DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Department of Health and Human Services
National Institutes of Health

Advisory Committee to the Director

97th Meeting

December 5, 2008

Contents

EXECUTIVE SUMMARY

The 97th meeting of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) was held on December 5, 2008, on the NIH campus. NIH Acting Director Raynard S. Kington, M.D., Ph.D., chaired the meeting. He gave thanks to five members who would be rotating off the committee. He welcomed three new ACD appointees—Maria C. Freire, Ph.D., President of the Albert and Mary Lasker Foundation; Beatriz Luna, Ph.D., Associate Professor of Psychiatry, University of Pittsburgh; and James Thrall, M.D., Radiologist-in-Chief, Massachusetts General Hospital.

Dr. Kington reported on personnel changes at NIH in the wake of the national Administration transition. These changes included Dr. Kington's acceptance of the position as NIH Acting Director. Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research, accepted the position of Acting Deputy Director of the NIH. Sally J. Rockey, Ph.D., accepted the position of Acting Deputy Director for Extramural Research.

Dr. Kington noted NIH grantees and former grantees who had recently won prestigious prizes, including the Nobel Prize in Chemistry and Lasker Medical Research Awards. Three longtime NIH employees received, from President Bush, Presidential Rank Awards for outstanding leadership and longtime service to government.

John J. Bartrum, M.B.A., J.D., Associate Director for Budget, reported on the NIH budget and the possibility of funds from the national economic stimulus legislation being directed to the NIH. These funds, through grants nationwide, would support research and boost local economies. The ACD members discussed the potential economic benefits of new NIH grant money as a result of the stimulus package. Marc Smolonsky, Associate Director for Legislative Policy and Analysis, reported to the ACD on upcoming legislation, which likely will feature initiatives in health care reform and comparative effectiveness research.

Dr. Kington reported that the Administration's transition is proceeding well and features NIH representatives working with the Department of Health and Human Services and the new Administration. He noted additional changes in NIH leadership. Francis Collins, M.D., Ph.D., stepped down as the Director of the National Human Genome Research Institute (NHGRI), and Alan Guttmacher, M.D., is now the Acting Director. Ting-Kai Li, M.D., stepped down as the Director of the National Institute on Alcohol Abuse and Alcoholism, and Kenneth Warren, Ph.D., is now the Acting Director. Lana Skirboll, Ph.D., Associate Director for Science Policy, will serve as Acting Director of the Division of Program Coordination, Planning, and Strategic Initiatives.

Adel Mahmoud, M.D., Ph.D., of Princeton University, presented a progress report from the Advisory Committee to the Director on the risk assessment for the proposed National Emerging Infectious Diseases Laboratory at Boston University. He described recent meetings devoted to the development of best practices for community engagement, and he presented results for draft principles and best practices. The ACD members proposed that the panel expand the initiative's focus to the clinical community, offering education and information. They encouraged the panel to develop broad messages about cost-effectiveness of such efforts and the appropriateness of the geographical area.

Dr. Tabak reported on progress in the initiative to enhance the NIH's peer review process for research grant applications. The initiative has entered a phase of implementation. The ACD members focused their discussion on the plan to limit applications to 12 pages, with an extra 6 pages allowed for studies with human subjects. They expressed concern that inequities might result.

Dr. Rockey reviewed efforts to address potential financial conflict of interest (FCOI) in NIH grantees. The NIH has provided oversight for FCOI issues for many years—inquiring into institutional procedures and actions, requiring corrective actions, and suspending funding when appropriate. It now is considering changes in regulations to strengthen oversight and management by institutions. The ACD members discussed a

wide range of issues, including the need for informatics tools, the impossibility of knowing the investments of investigators, a need to establish governing principles, and a need for new strategies, such as linking to incentives.

Elaine A. Ostrander, Ph.D., Chief, Cancer Genetics Branch, NHGRI, reviewed studies at her Institute of genes mapped to morphology in dogs. She emphasized a study of body size in Portuguese Water Dogs, in which investigators performed genome-wide scans to identify shared haplotypes among size-selected groups that reduced a quantitative trait loci region to a single gene. She concluded that identifying and mapping genes that contribute to complex morphological traits are feasible using breeds fixed for a trait.

