PMC Members Newsletter

The Personalized Medicine Coalition, representing scientists, patients, providers and payers, promotes the understanding and adoption of personalized medicine concepts, services and products to benefit patients and the health system.

Winter | 2012

Personalized Medicine Advances But Cost Questions Remain

The integration of personalized medicine into the health care system continues to be slower than many innovators would like, speakers said at the annual Personalized Medicine Conference hosted by **Partners Healthcare**, co-sponsored by the Personalized Medicine Coalition and held at Harvard Medical School in Boston, Mass.

Ezekiel Emanuel, M.D., Ph.D., a self-described skeptic who delivered the opening address, charged that personalized medicine is not just slow to develop, but virtually non-existent.

"Personalized medicine is hyperbole; personalized medicine is so expensive it's unaffordable; personalized medicine is a myth when it comes to saving American medicine," said Dr. Emanuel, a bioethicist at the University of Pennsylvania who served as special advisor for health policy to the director of the White House Office of Management and Budget from 2009 to January 2011.

Dr. Emanuel's remarks were deliberately provocative, said Raju Kucherlapati, Ph.D., the Paul C. Cabot professor in the Harvard Medical School Department of Genetics, but they represent an attitude held by many in medicine.

"There are many who believe we are experiencing the 'best of times' in personalized medicine as the field has experienced continued growth and is being implemented in clinical practice," said Dr. Kucherlapati. "There are others who believe personalized medicine has over-promised and under-delivered."

JUSTIN KNIGHT PHOTOGRAPHY

Attendees gather at Harvard's Personalized Medicine Conference.

Although attendees disagreed that personalized medicine is a myth, many

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FROM THE PRESIDENT

Answers Needed for Personalized Medicine Skeptics

BY EDWARD ABRAHAMS | PRESIDENT

Although he acknowledged he knew little about the subject, Ezekiel J. Emanuel, M.D., Ph.D., an oncologist and a former senior White House advisor on health care, established himself as the leading skeptic of personalized medicine at the Personalized Medicine Conference held at Harvard on November 9. He called its claims exaggerated hyperbole, in particular the contention that personalized medicine—by reducing inefficiencies and adverse events—has the power to cut systemic costs. In fact, in the most serious challenge yet leveled against the paradigm, Emanuel said that it "will be so expensive as to be unaffordable."

Emanuel, now a professor of health policy at the University of Pennsylvania, was not invited to deliver the conference keynote to be, as one journalist wrote, the "skunk at a garden party. " He was invited

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PMC Develops FDA Guidance Mosaic

Speaking at a PMC Public Policy Committee meeting, Larry Lesko, Ph.D., F.C.P., Former Director, Office of Clinical Pharmacology, Food and Drug Administration, (FDA), said that contrary to the expectations of many that FDA would produce a single guidance document to govern the entire field, instead a "mosaic" of FDA documents will guide the regulation of personalized medicine products and services. PMC's list of relevant guidance documents is available at http://www.personalizedmedicinecoalition.org/policy/executive/guidance.

PMC Launches Public Policy Discussion Series

In December, PMC launched a public policy discussion series with a forum about legal and intellectual property issues facing personalized medicine. The forum, which was held the day before the Supreme Court heard oral arguments in *Mayo v. Prometheus*, reviewed current court cases on gene and method patents and their implications for personalized medicine. It featured Sandra Park, Staff Attorney of the American Civil Liberties Union, and David Resnick, Partner, **Nixon Peabody LLP,** in a discussion moderated by Richard Meyer, Partner, **Kilpatrick Townsend & Stockton LLP.** The next panel in the series will discuss how to create incentives for the diagnostics industry. It will be held on February 15, 2012 at the American Association for the Advancement of Science in Washington, DC. Other planned discussions include:
April 25—PCORI and Personalized Medicine: A Conversation (Speaker: Joseph Selby, M.D., M.P.H., Executive Director, Patient-Centered Outcomes Research Institute).
July 18—FDA's "Mosaic" for Personalized Medicine Regulation: Current Thinking and What's Next (Invited Speaker: Stephen Spielberg, M.D., Ph.D., Deputy Commissioner for Medical Products and Tobacco, FDA).

PMC Celebrates First Personalized Medicine Awareness Day

The Personalized Medicine Coalition (PMC) joined the state of Georgia in celebrating Personalized Medicine Awareness Day on September 1, thanking Governor Nathan Deal for being the first governor to recognize personalized medicine's significance as both a driver of improved health outcomes and a way to increase the efficiency of health care delivery. The Personalized Medicine Awareness Day celebration included a symposium and reception at Morehouse School of Medicine, where Governor Deal was joined by Former UN Ambassador Andrew Young, Leroy Hood, M.D., Ph.D., Founder of the **Institute of Systems Biology,** and other personalized medicine leaders. The program was sponsored by Georgia Bio, Morehouse School of Medicine, **Iverson Genetic Diagnostics, Inc.,** Emory University and the Georgia Institute of Technology.

Public Comments Available for Draft Guidance on In-Vitro Diagnostics

In July, FDA released its Draft Guidance for Industry and Food and Drug Administration Staff—In Vitro Companion Diagnostic Devices, which offered a potential regulatory framework for drugs that depend on the use of a diagnostic device (or test). The docket received 33 public comments, including 16 from PMC member institutions. All public comments are available for viewing at www.regulations.gov, docket ID: FDA-2011-D-0215.

