



**Department of Health and Human Services  
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**Advisory Committee to the Director**

**99th Meeting**

**December 4, 2009**

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## **EXECUTIVE SUMMARY**

The 99th meeting of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) was held on December 4, 2009, on the NIH campus. NIH Director Francis S. Collins, M.D., Ph.D., welcomed the ACD members, other meeting participants, and visitors, noting that this was the first ACD meeting since he became the NIH Director in August 2009. He expressed his gratitude for the contributions of five ACD members who were rotating off the committee: Catherine D. DeAngelis, M.D.; Karen A. Holbrook, Ph.D.; Mary-Claire King, Ph.D.; John C. Nelson, M.D.; and Barbara L. Wolfe, Ph.D. He welcomed a new ACD member, Haile T. Debas, M.D.

Dr. Collins announced that Eric D. Green, M.D., Ph.D., had been appointed Director of the National Human Genome Research Institute (NHGRI).

Mr. John Bartrum, of the Office of Budget, reviewed budget activities. The NIH had received \$10.4 billion in stimulus funds under the American Recovery and Reinvestment Act (ARRA). To date, \$4.8 billion had been obligated (that figure would rise to about \$7 billion with commitments into 2010) with emphases on extramural research, instrumentation, and construction projects. Raynard S. Kington, M.D., Ph.D., NIH Principal Deputy Director, reported that of the total ARRA funds for the NIH, \$8.2 billion targeted extramural scientific research; \$1.3 billion targeted extramural repairs, improvements, construction, and scientific equipment; and \$500 million targeted intramural repairs, improvements, and construction. An additional \$400 million targeted comparative effectiveness research (CER) through the Agency for Healthcare Research and Quality. Joseph Ellis, of the Office of Policy for Extramural Research Administration, reviewed progress in developing new rules for extramural conflict of interest. Rosalind Gray, Acting Director of the NIH Office of Legislative Policy and Analysis, noted that in 2009, the NIH had taken part in 18 congressional hearings, 21 courtesy visits, and 27 briefings.

Dr. Collins reviewed exciting areas in which the NIH would move forward in the days to come, and he described five themes for the future of the NIH: high-throughput approaches for fundamental biology, translational medicine, science to benefit health care reform, global health, and reinvigorating the biomedical research community.

Lana R. Skirboll, Ph.D., of the NIH Office of the Director, described the NIH effort to produce guidelines for human stem cell research, including the convening of an ACD working group for stem cell eligibility review. In March 2009, President Obama signed Executive Order 13505, "Removing Barriers to Responsible Research Involving Human Stem Cells." Jeffrey R. Botkin, M.D., of the University of Utah School of Medicine and Chair of the ACD Working Group for Human Embryonic Stem Cell Eligibility Review, described the working group process and presented to the ACD the findings regarding a submission from Harvard University. The ACD members discussed the Harvard submission and the working group's recommendation. They formally recommended to restrict use of the Harvard lines to be consistent with the language in the formed consent form and to approve the finding (proposal) of the working group that the Harvard embryonic stem cell lines (27 of the 28 proposed) be eligible for use in NIH-funded research.

Richard J. Hodes, M.D., Director of the National Institute on Aging, reviewed the NIH's history of supporting CER, including patient-centered research on prevention, diagnosis, treatment, behavior change, health systems, and special populations. He described the NIH's leadership role in CER funded by ARRA, as a member of a Federal Coordinating Council and with the convening of a CER Coordinating Committee for all NIH CER programs. The NIH had obligated about \$342 million of a total of \$400 million in ARRA funding for CER. Key CER activities would be those that generated evidence to enable physicians and patients to make optimal health care decisions and those that provided training for a CER workforce for the future.

Beth Furlong, J.D., Ph.D., R.N., the NIH Director's Council of Public Representatives (COPR) liaison to the ACD, reviewed recent activities of the Council, which had

celebrated its 10th anniversary in the fall. During the week of October 26-30, the Council took part in “Engaging the Public in Research Week”, which included a “Partners in Research Investigator Workshop”, a “Nuts and Bolts of Community Engagement in Research” forum, and the COPR fall meeting.

Christopher P. Austin, M.D., Director of the NIH Chemical Genomics Center and Senior Advisor to the NHGRI Director, described the Therapeutics for Rare and Neglected Diseases program (TRND), which supports small molecule (drug) research with a goal of expediting basic research discoveries beyond the target identification stages towards assay development, screening, and probe development and to testing in Phase I clinical trials.