Beth Furlong, Ph.D., R.N., J.D., reported on activities of the NIH Director's Council of Public Representatives (COPR), which met on October 31, 2008. That meeting featured presentations by Dr. Guttmacher on the Science of Genomics; by John Burklow on Charting the Future of NIH Communications; by Vence Bonham, J.D., and Mr. Burklow on Genomics in the Public Domain; and by Patricia Grady, Ph.D., R.N., and Yvonne Maddox, Ph.D., on the Public Trust Initiative's Partners in Research Awards Program. The ACD members suggested that the COPR consider issues such as the development of metrics for gauging community engagement, the development of public engagement and communication for specific topical areas, and the targeting of groups such as school-aged children.

Josephine Briggs, M.D., Director, National Center for Complementary and Alternative Medicine, NIH, reported on activities at her Center, which seeks to explore complementary and alternative healing practices, using rigorous scientific methods, and to develop the evidence base for safety and efficacy of complementary and alternative medicine (CAM) approaches. She reviewed the Center's work during the past 9 years to support six high-quality randomized controlled trials of widely used natural products, to support rigorous processes to assess quality and consistency of herbal and other natural products used in research, and to maintain a portfolio of investigator-initiated research. The ACD members discussed issues for the Center, including the use of randomized

controlled trials, the importance of placebo effects, a lack of standards for testing CAM approaches, and a lack of regulation and consistency for CAM products.

Dr. Kington presented, for the ACD members' consideration, a new list of prescreened bona fide cash awards that NIH employees may receive. The ACD members approved the new list of awards, adding it to the list of previously approved awards. Dr. Kington also referred the ACD members to a report of the NIH ACD Working Group on Participant and Data Protection for the Genetic Association Information Network (GAIN) and Genome-Wide Association Studies (GWAS).

WELCOME AND NIH DIRECTOR'S REPORT

The 97th meeting of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) was held on December 5, 2008, on the NIH campus in Bethesda, Maryland, and Webcast globally. NIH Acting Director Raynard S. Kington, M.D., Ph.D., welcomed the ACD members, invited speakers, and other participants.

Dr. Kington reported on personnel changes at the NIH in the wake of the Washington Administration transition, including his acceptance of the position of NIH Acting Director. Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research, accepted the position of Acting Deputy Director of the NIH. Sally J. Rockey, Ph.D., accepted the position of Acting Deputy Director for Extramural Research. Michael M. Gottesman, M.D., continues as Deputy Director for Intramural Research; and Colleen Barros continues as Deputy Director for Management.

Dr. Kington recognized the extensive contributions of the following ACD members, who were attending their final meeting: Nancy E. Adler, Ph.D.; David Botstein, Ph.D.; Alexander R. Lerner (absent); Christine E. Seidman, M.D.; and Tadataka Yamada, M.D. He welcomed three new ACD appointees—Maria C. Freire, Ph.D., President of the Albert and Mary Lasker Foundation; Beatriz Luna, Ph.D., Associate Professor of Psychiatry, University of Pittsburgh; and James Thrall, M.D., Radiologist-in-Chief, Massachusetts General Hospital (unable to attend). Absent from the meeting were ACD members Catherine D. DeAngelis, M.D.; Alan I. Leshner, Ph.D.; and Keith R. Yamamoto, Ph.D. Beth Furlong, Ph.D., R.N., J.D., the liaison to the ACD from the NIH Director' Council of Public Representatives (COPR), was in attendance.

Dr. Kington reviewed the day's agenda, which included presentations and discussions of important issues such as enhancement of the NIH's peer review process and the risk assessment plan for a future infectious diseases laboratory at Boston University. He reported that the 2008 Nobel Prize in Chemistry was shared by two current NIH grantees—Martin Chalfie, Ph.D., of Columbia University, and Roger Tsien, Ph.D., of the

University of California, San Diego—and a former NIH grantee, Osamu Shimomura, Ph.D., of the Marine Biological Laboratory in Woods Hole. Over the years, the NIH provided a total of more than $29 million in support of the three researchers and their research programs.

The 2008 Albert Lasker Basic Medical Research Award was given to Victor Ambros, of the University of Massachusetts; David Baulcombe, of the University of Cambridge; and Gary Ruvkun, of Massachusetts General Hospital. The Lasker-DeBakey Clinical Medical Research Award was given to Akira Endo, of Biopharm Research Laboratories. The Lasker-Koshland Special Achievement Award in Medical Science was given to Stanley Falkow, of Stanford University. A variety of NIH grants have supported these researchers through the years.

