

**Department of Health and Human Services  
National Institutes of Health**

**Advisory Committee to the Director**

**95th Meeting**

**December 7, 2007**

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## **EXECUTIVE SUMMARY**

The 95th meeting of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) was held on December 7, 2007, on the NIH campus. NIH Director Elias A. Zerhouni, M.D., introduced five new ACD members: Mary C. Beckerle, Ph.D., Executive Director of the Huntsman Cancer Institute; Colleen Conway-Welch, Ph.D., Dean of Vanderbilt University's School of Nursing; Walter Isaacson, President and CEO of the Aspen Institute; Thomas J. Kelly, M.D., Ph.D., Director of the Sloan-Kettering Institute; and Keith R. Yamamoto, Ph.D., Executive Vice Dean of the School of Medicine, University of California, San Francisco.

Dr. Zerhouni provided an update on legislative matters. In recent months, Congress held more than 10 meetings with NIH representatives relating to appropriations. The NIH currently is operating under a continuing resolution pending a new budget. A significant part of the recent budget talks was an emphasis on reauthorizing the Small Business Innovation and Research Act to stimulate small companies and ventures. For 2007, the NIH will make no inflationary adjustments for non-competing renewal awards. It will seek to stabilize the number of competing grants and strengthen support for at-risk populations, including new investigators, first-grant renewals, and established researchers with no other support.

Dr. Zerhouni described a disturbing long-term trend in the biomedical sciences, in which the average age of first-time NIH grantees has risen significantly. He presented graphical analyses of demographic trends and asked the ACD members to consider factors and suggest possible actions to counter the trends.

Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research (NIDCR), reported on the progress of an NIH Steering Committee working group to enhance the NIH's peer review process for research applications. Dr. Yamamoto reported on progress by an ACD working group, which also has collected feedback and is identifying challenges, considering solutions, and discussing transformational changes. The working groups seek to revise the peer review process to reduce the administrative burden, recognize high-impact science, support investigators at various career stages, advance reviewer quality, and reduce strains on the system that supports research (e.g., resources, costs). Possible changes include the

use of outside reviewers, the use of “prebuttal” communication with applicants, and a reduction in the mentoring aspect of reviews.

Annelise E. Barron, Ph.D., reported on activities of the NIH Director’s Council of Public Representatives (COPR). COPR working groups have been developing ideas for communication programs and for strategies to educate investigators and reviewers about community engagement.

Griffin P. Rodgers, M.D., Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), presented background and current activities of the NIDDK. He described the Institute’s work in obesity, type 2 diabetes, and kidney disease as a paradigm of integrated research. NIDDK has created a working group to analyze successes and downstream outcomes of its investigator training award programs,

Raynard S. Kington, M.D., Ph.D., Deputy Director of the NIH, presented, for the ACD members’ consideration, a new list of prescreened bona fide cash awards that NIH employees may receive.

Christine E. Seidman, M.D., reported on efforts of the ACD Working Group on Participant and Data Protection for the Genetic Association Information Network (GAIN) and Genome-wide Association Studies (GWAS). NIH-supported GWAS produce data for the GAIN. The NIH has a goal of advancing GWAS to identify common genetic factors that influence health and disease. Dr. Seidman reviewed the GWAS data management procedures, which feature informed consent, data submission, removal of personal identifying information and replacement with a random unique code, placement in the repository, and access and secondary use by investigators.

Dr. Seidman asked the ACD members to consider recommending Freedom of Information Act (FOIA) exemptions, which would proscribe access to individual-level repository data and eliminate the risk of matching gene information and individuals. The ACD members voted to make such a recommendation and also voted for recommendations to provide aggregate genetic information to GWAS research participants and to develop a system for addressing public inquiries about GWAS and the repository.

