pregnancy; however, these tests are not always as accurate, sensitive, and specific as they should be. Using microfluidic integration, PATH attempted to make molecular assays as simple to use as strip tests, but the cost and failure rates proved too high to be practical for developing countries. Dr. Weigl's latest approach is to focus on component improvement, with the same goal of simplicity and sensitivity. He and his colleagues have developed two types of nucleic acid sample preparation devices with different heating modules that do not require any kind of instrumentation. Dr. Weigl provided several examples of sample preparation methods developed by PATH, including a proviral DNA capture card and visual detection.

PATH is collaborating with the Yager group to develop paper microfluidics, which would use multiplex assays on a strip or in a vial for chronic disease and syndromic diagnosis and HIV treatment assays.

The NIBIB-supported Center for Point-of-Care Diagnostics for Global Health (GHDx Center) conducts diagnostics validation, diagnostics research and development in the laboratory and field settings, and needs assessments; provides training and outreach; and funds external work. Unfortunately, funding for translation and introduction of products is limited—the Gates Foundation gives only limited funding, and NIH gives none. It takes approximately 5 years and $20 million to develop a new diagnostic product platform.

Dr. Weigl suggested that diagnostic tools should be developed specifically for low-resource settings. Some markets are quite attractive, and reverse technology transfer (from a developing nation to developed nation) is possible. More traditional arguments include preventing waste, preventing worsening problems, reducing health system costs, and improving lives. However, the challenges of developing diagnostic tools specifically for low-resource settings are enormous. These diagnostics must work just as well as those created for high-resource settings: they must work in adverse conditions; require little training; cost less to develop and produce; and sell for one-tenth to one-twentieth of the comparable assay in developed countries.

Discussion

One Council member suggested that money can be made in mixed settings, marketing low-cost diagnostics to those who can afford to pay more and using cost-shifting to support the low-resource settings. Dr. Weigl agreed that products must make money in order to ensure their ongoing support. PATH contracts stipulate that a company must commit to selling to certain markets at a certain cost for a specific period of time; however, they may also sell in the same market to private clinics or in developed countries at whatever price they choose.

Another Council member noted that many factors contributed to the decline of global health in the late 20th century, including economic turmoil, structural adjustment, and nutritional status change as a result of the switch from indigent farming to cash crops. HIV/AIDS made things worse, but countries also spent less on health care. It is necessary to consider what a country is willing to pay for, as the largest advances in public health are in sanitation and infrastructure. Dr. Weigl added that while HIV/AIDS was certainly not the only cause of the decrease in global health, it was a major factor. The Web site gapminder.com has graphs that illustrate other developing country parameters.

That same Council member also suggested that reverse technology transfer opportunities might exist for doctors' laboratories in the United States with regard to travelers' diseases. Dr. Weigl noted that FDA approval is an impediment to keeping costs low; generally, PATH-developed tests have only foreign, country-specific approvals, due to regulatory costs.

VIII. Adjournment

The open session of the NACBIB meeting was adjourned at 12:45 p.m.

IX. Closed Session

The grant application review portion of the meeting was closed to the public in accordance with 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). The closed session was adjourned at 2:45 p.m.

Certification:

We certify that to the best of our knowledge, the foregoing minutes and attachments are accurate and complete.[2]

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Anthony Demsey, Ph.D.
Executive Secretary,
National Advisory Council for Biomedical Imaging and Bioengineering
Director,
Office of Research Administration
National Institute of Biomedical Imaging and Bioengineering

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

[2] These minutes will be approved formally by the Council at the next meeting on September 13, 2010, and corrections or notations will be stated in the minutes of that meeting.