Linda S. Birnbaum, Ph.D., Director of the National Institute of Environmental Health Sciences (NIEHS), reviewed her Institute’s programs and activities. NIEHS is based in Research Triangle Park, North Carolina, and receives funding through three congressional committees (Labor [HHS-NIH], Interior, and Energy). Major activities include the National Toxicology Program, intramural laboratories, and extramural research. The Institute focuses on translating bench science into public health. NIEHS’s Superfund Program addresses mandates such as detecting hazardous substances in the environment and supporting worker training (e.g., chemical emergency responders).

Dr. Kington presented, for the ACD members’ consideration, a new list of prescreened bona fide cash awards that NIH employees could receive.

## **WELCOME AND NIH DIRECTOR'S REPORT**

The 99th meeting of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) was held on December 4, 2009, on the NIH campus. NIH Director Francis S. Collins, M.D., Ph.D., welcomed the ACD members, other meeting participants, and visitors, noting that this was the first ACD meeting since he became the NIH Director in August 2009. He stated that the meeting was open to the public and Webcast globally.

Dr. Collins expressed his gratitude for the contributions of five ACD members who were rotating off the committee: Catherine D. DeAngelis, M.D.; Karen A. Holbrook, Ph.D.; Mary-Claire King, Ph.D.; John C. Nelson, M.D.; and Barbara L. Wolfe, Ph.D. He welcomed a new ACD member, Haile T. Debas, M.D., and noted that three members, Joan S. Brugge, Ph.D.; Susan Hockfield, Ph.D.; and Alan I. Leshner, Ph.D., were unable to attend the meeting.

Dr. Collins asked the group to reflect on the life and work of Ruth L. Kirschstein, M.D., who passed away in October. Dr. Kirschstein served the NIH in many capacities for 50 years, performing work on vaccine safety in the 1950s, serving as the first female Director of the National Institute of General Medical Sciences beginning in 1974, and twice serving as Acting Director of NIH. Dr. Collins presented a brief video interview with Dr. Kirschstein, in which she recalled her early experiences in becoming a doctor and her focus on a diverse leadership.

Dr. Collins was nominated by President Obama in July 2009 to be the new NIH Director and was sworn in on August 17. He expressed his appreciation to Raynard S. Kington, M.D., Ph.D., Principal Deputy Director, for serving as Acting Director in the interim period and to Lawrence A. Tabak, D.D.S., Ph.D., for serving as Acting Deputy Director. Dr. Collins introduced Kathy Hudson, Ph.D., formerly of the Johns Hopkins University Genetics and Public Policy Center, as the new Chief of Staff.

Dr. Collins announced that Eric D. Green, M.D., Ph.D., had been appointed Director of the National Human Genome Research Institute (NHGRI). Dr. Green would bring to the position a strong background in comparative genomics research. Elizabeth G. Nabel, M.D., has moved from her position as Director of the National Heart, Lung, and Blood Institute (NHLBI) to become the President and CEO of Brigham and Women's Hospital. Susan B. Shurin, M.D., has been named NHLBI Acting Director during the search for a new director. After serving as Director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) for 23 years, Duane M. Alexander, M.D., has joined the Fogarty International Center (FIC) as a Senior Scientific Adviser on an initiative on Maternal and Child Health, which is a component of the White House Global Health Initiative. NHGRI Deputy Director Alan Guttmacher, M.D., has accepted assignment as the NICHD Acting Director.

The NIH also has searches under way for directors for the Office of Legislative Policy and Analysis; the Office of Behavioral and Social Sciences Research; the Office of Extramural Research; and the Division of Program Coordination, Planning, and Strategic Initiatives. Dr. Collins encouraged the ACD members to submit the names of appropriate candidates for the open positions. The NIH will soon be seeking a new Associate Director of the Office of Budget. John Bartrum, the current Associate Director of the Office of Budget, accepted an offer to join the House Majority Appropriations Committee as a senior professional member.

Mr. Bartrum reviewed the NIH budget activities. The NIH had received \$10.4 billion in stimulus funds under the American Recovery and Reinvestment Act (ARRA). So far, \$4.8 billion had been obligated (that figure would rise to about \$7 billion with commitments into 2010) with emphases on extramural research, instrumentation, and construction projects. The NIH was operating under a continuing resolution until December 18. The FY 2010 budget request was nearly \$31 billion. House and Senate versions of the budget were close to that amount. Both Appropriations Committees expressed reservations about proposed special initiatives for autism and cancer in the budget request, cautioning against earmarks for specific diseases. The accepted view was

that science should drive the research and, therefore, the amount of funding. The FY 2011 budget proposal is in process, having been submitted to the Department of Health and Human Services (HHS), and the Office of Management and Budget. The budget is expected to be rolled out in the first week of February.

