PUBLIC-PRIVATE PARTNERSHIPS PROGRAM

PPP ADVISOR

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MESSAGE FROM THE DIRECTOR

Dr. Barbara B. Mittleman

At this time of the year it seems fitting to look back to assess the outgoing year and to look forward to anticipating what the coming year will bring. I won't comment on the important issues of the economy, the wars in Iraq and Afghanistan, and the state of the environment. I also won't discuss here that this is a time of great change and hope, as we expect the new administration to provide new opportunities and the advent of a yet unnamed new National Institutes of Health (NIH) Director. From the vantage point of the Public-Private Partnerships (PPP) Program, however, there are several past and future items worthy of note.

Looking back, The Biomarkers Consortium (BC) is up and running and has ongoing projects as well as some moving toward completion. Dr. Shawnmarie Mayrand-Chung will update you on the BC and the new approach to generating high-impact projects likely to attract broad interest and funding in this newsletter. The PPP Coordinating Committee has been busy and continues to have a stimulating agenda with outside speakers from industry, other Federal agencies, and NIH, all addressing topics or issues of interest, or discussing why and how to partner. Coming months will bring discussions of ethical guidelines for PPPs; industry's view from a business consulting company's perspective; a presentation by Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research of the U.S. Food and Drug Administration (FDA); and other speakers.

PPPs are also becoming a more general topic of interest. We were featured as part of the Deputy Secretary's delegation on DHHS Approaches to Innovation, a tour reaching audiences in Washington, D.C., San Diego, San Francisco, Minneapolis, and Boston. (I gave the NIH presentation in San Diego, Alan Guttmacher from the National Human Genome Research Institute presented in San Francisco and Minneapolis, and Dr. Kington spoke in Washington and Boston.) This was a great opportunity to discuss innovation in general as well as how PPPs are relevant to it with diverse audiences in cities with many biotechnology, device, and IT industry representatives. It also allowed crosstalk among the agency representatives, from DHHS, FDA, NIH, CMS, and AHRQ on this topic. The Innovation tour was one of a number of presentations and visits—on campus to several Institutes and Centers (ICs), to the newly formed Translational Research Interest Group (by Dr. Wendy Smith), to the New York Academy of Sciences, to people at several companies, at AUTM, and at Biomarker meetings. We have participated in the NAS Government-Industry Roundtable Working Group on International Partnership Agreements and in the Clinical and Translational Science Awards (CTSA) PPP committee. Several publications reflecting progress in the BC have been authored by Dr. Mayrand-Chung. So we have really gotten around and have had a great deal of exposure this past year.

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SPOTLIGHT

The NIH Program on Public-Private Partnerships (PPP) is pleased to announce the formation of a broad PPP initiative to develop a robust Science of Health. As a way to incorporate the otherwise neglected concept of "health" in much of biomedical research and to refigure aspects of personalized medicine to focus on personalized health, we are planning a 3-day International Forum on the Science of Health in Bethesda, Maryland, June 1-3, 2009.

We would like to see several outcomes: a workable definition of health, a research agenda in very broad terms, a shared vocabulary, and a set of methodologies that require development in order to rigorously assess health status, interventions to optimize health, and the resulting health outcomes. We plan to include a wide range of stakeholders: scientists, government, academia, and clinicians in both usual and complementary modalities; public and patient advocates; professional societies/practitioner groups/networks; industry; insurers and payers; policymakers; and philanthropic organizations. This edition of the *PPP Advisor* newsletter provides a special focus on this meeting and partnership.

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Looking forward, we expect much more of the same. We are also planning to forge new opportunities as well. Dr. Smith's update in this newsletter will inform you of our newest broad initiative—to develop a PPP to develop a robust Science of Health. Evaluating disease has been the focus of medicine and biomedical research for a long time, but defining, quantifying, and assessing health per se have received less attention. Given the economic pressures on the health care system, given the desire of everyone to be as healthy as possible all the time, and given the investment made to accomplish that, we need definitions, metrics, and a basic understanding of what constitutes health! So, an international summit to address the question and to launch a PPP to accomplish it seems important and timely. See inside for more details, and we'll keep you posted as the agenda and Web site become available.