President Bush recognized three NIH employees with Presidential Rank Awards for outstanding leadership and longtime service to Government. Colleen Barros, NIH Deputy Director for Management, received the Distinguished Executive Award. Donald P. Christoferson, Associate Director for Administrative Management, National Heart, Lung, and Blood Institute; and Maureen E. Gormley, Clinical Center Chief Operating Officer, received the Meritorious Executive Award.

NIH Budget

Dr. Kington reported that he testified in November before the House Subcommittee on Health on the role of biomedical research in the economic stimulus. NIH staff members participated in 52 other hearings on topics including HIV prevention, NIH public access policy, implementation of the NIH Reform Act, health disparities and breast cancer, bisphenol A, and human embryonic stem cell research policy.

John J. Bartrum, M.B.A., J.D., Associate Director for Budget, reported to the ACD on the budget. He stated that the economic stimulus package includes a proposal to provide $1 billion to the NIH. Action likely will occur in January. The NIH is operating under a

continuing resolution, which expires March 6, 2009. The President's proposed fiscal year (FY) 2009 NIH budget is $29.5 billion, equal to the FY 2008 budget. House and Senate committees have proposed increases of 3.4 percent and 3 percent respectively for FY 2009.

Marc Smolonsky, Associate Director for Legislative Policy and Analysis, reported to the ACD on legislation. Legislators currently are focusing on bailouts for the financial and automobile industries. This likely will be followed by actions for short-term aid (food aid, Medicaid). Health care reform promises to be a high priority in the next congressional term, and this will have an impact on the NIH. In particular, Congress will continue to be interested in comparative effectiveness research. Other high priorities that will affect the NIH are the database clinicaltrials.gov, biosafety and biosecurity (oversight of labs), and financial conflict of interest.

Dr. Kington reported that the Government transition has proceeded smoothly. The Department of Health and Human Services Transition Team is led by Richard Turman, Deputy Assistant Secretary for Budget. Harold Varmus, M.D., former NIH Director; Francis Collins, M.D., Ph.D., former Director of the National Human Genome Research Institute (NHGRI); and Alta Charo, of the University of Wisconsin Law School, are leading the President-Elect Transition Team at the NIH.

Transitions

Dr. Kington reported the following changes at the NIH:

- Dr. Zerhouni stepped down from the position of NIH Director in October.

- Dr. Collins stepped down from the position of Director of the NHGRI. Alan E. Guttmacher, M.D., was appointed Acting Director of the NHGRI.

- Ting-Kai Li, M.D., stepped down from the position of Director, National Institute on Alcohol Abuse and Alcoholism (NIAAA). Kenneth R. Warren, Ph.D., will serve as Acting Director of the NIAAA during the search for a new director.

- The NIH Reform Act of 2006 authorized establishment of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) within the NIH Office of the Director. DPCPSI consolidates various program offices within the Office of the Director. Lana Skirboll, Ph.D., Associate Director for Science Policy, will serve as Acting Director of the DPCPSI. Amy P. Patterson, M.D., will assume Dr. Skirboll's responsibilities as Acting Director of the Office of Science Policy

- Linda S. Birnbaum, Ph.D., of the Environmental Protection Agency, will join the NIH in January as Director of the National Institute of Environmental Health Sciences.

Dr. Kington reported on a celebratory farewell event for Dr. Zerhouni, which took place October 30, 2008. The celebration featured messages of appreciation from several members of Congress and was attended by Dr. Zerhouni, his family, colleagues, and ambassadors from Algeria and Morocco.

Discussion

Dr. Botstein asked about the potential number of jobs that could be created as a result of the NIH receiving $1 billion in stimulus aid. He stressed that such a stimulus effort, using NIH grants, would create the jobs rapidly and reverberate through local economies (leveraging jobs). It would be especially helpful in places where academic institutions represent substantial fractions of the local economies. Mr. Bartrum stated that Congress is interested in supporting infrastructure projects, and this could include the NIH. Arguments about the leveraging of NIH funds in communities and the importance of such funds in particular communities were advanced in the committee hearings.