Joseph Ellis, Office of Policy for Extramural Research Administration, updated the ACD on progress in developing new rules for conflict of interest. He described the current regulations and the environment, in which grantee institutions were responsible for establishing policies and managing conflicts—a process that should continue because of each institution's responsibilities for their investigators. The NIH provides oversight and had recently presented an advance notice of proposed rulemaking, that asked for public comment on whether and how the Federal conflict of interest regulation should be amended. The NIH received about 70 responses, many from large organizations. The comments are being considered and proposed changes to the regulation are being drafted. A final rule likely would be published in the summer or fall of 2010, and Mr. Ellis noted that there would be additional opportunity for public input.

Dr. Collins expressed that it was crucial that the public trust the NIH. The ACD members discussed the importance of addressing conflicts that could arise in the research and publication processes. However, Beatriz Luna, Ph.D., stated that public-private interactions are often profoundly valuable and that the NIH should avoid creating the perception that interactions of NIH-funded researchers with pharmaceutical firms are somehow unethical.

Rosalind Gray, Acting Director of the NIH Office of Legislative Policy and Analysis, provided the legislative update, noting that in 2009 the NIH had taken part in 18 congressional hearings, 21 courtesy visits, and 27 briefings. In October, 16 members of Congress visited the NIH. Various provisions in the current health care reform legislation were of interest to the NIH, including aspects related to autism, comparative effectiveness, emergency medicine, health care quality, pain management, postpartum depression, and prevention. Ms. Gray outlined the organizational models for comparative

effectiveness research (CER), as described in the House and Senate bills. The House bill included a center within the Agency for Healthcare Research and Quality (AHRQ). The Senate bill called for a nonprofit institute to serve as the operational center with the NIH holding a seat on its governing board. The House had passed its version in November, and the Senate bill was still under consideration. There was a good chance that a final bill would not be voted on in the current congressional session.

In response to a question, Ms. Gray noted that CER would be funded from trust funds in addition to traditional mechanisms within the NIH. Ralph Horwitz, M.D., cited a need for fundamental work on CER methods. Dr. Collins noted the need to realize the strengths of both the AHRQ and the NIH in CER. Colleen Conway-Welch, Ph.D., cited a need to craft better messages to the public about CER. Dr. Wolfe suggested taking up the issue of cost-effectiveness as well. Dr. Collins stated that there were opportunities for the NIH to fund research into, for example, modeling incentives to lead to good outcomes and cost-effectiveness. James Thrall, M.D., emphasized that evidence-based research reflected not just science, but the intersection of science and social utility.

Dr. Kington updated the ACD on NIH ARRA funds. Of the \$10.4 billion given to the NIH, \$8.2 billion targeted extramural scientific research; \$1.3 billion targeted extramural repairs, improvements, construction, and scientific equipment; and \$500 million targeted intramural repairs, improvements, and construction. An additional \$400 million targeted CER through the AHRQ. ARRA-funded programs are intended to stimulate, accelerate, and expand biomedical research using a blend of existing mechanisms and new programs. To date, the NIH has awarded \$4.353 billion in grants. These include Challenge Grants, Grand Opportunities Grants, grants supporting new faculty recruitments, and administrative supplements for summer research for students and teachers. Many of these same funding mechanisms were used to support CER. Dr. Kington listed ARRA funding opportunities for FY 2010, including the pilot program “Biomedical Research, Development, and Growth To Spur the Acceleration of New Technologies;” the Small Business Catalyst Awards for Accelerating Innovative Research; the Academic Research Enhancement Award; and awards linking communities

to health science. Announcements for these programs can be found at <http://grants.nih.gov/recovery/>. The NIH has developed tools for reporting its ARRA funding and for tracking the investments. Data can be viewed at <http://report.nih.gov/recovery/index.aspx>. Dr. Kington commended the NIH staff for their tremendous effort in administering considerable funding in a short amount of time.

