PMC Conference Unites Personalized and Evidence-Based Medicine

By Kathi Hanna and Marcia Kean

One might expect the “intersection” between Personalized Medicine and Evidence-Based Medicine to be a quiet place, since these two disciplines have borrowed little from each other to date. But if the recent conference, 21st Century Medicine: Personalized and Evidence-Based, hosted by PMC and the Georgetown University School of Nursing & Health Studies, is any indication, there is indeed dynamic and intense traffic where the two meet.

Why now? As the U.S. confronts significant issues in improving healthcare quality and controlling costs, the combined benefits of personalized healthcare and evidence-based medicine are emerging as complementary approaches that could provide major fixes to a beleaguered system.

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Letter from the Executive Director

I know no other organization in Washington, D.C. as ambitious as the Personalized Medicine Coalition. Representing and seeking to unite a broad spectrum of academic, diagnostic, pharmaceutical, patient, provider, and payer communities—its a tall order—the PMC aspires to improve our healthcare system by changing fundamentally the way drugs are discovered, developed, and marketed as well as the way medicine will be practiced in the future.

Looking ahead to the third anniversary of the Personalized Medicine Coalition’s public launch on November 1, 2004, it is appropriate to ask how we are doing in advancing this bold agenda and what more we might do with additional resources.

Unfortunately, it is impossible to measure precisely when fundamental change has been accomplished, especially at the early stage of a paradigm shift. Before “personalized medicine” becomes just medicine, decision-makers across the spectrum of our healthcare system will have to come to believe that one-size-fits-all medicine is neither wise nor necessary. They must be willing to alter the way that they approach investment, regulation, and reimbursement, to name but three variables that will indeed shape the future of medicine. Although we may still be a long way from a concerted effort to personalize healthcare, it is, nevertheless, possible to achieve significant movement toward that goal.

First, in keeping with the exciting scientific discoveries reported almost daily that have generated enormous interest in molecular-based medicine, the PMC itself has quintupled in size in three years. It now has over one hundred members, including an expanding number of international institutions and companies. New members that have joined in the past quarter include Agendia BV (Netherlands), Curidium Medica (UK), Dako Denmark A/S (Denmark), OncoMethylome Sciences (Belgium), and TheraGenetics Ltd. (UK)—diagnostic companies whose research and technology aim to improve patient therapy in oncology, cardiovascular care, and CNS disorders.

Second, there have been a number of recent mergers designed to better position companies in the emerging science and technology underpinning personalized medicine.

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SAVE THE DATE:

Personalized Medicine Coalition Receptions:
East Palo Alto and Cambridge

December 10, 2007
Four Seasons Silicon Valley at East Palo Alto
East Palo Alto, CA

Please save the date for a Personalized Medicine Coalition reception, hosted by Brook Byers, Kleiner Perkins Caufield & Byers; William Young, Monogram Biosciences; and Susan Desmond-Hellmann, Genentech.

January 17, 2008
Broad Institute
Cambridge, MA

In January, the PMC will hold a reception in Cambridge, MA, hosted by Raju Kucherlapati, Harvard-Partners Center for Genetics and Genomics; Eric Lander, Broad Institute; and Mark Levin, Third Rock Ventures.

Both receptions are being sponsored by Feinstein Kean Healthcare in recognition of 20 years of service to the Life Science Community. Invitations will be distributed soon.

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Policy Brief  By Amy M. Miller

Over the past few years, the FDA has issued a number of guidance documents related to aspects of personalized medicine. Topics of these papers have covered the following subjects: In Vitro Diagnostic Multivariate Index Assays (IVDMIA), voluntary pharmacogenomic data submissions, and Analyte Specific Reagents (ASR). These and other federal regulation issues were discussed during our recent conference, 21st Century Medicine: Personalized and Evidence-Based.

