Department of Health and Human Services
National Institutes of Health (NIH)
Office of the Director (OD)
Office of Portfolio Analysis and Strategic Initiatives (OPASI)

Council of Councils Meeting
March 31–April 1, 2008

Meeting Minutes

I. WELCOME

Dr. Alan M. Krensky, M.D., Chair, welcomed participants, NIH staff members, and members of the public to the first official meeting of the Council of Councils (CoC). The meeting opened at 8:15 a.m. on Monday, March 31, 2008, in Building 31, 6th Floor, Room 6, on the NIH Campus, Bethesda, Maryland.

A. Attendance

1) Council Members Present

Chair: ALAN M. KRENSKY, M.D., Director, OPASI, OD, NIH
Executive Secretary: ELIZABETH L. WILDER, Ph.D., Acting Associate Director, OPASI, OD, NIH
RONALD L. ARENSON, M.D., University of California, San Francisco
ENRIQUETA C. BOND, Ph.D., Burroughs-Wellcome Fund, Research Triangle Park, North Carolina
DONNA BATES BOUCHER, Bates Group, Inc., Denver, Colorado
RICHARD CHABRAN, M.L.S., California Community Technology Policy Group, Los Angeles, California
COLEEN K. CUNNINGHAM, M.D., Duke University Medical Center, Durham, North Carolina
ROBERT M. DICKLER,[1] Association of American Medical Colleges, Washington, District of Columbia
EDWIN FLORES, Ph.D., J.D., Chalker Flores, LLP, Dallas, Texas
JOSEPH H. GRAZIANO,[2] Ph.D., Columbia University, New York, New York
BEVRA H. HAHN, M.D., University of California, Los Angeles
MARY J.C. HENDRIX, Ph.D., Northwestern University, Chicago, Illinois
DILIP V. JESTE, M.D., University of California, San Diego/VAMC
LENWORTH N. JOHNSON, M.D., University of Missouri-Columbia, Columbia, Missouri
WARREN A. JONES, M.D., F.A.A.F.P., University of Mississippi Medical Center, Jackson, Mississippi
ARTHUR M. KLEINMAN,[3] M.D., Harvard University Medical School, Cambridge, Massachusetts

[1] Attended intermittently because of a concurrent Clinical Center meeting, was not present on April 1.
[2] Arrived late because of travel issues.

JOSEPH LOSCALZO, M.D., Ph.D., Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts
MARJORIE K. MAU, M.D., University of Hawaii at Manoa, Honolulu, Hawaii
JUANITA L. MERCHANT, M.D., Ph.D., University of Michigan, Ann Arbor, Michigan
SERGIO R. OJEDA, D.V.M., Oregon Health and Science University School of Medicine, Beaverton, Oregon
ORIEN REID, M.S.W., Alzheimer's Disease International and Consumer Connection, Laverock, Pennsylvania
MARTIN ROSENBERG, Ph.D., Promega Corporation, Madison, Wisconsin
HAROLD T. SHAPIRO, Ph.D.,[4] Princeton University, Princeton, New Jersey
SANDRA MILLON UNDERWOOD, Ph.D., R.N., University of Wisconsin-Milwaukee
PHYLLIS M. WISE, Ph.D., University of Washington, Seattle, Washington
MARINA E. WOLF, Ph.D., Rosalind Franklin University of Medicine and Science, North Chicago, Illinois

2) Council Members Absent

CECILE A. FELDMAN, D.M.D., M.B.A., University of Medicine and Dentistry of New Jersey, Newark, New Jersey
DARIA MOCHLY-ROSEN, Ph.D., Stanford University School of Medicine, Stanford, California
RICHARD A. RUDICK, M.D., Cleveland Clinic, Cleveland, Ohio
GARY L. WESTBROOK, M.D., Oregon Health and Science University, Portland, Oregon

3) Ad Hoc Representatives Present

JOAN E. FOX, Ph.D., Case Western Reserve University, Cleveland, Ohio
VICTOR M. HESSELBROCK, Ph.D., University of Connecticut Health Center, Farmington, Connecticut

4) Presenters in Attendance

Timothy C. Hays, Ph.D., Chief, Portfolio Analysis and Scientific Opportunities Branch, OPASI, OD, NIH
Deborah Duran, Ph.D., Chief, Systemic Assessments Branch
Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research
Francis S. Collins, M.D., Ph.D., Director, National Human Genome Research Institute
Barbara Mittleman, M.D., Director, Program on Public-Private Partnerships, Office of Science Policy, OD, NIH
Amy McGuire Porter, Executive Director, Foundation for the National Institutes of Health
Julie Wolf-Rodda, M.A., Director of Partnership Development, Foundation for the National Institutes of Health

[3] Was not present on April 1.
[4] Arrived late because of travel issues.