## **DIRECTOR'S VISION FOR NIH: EXCEPTIONAL OPPORTUNITIES IN BIOMEDICAL RESEARCH**

Dr. Collins reviewed exciting areas in which the NIH would move forward in the days to come. He stressed the interests and support of President Obama and HHS Secretary Kathleen Sebelius, who had visited the NIH on September 30. The NIH serves two roles—supporting science in the pursuit of fundamental knowledge about the nature and behavior of living systems and supporting the application of that knowledge. Dr. Collins expressed his belief that the success and contributions of the NIH are largely dependent on the ideas and efforts of individual investigators, with large organized projects also playing a role. Dr. Collins described five themes for the future of the NIH.

- *High Throughput Technologies:* This would include genomic sequencing efforts, nanotechnology, small molecule screening, new imaging modalities, computational biology, and comprehensive approaches (e.g., all of the proteins in the cell). Computational biology would be critical.
- *Translational Medicine:* NIH-supported researchers could work to “de-risk” small-molecule investigations, making them attractive to the private sector for licensing.
- *Benefiting Health Care Reform:* Address CER, prevention, personalized medicine, health disparities, pharmacogenomics, large-scale prospective studies, and health information technology.

- *Global Health:* Recognize the value of research that could provide solutions for diagnostics and prevention, including vaccine development and solutions for chronic noninfectious diseases.
- *Reinvigorating the biomedical research community:* Emphasize innovation and transformative research.

With the conclusion of ARRA funding on the horizon, a large number of applications are expected in 2011. That possibility, combined with future budget uncertainty, will present the NIH with challenges and no easy answers. Dr. Collins cited a need to attend to the peer review process to ensure that current innovations were working. Other important issues include research supported by the Common Fund and career development. The NIH needs to seek ways to make the NIH-supported biomedical workforce more representative of the country as a whole. Dr. Collins raised the idea of creating more ACD subcommittees to deliberate on specific issues and make recommendations.

### *Discussion*

Dr. Nelson wondered about the NIH's ability to deal with even larger issues, such as clean air and clean water (and health effects), including reaching out to other agencies. Dr. Collins noted recent meetings dealing with, for example, designing new clinical trials, and developing relationships with other agencies such as the Centers for Disease Control and Prevention (CDC). Dr. Holbrook cited a need to address the health of military veterans who returned from war with disabilities.

Dr. Horwitz encouraged the NIH to address the issue of new technologies adding to the cost of health care. Dr. Collins stated that technology's influence on rising health care costs appears to be linked not just to the technology itself but also to the way in which the technology is utilized. Dr. DeAngelis suggested that the high costs of many new technologies are related to misapplication. Perhaps, said Dr. Collins, the NIH could consider experiments in which preventive information (e.g., about mammograms) was

offered to providers along with incentive systems and educational modules, with a goal of identifying good decision making. The NIH needs to identify where technologies should be translated into the health care system. Thomas Kelly, M.D., Ph.D., noted demographic changes in science and a need to understand the effectiveness of training programs. Dr. Wolfe wondered whether health care reform might provide opportunities to determine what prevention strategies worked.

Jeffrey Murray, M.D., encouraged the NIH to build on the idea of placing information in the public trust, as in the human genome project. Dr. Collins agreed, citing the need to find balance with intellectual property rights and privacy. Keith Yamamoto, Ph.D., encouraged the NIH to first consider principles regarding graduate training of medical researchers. What product did the NIH desire? The NIH should consider lengthening postdoc training and a need for focus to hold onto students. A workforce analysis was needed. Mary Beckerle, Ph.D., encouraged the NIH not to lose sight of the fact that the foundation of its knowledge came from basic science and discovery. Maria Freire, Ph.D., stressed the importance of reaching out through international efforts, including new world players such as China, India, and South Africa, to advance global health.

## **STEM CELL POLICY AND ACD STEM CELL WORKING GROUP REPORT**

Lana R. Skirboll, Ph.D., of the NIH Office of the Director, described the NIH effort to produce Guidelines for Human Stem Cell Research and the convening of the ACD Working Group for Human Embryonic Stem Cell Eligibility Review (hESC WG). In March 2009, President Obama signed Executive Order 13505, "Removing Barriers to Responsible Research Involving Human Stem Cells." The NIH released draft Guidelines for Human Stem Cell Research in April 2009 and solicited and received public comment. Final guidelines were published and became effective in July 2009. The Guidelines stated that human embryonic stem cells used in NIH-funded research had to be (1) derived by *in vitro* fertilization for reproductive purposes and were no longer needed for that purpose; and (2) donated by individual(s) who sought reproductive treatment and who gave voluntary written consent for embryos to be used for research purposes.