PMC Board of Directors Announces New Chairman

The PMC Board of Directors has elected D. Stafford O'Kelly, President of **Abbott Molecular,** as its new Chairman. Also elected were David King, Chief Executive Officer of **The Laboratory Corporation of America,** as Treasurer, and Jeffrey Cossman, M.D., President and Founder of **United States Diagnostic Standards, Inc.** as Secretary.

"I look forward to working with the PMC Board and its membership to promote the understanding and adoption of personalized medicine and put in place public policies to do so," Mr. O'Kelly said.

Mr. O'Kelly joined PMC's Board in June 2010 and previously was Vice Chairman.

D. Stafford O'Kelly

"We look forward to Stafford's leadership in helping increase PMC's impact in the public arena and in making the case for personalized medicine," said Edward Abrahams, PMC's President.

Mr. O'Kelly joined Abbott in 1984 and has served in various management positions across the company. He was appointed to lead Abbott's molecular division in 2007 and was instrumental in Abbott Molecular's partnership with Pfizer in developing the Vysis ALK Break Apart FISH Probe Kit, a companion diagnostic for the non-small cell lung cancer drug Xalkori®.

He earned his bachelor's degree in engineering and MBA from Trinity College Dublin, Ireland.

Public Policy Alignment Needed to Spur Innovation

BY AMY MILLER | VICE PRESIDENT, PUBLIC POLICY

Budget battles dictate policy debates on Capitol Hill and dominate the news right now, forcing the personalized medicine community to focus on low-cost ways to facilitate personalized medicine's development.

In 2011 the Personalized Medicine Coalition's public policy committee agreed that to enable personalized medicine, federal policy makers should:

- Improve and better coordinate the Food and Drug Administration's regulatory process for personalized medicines and co-developed diagnostic tests.
- Provide a clear reimbursement pathway for personalized medicine products and services at the Centers for Medicaid and Medicare Services.
- Engage a federal advisory committee on personalized medicine to help coordinate federal agencies' personalized medicine activities.
- Offer tax incentives for companies developing personalized medicines and the diagnostics that guide them.

With the 2012 election looming, we do not expect Congress to tackle significant health care legislation outside of "must-pass" bills. Because the Food and Drug Administration's drug and device user fees must be reauthorized in 2012, user fee legislation represents the best vehicle this year to enact policies that will benefit personalized medicine. To be considered as an amendment to the user-fee legislation, policies must meet four criteria: they must have the consensus support of the health care community, be budget-neutral or paid for through other revenue, be supported by the congressional leadership and be related to the content of the user fee agreements.

We believe that our proposals to better align FDA review of paired therapeutics and diagnostics and to create a personalized medicine committee to coordinate government activities meet these standards. Given the current political environment, however, securing even these changes will be difficult. We will continue to encourage the House sponsor of the Genomics and Personalized Medicine Act, Rep. Anna Eshoo (D-Calif.) to include these provisions as she prepares to re-introduce the bill.

Regardless of what Congress does, we expect the FDA to offer the personalized medicine community new regulatory guidance.

Regardless of what Congress does, we expect the FDA to offer the personalized medicine community new regulatory guidance. For example, we expect draft guidance documents related to the co-development of drug-diagnostic combination products, the enrichment of study populations for clinical trials and issues to consider in drug development tools. PMC looks forward to commenting on relevant FDA draft guidance documents, and we encourage members to participate in our process to develop these comments.

In recognition of the threats that the budgetary environment poses to health care innovation—in personalized medicine and more broadly—PMC, in collaboration with the **American Association for Cancer Research** and **Feinstein Kean Healthcare,** is planning a national conference in mid-2012 to consider the status and future of cancer research and care. The goals of the conference are to identify and build support for policy pathways to sustain and accelerate progress and improve patient care in this era of health care cost containment.

The conference will bring together stakeholders from all sectors of the health care community to discuss emerging science and technology, the impact of cancer research on clinical care, and policy and business environment that are necessary to support personalized cancer care. Among the topics to be discussed at the conference are how the value of new products and services can be defined for policymakers, how to address evidence challenges, and how to and empower patients.

We are also working with the **Biotechnology Industry Organization** (BIO) on meetings with payers and patients to inform a national summit that will examine coverage, coding, and payment challenges to personalized medicine, and consider possible solutions, such as the evidentiary requirements that different stakeholders require and how alternative payment models can incentivize personalized medicine's development.

We expect these activities and our speaker series, described on the opposite page, to inform discussions about how public policy can support personalized medicine. As outlined above, such policies do not have to cost a lot of money, but they require careful articulation and compelling arguments to support their adoption.

Improved Technology and New Targeted Therapies Drive Personalized Medicine Forward

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expressed frustration with the existing regulatory and reimbursement framework that is neither speeding its adoption and use nor catalyzing innovation.

"Personalized medicine products currently on the market are the leading edge of a front of products," said Randy Burkholder, Deputy Vice President, **Pharmaceutical Research and Manufacturers of America** (PhRMA), "but better alignment of public policy is needed to bring them to the market."

JUSTIN KNIGHT PHOTOGRAPHY

Ezekiel Emanuel, M.D., Ph.D. is questioned by Raju Kucherlapati, Ph.D. regarding his skepticism about personalized medicine.

However, while some presenters at the conference claimed that advances in personalized medicine were too slow, others highlighted how close partnerships between pharmaceutical and diagnostic companies have led to successful commercialization of personalized medicine products.