Alan M. Krensky, M.D., Director, Office of Portfolio Analysis and Strategic Initiatives (OPASI), presented the history and progress of the NIH Roadmap for Medical Research program, which is designed to foster the development of transformative solutions to grand challenges in health research. Initiatives chosen for the program demonstrate high potential to transform how research will be conducted, synergistic advancement of the mission of the Institutes to benefit health, applicability to issues beyond the scope of one or a few of the Institutes, and a public health benefit. The program's challenge, or theme, of seeking new pathways currently features two major initiatives—the Roadmap Epigenomics Program and the Human Microbiome Project.

Duane Alexander, M.D., Director, National Institute of Child Health and Human Development (NICHD), described the history and progress of the National Children's Study, the largest longitudinal study of children's health and development ever conducted. Between 2000 and 2007, an Interagency Coordinating Committee, a Federal Advisory Committee, working groups, multi-agency consortiums, teams of investigators, and more worked to plan and develop the study. The study will be conducted from 2007 to 2034, collecting information on more than 100,000 children across the United States, including important but less common outcomes. It will address a series of questions, such as: What are the health and developmental effects of persistent low-level chemical exposures?

## **NIH DIRECTOR'S REPORT**

The 95th meeting of the National Institutes of Health (NIH) Advisory Committee to the Director (ACD) was held on December 7, 2007, on the NIH campus in Bethesda, Maryland, and was Webcast globally.

NIH Director Elias A. Zerhouni, M.D., welcomed the ACD members, invited speakers, and other participants. He introduced five new members: Mary C. Beckerle, Ph.D., Executive Director of the Huntsman Cancer Institute; Colleen Conway-Welch, Ph.D., Dean of Vanderbilt University's School of Nursing; Walter Isaacson, President and CEO of the Aspen Institute; Thomas J. Kelly, M.D., Ph.D., Director of the Sloan-Kettering Institute; and Keith R. Yamamoto, Ph.D., Executive Vice Dean of the School of Medicine, University of California, San Francisco.

Dr. Zerhouni announced three retirements from the ACD—Annelise E. Barron, Ph.D.; C. Martin Harris, M.D., M.B.A.; and Joan Y. Reede, M.D., M.P.H., M.S. He noted that ACD members Martin Harris, M.D., and Karen A. Holbrook, Ph.D., were unable to attend the meeting. ACD member John C. Nelson, M.D., was announced as the new liaison to the NIH Director's Council of Public Representatives (COPR).

Dr. Zerhouni reviewed the day's agenda, with its emphases on efforts to revise and advance the NIH's peer review process and to safeguard the privacy of participants in genetic studies when there is a risk of identifying personal genome data. The ACD is positioned to play important roles in both efforts.

### *Legislation and the Budget*

Dr. Zerhouni provided an update on legislative matters. Congress has shown great interest in the NIH in recent months, holding more than 10 meetings with NIH representatives relating to appropriations. The NIH currently is operating under a continuing resolution, pending a new budget. Dr. Zerhouni suggested that this situation might continue for a year, leading to difficulties in managing the NIH's budgetary disbursements. In an appropriations conference, the Senate called for a \$1 billion increase over the NIH's 2007 budget, and the House of

Representatives called for a \$750 million increase. A conference report then cited an increase of \$1.1 billion. President Bush, however, vetoed the resulting budget bill.

A significant part of the budget talks was an emphasis on reauthorizing the Small Business Innovation and Research Act to stimulate small companies and ventures. The Congress passed a Food and Drug Administration act mandating that the NIH expand the Web site [www.clinicaltrials.gov](http://www.clinicaltrials.gov). The site has not been capturing all interventional trials. The new act calls for widening the site's scope and including a results section for each trial. These adjustments will create a resource burden for research institutions, and a phased-in strategy will be used.