Dr. Skirboll reviewed the requirements in the Guidelines, including those (sections IIB and IIC) that referred to the responsibilities of the ACD and its hESC WG. She outlined the paths to eligibility (or ineligibility) for embryos under the Guidelines, highlighting cases to be considered by the hESC WG. Section IIC of the Guidelines stated: “For embryos donated abroad on/after July 7, 2009 (if Section IIA is not met), the Working Group will consider whether alternative procedural standards of a foreign country where embryos were donated provide protections at least equivalent to those provided by Section IIA of Guidelines.” Dr. Skirboll referred to the many stem cell lines developed during more than a decade—in states, countries, and other entities—that featured many common policies, guidelines, and ethical bases. Nevertheless, requirements for implementation and compliance had evolved. The ACD was charged to consider such issues without performing a *de novo* evaluation of ethical standards. Dr. Skirboll noted that more than 100 additional human embryonic stem cell lines had so far been submitted and were currently being reviewed. On December 2, 2009, Dr. Collins approved 13 cell lines for NIH-funded research.

The ACD members wondered about issues relating to original consent forms and restrictions—for example, if the consent called for specific research uses of cell lines derived from the embryos. Dr. Skirboll noted that the uses in NIH-funded research would be restricted appropriately and on a case-by-case basis. Donors were not allowed to benefit financially from the use of the human embryonic stem cell lines, to avoid inducements to donate. Issues of the broad availability of the lines listed on the NIH Registry were yet to be resolved. Dr. Collins stated that the idea of a repository would be considered. Dr. Wolfe wondered whether, because the policy was the result of an Executive Order, it might be reversed in the future. Dr. Collins responded that Congress might establish a remedy for that issue.

Jeffrey R. Botkin, M.D., of the University of Utah School of Medicine and Chair of the ACD hESC WG, described the WG process and presented to the ACD its findings regarding a submission from Harvard University. Dr. Botkin noted that the consent for

clinical services that couples underwent for fertilization processes was distinct from the consent for research processes. The hESC WG reviewed the Harvard submission of 28 human embryonic stem cell lines for research; Dr. Murray served as the primary reviewer. The lines were donated prior to July 7, 2009, under a single Institutional Review Board (IRB)-approved protocol and informed consent form. The protocol was designed in 2000-2001. Dr. Botkin described the anonymization and other processes for donations. Relevant to use of the lines in NIH-funded research, the consent form indicated that cells would be used to study the embryonic development of endoderm, with a focus on pancreatic formation. The Harvard IRB determined that it was acceptable to use the cells more broadly based on interpretation of the Common Rule regarding the use of anonymized tissue. Finally, the hESC WG determined that one line (#HUES25) should not be approved, because its consent was obtained during a lapse in the IRB approval process. The hESC WG suggested that the ACD recommend the NIH approval of the remaining lines for NIH-funded research.

#### *Discussion and Vote*

Dr. DeAngelis wondered whether it would be necessary for researchers to have some background information about these and other anonymized embryos. Dr. Collins stated that such information would not be necessary for immediate basic research. In the long term (clinical implications), information would be gleaned from full genome analyses.

Dr. Luna proposed, for future submissions, that the NIH considers a standardized consent process. Dr. Beckerle expressed agreement with the hESC WG in excluding line #HUES25. The ACD members expressed some concern about determining authenticity of the informed consents. Dr. Murray, who was a member of the WG, described the extraordinary lengths to which Harvard had gone to ensure that no possible financial relationships existed for collection of the embryos. Dr. Wolfe wondered about possible uses of the embryonic stem cells beyond endoderm development and beyond the consent form requirements. Dr. Nelson stated a need for the ACD to vote on two aspects—(1) a

restriction on use of the cell lines related to the language in the informed consent, and (2) the finding of the hESC WG.

The ACD members considered charging the NIH with developing a policy to guide the ACD and the hESC WG in handling issues such as conditions listed in the informed consent form signed by the embryo donor(s).

The ACD drafted and voted on the following recommendations:

- 1. The ACD recommends that the use of the Harvard lines discussed today, December 4, 2009, in NIH-funded research be restricted to projects that are consistent with the wording of the consent form. This recommendation is specific to these lines.**
- 2. The ACD recommends that, consistent with Section IIB, 27 of the 28 lines (HUES 1–28) be eligible for use in NIH-funded research. It recommends that line #25 not be eligible.**

The ACD members approved each proposal unanimously (13 votes in each case).