Hakan Sakul, Ph.D., Executive Director and Head of Diagnostics, **Pfizer, Inc.**, and Stafford O'Kelly, President, **Abbott Molecular,** discussed their success in securing approval by the Food and Drug Administration for crizotinib (Xalkori ®), which is designed to treat about 3 to 5 percent of patients with non-small cell lung cancer that overexpresses the ALK protein and is 63 percent more effective in these patients than chemotherapy. Both the drug and its companion diagnostic were approved simultaneously. Until this past summer, the development and approval of a diagnostic and drug have typically been handled separately.

The need for a companion diagnostic became clear in 2009, Dr. Sakul said, and Pfizer began working with Abbott Molecular to develop a diagnostic to use in Phase II and III clinical trials. That helped Pfizer and Abbott Molecular gain approval of both the drug and the diagnostic from FDA in a record five months.

This summer, the FDA also cleared the therapy and companion diagnostic for Roche and Daiichi Sankyo/Plexxikon's vemurafenib (Zelboraf ®), which treats about half of melanoma patients with a mutated form of a protein called BRAF.

Many other leaders from a variety of health care industries discussed progress in personalized medicine. Officials from **Medco Health Solutions,** who last year announced that they would begin offering genetic tests, were joined this year by leaders from **Humana, McKesson Health Solutions,** and **Health Advances LLC.**

Louis Hochheiser, M.D., Vice President and Chief Medical Leader at Humana, said Humana is also willing to pay for genetic tests—if they meet certain conditions. "Give me the right information about a test—how doctors will use it and how patients will benefit, and we'll pay for it," he said.

That's a challenge advocates have yet to overcome, said Anna Barker, Ph.D., Professor and Director of Transformative Healthcare Networks at Arizona State University (formerly a Deputy Director at the National Cancer Institute). "We need good economic data quantifying the value personalized medicine can provide to the health system," she said.

Dr. Barker also noted that personalized medicine has made great strides. Presenting a report from the **American Association for Cancer Research,** she said that thanks in large part to targeted therapies such as Gleevec® and Tarceva®, cancer fatalities have declined by 22 percent in men and 14 percent in women over the past 40 years.

Another panel predicted that the pace of personalized medicine may soon speed up since the cost of sequencing the human genome is falling so fast. The personalized medicine community has long predicted that genome sequencing will become widespread once its cost is low enough, say $1,000.

"It's a game changer," said Howard Jacobs, Ph.D., founder of the Human and Molecular Genetics Center at the Medical College of Wisconsin, speaking about the utility of genome sequencing at a lower cost on a panel of experts from academic medical centers.

But as one panelist said, most doctors don't yet know enough about genetics to make use of the new information. Physicians and other health care professionals need more education about genetics to make clinically useful genomic information, said Kevin Davies, Editor-in-Chief of *Bio-IT World* magazine.

Michael Pellini, M.D., CEO of **Foundation Medicine,** summed up two of the major challenges facing personalized medicine: patients want access to new medical technologies, but genomic data must be medically useful and payment must be available in order to spur widespread adoption.

Complexity is Grand Challenge for 21st Century

Following is an excerpt from an acceptance speech by Leroy Hood, M.D., Ph.D., President and Co-Founder, ***Institute for Systems Biology*** *(ISB), who received PMC's 2011 Leadership in Personalized Medicine award. The award is given annually at the Personalized Medicine Conference at Harvard Medical School to recognize an individual whose contributions in science, business, and/or policy have helped advance personalized medicine.*

In 10 years, we'll have patients who each have a virtual cloud of billions of data points—and we'll also have the wherewithal to be able to reduce that enormous data dimensionality to simple hypotheses about health and disease.

That data cloud will be enormously heterogeneous, extending from genetic and molecular data all the way up to social data that will give us fundamental insights into environmental exposures. Critically, most of that data is noise with regard to creating actionable data and choices and options for patients.

The key to reducing noise is to use systems approaches to analyze information and to integrate different levels of information. A relevant question is, why do we need all of the data? The simple answer is that disease is enormously complex, and it's complex because of Darwinian evolution. It's not directed: it's random, it's chaotic. It builds systems on top of systems in a chaotic fashion. To simplify this systems complexity, we need systems approaches.

Systems biology has to recognize fundamental principles of information and biology. There are really two major types of information that are critical to thinking about disease: your genome, and the environment impinging on that genome. They create a phenotype. As we look across the dimensions of the development of physiologic responses or even the initiation and onset of disease, we can ask what connects the information with the phenotype. The connectors are biological networks and dynamic molecular machines. The essence of systems thinking about biology is really understanding the dynamics of those two information-handling units, networks and molecular machines.

In biology there is an information hierarchy of DNA to RNA to proteins, all the way up to individuals in populations. The environment impinges on every one of those levels of information. If you're to understand the system at any level, say cell replication at the single-cell level, you have to ascertain the preceding levels of information and carry out a process of integration that explicates the nature of that environmental information that's been added. Unless we understand the environment as well as we understand the digital genome, we don't have a chance of understanding complexity.

At ISB we've demonstrated that dynamically altered information not only explains the pathophysiology of the disease but it also suggests new strategies, new approaches to diagnostics and therapy and ultimately to prevention.

JUSTIN KNIGHT PHOTOGRAPHY

William S. Dalton, Ph.D., M.D., presents the 2011 Award for Leadership in Personalized Medicine to Leroy Hood, M.D., Ph.D.