In summary, we in the PPP Program wish you and all of our partners the best for the New Year! ❖

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The Science of Health Initiative: Next Steps and Upcoming Activities

Dr. Wendy B. Smith

One role of the Public-Private Partnerships (PPP) Program is to identify areas of broad interest to National Institutes of Health (NIH) Institutes and Centers (ICs), consistent with the NIH mission and also of interest to a variety of potential partners. The Biomarkers Consortium (BC), the NIH activities of which center in the PPP Program, is one such area. At this time, we would like to share the news about an exciting and novel effort of the PPP Program to develop an integrated and robust science of health.

"The general approach will be to build conceptual scaffolding with three (related and interpenetrating) parts: focus on the individual, the individual in relationship, and the individual in the world."

The first step of this initiative is an upcoming meeting to be held at the NIH. The International Forum on the Science of Health will be held June 1-3, 2009, in Bethesda, Maryland.

We are all aware that the aim of many activities and interventions by the public, patients, and health care providers is to optimize or improve health. The mission of the NIH is to improve the public health through biomedical research. Despite an enormous commitment by many people in many sectors, and a similarly enormous expenditure in efforts to ensure, provide, and monitor health, major gaps exist in our understanding of what "health" really means. Without a clear definition, and a robust set of research methodologies to study health, deciding the relative merit and value of the many health-promoting or restoring interventions likewise becomes a daunting challenge. Without such robust research, making regulatory decisions about which interventions or approaches are safe and effective is difficult, and making payment decisions based on safety and efficacy is similarly complicated.

In this context, the PPP Program, together with potential partners, proposes to bring wide-range stakeholders with important commitments to establishing, promoting, and restoring health together, to develop a shared and rigorous research agenda, and to thereby develop the knowledge base to inform lifestyle decisions, clinical decisions, and regulatory decisions, as well as policy and payment decisions.

To accomplish these ambitious aims, we propose to:

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The Science of Health Initiative: *Next Steps and Upcoming Activities* (CONTINUED FROM PAGE 2)

- Arrive at a working definition of health, recognizing that this may be context dependent, vary from person to person as a function of individual and cultural factors, and vary over time.
- Develop a shared vocabulary of terms and concepts relevant to research into health.
- Establish shared approaches to rigorous research related to health and interventions to optimize it.
- Initiate projects exemplifying the above and addressing questions of interest to personal life choices and/or clinical, regulatory, payment, and/or policy aspects of health.
- Develop a means and infrastructure to share ideas and information regarding the above.
- Develop public resources resulting from the activities described above.

The focus of this 3-day Forum will be to define the notion of health and optimal health, to identify areas that need measures and metrics for this, as well as potential methodologies to examine whether we are achieving it with various/particular interventions or strategies. Expected participants include representatives from government, regulators such as the U.S. Food and Drug Administraton (FDA), academia, basic and clinical investigators from traditional biomedical fields and allopathic medicine as well as related integrative and complementary fields, and professional societies/practitioner groups/networks; industry; insurers and payers; policymakers; patient and public advocacy groups; and philanthropic organizations.

The general approach will be to build conceptual scaffolding with three (related and interpenetrating) parts: focus on the individual, the individual in relationship, and the individual in the world. The *individual* focus includes the characterization of the genetic/genomic, biochemical, immunological, functional, psychological, behavioral, (spiritual), etc. features and mechanisms associated with health, and the worsening or improving of it. The *individual in relationship* will allow an examination of how an individual relates to others in life, in medical or health circumstances, and the health consequences of those relationships. The *individual in the world* allows for examining issues as diverse as health policy, resource allocation, nature and the built environment, global climate and geography, etc.

Each perspective raises several questions that could be considered. For example, with a focus on the individual: What characteristics (physical, genetic, immunological, psychological, historical, etc.) of the individual contribute to health in positive, negative, or neutral ways; which of these characteristics are amenable to modulation or change? Which interventions pose greater threats or likelihood of success to the individual at this time? How can those effects be measured and compared? How can outcomes be defined, measured, and compared? In terms of focusing on the individual in relationship(s), some topics that could be considered include: How can relatedness be defined and described? What qualities of relationship are relevant to health? To what extent can this be modulated to optimize health? How can the relationship of the individual to the intervention or the provider of that intervention influence or control the outcome? And lastly, when placing the focus on the individual in the environment, questions that arise include: How does the setting of the individual affect health? How do geography, climate, nature, built environment, etc. affect health? How can this be modulated and measured? What role do environmental exposures (light, temperature, toxins and other substances, nutrients, etc.) play in health, and how can this be measured?