### *The Scientific Workforce*

Dr. Zerhouni described a disturbing long-term trend in the biomedical sciences, in which the average age of first-time NIH grantees has risen. Also, the training period for researchers has increased to about 20 years. Other lengthenings have occurred—for example, the average appointment age in medical schools has risen. Dr. Zerhouni presented graphical analyses of such demographic trends. The ages of medical school faculty members and principal scientists/grantees have risen steadily within the past 26 years. Expert models predict a continuing trend. What are the policy implications? Dr. Zerhouni asked the ACD members to consider factors and suggest possible actions to counter the trends. Budget levels have not affected the number of R01 investigators. During bad budgetary years, however, the numbers of new investigators have dropped. Dr. Zerhouni cautioned against applying rigidity to the system to counter the rising-age trends.

In recent years, the numbers of applicants rose and the numbers of awardees decreased. As a result, the success rate diminished. There has been an increasing demand, or capacity, for science. Nevertheless, the NIH is maintaining a baseline of new R01 grants. During 2007, it funded 1,500 new R01 investigators, with a funding rate of 20 percent and a success rate of 18.5 percent.

For 2007, the NIH will make no inflationary adjustments for non-competing renewal awards. It will seek to stabilize the number of competing grants and strengthen support for at-risk

populations, such as new investigators, first-grant renewals, and established researchers with no other support. The NIH has continued to request funding for the NIH Director's Bridge Award (NDBA), which serves to support vulnerable scientists, and it has increased support for the New Investigator Award.

Dr. Zerhouni stressed the continuing need for the NIH to develop proactive policies, based on quantitative long-range forecasts that focus on preserving a dynamic and innovative scientific workforce.

### *Discussion*

Some ACD members suggested that the NIH stress new ideas as well as new investigators. Others stressed the importance of youth in the identification of new research ideas. Perhaps the NIH should better publicize its interest in funding new investigators and offer additional incentives. Dr. Reede encouraged the NIH to consider the importance of minority investigators as it seeks young investigators and new ideas.

In analyzing the trends in age to the first R01, the NIH should consider the dynamics involving training grants and faculty appointments. It might consider a new model in which the status of a new faculty investigator is considered as the end result or goal of a training award. The U.S. population is aging in general. What investigator age rates should the NIH seek? Perhaps it should consider absolute numbers of investigators rather than rates. The fraction of a grant that supports a principal investigator's salary may be related to the amount of research that occurs. Motivations of senior investigators receiving R01s may change over time. Some institutions are stepping up efforts to support young investigators using innovative programs.

Cultural dynamics play a role. Dr. Barron suggested that, for example, women often fail to move from K awards to R01 awards because of a fear of uncertainty. Some reassurance of success might help. Dr. Zerhouni stated that further analyses should be made. He cautioned against top-down planning and stressed the importance of independence for investigators. Resource issues will always play a large role in efforts to change or maintain the system.

## **REPORT FROM THE ACD WORKING GROUP ON PEER REVIEW**

Lawrence A. Tabak, D.D.S., Ph.D., Director of the National Institute of Dental and Craniofacial Research, reported on the ACD working group's progress in enhancing the NIH's peer review process for research grant applications. The NIH Steering Committee's working group studied the current environment in which the increasing breadth, complexity, and interdisciplinary nature of biomedical science present challenges to peer review. Changes under consideration include shortening the review cycle, assigning applications immediately to Integrated Review Groups (IRGs), realigning study sections, reviewing electronically, and shortening the applications.

The working group completed a diagnostic phase, involving the collection of feedback from institutions, councils, NIH staff, and more. It now is conducting an analytical phase, coding and analyzing the responses. Dr. Tabak reviewed themes that the working group's proposals will likely address. These include reducing the administrative burden, recognizing high-impact science, supporting investigators at various career stages, advancing reviewer quality, and reducing strains on the system that supports research (e.g., resources, costs). The Steering Committee working group may also propose a Select NIH Investigator Award, to recognize outstanding scientists conducting high-impact research.