5) Institute and Center (IC) and Office Directors Present

James F. Battey, Jr., Director, National Institute of Deafness and Other Communication Disorders
Jeremy Berg, Ph.D., Director, National Institute of General Medical Sciences
Paul Coates, Ph.D., Director, NIH Office of Dietary Supplements
Richard J. Hodes, M.D., Director, National Institute on Aging
Vivian Pinn, M.D., Director, NIH Office of Research on Women's Health
Antonio Scarpa, M.D., Ph.D., Director, Center for Scientific Review
Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research
Jack Whitescarver, Ph.D., NIH Office of AIDS Research

6) NIH Staff and Guests

In addition to Council members, presenters, and Directors, others in attendance included NIH staff and interested members of the public.

B. Planning Meeting Minutes, November 8, 2007

A motion to approve the minutes was forwarded and seconded. The motion passed unanimously.

II. REMARKS FROM THE NIH DIRECTOR

Dr. Elias Zerhouni, Director of NIH, noted the enormous impact and profile the CoC is expected to have and the large amount of interest in it. He stated that CoC must have the flexibility to explore and advise beyond the content of any one IC. Dr. Zerhouni acknowledged, however, that Council members also serve as liaisons to their individual councils and that the most important aspect of integration is clear, bidirectional communication.

The CoC has established subcommittees parallel to the function of OPASI: portfolio analysis, strategic coordination, and evaluation and assessment. Dr. Zerhouni cautioned that although most see portfolio analysis as a counting exercise, that aspect is only a snapshot. Another component of portfolio analysis involves looking forward and assessing where NIH is in relation to where the science is. Portfolio analysis should involve assessing the frontiers of knowledge and identifying real gaps.

Dr. Zerhouni emphasized that the Common Fund should not serve as backstop funding for projects that cannot get funding elsewhere. Rather, the Common Fund should support strategic initiatives that are based on intelligent, forward-looking analysis of the portfolio of science, rather than the portfolio of NIH. Ideas generated and proposed for Roadmap/Common Fund projects require oversight, improvement, and a wide range of input, but that input should challenge NIH to take risks. Dr. Zerhouni exhorted the Council to rise to the challenge of assessing where the frontiers are and promoting high-risk ideas.

Evaluation and assessment—and to some degree resource development and analysis—helps individuals to understand whether they are doing a proper job. One can evaluate

publications and regulatory requirements, but this approach does not account for discovery or the breakthroughs that often surprise scientists themselves. Evaluating the success of Common Fund programs will require the development of a different way of assessing science. However, Dr. Zerhouni pointed out that there is presently no science of science, and thus no scientific way to prospectively assess and evaluate science.

Dr. Zerhouni pointed out that Council members bring a large and diverse expertise, most important of which is the ability to think broadly. He also specified that the CoC differs from the Advisory Committee to the Director, which focuses on day-to-day policy and not the scientific portfolio. Its work will require rigor and discipline and be based on an exploration of how best to look at scientific priorities and portfolios of scientific ideas. This work, along with advice on priority setting in terms of public health burden and scientific opportunity, is what Congress envisioned when it established the CoC.

Dr. Zerhouni concluded his remarks by noting that the ability to do science ultimately depends on well-supported, talented, and creative scientists. Dr. Zerhouni thanked Council members for taking on this responsibility.

Discussion Highlights

- Dr. Zerhouni emphasized the importance of open, direct, and transparent communication between the CoC and individual IC councils. He encouraged Council members to report to IC directors or present a formal report at IC council meetings. However, he cautioned against directing projects toward support by the Common Fund simply because they cannot be funded elsewhere.

- In response to questions about private-sector examples of integrative functions, Dr. Zerhouni noted again that OPASI and the CoC should not constitute an additional layer of bureaucracy. He then cited successful examples of creativity and integration in the private sector, which relies on heavy brain trusts, rather than additional infrastructure, to manage their opportunity funds. This type of coordination—a brain trust, rather than a new structure—is what is envisioned for OPASI and the CoC. However, because of the complexity of the NIH mission, coordination will be an evolving, ongoing process.

- The CoC's recommendations should not supplant the ongoing training efforts of the NIH. However, workforce issues might be involved in the development of new scientific fields proposed by OPASI and the CoC. Thus the CoC will consider workforce and training issues within the context of identifying scientific gaps and trans-NIH needs.

- Dr. Zerhouni emphasized that assessment should accommodate the unpredictability of science, and he cautioned that no one approach will fit all. Focusing on prizes and publications merely assesses past success, but it does not give weight to the future.

- In response to questions about the inclusion of tacit knowledge from the bottom up—that is, from people who are not scientists but are connected with science—

Dr. Zerhouni further emphasized the need for input from a wide and diverse range of communities. Dr. Zerhouni recognized the work of many ICs in involving communities, particularly in clinical research, and he cited the accumulation of knowledge as one function of the CoC.

III. OPASI DIVISIONS

A. Resource Development and Analysis

Dr. Timothy Hays pointed out that the main goal of the Division of Resource Development and Analysis (DRDA) is to understand the frontiers of knowledge. The Division's mission is to employ existing resources, including databases, analytic tools, and methodologies, and to develop specifications for new resources needed to better understand science as it has and will evolve.