FDA's Draft Guidance for Industry, Clinical Laboratories, and FDA Staff - In Vitro Diagnostic Multivariate Index Assays (IVDMIA) was first issued on September 7, 2006. In response to community requests, FDA extended the comment period for this guidance and hosted a public comment period. The revised draft guidance (http://www.fda.gov/cdrh/oivd/guidance/1610.pdf), issued on July 26, 2007, reflected community engagement. For instance, in direct response to expressed concerns, FDA clarified the definitions of IVDMIA by using examples and by outlining a transition period for currently marketed products that will be reviewed by FDA for the first time.

Because the resulting draft was very different from the first, FDA extended the original 30 day comment period to October 17, 2007.

PMC responded to this draft with a comment letter designed to position the Coalition as the organization ready to help FDA work with all stakeholders in personalized medicine to develop a reasonable and predictable regulatory path that balances innovation and patient protection. We suggest that:

• FDA and CMS should work together to provide clear and consistent messages on oversight.
• FDA should convene a workshop on Quality Systems Regulation and publish a side-by-side comparison of relevant FDA and CLIA regulations.

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Leading figures in government—including HHS Secretary Michael O. Leavitt; Dr. Janet Woodcock, Deputy Commissioner and Chief Medical Officer, FDA; and Dr. Carolyn Clancy, Director, Agency for Healthcare Research and Quality (AHRQ)—gathered with industry and academia at the Georgetown University Law Center on September 18 – 19, 2007, to discuss the policies and the incentives for all stakeholders that will be needed to ensure that the healthcare of the future is both evidence-based and patient-centered.

Meeting participants included 225 senior-level representatives from across the healthcare spectrum, consisting of policymakers, regulators, healthcare professional workforce for the new realities of personalized medicine. We also need to focus attention on product regulation, insurance reimbursement, information technology infrastructure, medical privacy legislation, and ethical considerations.”

**“Personalized medicine requires personalized evidence.”**

Secretary Leavitt, in his keynote address, emphasized the value of personalized healthcare as both an effective and cost-effective approach to patient management, noting that many measures must be taken to achieve the promise of personalized healthcare, including:

- Developing evidence-based standards for measuring and improving quality of care;
- Building systems of health information technology to make the patient records available when and where they are needed;
- Using those same systems to gather medical evidence from the day-to-day practice of medicine so that clinicians can make the best decisions for each patient; and
- Ultimately, using our personal genetic information to tailor treatments more effectively to each patient.

Secretary Leavitt has appointed a team to implement his new Personalized Health Care Initiative, and he used the conference as an opportunity to release the department’s first report on personalized medicine: Personalized Health Care Opportunities, Pathways, Resources (http://www.hhs.gov/myhealthcare/news/phc-report.pdf).

In the opening keynote address, former congressman W.J. Billy Tauzin, now President and CEO of PhRMA, described his own struggle against cancer, placing his personal battle in the context of a healthcare system with exponentially rising costs. Yet, he noted, we have the most vibrant pharmaceutical research enterprise in the world—that drives new therapeutics with a $55 billion annual investment in research.

"The more new knowledge we uncover about the molecular underpinnings of disease," Tauzin said, "the greater our understanding of the role that genetic variations play in response to treatment. As a result, we, and everyone involved, are going to be able to put together a better healthcare delivery system that is personalized, individualized, and hopefully—if we do this right—economically bearable."
MCiellan went on to differentiate some of the nuances of personalized medicine.

“One point to make is that when you’re talking about personalized medicine, what’s important is not an average effect that you estimate for a whole population, but personalized evidence for an individual patient or type of patients. Personalized medicine requires personalized evidence,” he said.

Many speakers addressed the tensions in the current environment and discussed how best to build the evidence base needed to develop and adopt personalized healthcare technologies and approaches to care management.

**Dr. Lewis Sandy**, Senior Vice President, UnitedHealth Group, observed that as personalized healthcare advances, it will be critical to find ways to integrate the research methods of individual-based versus population-based studies and to identify what levels of evidence are required for prevention and treatment decisions.