## **COMPARATIVE EFFECTIVENESS RESEARCH**

Richard J. Hodes, M.D., Director of the National Institute on Aging (NIA), stated that the NIH has a long history of supporting Comparative Effectiveness Research (CER), including patient-centered research on prevention, diagnosis, treatment, behavior change, health systems, and special populations. He reviewed some landmark CER studies, such as the ALLHAT study, which compared antihypertensive drugs, and the lifestyle-versus-drug (metformin) trial for the prevention of diabetes. The NIH has addressed CER in trial networks, in its consensus development program, in the National Information Center on Health Services Research and Healthcare Technology, and in other ways. Its HMO Research Network is a consortium of 16 integrated health systems that is supported by funding from the AHRQ, the CDC, and the Food and Drug Administration (FDA) in

addition to the NIH. The NIH extensively disseminates CER findings through its Web site, education programs, patient groups, and professional organizations.

The NIH is taking an active leadership role in CER funded by ARRA, both as a member of a Federal Coordinating Council and by convening the NIH CER Coordinating Committee for all the NIH CER programs. CER subcommittees coordinate with activities at the AHRQ, the Department of Veterans Affairs, and the FDA. The NIH has obligated about \$342 million, of a total of \$400 million, in ARRA funding for CER. Dr. Hodes presented a list of funded CER projects. Key CER activities were those that generated evidence to enable physicians and patients to make optimal health care decisions and those that provided training for a CER workforce for the future. CER centers were being developed to support research, training, and dissemination of knowledge, and investigators were applying behavioral economics to increase the uptake of CER findings. Dr. Hodes described CER efforts by the AHRQ using ARRA funds. He also described projects of the Office of the Secretary for which the NIH would be taking the lead, including Centers of Excellence for Racial and Ethnic Minority-Focused CER and Behavioral Economics and Change. He said that CER should be guided by the emerging sciences of genomic and personalized medicine. Researchers would generate and test hypotheses in personalized medicine relating to why individuals and groups do or do not respond to treatments.

In discussion, Dr. Conway-Welch encouraged the NIH to examine, for the benefit of CER, studies of public dissemination in other cases, especially noting the use of language. Dr. Nelson suggested reaching out to professional societies to disseminate findings. Dr. King encouraged the NIH to include pharmacogenetic studies in the work of the Centers of Excellence for Racial and Ethnic Minority-Focused CER. David L. Demets, Ph.D., cautioned that many CER results would feature only modest differences. Experience and trial designs would be important. Dr. Horwitz stressed that researchers needed to get good data from good study designs, and Dr. Hodes added that data from existing databases should also be included. Dr. Wolfe proposed that a national

group—perhaps the Institute of Medicine—develop guidelines for performing CER (e.g., methodologies).

## **NIH DIRECTOR'S COUNCIL OF PUBLIC REPRESENTATIVES (COPR) LIAISON REPORT**

Beth Furlong, J.D., Ph.D., R.N., the COPR liaison to the ACD, reviewed recent activities of the Council, which had celebrated its 10th anniversary in the fall. During the week of October 26-30, the Council took part in “Engaging the Public in Research Week,” which included a “Partners in Research Investigator Workshop”, a “Nuts and Bolts of Community Engagement in Research” forum, and the COPR fall meeting. The community engagement forum was part of the NIH Staff Training in Extramural Programs (STEP) initiative.

Prior to its public meeting on October 30, the COPR held a work group day, or information-gathering session, featuring presentations by Philippa Yeeles of the United Kingdom Clinical Research Collaboration; Adel Mahmoud, M.D., Ph.D., of Princeton University; and representatives from the NIH Institutes and Offices. The COPR meeting on October 30 featured presentations by Josephine P. Briggs, M.D., Director, National Center for Complementary and Alternative Medicine (on current research directions); Roger I. Glass, M.D., Ph.D., Director, FIC (on international biomedical initiatives); and Dr. Hodes, Director, NIA (on CER).

The COPR Communications Work Group released a request for information (RFI) on consumer health information-seeking behaviors. Responses to the RFI will assist the NIH in developing health, medical, and scientific information and disseminating it to a broader variety of audiences. It had been created in response to the President’s directive for transparency and open government and would reveal processes for future information-gathering activities.