DRDA comprises three branches:

- The Public Health Burden Branch aims to refine metrics to measure the contribution of different diseases to ill health, an effort that requires rigorous inquiry based on established techniques in fields such as epidemiology, biostatistics, economics, and psychometrics. The Branch also assists other OPASI Divisions in mapping multiple dimensions of public health need against the NIH portfolio; addresses difficulties that arise in measuring disease burden, comparing the burden of different diseases, and projecting those burdens into the future; and works closely with other Federal agencies responsible for monitoring the nation's public health needs.

- The Data Tools and Analysis Branch is responsible for pulling together a central repository and analyses from various sources to provide researchers and staff a better way to understand large amounts of information. The Branch will devise analyses to increase understanding of research portfolios and other measures beyond OPASI into other areas of NIH.

- The Portfolio Analysis and Scientific Opportunities Branch focuses on scientific content in both intramural and extramural research. This effort includes the Research, Condition, and Disease Categories (RCDC); an examination of internal and cross-agency funding trends; and analyses of research overlaps and research gaps.

<u>Discussion Highlights</u>

- One difficulty faced by the RDCD involves different definitions of the same term by different groups. Dr. Hays noted that a large amount of time is spent on defining areas and adapting the tool to capture the right projects for each category.

- DRDA is collecting both U.S. and international data. Council members suggested keeping these sources distinct in its categorizations.

- Council members pointed out that many areas of interest to NIH begin in childhood and that children should therefore be included in DRDA's categories. Dr. Hays responded that every age group will be important and that the National Institute on Aging (NIA) and the National Institute of Child Health and Human Development have been involved in discussions for many research areas and categories.

- Dr. Hays acknowledged that portfolio analysis is an enormous undertaking and that CoC input will be helpful in identifying the highest priorities. He also noted that the RCDC covers 350 different categories but that thousands of other categories are not addressed at present, although the ultimate goal is to cover all of them.

- In response to questions about how to move from burden of disease to frontiers in knowledge, Dr. Hays noted that approaches to do that effectively need to be worked out and that many datasets must be mined. At present, DRDA has focused on research content—titles, abstracts, and specific aims—and not tapped into datasets.

- In response to Council members' concerns that DRDA efforts will merely duplicate those of other agencies focused on public health, Dr. Hays clarified that DRDA aimed to examine what has already been collected and not to collect new data.

B. Strategic Coordination

Dr. Elizabeth Wilder stated that everything the Division of Strategic Coordination (DSC) does involves coordination with ICs or other OPASI Divisions. DSC serves as a focal point for coordination of trans-NIH programs and for development and implementation of strategic initiatives at the NIH. The mission of the DSC is to:

- Foster coordination of research that spans the missions of multiple ICs.

- Implement a process of strategic planning in those areas for which emerging opportunities and specific grand challenges meet the criteria for funding via the Common Fund.

Dr. Wilder clarified that the Common Fund represents a relatively small portion of the NIH budget and that only a small subset of trans-NIH ideas meet the criteria for Common Fund support. Most importantly, Common Fund projects are designed to meet emerging areas in which large roadblocks are apparent, and they are designed to transform science. OPASI aims to implement a process to identify those areas and implement programs.

DSC is still growing and has not yet divided formally into branches. However, two branches are specified in the current organizational chart: the Analysis Branch will ensure communication, develop concepts for new Common Fund Programs,

implement new Common Fund programs, and articulate questions for evaluations of these programs; the Operations Branch will administer the Common Fund, interacting with the NIH Office of Budget and with ICs to facilitate the transfer of money from the Common Fund to the ICs that administer individual awards.

Dr. Wilder outlined DSC activities for the current Common Fund program cohorts, and closed her presentation by noting that OPASI expected to develop suggestions for new programs during spring CoC meetings and for CoC to approve concepts during its fall meetings.

Discussion Highlights

- NIH expects that the Common Fund will serve as an incubator space for trans-NIH programs and that these programs will end or move to individual ICs once Common Fund support ends.

- The Council will help to generate ideas during its spring meetings, NIH staff will develop a subset of ideas into concepts with supporting data, and the Council will approve concepts at its fall meetings. Dr. Wilder emphasized that ideas could come from portfolio analysis, IC staff, the larger community, and NIH leadership and that the process for collecting, vetting, and approving ideas is still evolving. Dr. Wilder also pointed out that although Council opinions will be given considerable weight, the broader community cannot be excluded from this process. The Council will approve concepts and make recommendations to the NIH leadership, and the Council has the opportunity to comment on any concepts it deems unacceptable for the Common Fund. Although the subcommittee for strategic coordination will have more indepth discussion of the concepts, the entire Council will have the opportunity to comment..

- The NIH leadership sees training as critical, and a trans-NIH group has begun a strategic planning process that assesses all NIH training programs and the career path and identifies critical training needs. The Common Fund might support new training mechanisms to encourage investigators to enter a new or underserved field, but training in general is not in the purview of OPASI or the CoC.

- DSC communicates with the other Divisions but its roles are distinct. DRDA examines the entire NIH portfolio, reports on it, and enables ICs to use data for their own planning. The job of DSC is smaller: to identify a subset of topics as possible Common Fund programs. In terms of assessment, DSC coordinates a process for gathering input on the needs of the Common Fund programs; DESA works with all the ICs to help them with their needs assessments..