Such approaches should result in evidence that a) is sub-stratified for particular subpopulations based on genetic, molecular, imaging, or patient subtypes, and b) compares effectiveness of diagnostic and treatment options across these groups. Sandy added that we need better analytical tools—simulations and models, for example—to assess the range of possible effects of personalized healthcare and to drive out ineffective care.

Another tension is the need to move beyond the randomized clinical trial as the only design for gathering evidence. **Dr. Michael McGinnis**, Senior Scholar, Institute of Medicine, stressed the importance of observational studies to lower the threshold costs for clinical validation or diagnostic tests and drugs. **Dr. George Poste**, Director, The Biodesign Institute at Arizona State University, argued for more efforts aimed at demonstrating the value of personalized healthcare, suggesting that technology assessment and forecasting should be a part of the discovery and development process.

> “We need to combine mechanistic understanding from pharmacogenomics, from functional imaging and other things, and combine that with the classic evidence-based medicine empirical outcomes.”

A critical issue to confront is reimbursement policies. Dr. Clancy said that there must be core changes in the policies for reimbursement, especially for diagnostic tests. Reimbursement decisions should not only be focused primarily on cost containment, but also on weeding out the overuse of inappropriate treatments and the misuse of others.

Above all, reimbursement policies should guide disease prevention strategies and facilitate the smarter use of therapies—that is, select treatments that are more likely to be effective and less likely to cause harmful side effects for the individual patient.

**Newly Published: The Landscape for Personalized Medicine**

The PMC is pleased to announce the publication this month of two important essays regarding the promise of and barriers to the advancement of personalized medicine. The first, “Integrating Molecular Medicine into the U.S. Health-care System: Opportunities, Barriers, and Policy Challenges” by PA Deverka, T Doksum, and RJ Carlson in the October issue of *Clinical Pharmacology & Therapeutics*, is the peer-reviewed study based on the PMC’s Landscape Analysis conducted last year. The second, “Realizing the Promise of Personalized Medicine” by Mara G. Aspinall, President of Genzyme Genetics and Vice Chair of the PMC, and Richard G. Hamermesh of the Harvard Business School, appears in the current edition of the Harvard Business Review, and it reflects discussions the PMC has hosted and encouraged since its inception.

Both essays contend that while personalized medicine has widespread support, its adoption depends on our collective ability to reconfigure the regulatory structure, reform reimbursement policies, integrate pharmacogenomics into medical education, and, not least, revise business models so that all will not, as is often the case today, inhibit the new paradigm but instead encourage its adoption. According to Aspinall and Hamermesh, “Although science is always ahead of practice, the gap today in the area of personalized medicine is inexcusably large.”

Based on interviews of sixty executives across the entire healthcare spectrum, Deverka, et al. contend that the key barriers to “molecular medicine” are lack of evidence of clinical utility of many diagnostic tests, high barriers to value-based reimbursement, an undefined regulatory environment, and the inability of providers to swiftly integrate new genomic-based technologies into clinical practice.

Aspinall and Hamermesh concur that these indeed are significant barriers, and add that, in their view, pharmaceutical companies are still too wedded to the “blockbuster business model,” hoping for home runs rather than a series of base hits that would put them on a new trajectory. Corporations, therefore, do not invest sufficiently in biomarker discovery programs, nor do they proactively seek to co-develop diagnostic and therapeutic products. Unless these changes occur, the authors contend, patients will not reap the benefits of the new science, and the pharmaceutical industry will face “a frustrating future of declining sales and profits.” The authors also criticize FDA and CMS for not being more aggressive in promoting personalized medicine through regulatory and reimbursement incentives.

In a rejoinder to “Integrating Molecular Medicine” published in the same issue of *Clinical Pharmacology & Therapeutics*, Janet Woodcock of FDA takes issue with some of the essay’s contentions, but notes correctly that “the most important goal for this new field will be to generate some quick wins demonstrating proof of concept to move the field from theoretical opportunity to proven value in healthcare.”