Dr. Yamamoto reported on progress by an ACD working group, which, operating in parallel, collected feedback from the extramural community and is identifying challenges, considering solutions, and discussing transformational changes. This working group is seeking a system that will reaffirm and emphasize core values of review, support new investigators, reduce administrative burden, and strengthen the leadership and culture of review. Numerous potential approaches or solutions are under active consideration. For example, the working group may recommend the use of study sections as "editorial boards," which make use of outside reviewers and expanded reviewer expertise. It may recommend a "prebuttal" phase, in which the applicant responds to a pre-meeting assessment. Two separate R01 tracks are being discussed—one for innovative research (99 percent) and one for transformational research (1 percent). The working group is also considering a possible change in the triage of applications, instituting a single criterion—impact—and a ranking of applications (e.g., each reviewer ranking a top 10) rather than scoring. Other changes under discussion include a shorter application and 1-page reviews based on merit only and with

no mentoring.

### *Discussion*

Dr. Zerhouni stated a main goal of ensuring that scientists do not suffer from unnecessary restrictions. He noted that the process of enhancing peer review continues, and he will seek input from the ACD members. Dr. Kelly stressed the need to enlist the best scientists in study sections. Dr. Yamamoto responded that the proposed ideas, such as shorter applications and mailed reviews, would make it easier to enlist the best and most appropriate reviewers.

The ACD members noted that a shift to an editorial model, with the mailing of reviews, would likely require increased work by the NIH staff—although efficiencies are possible. David Botstein, Ph.D., cautioned that the categories of innovative and transformational research might not account for studies that are valuable yet not quite either innovative or transformational (e.g., studies featuring “essential continuation”). Rules about percent effort should take into account different types of investigators. Dr. Nelson encouraged both working groups to consider ways in which the NIH communicates with investigators. The criterion of impact will involve subjective considerations.

Antonio Scarpa, M.D., Ph.D., Director of the Center for Scientific Review (CSR) confirmed that the CSR has expanded the use of technologies for reviewing (e.g., electronic applications, interactive chat). Dr. Barron stated that, nevertheless, face-to-face meetings of reviewers produce benefits, such as accountability. Dr. Zerhouni noted that, despite the benefit of experts, it has been shown that, in general, a group of diverse persons tends to make the best decisions.

Christine E. Seidman, M.D., encouraged the working groups to consider ways to accommodate collaborative science—for example statisticians and biologists working together. Dr. Botstein suggested that review panels contain generalists, and he praised the working groups’ efforts to increase the recognition of scientific significance in applications.

Dr. Zerhouni stressed that one goal of the new reviewing scenario is to reduce the traffic jam that occurs when weak applications are returned with changes yet redundancy (a mentoring process). Reviewers may be more willing to take part in the process if this aspect is reduced. Wendy

Chaite, Esq., noted the ongoing independent effort to find alternative funding for applications that “just miss” acceptance.

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

Dr. Barron reported that COPR members recently served or participated in NIH committees and councils, made presentations, and provided interviews and consultations. The COPR’s three working groups—Agenda, Communication, and Role of the Public in Research—have moved forward with various activities. In particular, the Communication Working Group developed a series of recommendations, including a NIH Ambassador Program, an Ad Council campaign, and partnerships with non-Federal groups. The Working Group on the Role of the Public in Research developed ideas to pursue, such as creating criteria with which review panels can gauge community engagement, creating guidelines for educating researchers about community engagement, and defining community engagement. In a public meeting session on October 26, 2007, the COPR members received updates from representatives from a series of NIH initiatives, including the NIH Public Trust Initiative, the NIH Pioneer Award, the New Innovator Awards, and NIH Peer Review.

Dr. Seidman suggested that young investigators be given “service” credit for taking part in COPR-related community engagement activities. Ms. Chaite encouraged the ACD members to become more involved with the activities of the COPR. Dr. Barron noted that a joint ACD-COPR meeting is being planned.