- Transparency and communication. The Common Fund is now a separate line item for appropriations to the NIH Office of the Director; ICs no longer pay for it. However, OPASI still strives for transparency and tries to be clear about how topics are selected.

C. Evaluation and Systematic Assessments

Dr. Deborah Duran noted that DESA's mission is to conduct NIH-wide evaluations and system assessments, provide technical assistance for these assessments, facilitate the development of more appropriate performance assessments of science, provide findings integrated with portfolio analyses that foster scientific planning, and maximize effective use of the NIH's 1% set aside for evaluation.

The Division consists of two branches:

- The Evaluation Branch is guided by Federal regulations as it manages the 1% of the NIH budget set aside for evaluation.

- The Systemic Assessments Branch evaluates the performance of NIH as a whole and conducts internal assessments. The Branch also complies with and responds to Federally mandated performance reporting mechanisms. In addition, the Systemic Assessments Branch fosters the development of more appropriate assessments for innovative science and large complex systems and organizations, and it facilitates "science of science" activities.

The two DESA branches work together in coordinating, planning, managing, tracking, and reporting program performance data to assess how programs perform and to do the required reporting. Thus, staff within a particular program are not responsible for evaluating that program.

Dr. Duran devoted the bulk of her presentation to "the science of science." The rationale for assessing science arises from a desire for evidence-based information for planning and budgeting. This is critical in the current environment of accountability, which asks about impact, value, effectiveness, and efficiency. Existing methodologies for evaluating and assessing science work for only a portion of the NIH portfolio, but they do not work for highly innovative, high-risk-high-reward projects, which are difficult to plan and predict. Moreover, these methodologies can assess individual sites, but not the impact of the overall system.

No definition exists for the science of assessing science. DESA has developed the following draft definition for NIH, although no consensus has been reached: "The science of science management is a systematic approach to determine how to enhance scientific productivity to improve public health."

DESA is sponsoring a Science of Science meeting on October 2–3, 2008, to foster crosstalk among disciplines such as economics, information technology, evaluation, organizational psychology, and systems. The meeting will be supported as a working group to the CoC, and there will be a report at the fall 2008 meeting of the Council.

<u>Discussion Highlights</u>

- Better methodologies are needed to determine when to end a program. Dr. Wilder added that some evaluation aspects, such as midcourse reviews, were built into

the Common Fund programs and that the NIH leadership had considered these reviews in its decisions to continue programs. It is not yet clear how the Council would decide it was time to end a program or move to the next generation.

- The concept of failure was discussed. Dr. Duran noted that in assessment terms, "failure" means a program did not achieve what was intended. One Council member suggested that the term "failure" should not be avoided; instead, it should be defined in a clear way.

- Bureaucratic assessment, which is relatively straightforward, should be separated from science assessment.

- One Council member discussed the need for a common database to assess the translational impact of science and to identify new areas of funding. She suggested pulling from PubMed Central, where NIH-funded investigators are required to enter their publications; patent databases, which would provide information about provisional and granted patents and licenses; and databases of NIH grantees. DESA's demonstration project with the OER aims to compile such a database.

- Science of science metrics. Measures historically used for assessment, such as publications, patents, drugs, and number of associated startup companies, usually improve social benefit. However, they do not necessarily derive directly from funded data. Links between endpoints and something stakeholders value are not linear, but complicated, and the logic and validity of those links will have to be demonstrated in a way that the public can understand.

<u>General Discussion Highlights of OPASI Divisions Presentations</u>

- Dr. Krensky began the discussion by noting that OPASI and the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) represent a new evolution. The CoC can advise on that evolution, although how it will do so is not yet clear. The talks from Drs. Hays, Wilder, and Duran provided the CoC with an idea of how activities would be integrated within OPASI and in DPCPSI as a whole: portfolio analysis will lead to strategic planning, which will lead to evaluation, which will circle back to portfolio analysis.

- Council members cautioned against collecting large amounts of data without having some idea of how that data will be used.

- There is a sharp distinction between assessments done as mandated by Congress and those done to improve the management of science. Applying traditional evaluation metrics to high-risk-high-reward projects will not assess performance accurately. Council members also suggested that some of them attend the October meeting on the science of science.

- OPASI intends to compile libraries or databases for others to examine the science.

- Dr. Krensky emphasized that although OPASI has been charged with some bureaucratic tasks, it is about science and transparency first. Its portfolio analysis, strategic coordination, and evaluation processes must go beyond bureaucratic parameters and explain what science is.

- OPASI and DPCPSI are designed to define new areas, and the CoC can play a critical role by providing input in the generation and vetting of ideas. OPASI is still looking for better ways to engage the Council, beyond its regularly scheduled meetings. Subcommittees and working groups might help in this regard. OPASI also will have to address the tension between the natural resistance of the scientist to new ideas and the value of those ideas. There is a demonstration oversight group for high-risk-high-reward projects, and NIH is reviewing the peer-review system.

- Importance of "failures." Because "failures" can represent vital steps, OPASI should consider a reservoir for investigators to deposit results for projects that do not work.