The ultimate goal of this effort is to develop a broad-based partnership to promote and advance an individualized and rigorous science of health, such that each individual can make informed and customized choices to optimize individual health, and clinicians, payers, policymakers, and regulators can make informed decisions about health promotion at the societal level. As a result of the Forum activities, we expect that working group meetings and discussions will continue after the Forum has concluded, leading to substantive collaborations on research projects and the formation of a broad-based PPP.

For more information about the International Forum on the Science of Health, see http://ppp.od.nih.gov. ❖

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BIO 2009: *Increasing NIH Presence and Participation*

Dr. Shawnmarie Mayrand-Chung

The Biotechnology Industry Organization (BIO) International Conference 2009, the annual meeting of the trade organization of the biotechnology industry, will be held in Atlanta, Georgia, from May 18 to 21. At the invitation and request of BIO, the meeting will feature an opportunity for an increased National Institutes of Health (NIH) presence. The program comprises scientific and business presentation sessions, an exhibit hall, and prearranged and orchestrated business opportunities for potential partners to meet and share information.

PPP Program staff is working closely with representatives from several Institutes and Centers (ICs) to develop speaker opportunities, an NIH presence within the business forum, and a dedicated NIH Pavilion exhibit space.

Speaker Opportunities

In conjunction with the Centers for Disease Control and Prevention (CDC) and other Federal agencies (e.g., U.S. Food and Drug Administration [FDA], Centers for Medicare & Medicaid Services [CMS], and others), NIH will participate as part of a Super Session to spotlight the use of public-private partnerships to leverage government resources.

A half-day program devoted to "Federal Programs" is also currently being developed. The proposed topics for the session on Federal Programs include:

1. Biomedical Advanced Research and Development Authority (BARDA): Nuts and bolts for the urgent development, expedited approval, and distribution of countermeasures. This session would review Emergency Use Authorization (EUA).
2. Biomedical High Performance Computing: The high-volume and complex data that are generated from advances in biotechnology exceed current capabilities (e.g., genomic sequences, proteomics, cell biology). Furthermore, untapped potential exists to forge interfaces between these data and existing data collection systems that contain clinical information (e.g., EMRs, surveillance systems, large-scale surveys). Leveraging the significant Federal funding for computing (>$3 billion in FY08) will promote the development of shared approaches and maximize the value of both new and existing data.
3. Occupational Safety: How Federal policy and regulation influence R&D.
4. Hot Federal Biotechnologies for Licensure Survey: Includes all aspects of the Federal Government (e.g., U.S. Department of Health and Human Services [DHHS], National Aeronautics and Space Administration [NASA], U.S. Department of Defense [DoD]) to showcase technologies that need partners to commercialize.
5. How To Partner With Government
   - Funding opportunities: Small Business Innovation Research and Small Business Technology Transfer (SBIR/STTR) grants and contracts
   - Technology Transfer: Cooperative Research and Development Agreement (CRADA), Material Transfer Agreement (MTA), licensing/patents
   - Collaborations: public-private partnerships through federal foundations (e.g., FDA, CDC, NIH)
6. Federal Laboratory Consortium: The Federal Laboratory Consortium for Technology Transfer (FLC) is the nationwide network of Federal laboratories that provides the forum to develop strategies and opportunities for linking laboratory mission technologies and expertise with the marketplace.

Business Forum

A coordinated NIH business forum would provide ICs an opportunity to arrange meetings at BIO 2009 with other BIO participants. Several ICs participated in the BIO business forum at BIO 2008 and found it very useful. For more details on this possibility soon, stay tuned.

NIH Pavilion

We are working with the Foundation for the NIH (FNIH) and the State of Maryland to explore the possibilities for

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BIO 2009: *Increasing NIH Presence and Participation*

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combining all NIH exhibit booths into a shared space—either within the State of Maryland Pavilion or in a standalone space housing all NIH entities (e.g., an NIH Pavilion). FNIH has negotiated a prime space on the exhibit floor at BIO 2009 and is working with BIO to secure a favorable package rate, including space, business forum participation, and publicity.

In order to coordinate, please let us know whether your IC has plans to attend BIO and we will keep you informed of the developments of this effort. Please e-mail Dr. Shawnmarie Mayrand-Chung at mayrands@od.nih.gov for answers to your inquiries or to be added to the list. ❖

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The Biomarkers Consortium: *Introducing HIBOs—"High-Impact Biomarker Opportunities"*

Dr. Shawnmarie Mayrand-Chung

As you know, The Biomarkers Consortium (BC) is an opportunity for public and private entities to join forces and pool resources in order to advance biomarkers research, an exciting and challenging mission. This novel experiment is an exciting and challenging endeavor that is undergoing evaluation and restructuring in some areas to improve and optimize the identification, funding, and implementation of cross-sector biomarker projects.