How do we deal with hundreds of billions of data points for each individual? It isn't all the data that's the problem—it's how you increase the signal to be heard through noise. The tsunami of data is over-hyped. The cloud will handle as much data as you want, and we'll put our analytic tools in the cloud to be controlled by our desktops. The grand challenge for 21st century is complexity. It's true of all disciplines, scientific and engineering. For our purpose, biology has powerful systems approaches that can attack complexity in a fundamental way.

Personalized Approach to Cancer Care Begins to Spread Across Country

At top-tier cancer centers, patients now receive personalized care in the form of molecular tumor analysis and some targeted therapies; personalized medicine is here, and beginning to change health care.

The 'if you build it, they will come' model will never work for personalized medicine. Our idea is to export the technology, the know-how, the capability, to the patients and their doctors.

–William S. Dalton, Ph.D., M.D.

So far, however, access to these advances is limited to relatively few people. Personalized cancer treatment based on genomic information isn't available to the vast majority of cancer patients treated outside of big-name cancer centers.

"There are two models of cancer care," says Jeff Elton, Ph.D., founder of the KEW Group in Concord, Mass. "One is the clinical center that is funded by research grants, has a staff of 450 professionals, and access to the latest treatments and experimental techniques. The other is a general oncologist, working for a commercial entity or with his own practice. He has no access to the expertise or interpretive skills of the clinical centers. He's swamped with patients." The KEW Group seeks to build a network of community cancer centers where personalized care will be offered.

That community setting is key, says Jerry Callahan, Ph.D., CEO of **Intervention Insights,** a medical information service provider in Grand Rapids, Mich.

"Eighty-five percent of our patients live and die in their communities," he says. "They never make it to an academic setting."

These men and their companies are among a number of organizations that hope to spread personalized cancer into every community, no matter how small, by changing the way doctors receive medical information. Many large cancer centers are also engaged in the effort.

"The 'if you build it, they will come' model will never work for personalized medicine," says William S. Dalton, Ph.D., M.D., President and CEO of **Moffitt Cancer Center** in Tampa, Florida. "Our idea is to export the technology, the know-how, the capability, to the patients and their doctors."

The approach these organizations are seeking to pioneer represents a change for oncologists, who are used to choosing tests and therapies for their patients. Now, they will be asked to rely on outside experts to aid them. It's not clear how receptive local oncologists will be to the new idea. But some believe that it's inevitable.

"The practice of oncology must change," says Michael J. Pellini, M.D., CEO of **Foundation Medicine** in Boston, a company which uses a multivariate test to look for all known cancer mutations in a single tissue sample. Five years ago, it cost $300 to $500 to run all the available tests on a non-small cell lung cancer tumor sample, he said. Today, a complete workup for a patient runs $3,000 to $7,000, making a single multivariate test a more affordable option. Further, many oncologists don't have time to keep up with the rapidly-developing science on their own.

"Somebody has to take the lead in pulling all that information together so that it's presented in context," Dr. Pellini says.

In addition to molecular sequencing of cancer tumors for mutations, the new companies provide doctors with information on all drugs that have been approved for those mutations.

The effort has promise beyond the limited number of targeted therapies now available to treat gene mutations tied to particular cancers, says Roy Herbst, M.D., Ph.D., chairman of the Task Force on Tobacco and Cancer at the **American Association for Cancer Research.** When there is no drug for the specific cancer, researchers can seek drugs that are effective against the mutation in other types of cancer. Doctors may

The practice of oncology must change. Somebody has to take the lead in pulling all that [genetic] information together so that it's presented in context.

–Michael J. Pellini, M.D.

DICK DICKINSON FOR MOFFITT CANCER CENTER

A researcher checks the automated freezer that stores tissue samples of cancer patients at the Moffitt Cancer Center in Tampa, Florida. The biobank is used to identify patients for clinical trials of targeted therapies.

even decide to treat a nonresponsive cancer by developing a kind of cocktail containing several different drugs, much as AIDS patients now receive cocktails of antiretroviral therapies, says Dr. Herbst, who is also chief of medical oncology at Yale University.

However, Roy Beveridge, M.D., chief medical officer for the U.S. Oncology Network (owned by **McKesson**), warns that outside a research setting such as Yale's, doctors need to be careful about giving their patients false hope by treating them with medications that have not been proven for a condition.

"We're concerned that when a therapy has not been proven in a trial, there is the potential to overpromise benefits from the therapy that may not be delivered," he said. "We need to be true to patients by insisting on collecting data and conducting clinical trials," as Moffitt is doing, he says. U.S. Oncology is working with Moffitt to spread its cancer care methodology, tests and treatments throughout Florida.

The need to wait for a clinical trial before trying an unproven approach could leave some patients without other options, but new hope is offered by the fact that the number of clinical trials for targeted therapies is proliferating rapidly. There are some 500 such trials underway now, and patients can be put into them very quickly, thanks to numerous biobanks where tissue can be tested for new mutations, as well as molecular tumor analysis, which quickly establishes eligibility for ongoing trials.

"The traditional approach was to wait for patients to come in and then test them to see whether they qualified for clinical trials," Dr. Dalton says. "We can use our biobank to identify patients for trials. We found 37 patients for a colon cancer trial in three and a half months. That's unheard of. We were able to complete the trial in less than a year."