IV. INTERDISCIPLINARY RESEARCH

Dr. Lawrence Tabak, Director of the National Institute of Dental and Craniofacial Research, began his presentation by thanking members of the NIH Interdisciplinary Research Implementation Group (IRIG). IRIG is a trans-NIH group that develops initiatives to incubate interdisciplinary research, with the goal of supporting significant advances in public health by stimulating research that crosses boundaries. Specifically, IRIG identifies barriers and supports initiatives to remove those barriers. In so doing, the group has discovered that it is not crossing boundaries that is difficult so much as the approaches that lie at the interface of those boundaries.

Dr. Tabak then discussed the context and background for interdisciplinary research, challenges to interdisciplinary research, and evaluation of IRIG activities. Team science does not necessarily equate to multidisciplinary or interdisciplinary science. In multidisciplinary research, for example, a dentist might work with an organic chemist on a common problem, but each one remains in his or her own field. In interdisciplinary research, the dentist and organic chemist interact and create a new discipline.

Dr. Tabak highlighted the following challenges to interdisciplinary research:

- The current system of academic advancement favors the independent investigator.

- Most institutions house scientists in discrete departments.

- Interdisciplinary science requires interdisciplinary peer review.

- Project management and oversight is performed by discrete NIH ICs.

- Interdisciplinary research teams take time to assemble and require unique resources.

To address the need for infrastructure to support interdisciplinary research, initiatives were created for a series of interdisciplinary research consortia. Dr. Tabak outlined other IRIG responses to barriers:

- The support of research collaborations between behavioral and social sciences and biomedical science, through supplements, specific grant mechanisms, and networks.

- A change in NIH policy to recognize multiple principal investigators, brought about by many NIH groups, including IRIG.

- Establishment of new training programs, including the K07 Curriculum Development Award in Interdisciplinary Research; the R13 Short Program for Interdisciplinary Training; the T32 Interdisciplinary Health Research Training: Behavior, Environment, and Biology; and the T90/R90 Training for a New Interdisciplinary Research Workforce.

The parameters of evaluation for these initiatives are still evolving, but scientific excellence is superimposed over all aspects. The overall contribution of a team is one aspect of evaluation: has it contributed anything new, how much of its work depends on antecedent knowledge, what kind of impact does it have on a single field or does it contribute to a network of knowledge, and what is the degree to which the team's work yields practical answers to societal questions? Yet evaluation processes also must assess individual team members, and groups are beginning to agree on the types of questions that should be asked.

IRIG has focused its evaluation plan on process and short-term outcomes. The quality of training is important, and scientific rigor should be built into programs. IRIG evaluation activities also identified program-specific issues such as the development of degree-granting programs, the use of mentoring committees or teams versus co-mentors, core competency courses versus an individually tailored menu of courses, whether courses should be front-loaded before students engage in research, and involvement of basic research students in clinical work.

In preparation for life after Roadmap/Common Fund, IRIG is working with the leadership of training programs to match funded interdisciplinary research training programs with relevant and interested ICs.

Discussion Highlights

- Universities typically do not pay for teaching, and NIH training grants do not pay for mentors. Dr. Tabak acknowledged the importance of these comments and noted the tension between the desire to attract new investigators to interdisciplinary research. He clarified that a newT90/R90 training program allows mentors a modest salary recovery.

- Dr. Tabak speculated that the better or stronger institutions have embraced interdisciplinary research most quickly. Yet metrics beyond the traditional measures are needed to assess the impact of interdisciplinary teams and the individuals within them.

Council members suggested press coverage as a surrogate marker for measuring impact of interdisciplinary research on society.

- One Council member emphasized the need for a balance between interdisciplinary research and R01-supported research. In some cases, projects are best served by independent research.

V. THE MOLECULAR LIBRARIES ROADMAP INITIATIVE

Dr. Francis Collins, Director of the National Human Genome Research Institute (NHGRI), explained that the Molecular Libraries Initiative (MLI), a marriage of chemistry and biology, is the largest Roadmap/Common Fund initiative and one of the earliest ones adopted. It offers academic investigators a new entry in their toolkits: small molecules, or small organic compounds, as "perturbogens" of their favorite molecular pathways or as first steps in the development of therapeutics. Several developments have made MLI possible. The sequencing of the human genome yielded new targets, far more than the private sector can pursue. High-throughput mechanisms have been developed to build compound libraries of considerable diversity, and robotic and assay technology allows high-throughput screening.

MLI fits into the New Pathways to Discovery component of the Roadmap. It was proposed because of an urgent need to understand genes, proteins, and pathways at a sufficient level of detail to allow the consideration of novel ideas. MLI also arose from an urgent need to catalyze the development of therapeutics for rare and neglected diseases.

MLI fits in with the pipeline for drug development. This pipeline usually begins with the identification of a target, the development of an assay to allow one to identify small molecules active against that target, and the use of high-throughput screening to identify initial molecules to be modified by medicinal chemistry. Further steps are taken to make these molecules more potent and soluble, creating a research probe, and after further lead development and optimization, the compounds undergo clinical development in Phase I, II, and III trials that ultimately lead to approval by the U.S. Food and Drug Administration (FDA).