The method for the solicitation and selection of biomarkers projects undertaken by the BC has been modified. The adoption of a new proactive approach for the identification of High-Impact Biomarker Opportunities (HIBOs) represents an effort to identify biomarker projects that are cross-cutting and arch over multiple therapeutic areas. The impetus for supplementing the original "bottoms-up" approach with the newer "top down" approach is to identify biomarker projects of sufficient urgency and promise that all sectors (industry, government, private organizations, and academia) can champion and support. A more tightly coordinated approach increases the likelihood that a project selected for development will be funded for implementation.

While the BC has successfully approved, funded, and implemented the following biomarkers projects, there is a continued need to identify and develop even bigger and broader reaching biomarkers projects. Current BC projects under way include the following:

- **Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) for Lung and Lymphoma.** These two studies are NIH-managed via the National Cancer Institute (NCI) and aimed at evaluating the use of FDG-PET as a potential biomarker for clinical trials conducted in cancer, specifically, non-Hodgkin's lymphoma and non-small cell lung cancer. One goal of this project is to improve patient management and care by validation of a tool that can measure response to treatment and accelerate drug development. Additionally, it is anticipated that these first two trials to evaluate FDG-PET in non-Hodgkin's lymphoma and lung cancer will provide guidance to the U.S. Food and Drug Administration (FDA) in its regulatory review process, and deliver to the Centers for Medicare & Medicaid Services (CMS) an evidence-based measure by which to inform reimbursement decisions. (This project is supported by a core investment from the NIH-NCI in conjunction with contributions from Amgen, AstraZeneca, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Johnson & Johnson, Merck & Co., Inc., Pfizer Inc., and Wyeth, in conjunction with substantial core investment by NCI.)
- **Evaluate the Utility of Adiponectin as a Biomarker Predictive of Glycemic Efficacy.** This project involves pooling existing clinical trial data from previously

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The Biomarkers Consortium: Introducing HIBOs—"High-Impact Biomarker Opportunities" (continued from page 5)

conducted studies in an effort to evaluate whether adiponectin, a soluble protein, has utility as a predictive biomarker of glycemic control in normal non-diabetic subjects and patients with type 2 diabetes following treatment with peroxisome proliferator-activated receptor (PPAR) agonists. If validated, adiponectin would be a useful biomarker in the development of new therapies. The data for this study are being provided from Phase II clinical trials conducted by GlaxoSmithKline, Eli Lilly and Company, Merck and Co., Inc., and F. Hoffmann-La Roche. The statistical analysis for this study is being provided (in-kind) by the National Institute of Diabetes and Digestive and Kidney Diseases and Quintiles Transnational Corp.

- **Carotid Magnetic Resonance Imaging (MRI) Reproducibility Study.** This study is being conducted in conjunction with the National Heart, Lung, and Blood Institute (NHLBI) AIM-HIGH (Titled: Atherothrombosis Intervention in Metabolic Syndrome with Low HDL-cholesterol/High Triglyceride and Impact on Global Health Outcomes). This AIM-HIGH substudy is aimed at improving patient management by validating a tool that can help identify therapeutic response and facilitate drug development. Specifically, this substudy involves an 80-patient reproducibility study, being conducted at 15 established clinical sites, to determine the reproducibility of the noninvasive technique of carotid MRI, a well-known imaging biomarker. (This project is supported by a core investment from the NIH-NHLBI in conjunction with contributions from Abbott, Merck & Co., Inc., and Pfizer Inc.)

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Changing gears is challenging, and after much discussion, the BC has developed a number of criteria for defining HIBOs, with the projects intended to be of sufficient interest and scope to capture the attention of industry and/or philanthropic groups that presently provide a good portion of the financial backing for BC projects. The criteria require a HIBO to be:

- **Important:** Addresses a significant unmet medical or scientific need in biomarkers with a potentially considerable impact on public health.
- **Translational:** Will result in significant improvement in the development, approval, or delivery of care to patients (i.e., diagnostics, therapeutics, clinical practice).
- **Transformational:** Addresses critical gaps in the biomarkers qualification/validation process and/or may otherwise transform the process of how biomarkers are developed, approved, and applied in the future.
- **Feasible:** An idea or program whose end goals can likely be achieved in a specific timeframe, and that has a reasonable prospect of producing the expected outcomes; ideal programs are those which could result in regulatory qualification of a biomarker in 3 years.
- **Practical:** Leverages preexisting resources (e.g., intellectual capital, personnel, facilities, specimens, reagents, data) wherever possible.
- **Fundable:** Is capable of generating the required funding and stakeholder support needed for implementation.
- **Collaborative:** Would uniquely benefit from the multi-stakeholder composition and approach of the BC and could feasibly be executed under its policies.