## **NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK): CORE PRINCIPLES**

Griffin P. Rodgers, M.D., Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), presented background and current activities of the Institute. The NIDDK's core principles/activities include maintaining a vigorous investigator-initiated research portfolio, supporting pivotal clinical studies and trials, preserving a stable pool of new investigators, fostering exceptional research training and mentoring, and disseminating knowledge.

Dr. Rodgers reviewed the NIDDK's FY 2007 budget and showed 10-year graphs of NIDDK grant paylines and application funding requests. The Institute hopes to increase paylines in 2008. Dr. Rodgers described the Institute's work in obesity, Type 2 diabetes, and kidney disease as a paradigm of integrated research. It supports a strategic research plan that targets lifestyle modifications, pharmacologic, surgical, and other prevention and treatments, methods for breaking the link between obesity and health conditions, and a variety of cross-cutting research areas. Dr. Rodgers described current and future trials that target stages in Type 2 diabetes.

The NIDDK created a working group to analyze successes and downstream outcomes of its investigator training award programs. It found, for example, that 60 percent of T32 award trainees remained in research during the period 1994 to 2005. The Institute funds large knowledge dissemination programs focusing on weight control, diabetes, and kidney disease. Dr. Zerhouni applauded Dr. Rodgers for applying a quantitative approach to analyzing and forecasting the nation's need for research in obesity, diabetes, and kidney disease.

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

Raynard Kington, M.D., Ph.D., Deputy Director of the NIH, 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 ACD members Dr. Reede and Dr. Barron. 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. Seidman reported on efforts of the ACD Working Group to review data protection and use policies for the Genetic Association Information Network (GAIN) and NIH-supported or conducted Genome-Wide Association Studies (GWAS). In the past 4 or 5 years, genetic research has advanced from the analyses of a few genetic markers in a small number of families with single gene defects to the study of genetic variations, or single nucleotide polymorphisms (SNPs), in patients and populations with common disorders such as diabetes, heart disease, and inflammatory disorders. To assess the relevance of human genetic variation on disease, researchers perform whole GWAS in which almost a million SNPs are determined throughout the genome of hundreds to sometimes thousands of study participants. As such, the amount of clinical and genetic data in these studies is considerable. Because these very large datasets have potential to empower other studies and discoveries, the NIH has put forward mechanisms to share these clinical and genetic datasets through GAIN and the development of an NIH policy for sharing data from NIH-supported GWAS. A very important consideration for sharing GWAS data is the protection of subject privacy and the confidentiality of the data.

The overarching NIH goal for advancing GWAS is to identify common genetic factors that influence health and disease. To promote the sharing of GWAS data for research, a central NIH repository, database of Genotype and Phenotype (dbGaP), has been created through the National Center for Biotechnology Information (NCBI). The policy for the repository includes data submission procedures, data access principles, protection of research participants, scientific publication, and intellectual property. Dr. Seidman reviewed the GWAS data management policies and procedures, including those addressing informed consent, data submission, removal of personal identifying information and replacement with a random unique code, placement in the repository, and access and secondary use by investigators.

Data Access Committees (DAC) review requests for GWAS data to determine whether the proposed use is consistent with the use that the submitting institution indicated is appropriate, based on its review of the study's informed consent document. The DACs also monitor data usage via annual reports from data users. Two steering committees and a Senior Oversight

Committee, together with the NIH Director, form a governance structure for GWAS. The Senior Oversight Committee reports to the ACD and the NIH Director. The ACD Participant and Data Protection (PDP) Working Group makes recommendations to the ACD on data protection and management policies. It has determined that policies for data access and review currently are robust. It has been considering the potential scope of secondary use of data for research and determined that some uses—for example, methodological studies—are acceptable. Other issues being discussed include the potential for group harm and the communication of research results to individuals. A system is needed that ensures inquiries about the GWAS repository from investigators, study participants, and members of the public are addressed in a complete and timely manner.