MLI consists of interlocking initiatives, the centerpiece of which comprises 10 screening centers with high-throughput capabilities. Located throughout the United States, the screening centers represent an NIH-academic partnership and form a cooperative network, and center directors meet regularly. Components of MLI include technology development efforts, such as chemical diversity, assay development, and instrumentation, as wells as components for data analysis and dissemination, such as chemoinformatics research centers. Dr. Collins pointed out that creative genius drives this enterprise.

Dr. Collins presented two examples of projects: inhibitors of measles virus RNA polymerase and inhibitors of *Schistosoma mansoni* peroxiredoxins. Dr. Collins cited the latter project as an example of something that never would have happened in the private sector.

The MLI has almost reached the end of the pilot phase, and it is undergoing an intense and rigorous peer review. Dr. Collins closed his presentation by noting the excitement of merging what has been learned about the genome and proteins with opportunities to further therapeutics. He pointed out that the pharmaceutical industry would provide the best partners but that NIH could step into the void and push the process forward for rare and orphan diseases. He referred the CoC to the MLI Web site (http://mli.nih.gov/mli) for further information.

Discussion Highlights

- MLI leadership have emphasized that PubChem was not meant to compete with the Chemical Abstracts Service, but to place small molecule technology into the hands of academic investigators.

- Dr. Collins stated MLI's hard and fast policy that neither the assay developer nor screening center can make an intellectual property claim on connections arising from MLI assays. He further noted that intellectual property normally arises downstream from the initial assay and hit or early medicinal chemistry steps. In response to concerns that NIH and original contributors will not benefit from lucrative projects based on MLI, Dr. Collins acknowledged the tension between the need to capture intellectual property supported by NIH and the need for public access. However, he expected that most compounds taken further would address rare or orphan diseases and would likely have limited profits.

- Council members and Dr. Collins agreed that the chemistry step of drug development could represent a roadblock. Dr. Collins noted that approximately one-third of the budget is devoted to chemistry.

- MLI aims to learn about biological function and determine the functions of molecular pathways and their possible relevance to disease.

- Exit strategies should be considered for long-term Roadmap initiatives that cannot be transferred to a single IC.

- Dr. Roderic Pettigrew, Director of the National Institute on Biomedical Imaging and Bioengineering reminded the Council that early on in the MLI, there were two separate activities for molecular libraries and molecular imaging. These activities have been brought together administratively, although projects are still specific and distinct.

VI. NEW CONCEPTS AND CURRENT ROADMAP TOPICS

Dr. Wilder briefed the Council on other Common Fund projects and concepts and asked Council members to consider what types of information they need to make recommendations in the future. She reported that the NIH leadership had met on February 29, 2008 to select Common Fund programs that will initiate funding in FY2009 or FY2010.

Discussion Highlights

Possible exit strategies for Common Fund projects were discussed: (a) transition from Common Fund into IC; (b) selection for longer-term Roadmap funding; (c) support from a group of ICs; (d) a new funding mechanism from the NIH Director that would allow long-term support without compromising the intent of the Common Fund; (e) partnerships with entities outside NIH; (f) developing metrics of success to judge which projects represent "home runs" for the initial investment; and, (g) setting a "sunset" for current entitlements, forcing centers to develop strategies for sustainability.

Information needed by the Council to make recommendations: (a) a two-page description of each concept and proposed funding amount, with an opportunity for Council members to find more information; (b) a list of exit strategies for a proposed concept; and, (c) information about the overall budget in different research categories.

- Budget and funding can be considered in the Council's decisions, but OPASI seeks input in terms of the "scientific excitement factor" for proposed concepts. Some Council members suggested that CoC should focus more on bringing new ideas into the Common Fund, leaving issues of funding and exit strategies to NIH as a whole.

- Council members were reminded that Roadmap/Common Fund is not the only mechanism for trans-NIH efforts. Historically, ICs have worked together on projects. The Neuroscience Blueprint is an example.

- Council members also were reminded that DPCPSI, OPASI, Common Fund, and CoC are law as a result of the NIH Reform Act of 2006. These entities will remain in place regardless of changes in NIH Directors.

VII. CLOSED SESSIONS—SUBCOMMITTEE BREAKOUT SESSIONS

These sessions were closed to the public to allow subcommittees to conduct confidential, preliminary discussions leading to the presentation of advice and recommendations to the overall Council and ultimately to the NIH Director.

VIII. PUBLIC-PRIVATE PARTNERSHIPS AND THE FOUNDATION FOR THE NATIONAL INSTITUTES OF HEALTH

A. Public Private Partnerships

Dr. Barbara Mittleman, Director of the Program on Public-Private Partnerships, noted that although the public-private partnerships (PPP) program began slowly, many recognized that it would have a life beyond the 5- to 10-year lifetime of a Common Fund program. The initiative was a mechanism relevant to all science, not to a single IC; thus it was transferred to the NIH Office of Science Policy. The goal of PPP is to promote public health in a way that is science driven and rigorous, leverages NIH resources to achieve synergy, and is compliant with Federal law, regulations, and policies.