The final hurdle for the new business model is persuading insurance companies to pay for the tests, but even the new companies say they have had few problems so far.

"We have had no payers deny us yet, although we fully expect some amount of loss," says Dr. Callahan of Intervention Insights. "But all boats are rising at this point. Everyone's trying to change the industry."

Europe Must Better Align Coverage, Coding and Reimbursement to Advance Personalized Medicine

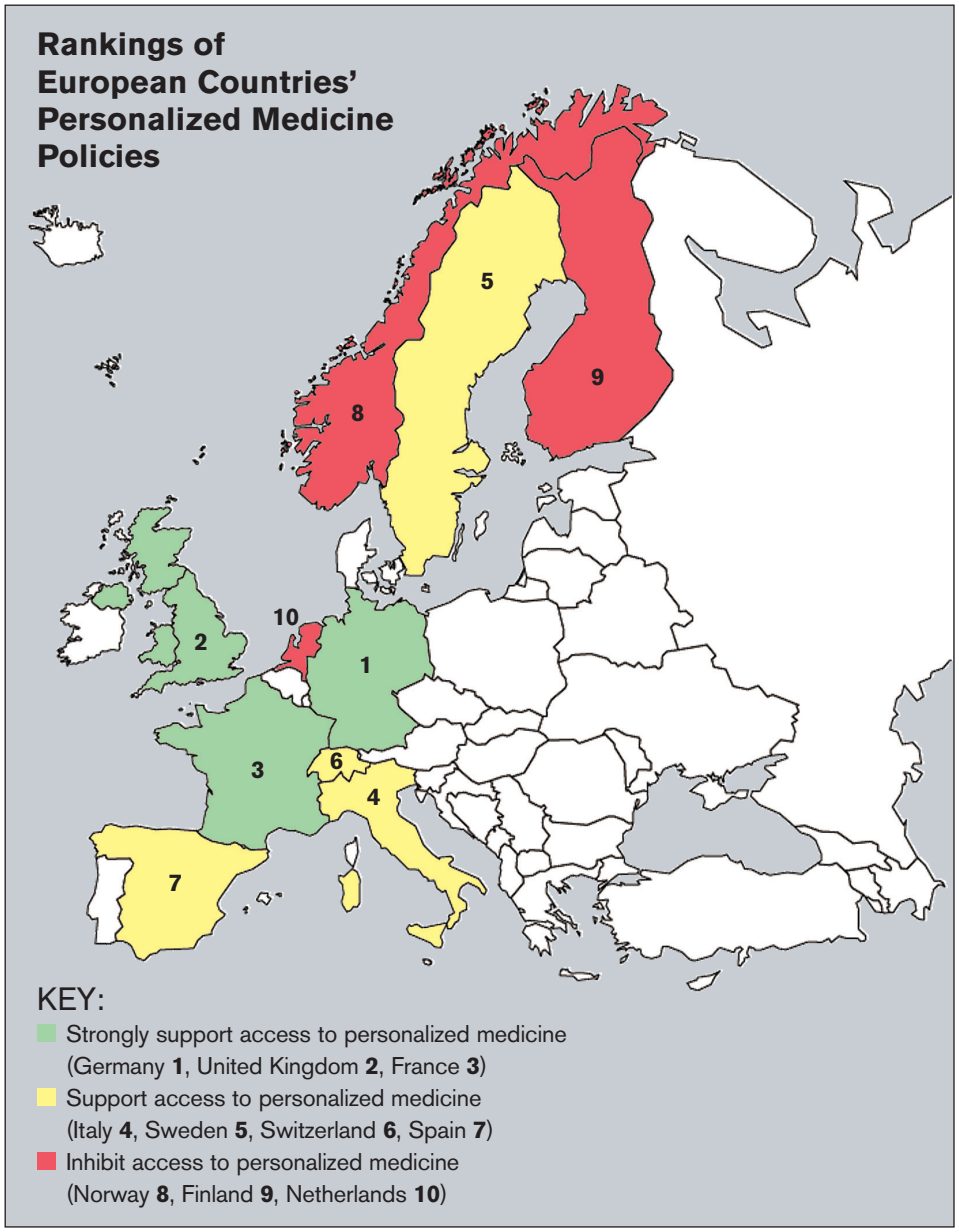
Germany leads nine other countries in the European Union when it comes to fairly reimbursing the costs of personalized medicine, according to a new Personalized Medicine Coalition white paper.

But while Germany's health system scored higher than other EU countries in terms of reimbursement and market access, many reforms are needed to coverage, coding and reimbursement systems across the EU to stimulate future investments in personalized medicine, according to the white paper, *Advancing Access to Personalized Medicine: A Comparative Assessment of European Reimbursement Systems*.

"Companies developing innovative personalized medicine products in Europe face similar challenges to innovators in the United States," said PMC President Edward Abrahams during a panel discussion of EU reimbursement issues at **Cambridge Healthtech Institute**'s Molecular Diagnostics Summit Europe in Hanover, Germany. PMC's white paper was released at the conference, which was held in October. "Regulatory systems on both continents are not well-positioned to evaluate personalized medicine products nor are reimbursement systems configured to provide companies with a predictable, value-based return on their investments," he said.

A number of country-level reimbursement factors can support or inhibit investment in and access to personalized medicine technologies, according to the paper's lead author, Susan Garfield, DrPH, Vice President, **Bridgehead International.**

"For personalized medicine to reach its full potential, policies across Europe need better coordination. The fragmented system whereby regulatory decisions are made by the entire European Union, but reimbursement, coding and pricing are determined by individual countries compounds the problem," said Garfield.