Mary Beckerle, Ph.D., noted that some academic institutions have hiring freezes, which might affect efforts to advance economies with new grant money. The ACD members encouraged the NIH to inform academic institutions of these issues and efforts. Dr. Yamada stated the importance of indicating that reductions in NIH funds can lead to negative economic consequences.

Mr. Smolonsky noted that activities in biosafety and biosecurity are in need of advances in uniform oversight. Dr. Botstein called for attention to the scientific substance in areas of biosafety—for example, supporting and performing the right science. Dr. Seidman cautioned about the need to avoid administrative burden and inefficiency.

Dr. Kington noted that discussions about which part of the overall NIH portfolio should handle the issue of comparative effectiveness research continue. Some NIH Institutes and Centers address the issue in their portfolios.

REPORT FROM THE ACD BLUE RIBBON PANEL ON THE NATIONAL EMERGING INFECTIOUS DISEASES LABORATORY AT BOSTON UNIVERSITY MEDICAL CENTER

Adel Mahmoud, M.D., Ph.D., of Princeton University, presented a progress report from the ACD Blue Ribbon Panel on the risk assessment for the proposed National Emerging Infectious Diseases Laboratory at Boston University. The panel briefed the ACD in June 2008 on a scope and analytical approach for risk assessment. The ACD accepted the recommendations with provisions. The NIH then awarded a contract for supplemental risk assessment studies. The panel proceeded to work to advise the NIH on strategies to address local community relations and communications. It has held meetings devoted to the development of best practices for community engagement. A May 2008 meeting was held in Boston. At a meeting on the NIH campus in July 2008, members of the Boston community, Boston officials, researchers, and social justice advocates explored ideas about community engagement. As a result, the panel developed draft principles for oversight and proposed the following three best practices:

- Rigorous, balanced, transparent local institutional biosafety review and oversight of high- and maximum-containment research.

- Community liaison activities to promote openness and transparency with respect to the research agenda of the institution.

- A communications plan regarding phase-in of research operations.

Dr. Mahmoud reviewed details of the draft principles and best practices and asked the ACD members to comment. He stressed that translating the principles and best practices into concrete programs will be the responsibility of institutions, in accordance with their research programs and needs.

Discussion

John Nelson, M.D., M.P.H., applauded the work of the panel and encouraged it to expand the focus to the clinical community, offering education, information, etc., to clinical professionals. In response to questions about legal cases regarding the Boston initiative, it was noted that a federal case is on hold until the risk assessment is completed. A state court case was resolved. A third complaint, by the Office for Civil Rights, is on hold. Dr. Seidman and Dr. Botstein suggested that the panel consider developing broad messages about cost-effectiveness of such efforts and the appropriateness of the geographical area.

Dr. Patterson noted that the panel considered the idea of a worst case scenario and avoided its use in favor of a focus on where risks come from and the plurality of possible risks. Dr. Yamada wondered about expanding the consideration to broader health practices that might be involved in risk scenarios. Dr. Mahmoud noted that such issues were beyond the panel's scope. Dr. Nelson encouraged the panel to consider long-term effects.

ENHANCING PEER REVIEW: IMPLEMENTATION OF RECOMMENDED ACTIONS

Dr. Tabak reported on progress in the initiative to enhance the NIH's peer review process for research grant applications. The initiative achieved the completion of two phases—a diagnostic phase of gathering feedback and input and a phase of designing an implementation plan. It has begun a third phase of proceeding with implementation.

Dr. Tabak reviewed the implementation activities within three areas:

- Engaging the best reviewers (recruiting the best reviewers, improving retention and training, allowing flexibility through virtual reviews).

- Improving the quality and transparency of reviews (improving scoring transparency and scale, providing scores for streamlined applications, shortening and restructuring the applications).

- Ensuring balanced and fair reviews across scientific fields and career states and reducing administrative burden (funding meritorious science earlier, reviewing like applications together).

The initiative currently is generating baseline surveys that can be used to assess changes in results as the new program moves forward—in other words, for continual review and adjustment. The NIH is developing a program for education and training in the new processes.