Dr. Mittleman discussed several foci of PPP and emphasized that there is no new PPP authority; rather, PPP represents business as usual as NIH carries out its official duties. She also discussed authorities relevant to PPP, including Gift Authority, in which monetary donations support research or other NIH activities, and the Foundation for the National Institutes of Health (FNIH), which facilitates co-equal governance in partnerships and mediates support from prohibited donors or donors wishing for distance from the work they want to support.

Dr. Mittleman stressed that PPP should not be built if an activity can be accomplished by a single entity. Instead, PPP should build synergy. Dr. Mittleman added that PPP can be constructed at any point in the spectrum from basic to translational to clinical research.

Examples of ongoing PPPs include: Osteoarthritis Initiative; Alzheimer's Disease; Neuroimaging Initiative; Genetic Association Information Network; and Biomarker Consortium. Dr. Mittleman closed her presentation by providing the Council with several links for more information.

B. Foundation for the National Institutes of Health

Ms. Amy McGuire Porter, Executive Director of FNIH, provide an overview of the Foundation. Created by Congress in 1990 and incorporated as a non-profit in 1996, FNIH raises private funds in support of NIH's mission of improving health through scientific discovery and translational research. Where once the Foundation aimed to fill the gaps in NIH activities, it now looks for difficult projects and devotes strategic thought to negotiating partnerships in those areas. As Dr. Mittleman had noted, FNIH now works with the Program on Public-Private Partnerships. It also continues to work with ICs.

Ms. Porter informed the Council that for 2008, FNIH aims to align as closely with NIH as possible, track its activities, and identify discoveries that can be promoted externally. FNIH continues to build on existing NIH programs as its core business. It ability to expand the number of funded NIH grants, through parallel grants or additional funds from other agencies, has increased. The Foundation also works with intramural research laboratories and collaborative networks, and it is interested in doing more training and mentoring activities.

Ms. Julie Wolf-Rodda, Director of Partnership Development at FNIH, described three ways in which FNIH facilitates PPP: (1) NIH-managed PPP; (2) parallel PPP through which projects are supported by NIH funding, but private partners support additional pieces or aspects that NIH cannot do on its own; and (3) FNIH-managed PPP. The latter category allows FNIH full grant-making authority.

In closing, Ms. Wolf-Rodda emphasized that FNIH helps underwrite biomedical research by facilitating PPP, with NIH priorities as its points of references or guiding factors.

<u>Discussion Highlights</u>

- Dr. Mittleman noted that "public" is a collective term that includes all Federal agencies and that Dr. Zerhouni has appointed liaisons to all these agencies.

- Dr. Mittleman noted that the amount of time needed to begin a project depends on the project's complexity and how much must be constructed *de novo*. The time can range from less than 1 week to18 months.

- The Program on Public-Private Partnerships can serve as an off-ramp for Common Fund programs, such as PROMIS or MLI, if they can be sustained in the long term as PPP.

IX. WORKING GROUP AND SUBCOMMITTEE REPORTS

A. Research, Condition, and Disease Categorization Update

Dr. Hays provided an update on the activities of two working groups that reviewed the Research, Condition, and Disease Categorization (RCDC) following the November CoC planning meeting. Dr. Hays reported that the Public Review group had had its introductory meeting and that members were now receiving access to the RCDC system.

B. Resources Development and Analysis Subcommittee

Dr. Sergio Ojeda presented the subcommittee's recommendations:

Recommendation 1. Ensure complete analyses are carried out to satisfy several requirements, including those intrinsic to RCDC, biennial reports to Congress, public reporting of data on NIH-funded research, and easy access to information by key groups and individuals, including ICs and the larger scientific community. These analyses should be user-friendly.

- Initiate analyses by performing a pilot "proof of principle," using Roadmap as primary material.

- Identify gaps by exploring other Federal government research databases. Identifying areas that are not funded but could be important might provide another dimension to understanding ICs' priorities.

Recommendation 2: Begin to define public health burden by identifying an example of a disease or syndrome addressed by Roadmap and exploring methods for investigating how that disease or syndrome relates to clearly connected diseases and to various, seemingly unrelated aspects of public health, for example addictive behavior, neurodegenerative diseases, and intrauterine health.

Dr. Hays added that the subcommittee discussed the wealth of activities that could be done as a part of portfolio analysis and the need to narrow the focus. The pilot discussed by Dr. Ojeda would allow DRDA to assess a Roadmap initiative, which represents something NIH and others have identified as a critical step forward, and ensure that research is being carried out at NIH and not elsewhere.

C. Strategic Coordination Subcommittee

Dr. Joseph Loscalzo, Chair of the subcommittee, reported that the subcommittee considered a process for culling through pools of ideas to bring forward for the Common Fund, as well as any ideas they themselves might have.