In order to move past traditional medicine's one-size-fits-all paradigm, the report recommends best practices to improve the reimbursement environment in Europe and proposes reforms that would improve access to personalized medicine by modernizing coding systems, developing new reimbursement processes, and clarifying evidence requirements needed to bring products to market.

The EU paper follows a similar PMC research product on US reimbursement policies released in 2010. That paper, written by David Parker, Ph.D., Vice President, **Boston Healthcare**, examined the impact of U.S. coverage, coding and reimbursement policies on the development of new molecular diagnostic tests. Both papers are available for download on PMC's website.

Reading the Tea Leaves in *Mayo v. Prometheus*

VERN NORVIEL AND MARK D. MCNEMAR, ATTORNEYS WITH WILSON SONSINI GOODRICH & ROSATI

Biotech companies are eagerly awaiting a Supreme Court decision that could either boost personalized medicine by clarifying the rules on diagnostic-related patents—or significantly harm the sector by making such patents vastly harder to obtain.

Fortunately, the second outcome seems unlikely, according to our analysis of oral arguments in the case, *Mayo Collaborative Services, DBA v. Prometheus Laboratories, Inc.* While the Justices seemed concerned about the patentability of the Prometheus claims, they also recognized the negative effects a sweeping change would have to existing patents and the U.S. biotech industry. But until the decision is made, uncertainty remains as to how U.S. courts will apply patent law to diagnostic claims.

Courts have struggled to apply exceptions to patent eligibility in cases that involved diagnostic claims, and the current debate is fueled by an influential dissenting 2006 opinion in *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.* where three dissenting justices argued that the underlying patent-eligibility should have determined if the claim was invalid on the merits because the correlation step was an unpatentable "law of nature."

United States Supreme Court

In the 2010 case, *Bilski v. Kappos,* justices reaffirmed the judicially established principle that laws of nature, physical phenomena, and abstract ideas cannot be patented, despite broad language in federal patent law, which states that "any new and useful process, machine, manufacture, or composition of matter" can be patented.

After deciding *Bilski*, the Supreme Court directed the Federal Circuit to reexamine two opinions on diagnostic patents, including Prometheus. For one of the Prometheus patents, the claim at issue involves a method for "optimizing therapeutic efficacy" by first administering a particular drug to a subject and then using the subject's metabolite level to adjust future drug doses. In another patent, the administering step is implied; the claim is for merely "determining the level of [a metabolite]" in a subject who has been administered a particular drug.

The district court had said the claims lacked patentable subject matter, but the Federal Circuit reaffirmed the patentability of the claims at issue and the Supreme Court granted review.

All sides made broad-brush arguments before the court. Prometheus asserted that its claims were drawn to research and therapeutic processes in personalized medicine and warned that the U.S. biotech industry would be severely harmed if such processes couldn't be patented. The Mayo Clinic portrayed the patent as an attempt to monopolize a law of nature. The U.S. Solicitor General, on behalf of the Department of Justice, argued that while the claims are patent eligible, they are probably invalid for other reasons.

The justices' questions focused on identifying the threshold of "other matter" that transforms a claim from an unpatentable law of nature to an application of a law of nature. They seemed to conclude that merely observing a law of nature is insufficient, but they also seemed undecided as to where the actual sufficiency lay.

The Court questioned whether standards of novelty and obviousness contained in other sections might apply when analyzing the patentability of medical process claims. Mayo argued that such an approach is appropriate to protect the medical community from over-reaching patent claims and argued that this approach was taken in the *Bilski* case. However, the Solicitor General asserted that such an approach would complicate patent eligibility analysis by the courts and that the threshold test from *Bilski* requires simply that there be a process.

Prometheus argued that its claims applied to administering and measuring steps, not just observation. It said these steps mean that its claim meets the law's intentionally low eligibility threshold and patentability should be determined under other sections of the law.

If the Court is cautious in its final decision, it will reaffirm earlier holdings and make no changes to the current law of patent eligibility. In that case, most diagnostic/therapeutic process claims that contain a treatment or analysis step would remain eligible for patents and there would be little impact on the personalized medicine industry.

However, the Supreme Court may require that a claim show novelty in a "mechanical" step rather than a "transformation" step. For example, the Court may find that the Prometheus diagnostic can't be patented because administering a drug and measuring a metabolite are not novel steps, even though the approach is novel in the "transformation" step, where this measurement is used to guide dosing.

While we believe it is unlikely, such an outcome could prove very troublesome to the U.S. biotech industry. Were the Supreme Court to so radically change the law of patent eligibility, the value of investment in personalized medicine companies would be undermined.

The views expressed in this article are those of the authors and do not necessarily represent the opinions of the Personalized Medicine Coalition.