Discussion

The ACD members' discussion focused on the plan to limit applications to 12 pages, with an extra 6 pages allowed for studies with human subjects. They expressed concern that inequities might result, as many research projects, such as those performing human DNA studies, would create an opportunity to submit the longer, 18-page application. This

could introduce biases into the process and defeat the goal of making applications shorter. Dr. Kington emphasized that clear criteria will be applied. Dr. Botstein proposed that in such cases, the extra six pages be used specifically to describe the human subject aspects of a research project. It might be referred to as a "special section." Dr. Tabak assured the ACD members that these issues had been raised in the process, with NIH program staff arguing for the need for greater space in the application for investigators using human subjects. Dr. Luna suggested providing very specific definitions of studies for which the expanded page count could apply. With a unanimous voice vote, the ACD members agreed that the initiative should revisit the proposed rule about a subset of expanded applications.

Dr. Seidman proposed allowing applicants to see, prior to grant submission, the toolbox used by the reviewers in order to understand the criteria under which they are being judged. Applicants also might be provided with model applications—although, noted Dr. Botstein, that can lead to improper suggestions of mandated content (and cookie-cutter responses). Dr. Tabak noted that some aspects of an editorial board approach, in which reviewers can question applicants, are being considered. However, it is important that the process not be lengthened—in fact, a goal is to shorten the process. It is also important that the peer review process not be considered a mentoring process, as in teaching applicants how to enhance applications. The goal of the process is to reward good, or meritorious, science. Dr. Botstein stressed that investigators should not write applications with the aim of appealing to a certain study section. A long process with many amendments to an application in response to comments by a study section could lead to a project that is obsolete.

Antonio Scarpa, M.D., Ph.D., Director of the NIH Center for Scientific Review, briefly described current processes for triaging new and revised applications that are submitted.

ASSURING OBJECTIVITY IN RESEARCH: NIH AND FINANCIAL CONFLICT OF INTEREST

Dr. Rockey reviewed efforts to address potential financial conflict of interest (FCOI) for NIH grantees. Current Public Health Service (PHS) regulation aims to ensure that the design, conduct, and reporting of research funded under NIH grants and cooperative agreements will not be biased by any conflicting financial interest of the investigators responsible for the research. Dr. Rockey reviewed FCOI reporting requirements. These include submission by the applicant at the time of application of known significant financial interests and a report by the institution, prior to the expenditure of funds, of any identified FCOI. Institutions must have policies in place. Dr. Rockey explained procedures for resolving potential disclosure, compliance, and policy issues.

The NIH has provided oversight for FCOI issues for many years, inquiring into institutional procedures and actions, requiring corrective actions, and suspending funding when appropriate. It now is considering changes in regulations to strengthen oversight and management by institutions. It has published an advanced notice of proposed rule making and is seeking input on potential changes. Dr. Rockey asked the ACD members to discuss possible expansion of the scope of the regulation and the disclosure of interests, definition of "significant financial interest," and ways to identify and manage conflicts.

Discussion

Dr. Kington stressed that the FCOI regulations originate in the PHS and are not NIH-developed policy. Dr. Yamada wondered whether an informatics tool is needed to scan investigators for conflicts. In cases of conflict, grants must be suspended; otherwise, the policy will be ineffective. Barbara Wolfe, Ph.D., noted the impossibility of determining all investments of investigators (although financial support is easier to establish). She suggested new and different strategies, such as linking to incentives. Dr. Luna cited a problem of perception—the false idea that investigators become unethical when they

receive support. There is a need, stated Dr. Kington, to develop governing principles. The NIH should be proactive in this area and must be thoughtful and fair.

Dr. Freire noted that the issues are complex. One key is the basic link of oversight to the health of people. Because of this, links to private industry are important. Oversight should be provided by institutions rather than the NIH. Too much bureaucracy, noted Dr. Botstein, will be harmful. The focus should be on persons who do not disclose conflicts and whether institutions are being responsible for what they disclose. Only substantial conflicts should be addressed. Dr. Seidman noted that some scientific journals require tax forms for disclosure by authors. Dr. Wolfe emphasized that we need to encourage the private sector to provide research funds. Perhaps, noted Dr. Seidman, the Foundation for NIH might provide ideas for avoiding conflict.

Dr. Kington stated that the NIH recognizes the need for regulations that are responsible to real conditions. It is reviewing cases, tallying inputs, and analyzing responses. The goal is to provide input for new department regulations during the next 6 months. However, Congress may act on its own in the area of FCOI.