The Freedom of Information Act (FOIA) would allow requests for de-identified genetic data under traditional FOIA interpretations. Because of the personal and sensitive nature of the data, the agency intends to redact individual-level genotype and phenotype data from disclosures made in response to FOIA requests and the denial of requests for unredacted datasets under FOIA Exemption 6, 5 U.S.C. § 552 (b)(6). However, FOIA affords requesters an opportunity to contest an agency's determination.

Dr. Seidman asked the ACD members to consider recommending that NIH pursue an additional FOIA exemption. Exemption 3 (as suggested by the working group) would specifically prohibit access to individual-level repository data, to eliminate the risk of matching gene information and individuals.

### *Discussion*

The ACD members discussed complex issues surrounding the use of genetic data. Confidentiality of a person's genetic data should be maintained, yet data should be used for research purposes. Revealing genetic risk associations to a patient may do more harm than good to the patient. What is the responsibility of the clinician? Dr. Nelson stated that clinicians need a safe harbor for revealing or not revealing genetic information to patients. Mary-Claire King, Ph.D., cited a practical example in which a parent's involvement in a genetic study (and data, therefore, in a repository) could be introduced as a factor in a child-custody fight. Dr. Zerhouni

noted that misuses of the data could undermine public trust that could have adverse consequences on public support for genetic research. Dr. Reede pointed out that the general public lacks a basic understanding of genetics and the role that genetics plays in health and research. Additional efforts are needed to determine how best to convey information on genetics to research participants and the public.

The ACD members agreed with the working group's recommendation to seek a FOIA Exemption 3 statute, which would enhance legal safeguards to protect the privacy of individual genotype and phenotype data held by the Federal Government. They suggested adding the phrase "...and other means or safeguards..." to the proposed recommendation to provide such protections. The ACD members also voted for recommendations to provide aggregate genetic information to GWAS research participants and to develop a system for addressing public inquiries about GWAS and the repository. A final recommendation was to develop a strategy for communicating to the community the value of the GWAS and its protections.

As amended by the ACD, the final recommendations that the committee agreed to read as follows:

**Recommendation 1: Privacy Protections for Federal Databases Containing Individual Genotype-Phenotype Data Should Be Strengthened**

The potential for inappropriate and unauthorized uses of research data highlights the obligation of the Federal Government to rigorously protect genomic data and to establish strict standards of data protection to preserve the privacy of individual research participants. NIH and the NIH FOIA Officer consider genotype-phenotype datasets and similar types of individual-level genetic information held by the NIH to be exempt from disclosure under FOIA pursuant to Exemption 6. The NIH and the NIH FOIA Officer are to be commended for attempting to protect data from release under FOIA using Exemption 6; however, the discretionary withholding of the information under FOIA Exemption 6 is subject to change as well as to appeal mechanisms. A statutory-based exemption, called an Exemption 3 statute, would provide more secure and more permanent legal protection of individual-level genotypic and phenotypic data. As such, the NIH Director should seek an Exemption 3 statute and other means or safeguards to enhance legal safeguards to protect the privacy of individual genotype-phenotype data held by the Federal

Government.

**Recommendation 2: Information Should Be Provided to Research Participants and Members of the Public**

NIH should develop a strategy for disseminating information about GWAS to study participants, including information about the purpose of the GWAS repository, the types of genetic studies being carried out with GWAS data, the nature of the findings resulting from those studies, and the potential risks and benefits of broad data sharing. It is also important for NIH to develop a better understanding about the different ways in which such information will be received by participants and to design its dissemination strategy accordingly. In addition, the general public would also benefit from a better understanding of the value of GAIN and GWAS and their unique roles in advancing knowledge of the genetic basis of common diseases.

**Recommendation 3: A System Is Needed to Ensure That Public Inquiries Are Addressed**

The number of members of the public whose genomic data is included in large NIH databases such as dbGaP will continue to increase. As such, a system should be developed to ensure that inquiries from investigators, study participants, and members of the general public about dbGaP are addressed in a thorough and timely way.