The PMC will be mailing reprints of both articles to its members, and within the confines of copyright restrictions, will also send electronic versions to those who request them as well. The PMC would like to acknowledge the generous financial support of Abbott, Apligraf Corporation, AstraZeneca, Burrill & Company, and the Centers for Disease Control, Duke University, Epstein Becker & Green, Expression Analysis, Genetic Alliance, Genomic Health, IBM, Monogram Biosciences, Perlegen, Pfizer, PhRMA, Quest Diagnostics, and Wellpoint whose contributions made possible the research upon which “Integrating Molecular Medicine” is based.
Dr. Woodcock stated: “I believe the future is that medicine has to move away from being strictly empiric... we need to combine mechanistic understanding from pharmacogenomics, from functional imaging and other things, and combine that with the classic evidence-based medicine empirical outcomes.” She added: “FDA is trying to drive these mechanistic technologies forward, so that we can very rapidly understand better the sources of adverse events and who stands to benefit from medicine...”

Dr. Gregory Downing, Program Director of the HHS Personalized Health Care Initiative, synthesized the themes of the conference in his closing panel. Achieving personalized healthcare will be the “work of a generation,” he noted, and, increasingly, it will not be enough for providers and patients to rely on instinct when evidence is lacking—there must be a concerted effort to break down barriers that currently impede the collection and sharing of data. Once assessed, we must use health information technology and other tools to ensure that the right information is available at the point of care.

In concluding the conference, PMC’s Chairman Dr. Wayne Rosenkrans, Jr., reiterated that collaboration among all the stakeholders would be critical to the achievement of new policies to improve healthcare. The PMC, he noted, would continue in its role of convener of such policy dialogues, bringing together all the best thinkers to identify, synthesize, and act on the best ideas for change.

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**Policy Brief** By Amy M. Miller continued from page 2

- A policy coordinating office for personalized healthcare at HHS should ensure a smooth transition between FDA pre-market regulation and CMS reimbursement while maintaining the agencies’ separate jurisdictions.

- FDA should develop materials explaining how Medical Device Reporting requirements can be met without duplication of effort and extend the transition period while a submission is under review.

Read PMC’s full response at: http://www.personalizedmedicinecoalition.org/PMC_FDA_IVDMIAPDF.pdf

FDA’s Guidance for Industry, Pharmacogenomic Data Submissions – Companion Guidance (http://www.fda.gov/OHRMS/Dockets/07d-0310-gdl0001.pdf), issued in August, 2007, is an excellent example of how FDA should work with industry when developing procedures. The draft guidance was first issued in 2005. A concept paper was distributed in 2006, and later that year, industry was invited to participate in a workshop where the draft guidance and issue paper were discussed. Stakeholder feedback on the guidance, the concept paper, and from the workshop were combined with the real-life experiences that FDA and industry had with the outlined procedures to develop the next draft guidance. Moving forward, FDA and industry will work with this guidance before FDA issues the final version.

On September 7, 2006, FDA issued Draft Guidance for Industry and FDA Staff – Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions (http://www.fda.gov/cdrh/oivd/guidance/1590.html), designed to clarify how the agency would treat these products. FDA considered over 30 sets of comments on the original document when drafting the final guidance. M any of the public comments focused on the altered definition of ASR. In simple terms, an ASR is an active ingredient of a laboratory developed test (LDT). The revised guidance, released on September 14, 2007, attempted to address community concerns about definitional changes. In the Federal Register notice that accompanied the new guidance, FDA reiterated that some products currently labeled as ASRs are actually Class II or Class III in vitro diagnostic devices and are inappropriately labeled as ASRs. FDA has indicated that it will use enforcement discretion until September 15, 2008, meaning that FDA will not enforce regulatory requirements before that date. This indication gives industry one year to comply with the new regulation through proper labeling and following the regulatory path outlined by FDA.

Further guidance can be expected from FDA on these and issues related to personalized medicine, and PMC will continue to look for opportunities to engage stakeholders in an active and constructive dialog with the FDA.