DOG GENES TELL SURPRISING TALES: FINDING GENES FOR COMPLEX TRAITS

Elaine A. Ostrander, Ph.D., Chief, Cancer Genetics Branch, NHGRI, reviewed studies at her Institute of genes mapped to morphology in dogs. In one case, considering body size, investigators performed genome-wide scans of a single breed, the Portuguese Water Dog, to identify shared haplotypes among size-selected groups that reduce a quantitative trait loci region to a single gene. The 10,000 or so Portuguese Water Dogs in the United States all descended from 30 dogs brought to the country 50 years ago.

The investigators genotyped more than 500 dogs and collected skeletal measurements. They narrowed the interval associated with size using single-nucleotide polymorphism–based markers and found an association for the insulin-like growth factor-1 (IGF1) gene. A shared sweep haplotype among small breeds suggested that a single ancient mutation

contributed to small dog size. Further analyses found that at least three genes are associated with body size. Dr. Ostrander described additional studies completed and under way to find genetic associations for morphologies including short limbs and muscle mass. Asymmetrical dwarfism in dogs appears to be controlled by insertion of a transcribed growth factor gene. A mutation in the myostatin gene is associated with increased muscle mass and racing performance. Dr. Ostrander concluded that identifying and mapping genes that contribute to complex morphological traits are feasible using breeds fixed for a trait.

Discussion

Dr. Ostrander stated that the results of work with dogs suggest that they could serve as models for human studies involving skull morphology (cleft palate) and leg length/leg width (osteosarcoma). A number of investigator groups are studying dog breeds that are predisposed to certain lymphomas. Dr. Botstein suggested that researchers consider the population genetics of preferred sire animals (e.g., cattle, work horses).

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

Dr. Furlong reported on activities of the COPR, which met on October 31, 2008. That meeting featured presentations by Dr. Guttmacher on the Science of Genomics; by John Burklow on Charting the Future of NIH Communications; by Vence Bonham, J.D., and Mr. Burklow on Genomics in the Public Domain; and by Patricia Grady, Ph.D., R.N., and Yvonne Maddox, Ph.D., on the Public Trust Initiative's Partners in Research Awards Program. The meeting also featured a brief farewell ceremony for Dr. Zerhouni.

Dr. Furlong described progress by two COPR work groups—the Role of the Public in Research Work Group and the Communications Work Group—both of which conducted sessions during the October meeting. She referred the ACD members to written frameworks for public engagement developed by the former work group, which were in the ACD meeting binder. She distributed to the ACD members a new NIH promotional

brochure, developed by the COPR, and she described the COPR's intention to develop a manuscript about recommendations for community engagement.

Discussion

Dr. Nelson, who is the ACD liaison to the COPR, applauded its efforts, stressed the different memberships of the two groups, and suggested that ACD members consider attending a COPR meeting. Dr. Freire asked whether the COPR has discussed the development of metrics for gauging community engagement. Mr. Burklow noted that only proxy measures (e.g., Web site hits) are available now. He also noted that various NIH Institutes are engaged in disseminating health information. Dr. Seidman suggested that the COPR (and the NIH communications office) consider developing public engagement and communication activities in specific topical areas, such as genetics and genomics. Such efforts might target, for example, school-aged children. Perhaps NIH-funded investigators could make presentations to schoolchildren. Dr. Adler wondered whether the COPR could promote the issue of effects of the status of the NIH budget.

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM) DIRECTOR'S REPORT: PROMISE IN RESEARCH ON COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Josephine Briggs, M.D., Director, NCCAM, NIH, reported on activities of the Center. As stated in the legislative document, "The general purposes of the NCCAM are the conduct and support of basic and applied research…research training, and other programs with respect to identifying, investigating, and validating complementary and alternative treatment, diagnostic, and prevention modalities, disciplines, and systems" (P.L. 105-277).

NCCAM is a small center with a budget that is 0.4 percent of the total NIH budget. It seeks to explore complementary and alternative healing practices using rigorous scientific methods and to develop an evidence base for safety and efficacy of CAM approaches. About 40 percent of Americans use CAM of any type, and natural product supplements

compose the largest fraction of uses. The most commonly taken non-vitamin/non-mineral dietary supplement is fish oil/omega 3 fatty acids. The condition most responsible for adult use of CAM is back pain. Dr. Briggs reviewed evidence that negative results of studies of CAM can lead to reductions in the sales of products.