Generation and Clearance of Ideas

- Invite a task force of thought leaders annually to provide ideas by email. Conference calls will take place to clarify and sharpen concepts and to allow subcommittee members to cull those they wish to bring to the entire Council. The near-final list of proposals will be presented as two- to three-page summaries, assigned to individual subcommittee members who, on occasion, will seek input from the originating working group or other source and provide opinions online. All subcommittee members will vote on topic priority, then bring the prioritized list forward to the entire Council.

Subcommittee Ideas

- ATCC-like stem cell resource
- Core of mentors for underrepresented minority trainees, who might not be at the same institutions
- "Genetic code" for complex biological system components
- Molecular determinants of intermediate phenotypes, such as fibrosis, apoptosis, proliferation, inflammation, and thrombosis
- Infrastructure for clinical trials involving medically underserved populations
- Biomarker pool built from existing resources for diagnosis, prognosis, and therapeutic response
- Biologically inspired engineering principles and derivative devices, for example how can a gecko climb walls

The subcommittee also suggested that they be told why certain ideas were not approved, which will help members learn from the process and apply that learning to future iterations.

D. Evaluation and Systematic Assessments Subcommittee

Dr. Juanita Merchant reported that the subcommittee had been charged with designing methods to evaluate science. She presented two recommendations.

Proposal 1

Use the history of "innovative" discoveries, such as angiogenesis, *H. pylori*, prions, nanotechnology, and vitamin B12 deficiency. Scrutinize patterns to identify what pushes advances in science. Specifically, identify the tipping points and what enabled an advance to proceed.

Proposal 2

Perform a narrow analysis and define scientific successes, identify at least four known metrics of success, and apply these metrics to current Common Fund projects as a test case. Use the algorithm established with the test case to identify enabling or tipping factors.

The subcommittee focused on issues of novelty: changes in research emphasis, directions, or dogma; enabling of major breakthroughs; achievement of "science fiction"; facilitation of discovery, innovation and capacity building. The following questions were suggested for evaluation of high-risk projects:

- Does the project enable a breakthrough?
- Did it build capacity?
- Can NIH predict successful projects faster and more efficiently?
- What is the value added over traditional reviews or metrics?
- What is the impact across multiple areas?
- Is the overarching goal achieved?
- What is the impact on human health?

Dr. Merchant reported that for the next meeting, both approaches would be undertaken, and each approach would be assessed to determine whether metrics that advance science can be identified.

Discussion Highlights

The bulk of discussion focused on how OPASI could use CoC most efficiently. The NIH Reform Act of 2006 mandated the CoC, but it did not outline the responsibilities of this Council other than the review of high-risk, high-reward projects. Dr. Krensky pointed out that OPASI will rely on the expertise of CoC as it addresses the scope and complexity of its task. Yet the role of OPASI, and what it will need from CoC, is evolving. CoC members requested more guidance from OPASI staff; OPASI should articulate what problems it wants to address, and CoC can provide input.

Other topics of discussion included:

- Scope and complexity. Unlike the major ICs, OPASI is a new entity, designed to face difficult issues. OPASI's role is large and complex, but the Office must begin with a narrow focus. Council members suggested having all three OPASI Divisions select an existing Roadmap initiative as a pilot project for analysis and reporting. CTSAs and the Pioneer Awards were suggested, as well as the microbiome and epigenome projects or a complex condition such as obesity. Such a pilot project could generate a model for integration of OPASI activities, and CoC could participate in both the development and refinement of that model. Dr. Wilder also suggested that pilot projects be chosen from the fourth cohort of Common Fund initiatives, which is just beginning.

- Defining public health burden. Discussions of scope and complexity focused on how to define and assess public health burden. Council members suggested talking with the NIH Obesity Task Force to determine how Roadmap efforts could align with or add value to existing efforts.

- Council members also discussed scientific opportunities and program priorities versus public health need. For example, the National Institute of Deafness and Other Communication Disorders funds far more grants on echolocation in bats than on tinnitus, which affects up to 30 million Americans. Although it is clear where the public health burden is, NIDCD peer review still favors echolocation grants. Council members suggested that program priorities assume one can predict which science will drive the public health agenda.

- Dr. Krensky and CoC agreed that the role of NIH among the larger group of entities attacking a public health should also be defined clearly.

- DPCPSI. Dr. Krensky reminded CoC that although the meeting has focused on the complexities faced by OPASI, the Office works within the broader DPCPSI. This Division also includes the NIH Office of AIDS Research, the NIH Office of Research on Women's Health, and NIH Office of Prevention, and the NIH Office of Behavioral and Social Science Research. As OPASI's role evolves, its relationships with these other offices will also evolve.

X. NEXT STEPS

Dr. Krensky outlined the following steps:

- CoC subcommittees will engage in ongoing interactions with their OPASI contacts.

- The next CoC meeting is scheduled for November 20–21, 2008. OPASI will invite representatives from the NIH Obesity Task Force to speak at this meeting.

- OPASI will disseminate information about Council members' terms.

Dr. Krensky adjourned the meeting at 11:37 a.m.

CERTIFICATION

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

for Alan Krensky

Alan M. Krensky, M.D.
Chair, NIH Council of Councils
Director, Office of Portfolio Analysis and Strategic Initiatives
Office of the Director
National Institutes of Health