Personalized Medicine Promises to Cut Health Care Costs

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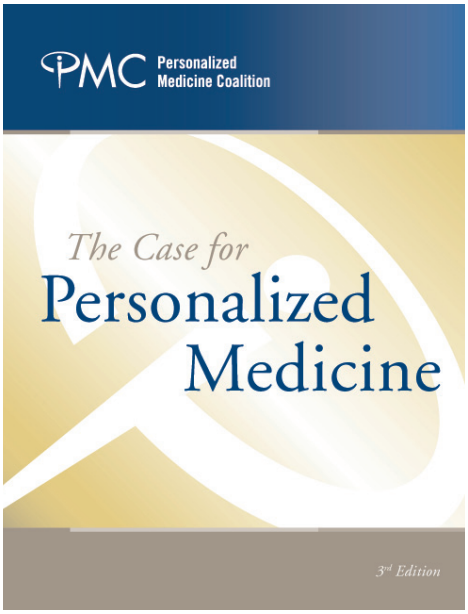
because the proponents of personalized medicine need to engage his views, or rather his fears, which are serious obstacles to convincing policymakers to support the paradigm.

Indeed many in governments across the globe do fear innovation. They claim it raises costs without improving health, ignoring for example that HIV was essentially turned from a death sentence to a chronic condition by implementing the principles of personalized medicine or that molecular medicine has helped improve survival rates for cancer patients over the past 40 years, as the **American Association for Cancer Research** documented in its 2011 annual report.

On November 16, in part to answer these critics, PMC issued the 3rd edition of *The Case for Personalized Medicine*, a document that illuminates the benefits of personalized medicine and outlines a pathway to improve the regulatory, payment, and educational systems that will shape the speed with which it reaches patients.

To those who contend that personalized medicine represents a dream of the future, the report points to the growth of commercially available personalized medicine products, which have risen from 13 in 2006 to 72 today, including two new targeted drugs, linked to diagnostic tests, for non-small cell lung cancer and melanoma. These products, listed in a compendium in the back of the document, point to a future in health care that moves away from one-size-fits-all, trial and error medicine.

The report, which suggests that we are likely to see many more personalized products come on the market in the near future, also notes that 30 percent of surveyed biopharmaceutical companies require all compounds in development to



have a biomarker strategy; 50 percent of clinical trials collect DNA from patients to assist that strategy; and that the pharmaceutical industry has increased its investment in personalized medicine by 75 percent in the last five years.

While acknowledging that the clinical utility of genome sequencing has not yet been established, the report also notes that the dramatic fall of the cost of sequencing from $300 million in 2001 to $5,000 in 2011 will undoubtedly provide new data-driven understanding of individual variation, leading to tailored approaches to health care.

But with health care costs spiraling to the point that they threaten the economies of the developed world, part of the appeal of personalized medicine is its promise of reducing systemic costs. And here *The Case for Personalized Medicine* notes that a 34 percent reduction in chemotherapy use would occur if women with breast cancer receive a genetic test prior to treatment; 17,000 strokes could be prevented each year if a genetic test is used to properly dose the blood thinner warfarin; and $604 million could be saved if patients with metastatic colorectal cancer receive a genetic test for the KRAS gene prior to treatment. Moreover, because they believe that it can help them get a handle on costs while improving outcomes, pharmacy benefit managers and some payers are, as the report notes, studying personalized medicine closely and implementing it where appropriate.

Unfortunately, to truly move the field forward what we need are not only single, product-specific studies such as those referenced above. Rather, what is required to change minds like Dr. Emanuel's are large-scale, system-wide economic analyses that compare today's standard of care with personalized approaches, to determine if improved outcomes and cost reductions can be achieved.

Making a Case for Personalized Medicine: Top Officials Highlight Opportunities, Challenges

Thanks to personalized medicine, doctors today can choose from different cancer treatments based on the characteristics of a particular cancer tumor, and can prescribe medicines in doses that are more effective for specific patients with diseases ranging from depression to inflammatory bowel disease, according to the third edition of PMC's report *The Case for Personalized Medicine,* released November 16 at a symposium at the North Carolina Biotechnology Center in Research Triangle Park, N.C.

The report documents the growth of commercially available prominent personalized medicine products from 13 in 2006 to 72 today. Diverse personalized medicine drugs and diagnostic tests are now available for arthritis, cancer, cardiovascular disease, infectious diseases, organ transplants and psychiatric disorders, among other conditions.

JIMMY CRAWFORD FOR RTI INTERNATIONAL

Jennie Hunter-Cevera, Ph.D., Amy Abernethy, M.D., David King, Jonathan Roy, and Eric Linsley offer perspectives on personalized medicine's development.

In a panel discussion of opportunities and challenges facing personalized medicine moderated by Jennie Hunter-Cevera, Ph.D., Executive Vice President, **RTI International**, speakers discussed how North Carolina institutions are playing a role in the development of the personalized medicine paradigm as the pharmaceutical industry increases its commitment to personalized approaches to drug development, the declining cost of genetic sequencing generates volumes of health care data, and the public policy landscape evolves.

Jonathan Roy, Senior Director and Head of Commercial Diagnostics for **GlaxoSmithKline**, discussed how the biopharmaceutical industry is evolving through cross-industry partnerships to develop diagnostic tests to help target new medicines and help demonstrate the tests' value for payers. "Drug and diagnostic development partnerships must be designed to provide value for all parties," he said, noting that his company is collaborating with **Abbott Molecular** and other diagnostic partners.

Since 2001, the cost of sequencing the human genome has fallen from $300 million to just $5,000, according to the report. But with the opportunity for physicians to use genetic information to optimize patient treatment have come the challenges of analyzing and storing genetic data.

"The personalized medicine paradigm is threatened by an overwhelming amount of data," David King, CEO of the **Laboratory Corporation of America**, told the symposium audience, evoking images of tsunamis of health information inundating providers and overwhelming the still-developing electronic health record system.