**ROADMAP 1.5**

Alan M. Krensky, M.D., Director, Office of Portfolio Analysis and Strategic Initiatives (OPASI), presented the history and progress of the NIH Roadmap for Medical Research program. The Roadmap is designed to foster the development of transformative solutions to grand challenges in health research. It funds cross-cutting research through a shared fund (the Common Fund); performs collective planning and prioritization; manages programs through inter-institute teams; pilots new awards; and operates as a single entity for programs with shared interest. For FY 2007, Roadmap initiatives received \$483 million, or 1.7 percent of the NIH budget.

The Roadmap is a dynamic program with shifting areas of emphasis. A first cohort of initiatives will transition out of this “incubator” space by FY 2014. Initiatives chosen for the program demonstrate the following:

- High potential to transform how research will be conducted
- Synergistic advancement of the mission of the Institutes to benefit health
- Applicability to issues beyond the scope of one or a few of the Institutes
- The likelihood that no other entity is likely to perform the work
- A public health benefit.

Dr. Krensky reviewed the process for choosing initiatives, featuring review steps involving scientists, the COPR, NIH staff, Institute Directors, the ACD, and the NIH Director. Grand challenges that the program considers include reengineering the clinical research enterprise; seeking new pathways to discovery (tools, technology, etc.); and new interdisciplinary research partnerships.

The challenge, or theme, of seeking new pathways to discovery currently features two major initiatives—epigenomics and the human microbiome. Dr. Krensky described the two initiatives and listed current funding opportunities for each within the Roadmap. Other ideas that may join the Roadmap program in the future include human phenotyping, protein capture/proteome tools, and connectivity mapping. It also will support demonstration programs in bridging the sciences and high risk/high reward research. The NIH will solicit ideas from the community on a regular basis.

In discussion, the ACD members sought ways to promote the Roadmap and disseminate its ideas. Dr. Krensky reminded them of the fact that the discoveries from the program will be transformative and will serve the health services. Dr. Zerhouni emphasized the Roadmap's focus on new tools, which the biomedical sciences need. Nancy E. Adler, Ph.D., wondered whether the Roadmap might consider an environome project in the future.

## **THE NATIONAL CHILDREN'S STUDY**

Duane Alexander, M.D., Director, National Institute of Child Health and Human Development (NICHD), described the history and progress of the National Children's Study, the largest longitudinal study of children's health and development ever conducted. The study originated in 1998 when a Presidential Task Force cited a need for a better science base with which to make recommendations about environmental health exposures for children. Children are especially vulnerable to environmental exposures. In 2000, a congressional act directed the NICHD to conduct a longitudinal study of environmental influences on children's health, following a prospective cohort from birth to adulthood.

Between then and 2007, an Interagency Coordinating Committee, a Federal Advisory Committee, working groups, multi-agency consortiums, teams of investigators, and more worked to plan and develop the study. The study will be conducted from 2007 to 2034 and will collect information on about 100,000 children, including important but less common outcomes. It will address questions such as the following:

- What are the health and developmental effects of persistent low-level chemical exposures?
- How are asthma incidence and severity influenced by the interaction of early life infection and air quality?
- How does high-level exposure to media content in early childhood affect development and behavior in children?
- Do pre- and post-natal exposures to endocrine-active environmental agents alter age at onset, duration, and completion of puberty?

Dr. Alexander presented lists of priority exposures to be examined, and samples to be collected. The study will recruit a national probability sample, using centers of excellence to conduct measurements. Investigators will analyze core hypotheses. Data sets by study phases will be made available for public use. Pending funding, the Children's Study will begin enrollment in 2008, extending over the first few years. Projected costs are \$110.9 million for 2008, \$192 million for 2009, and a tapering down to \$100 million per year during the period 2013 to 2034.