In the past 9 years, NCCAM has supported six high-quality randomized controlled trials of widely used natural products. It has supported rigorous processes to assess quality and consistency of herbal and other natural products used in research. It has maintained a portfolio of investigator-initiated research, currently supporting about 300 projects. Dr. Briggs listed areas of promise in natural product research and noted that NCCAM-supported work has been helpful in the medicine regulation process. A current NCCAM initiative focuses on non-pharmacological management of back pain. The Center faces challenges including the following:

- The fact that it covers a broad range of science and necessary expertise.
- A lack of mature methodologies to explore CAM approaches.
- A broad range of constituencies.

NCCAM currently is developing a 10-year strategic plan for extramural and intramural research. In developing the plan, a Blue Ribbon Panel is considering whether NCCAM should develop an intramural program, how an intramural program would be focused, and how NCCAM could structure its resources to produce information for the public and practitioners.

Discussion

Dr. Yamada cautioned the Center about randomized controlled trials. In cases where a high placebo effect is possible, multiple trials may be needed to obtain reliable results. In other words, in many cases it can be difficult to see effects beyond the placebo.

Dr. Wolfe cited the problem of a lack of standards for testing many CAM approaches. Many strengths and production methods are possible and have not been tested. Also, with a lack of regulation, the content of a substance may differ from manufacturer to manufacturer. Dr. Briggs recognized such difficulties and pointed to the existence of partial standards for some agents based on past tests and the evolving nature of CAM science. Dr. Seidman suggested that the Center consider supporting studies of products being used by young athletes for performance enhancement.

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 may receive. The awards were screened by the NIH legal staff and by Dr. Wolfe and Karen Holbrook, Ph.D. The ACD members approved the list with a unanimous vote. The awards will be added to the list of awards previously approved.

REPORT OF THE ACD WORKING GROUP ON PARTICIPANT AND DATA PROTECTION FOR THE GENETIC ASSOCIATION INFORMATION NETWORK AND GENOME-WIDE ASSOCIATION STUDIES

Dr. Kington referred the ACD members to a report (in the meeting binder) of the NIH ACD Working Group on Participant and Data Protection for the Genetic Association Information Network and Genome-Wide Association Studies. The report presents results of the discussions in two working group meetings held after June 2008. It does not feature policy recommendations. The working group will continue discussions—including conferring with the new NIH Director—and report at a future ACD meeting. Future discussions will include the issue of whether the working group should continue.

ADJOURNMENT

Dr. Kington thanked the ACD members, invited speakers, and guests and adjourned the meeting.

SUMMARY AND CONCLUSIONS

The Advisory Committee to the Director (ACD) of the National Institutes of Health convened on December 5, 2008, in Bethesda, Maryland, to receive updates on the NIH budgetary process; to receive a Blue Ribbon Panel report on the initiative to create a biocontainment laboratory in Boston; to learn of progress in initiatives (1) to improve the NIH peer review process, (2) to ensure that institutions are avoiding financial conflicts of interest in their NIH-funded investigators, and (3) to protect participants and data within the Genetic Association Information Network and genome-wide association studies; and to hear about activities at the NIH National Center for Complementary and Alternative Medicine. A representative from the National Human Genome Research Institute described studies using dogs to find genes for complex morphological traits. The ACD members received a report from the NIH Director's Council of Public Representatives and accepted a new list of bona fide awards that NIH employees may receive.

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

_____

Lawrence A. Tabak, D.D.S., Ph.D.
Executive Director, Advisory Committee to the Director
Acting Deputy Director, NIH

_____

Raynard S. Kington, M.D., Ph.D.
Chairman, Advisory Committee to the Director
Acting Director, NIH

ABBREVIATIONS AND ACRONYMS

ACD	Advisory Committee to the Director
COPR	NIH Director's Council of Public Representatives
CSR	Center for Scientific Review
FCOI	Financial conflict of interest
FDA	U.S. Food and Drug Administration
FNIH	Foundation for NIH
FY	Fiscal year
GAIN	Genetic Association Information Network
GWAS	Genome-wide association studies
NEIDL	National Emerging Infectious Diseases Laboratories
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIDCR	National Institute of Dental and Craniofacial Research
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
OSP	Office of Science Policy
PHS	U.S. Public Health Service
RPG	Research project grant
SNP	Single-nucleotide polymorphism