Amy Abernethy, M.D., Director, Cancer Care Research Program at **Duke University**, agreed with King. "Better health information technology and clinical decision-support tools are needed to help providers match treatments to patients," she said.

Despite the Food and Drug Administration's approval of two pairs of personalized drug-diagnostic products this past summer to stratify and treat melanoma and non-small cell lung cancer patients, panelists agreed that an unclear regulatory environment hampers personalized medicine's development.

"When evaluating potential deals, we look for management teams who know how to navigate the complex regulatory and reimbursement challenges that personalized medicine companies face," said Eric Linsley, Managing Partner, **Pappas Ventures**. "It's a red flag if they don't know the difference between a PMA and a 510k," he said, referring to two regulatory pathways for medical devices to come to market.

The Case also identifies the steps required to align regulatory and reimbursement systems to speed the adoption of the personalized medicine.

"The case for personalized medicine is not closed," said Brian Munroe, Chairman of PMC's Public Policy Committee. "The document illustrates the regulatory, reimbursement, and educational challenges that still need to be overcome to complete the transition from one-size-fits-all medicine to personalized medicine."

Printed copies of the *The Case for Personalized Medicine* can be requested by contacting PMC at (202) 589-1770; it is also available for free download at http://www.personalizedmedicinecoalition.org/sites/default/files/files/Case_for_PM_3rd_edition.pdf.

PMC IN THE PRESS

The 3rd edition of *The Case for Personalized Medicine*, and the news that since 2006 there has been a five-fold increase in the number of personalized medicine products on the market was covered by **The New York Times** and **Drug Discovery and Development Magazine**, on the **Science Roll** and **The DNA Exchange** blogs and **Expatriate Healthcare** website. A number of PMC members also featured the new publication in their communications, including ***FasterCures'*** **SmartBrief**, **PhRMA**'s **Innovation.org** website, and **Foley and Lardner's Personalized Medicine Bulletin**.

"PMC is working to blaze the way for personalized medicine projects" noted a new e-book published by **Fierce Medical Devices**. Drawing extensively from PMC's recent publications, *Companion Diagnostics: The Future of Medicine* quotes PMC President Edward Abrahams, Vice President Amy Miller, and Founder Brian Munroe. It highlights PMC's leadership in making the business case for personalized medicine while advancing widely-supported policy solutions to address legislative, regulatory and reimbursement challenges facing personalized medicine innovators.

BNA's Life Sciences Law & Industry Report covered a panel discussion held in conjunction with PMC's December 6 public policy meeting. The session, "Gene and Method Patents: Review of Court Cases and the Implications for Personalized Medicine" was held the day before the Supreme Court heard oral arguments in the *Mayo v. Prometheus*.

Investment website **Seeking Alpha** examined "Winners in the Shift to Personalized Medicine" in a review of breakthrough technologies and companies facilitating the transition from one-size-fits-all medicine. Paraphrasing *The Case for Personalized Medicine*, it said, "Physicians have always tried to tailor their therapies to the patients; the only difference is now they have the genetic tools to do it better."

MedCityNews covered the launch of the new edition of *The Case for Personalized Medicine* on November 16, which included a panel discussion of the opportunities and challenges facing personalized medicine. Highlighting a key theme from the discussion, the article concluded: "the FDA must encourage innovation and payers must modernize how they reimburse new technologies."

In a video shot during the Personalized Medicine Conference at Harvard Medical School that was posted on **GenomeWeb**, Amy Miller and Heidi Rehm of **Partners Center for Personalized Genomic Medicine** discuss personalized medicine, public policy and bringing new scientific tools from bench to bedside. The video is available at www.genomeweb.com/video/personalized-medicine-and-public-policy.

An article published in **The Telegraph** in October described how targeted approaches to treatment could help expensive cancer drugs win approval from the UK's National Institute for Health and Clinical Excellence (NICE). Quoting PMC's report on EU reimbursement, the article noted that "patients are often deprived of the most advanced drug and diagnostic treatments while health systems bear the costs of outdated trial-and-error approaches to medicine."

GenomeWeb reported on the PMC's white paper on EU reimbursement and discussed the variation in regulatory, coding and reimbursement methodology across European countries. "The wide variance in the reimbursement system across European nations is often cited as a barrier to market entry for many drug developers and test makers," it noted.

In an October interview with **Pharmaceutical Approvals Monthly**, Edward Abrahams discussed a recent report in *Lancet Oncology* that questioned the value of biomarkers and genetic tests. "Targeted therapies help avoid side effects and treatment in people who won't respond, reducing unnecessary costs," he said.

A **Pharmacogenomics Reporter** article in September about the MODDERN Cures Act, a piece of legislation drafted by patient advocate members of the National Health Council, quoted Amy Miller in discussing how the proposal could bring new treatments to the market. "Drugs that failed for one type of patient may have utility for other types of patients," she said.

Pharmacogenomics Reporter, **The Pink Sheet**, **The Gray Sheet**, **Inside CMS**, **Genetic Engineering & Biotechnology News** and **Personalized Medicine Bulletin** reviewed the history of the Genomics and Personalized Medicine Act (GPMA) and outlined suggestions PMC made that are designed to help Rep. Anna Eshoo (D-Calif.) redraft the bill. Rep. Eshoo is "looking to redraft GPMA in a way that will enjoy wide community support…we only presented her with ideas that the entire community favors," Amy Miller told *Pharmacogenomics Reporter*.