Amy M. Miller, Ph.D., is Public Policy Director at the Personalized Medicine Coalition
New BOD Members

The PMC is pleased to announce two new members of the Board of Directors. With backgrounds in biopharmaceuticals and in the payer community, Nancy Simonian, M.D., and Joanne C. Armstrong, M.D., respectively, add key expertise across the healthcare continuum.

Joanne C. Armstrong, M.D., is a senior medical director for Aetna, one of the nation's largest health-benefits companies. She is the clinical and strategic lead for genomic medicine-related activities since 2003. Aetna has led its industry in recognizing the importance of personalized medicine and in promoting access to medically appropriate genetic services. Dr. Armstrong also directs Aetna's women's health-related programs and services. Dr. Armstrong is also Assistant Professor, Department of Obstetrics and Gynecology, Baylor College of Medicine, a position she has held since 1999. Dr. Armstrong earned her M.P.H. degree in Epidemiology at the University of Michigan School of Public Health, and her M.D. degree at the University of Medicine and Dentistry of New Jersey at New Jersey Medical School.

Nancy Simonian, M.D., serves as the Chief Medical Officer of Millennium Pharmaceuticals, Inc., a leading biopharmaceutical company. She is responsible for clinical development, regulatory and pharmacovigilance and development project management. Prior to joining Millennium, Dr. Simonian was Vice President of Clinical Research at Biogen, where she was responsible for the clinical development of AVONEX® (Interferon beta-1a), Tysabri (natalizumab) and their oncology programs. Dr. Simonian earned a bachelor's degree in Biology from Princeton University and received her M.D. from the University of Pennsylvania, School of Medicine. She completed her medical residency at Massachusetts General Hospital (MGH) in Neurology, was an Assistant Clinical Professor at MGH and Harvard Medical School, and is board-certified in Neurology.

PMC in the Press

In October, BusinessWeek reported on the recent trend of simultaneous development of targeted treatments and accompanying genetic diagnostics with the article, “A Dream Te am Of Drugs And Diagnosis?” The writer spotlights Roche Holdings’ recent bid on Ventana Medical Systems to emphasize this increasingly common approach, noting that Roche and Ventana share an understanding of the next revolution in medicine. In the coming decade, pharmaceutical products—especially cancer drugs—will be created in tandem with diagnostic tests that tell doctors which patients are likely to benefit. Edward Abrahams, Executive Director of the Personalized Medicine Coalition, also emphasized the important role this new type of tandem development will play. He states, “Roche seems to understand” the need for customized treatments. The goal “is to figure out which drugs work for which people.”

U.S. News and World Report reported in September on recent trends and research in personalized medicine. In this feature article, “Moving Closer to Personalized Medicine,” the author uses J. Craig Venter’s recent sequencing of his own genome and the FDA’s new labeling recommendation for Coumadin (warfarin) as a backdrop for an overall examination of trends in personalized medicine. The writer believes that the real promise of genetic diagnostics may be the prospect of applying them to the prevention of common conditions such as diabetes and heart disease. In the article, Edward Abrahams, the Executive Director of the Personalized Medicine Coalition confirms that, “Medicine ought to be targeted to individuals. One size doesn’t fit all anymore.”

Pharmacogenomics Reporter reported in June on potential federal legislation that would regulate pharmacogenomics and personalized medicine, including a bill submitted by Illinois Senator and Democratic presidential candidate Barack Obama. Lawrence Lesko, Director of FDA’s Office of Clinical Pharmacology & Biopharmaceutics, stated that the regulations may be premature and could stifle potential breakthroughs in a nascent scientific field. An FDA spokesperson stressed, however, that Congressional “regulations are different from [FD A-issued] guidelines.” The “Genomics and Personalized Medicine Act,” proposed by Senator Barack Obama in 2006, has been both commended for its timeliness and criticized as too broad. Edward Abrahams, Executive Director of the Personalized Medicine Coalition, disagreed that Obama’s bill would stifle pharmacogenomics innovation. Instead, he said, the bill “heightens the discussion regarding personalized medicine. It is really exciting that someone who is running for President of the United States has taken an interest in this issue.”