Total cost will be about \$3.2 billion, including costs of the early planning years. Information is on the Web at <http://NationalChildrensStudy.gov>.

In discussion, the ACD members wondered whether the Children's Study could address additional components that affect health, such as state and local policies. They suggested investigating low-income families and the influences of changes. Dr. Alexander indicated that the data collection will allow for studies of various effects, including the influences of geographic location. He encouraged the ACD members to stimulate organizations and other research entities to expand the scope of the study by performing supplemental or derivative studies. Because of the long length of the National Children's Study, retention would be a key concern. The planners have addressed that issue up-front and have developed strategies.

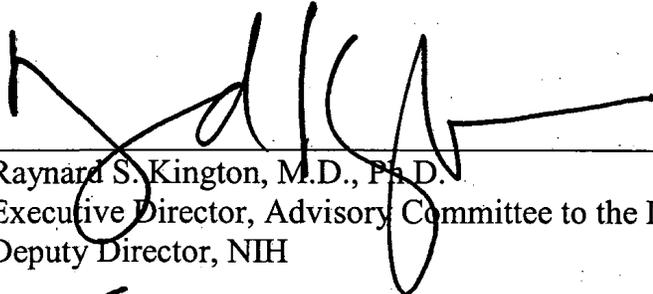
## **ADJOURNMENT**

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

## SUMMARY AND CONCLUSIONS

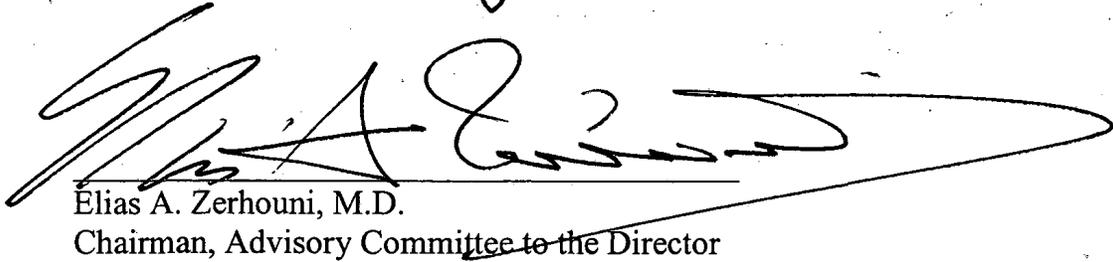
The NIH ACD convened on December 7, 2007, to receive updates on the NIH budgetary process; discuss the issue of rising average ages of first-time grant recipients; receive news on the NIDDK, the National Children's Study, and the NIH Roadmap for Medical Research; and receive reports from the ACD Working Group on Peer Review and the Working Group on Participant and Data Protection for GAIN and GWAS. The ACD members received a report from the COPR 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.



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Raynard S. Kington, M.D., Ph.D.  
Executive Director, Advisory Committee to the Director  
Deputy Director, NIH



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Elias A. Zerhouni, M.D.  
Chairman, Advisory Committee to the Director  
Director, NIH

## **ABBREVIATIONS AND ACRONYMS**

ACD	Advisory Committee to the Director
COPR	NIH Director's Council of Public Representatives
CSR	Center for Scientific Review
DAC	Data Access Committee
dbGaP	database of genotype and phenotype
FOIA	Freedom of Information Act
FY	fiscal year
GAIN	Genetic Association Information Network
GWAS	genome-wide association studies
ICs	(NIH) institutes and centers
IRG	Integrated Review Group
K Award	An NIH training grant program
NCBI	National Center for Biotechnology Information
NDBA	NIH Director's Bridge Award
NICHD	National Institute of Child Health and Human Development
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
OPASI	Office of Portfolio Analysis and Strategic Initiatives
PI	principal investigator
PDP	participant and data protection
R01	An NIH large research project grant program
SNP	single nucleotide polymorphisms
T Award	An NIH training grant program