Charles A. Sanders, M.D., Chairman of the Consortium's Executive Committee and Chairman of the Foundation for the NIH Board of Directors, comments, "We believe the High-Impact Biomarker Opportunities we have identified are those most critical to move forward: those which will have the greatest and most proximal impact on future diagnosis and treatment of patients and drug development, helping the medical community realize the promise of personalized medicine."

The BC anticipates launching four to five new "high-impact" biomarker projects this year, while a second wave of HIBOs is being developed concurrently to commence during 2009. The candidates for launch in the first quarter of 2009 include:

- **Plasma-Based Biomarkers in Alzheimer's Disease.** This study is an extension of a large 5-year longitudinal natural history study known as the Alzheimer's Disease Neuroimaging Initiative (ADNI), which was conducted

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The Biomarkers Consortium: *Introducing HIBOs—"High-Impact Biomarker Opportunities"* (CONTINUED FROM PAGE 6)

as a partnership among the National Institute on Aging and private and pharmaceutical companies in an effort to identify imaging and biochemical biomarkers for disease state and disease progression. The goal of the add-on biomarker project is designed to use targeted approaches and whole proteome profiling approaches to identify and validate plasma-based biomarkers of Alzheimer's disease. Results from this study aid in the identification of biomarker candidates to study disease state and/or disease progression in Alzheimer's disease, and serve as tools for clinical drug development and assessment of disease in Alzheimer's disease patients.

- **Evaluation and Validation of Circulating Tumor Cells (CTC) as Biomarkers of Castration-Resistant Metastatic Prostate Cancer.** This project is aimed at predicting response and survival to an investigational agent to treat men afflicted with progressive castration-resistant prostate cancer. The goal of this research is to validate the CTC number as a biomarker for survival, which could ultimately guide treatment and accelerate drug development. The project proposes to conduct CTC analyses on blood samples from men already participating in a Phase III randomized registration trial in order to evaluate the association between post-treatment change in the CTC number and survival.
- **Comparison of Two Positron Emission Tomography (PET) Radioligands Labeled With 11C or 18F to Quantify the Peripheral Benzodiazepine Receptor, a Potential Biomarker of Inflammation.** The goal of this project will be to assess the utility of two newly developed PET radioligands to image and quantify inflammation in periphery and brain. These newly developed PET radioligands will be tested in Alzheimer's disease and atherosclerosis, which were selected because both result in significant disability and often death. Also, these two diseases are representative of inflammation in the brain or periphery, respectively. An ultimate application of the results of this study might extend to neurodegenerative and psychiatric diseases and serve as a tool for developing new drug delivery systems and brain cancer treatment regimens.

It is the ability to step back and evaluate the structures and methods being used to implement projects that improves the likelihood of success. The promise of biomarkers to streamline and even revolutionize investigations of pathobiology, the conduct of clinical trials, and regulatory decision-making for drugs and therapeutics needs to be realized in an efficient, rapid, and effective manner. It is the hope of the BC that the identification of HIBOs will help make this happen! ❖

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Visit us at **http://ppp.od.nih.gov**

Looking for PPP information?

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Calendar

Date	Meeting	Time	Location	Speaker	Subject
1.15.09	PPP Coordinating Committee	1 - 3 pm	NIH Campus Bldg 1/ Wilson Hall	Janet Woodcock, FDA	Partnerships and the FDA
2.19.09	PPP Coordinating Committee	1 - 3 pm	NIH Campus Bldg 1/ Wilson Hall	TBA	TBA
3.19.09	PPP Coordinating Committee	1 - 3 pm	NIH Campus Bldg 1/ Wilson Hall	TBA	TBA
6.1.09-6.3.09	International Forum on the Science of Health		NIH Campus Natcher Conference Center		

Please check the PPP Web site for updates and additions.

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