For links to these and other PMC-related articles, visit the Communications section of our website at: http://www.personalizedmedicinecoalition.org/communications/overview.php

Sign up

To receive the PMC Newsletter and other announcements from PMC, sign up at our website: www.PersonalizedMedicineCoalition.org
Society for Neuroscience Annual Meeting - Panel Presentation: Identifying the best Genomic-Neuromarker profiles for brain-related “Personalized Medicine”

November 5, 2007
San Diego, CA

The Brain Resource Company Limited, a PMC member company, is hosting the panel presentation “Identifying the Best Genomic-Neuromarker Profiles for Brain-Related ‘Personalized Medicine’” as part of the Society for Neuroscience Annual Meeting. This panel will present the opportunities and challenges for utilizing neuroscientific data in Personalized Medicine. Edward Abrahams, Executive Director of the PMC, will moderate a panel on which Evian Gordon, Brain Resource Company, and Thomas Insel, National Institute of Mental Health, will participate. For more information, visit the conference website: http://www.brainresource.com/about_us/index.php?parent=26&id=29

3rd Annual Burrill Personalized Medicine Meeting
November 12 - 13, 2007
San Francisco, CA

The Burrill Life Sciences Media Group, with sponsor support from the PMC, will hold its 3rd Annual Personalized Medicine meeting on November 12 - 13, 2007, at the University of California San Francisco Mission Bay Conference Center. This conference brings together the thought leaders in science, healthcare, government, payers, regulators, the financial community, and pharma and biotech CEOs to discuss how the 3Ps—Personalization, Prediction, and Prevention—will impact the future of healthcare. PMC members may register for a discounted fee of $495.00 (use code PPCLN). For more information, visit the conference website: http://www.personalizedmedicinemeeting.com/index.htm

Oncology Leaders Forum 2007
November 14 - 16, 2007
Boston, MA

Hosted by Phacilitate Limited, the 2007 Oncology Leaders Forum will focus on defining the oncology therapeutics marketplace of 2017, driving efficiency in oncology clinical development through the application of innovative clinical trial designs and biomarkers, and delivering a blueprint for the successful oncology R&D portfolio of the future. Keynote speakers include Mara Aspinall, Vice Chair of the PMC and President of Genzyme Genetics. PMC members receive a 10% discount on registration fees. Please contact Nicola McCall at Nicola@phacilitate.co.uk.

For more information, visit the conference website: http://www.phacilitate.co.uk/pages/oncology/index.html

Personalized Medicine: A Call for Action
November 29 - 30, 2007
Boston, MA

The PMC will present its annual Leadership in Personalized Medicine Award at the Harvard Medical School-Partners HealthCare Center for Genetics and Genomics and Harvard Business School’s 3rd annual personalized medicine conference. The conference will explore how the Personalized Medicine revolution has been put into practice and what is required on the part of physicians, patients, payers, provider organizations, pharmaceutical innovators, and the business community to ensure its future success. For more information, visit the conference website: http://www.hpcog.org/PM/2007/index.jsp

 PMC Welcomes the Following New Members since April 2007:

Agenda BV
Baylor College of Medicine
Biosearch Technologies, Inc.
Brown University
CardioDX, Inc.
Center for Medicine in the Public Interest (CMPI)
Center for Molecular Medicine
Cleveland Clinic Genomic Medicine Institute
The Critical Path Institute (C-Path)
Curidium Medica
Dako Denmark A/S
Deloitte Center for Health Solutions
The DNA Repair Company
The George Washington University Medical Center
Helicos BioSciences
Institute for Genomics & Systems Biology, The University of Chicago and Argonne National Laboratory
Manatt Health Solutions
McKesson
Mirixa Corporation
National Jewish Medical and Research Center
National Foundation for Cancer Research
National Jewish Medica and Research Center
OncoM ethylene Sciences
Penn Medicine
Pensay, Inc.
Riley Genomics
The RPM Report
Thera Genetics Ltd.