Dr. Furlong reported that COPR alumnus Douglas Yee, M.B.A., had arranged for NHGRI Acting Director Alan Guttmacher, M.D., to speak to high school anatomy classes

at Punahou School in Hawaii. COPR alumna Valda Ford took part in the NHLBI's (and partners') campaign, The Heart Truth, to spread awareness about heart disease to middle-aged women nationally and internationally. Future topics for discussion and action by the COPR included obesity, human subjects protections, and the communication of research stories.

Dr. Luna encouraged the COPR to consider a focus on making research findings translatable to the media and public. James S. Jackson, Ph.D., encouraged the NIH to work with communications offices at universities. John Burklow, M.P.H., the NIH Associate Director for Communications and Public Liaison, noted that all institutional publication officers were invited to participate in the NIH listserv and periodic conference calls.

### **THERAPY FOR RARE AND NEGLECTED DISEASES**

Christopher P. Austin, M.D., Director, NIH Chemical Genomics Center, and Senior Advisor to the NHGRI Director for Translational Research, summarized the difficult issues surrounding attempts to translate human genomic information into biological insights and therapeutics. He noted that rare diseases, although individually rare, represent a large cumulative prevalence (25 to 30 million cases in the United States). To that could be added neglected diseases that are prevalent but not addressed, which mainly occurs in impoverished areas of the world. A small percentage of these diseases and genome-encoded targets are being addressed for drug development, and drug approvals are flat or declining.

Dr. Austin outlined the steps in the drug development process and described the conventional roles of the NIH and biopharmaceutical companies. The NIH funds basic science, and pharma and biotech fund the multi-year developmental and testing processes, which includes much failure and great expense. Through the NIH Roadmap for Biomedical Research, the Molecular Libraries Program provides resources for

researchers, including the NIH Chemical Genomics Center, which is now directing efforts to target rare and neglected diseases.

This work is included in the Therapeutics for Rare and Neglected Diseases (TRND) program. The TRND's approaches to therapeutics include both traditional development from target to clinical trial and a strategy of identifying all drugs approved worldwide for human use (about 3,000 small molecule drugs) followed by repurposing. Dr. Austin described TRND work in Gaucher disease, schistosomiasis, and trypanosomiasis. He emphasized the development of probes, which are the start of drug development. The goal of the TRND is to move developmental progress beyond the target identification stages through the assay development, screening, and probe phases in hopes of "de-risking" drug development and encouraging subsequent research in these diseases by pharmaceutical and biotech companies. It is hoped that the TRND program will receive about \$24 million per year. The program is centered at the Office of Rare Diseases Research and receives input from a trans-NIH staff advisory group and an expert external panel. TRND will receive projects from extramural and intramural researchers, foundations, and biotech/pharma firms.

### *Discussion*

Dr. Holbrook wondered whether basic scientists would be able to follow up on projects as they moved forward. Dr. Austin responded that they would. He noted that metrics for success within the program are being determined. A hope was to reach proof of concept in humans and be able to license the compound to the private sector for further research. Dr. DeAngelis proposed that the program get to the point where it could make a deal with pharma whereby pharma would fund an RFA through which grantee investigators would develop mechanisms for clinical trials. That could be followed by a deal for future royalties. The program could serve as a library (in a collaborative sense) for academic researchers. The collaborations, noted Dr. Collins, should lead to economies. Dr. Beckerle noted that the program could lead to a large demand, and she encouraged the program to consider ways to direct the work toward individualized medicine.

Dr. Yamamoto wondered about further possibilities for financial support from pharma as part of public/private cooperatives. Perhaps the program also could consider partnerships with emerging countries (e.g., Chile, South Africa).

## **INSTITUTE DIRECTOR'S REPORT: NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES**

Linda S. Birnbaum, Ph.D., Director of the National Institute of Environmental Health Sciences (NIEHS), reviewed her Institute's programs and activities. NIEHS is based in Research Triangle Park, North Carolina, and receives funding through three congressional committees (Labor [HHS-NIH], Interior, and Energy). Major programs include the National Toxicology Program, intramural laboratories, and extramural research. The Institute focuses on translating bench science into public health.

The NIEHS Division of Intramural Research conducts basic, applied, and epidemiological research to understand biological consequences of environmental exposures. Areas of interest include the epigenome, asthma, neurodegenerative diseases, altered DNA repair, gene-environment interactions, and cancer. The Institute supports the Environmental Polymorphism Registry. The NIEHS Division of Extramural Research and Training supports the Children's Environmental Health and Disease Prevention Research Centers (co-funded with the Environmental Protection Agency (EPA)); the Centers for Oceans and Human Health (co-funded with the National Science Foundation (NSF)); the Obesity and the Built Environment Program (with the CDC); and the Early Autism Risk Longitudinal Investigation (with the National Institute on Mental Health (NIMH), the National Institute of Neurological Disorders and Stroke (NINDS), and the NICHD. The Genes, Environment, and Health Initiative, co-led with NHGRI, seeks to identify genetic susceptibility and link exposures to disease. The NIEHS-National Cancer Institute (NCI) Breast Cancer and the Environment Program employs the same strategy while addressing concerns of communities and providing educational messages.

Within the Superfund Program, NIEHS addresses mandates such as understanding the health effects from exposures at hazardous waste sites, developing technologies to support clean-up, and supports worker training (e.g., emergency response; hazardous waste clean up). The National Toxicology Program is an interagency program established in 1978 to coordinate toxicology testing across the Federal Government. It has evaluated thousands of agents in toxicology studies and provided analyses and reports. The program is being revised to include new areas of emphasis, such as exposure-response relationships and the integration of data-rich techniques. A conceptual shift has occurred in the environmental health sciences with the recognition that environmental chemicals can act like hormones and drugs to disrupt the control of development and function at low levels of exposure. A confounding problem remains—people are exposed constantly to multiple environmental agents. Linking exposure and disease requires taking multiple exposures into account. Dr. Birnbaum ended by noting two new key initiatives being undertaken by the Institute: evaluating the safety of engineered nanomaterials (e.g., nanomedicine) and studying effects of climate change on health.

## **REVIEW OF OUTSIDE AWARDS FOR ACD APPROVAL**

Dr. Kington presented, for the ACD members' consideration, a new list of prescreened bona fide cash awards that NIH employees could receive. The awards had been screened by the NIH legal staff and by Drs. Wolfe and Holbrook and would be added to the list of awards previously approved. Dr. Freire recused herself from the vote. The other ACD members voted and approved the current list.

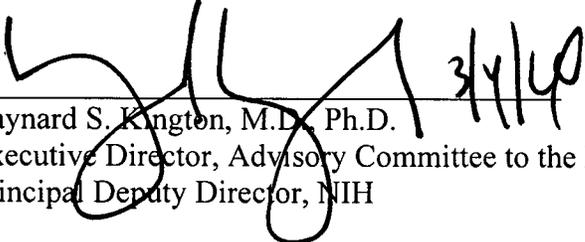
## **ADJOURNMENT**

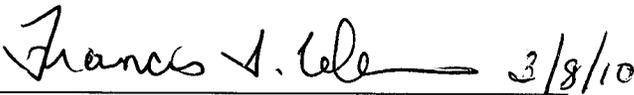
Dr. Collins thanked the ACD members, speakers, and guests and adjourned the meeting at 3:31 p.m. EST.

## SUMMARY AND CONCLUSIONS

The Advisory Committee to the Director of the National Institutes of Health convened on December 4, 2009, in Bethesda, Maryland, to learn of changes in staffing at the NIH; to receive updates on the NIH budgetary process, including the disposition of ARRA funds; and to hear reports of legislative hearings and initiatives addressing conflict of interest issues. The Committee received a presentation from the new NIH Director on his vision for the NIH, received a recommendation from the ACD Human Embryonic Stem Cell Working Group (and considered new lines for NIH-supported stem cell research), and learned about an initiative for small molecule research to address rare and neglected diseases. The ACD members received reports from the NIH Director's Council of Public Representatives and the Director of the National Institute of Environmental Health Sciences and accepted a new list of bona fide awards that NIH employees could receive.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

 3/4/10  
Raynard S. Kington, M.D., Ph.D.  
Executive Director, Advisory Committee to the Director  
Principal Deputy Director, NIH

 3/8/10  
Francis S. Collins, M.D., Ph.D.  
Chairman, Advisory Committee to the Director  
Director, NIH

## ABBREVIATIONS AND ACRONYMS

ACD	Advisory Committee to the Director
AHRQ	Agency for Healthcare Research and Quality
ARRA	American Recovery and Reinvestment Act
CDC	Centers for Disease Control and Prevention
CER	comparative effectiveness research
COPR	NIH Director's Council of Public Representatives
FDA	U.S. Food and Drug Administration
FIC	John E. Fogarty International Center
FY	fiscal year
HHS	U.S. Department of Health and Human Services
NCI	National Cancer Institute
NICHD	<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NIMH	National Institute on Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
RFI	request for information