Personalized Medicine
Part 1: Evolution and Development into Theranostics

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This article is the first in a three-part series on the topic of medicine that is geared toward the individual patient. Part 2 will explore key ethical, legal, and regulatory issues facing the future of personalized medicine, and Part 3 will cover the anticipated challenges in implementing pharmacogenomics and genetic testing into routine clinical practice.

Key words: personalized medicine, pharmacogenomics, pharmacogenetics, pharmacodiagnostics, theranostics, personal genomics, human genome, gene testing

INTRODUCTION

Personalized medicine (PM) has the potential to tailor therapy with the best response and highest safety margin to ensure better patient care. By enabling each patient to receive earlier diagnoses, risk assessments, and optimal treatments, PM holds promise for improving health care while also lowering costs.

For device and drug manufacturers, PM provides an opportunity to develop agents that are targeted to patient groups that do not respond to medications as intended and for whom the traditional health systems have otherwise failed. The successful practice of PM requires changes in practice patterns and management strategies for health care practitioners as well as for manufacturers in reimbursement, regulatory practices, and knowledge sharing. New value assessments for PM products, along with return-on-investment (ROI) models, will also be required as these new strategies for pharmaceutical and diagnostic products emerge. All stakeholders will also need to address barriers to implementation if we proceed down the path of harnessing the ability to alter individualized diagnoses and prognoses.

For hospitals, health care providers, and health plan sponsors, PM represents yet another challenge in uncertain times. Innovation in provider and benefit management, along with clarity in regulatory and legal constructs will be required, just as new national health insurance reforms begin to emerge. Allowing for earlier and more efficient decision-making will require redesigning systems of care and payment just as we are now addressing health care insurance reform in the U.S.

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HISTORY AND LANDSCAPE

Over the past six decades, much evidence has emerged indicating that a substantial portion of variability in drug response is genetically determined, with age, nutrition, health status, environmental exposure, epigenetic factors, and concurrent therapy playing important contributory roles. To achieve individual drug therapy with a reasonably predictive outcome, one must further account for different patterns of drug response among geographically and ethnically distinct populations.

These observations of highly variable drug response, which began in the early 1950s, led to the birth of a new scientific discipline arising from the confluence of genetics, biochemistry, and pharmacology known as pharmacogenetics. Advances in molecular medicine have spawned the newer field of pharmacogenomics, which seeks to understand all of the molecular underpinnings of drug response. Commercialization of this research application is now known as personalized medicine (PM). Demonstrated success is emerging for several conditions and treatments, but whether PM will achieve widespread benefits for all remains as yet unrealized.

For the average patient, the benefits have not yet been realized, but ultimately PM will affect the entire landscape of our health care system. Since the mapping of the human genome in 2003, the pace of discovery, product development, and clinical adoption of what we know as PM has accelerated.

PM may be considered an extension of traditional approaches to understanding and treating disease but with greater precision. A profile of a patient's gene variations can guide the selection of drugs or treatment protocols that minimize harmful side effects or ensure more successful outcomes. PM can also indicate an individual's susceptibility to certain diseases before they become manifest, allowing physicians and patients to design a plan for monitoring and prevention. Physicians can now go beyond the one-size-fits-all model of prescribing to make more effective clinical decisions for each patient.

PM offers a structural model for efficient health care; it is preventive, coordinated, and proven. PM works best with a network of electronic health records that link clinical and molecular information to make it easier to help patients and their physicians make appropriate treatment decisions. PM is participatory, engaging patients in lifestyle choices and active health maintenance to compensate for genetic susceptibilities.

Substantial progress has been made toward implementing PM. When all of the pieces of infrastructure fall into place; when we begin to classify and treat diseases not only by their most obvious signs and symptoms but also by their molecular profiles; when physicians combine their knowledge and

judgment with a network of linked databases that help them interpret and act upon a patients' genomic information; when insurance companies pay for tests and treatments that anticipate the needs of the patient as well as react to them; and when regulators insist on using all information available to the physician, including genetic tests, to ensure the safety and efficacy of an approved drug—then PM will be known, simply, as "medicine."

Within five major categories affecting the evolution of PM, the following examples illustrate areas of change that will redefine clinical practice as we know it today:

- real-world demonstrations currently showing how PM is:
  - shifting emphasis in medicine from reaction to prevention.
  - enabling the selection of optimal therapy and reducing trial-and-error prescribing.
  - making the use of drugs safer by avoiding adverse drug reactions.
  - increasing patient compliance with treatment.
  - reducing the time and cost of clinical trials.
  - reviving drugs that failed early in clinical trials or on the market, based on genomics advances that demonstrate variations in receptors that may make the drug work well for a select group within the general population.
  - reducing the overall cost of health care.
- key technology advances, making PM possible and at a faster pace of growth, including:
  - new tools to decode the human genome more rapidly and accurately using physically smaller yet more powerful machines.
  - large-scale studies and sample repositories that help link genetic variations to disease across multiple countries and continents.
  - health information technology (HIT) that fosters the integration of research and clinical data, which is already growing faster in the U.S. as a result of aggressive government incentives for adoption.
- explorations of "personal genomics" and direct-to-consumer genetic testing and how the field affects PM.
- information about ground-breaking policy, legislation, and government initiatives in place and in development to support PM, including the Genetic Information Nondiscrimination Act (GINA), passed in 2008, and proposed changes to health plan reimbursement policies.
- real-world examples of hospitals, regional health care systems, and educational institutions promoting clinical adoption of PM through research, clinical practice, and medical education reform.

PHARMACOGENOMICS AND GENE TESTING

Physicians have known for centuries that certain medicines work better in certain patients, but they have not learned why and surely have not been able to predict which drug will be safe and effective for any particular patient. For instance, 10 people who take the same medication for seizures, heart disease, or cancer might respond very differently. One person might have severe, even life-threatening side effects, whereas another might experience few, if any, adverse effects and may seem to sail through treatment; or an anticancer drug may shrink a tumor in one person but not in another.

One major cause of this difference is that people inherit variations in their genes, and even slight variations can affect how the body responds to certain medications. Pharmacogenetics is the science that studies how genetic variations in individuals affect their response to medications. Pharmacogenomics is the broader study of how genetic variations affect drug development.

Generally speaking, pharmacogenetics and pharmacogenomics deal with the genetic basis underlying variable drug responses in individual patients. The traditional pharmacogenetic approach relies on studying sequence variations in candidate genes that are thought to affect drug response, whereas pharmacogenomic studies encompass the sum of all genes (i.e., the genome). Numerous genes may play a role in drug response and toxicity, introducing a daunting level of complexity into the search for candidate genes. However, most currently available drugs are metabolized by the enzymes in the cytochrome P450 (CYP 450) system. These enzymes, and variations thereof, are responsible for individual variation in absorption, distribution, metabolism and excretion of drugs. Hence, just a minor variation, such as one nucleotide base "misspelling," can have clinically profound consequences. The high speed and specificity associated with newly emerging genomic technologies enable broader identification within the entire genome.

These new technologies have essentially spawned a new discipline—pharmacogenomics—that seeks to identify the variant genes affecting the response to drugs in individual patients and, in so doing, can identify disease susceptibility genes representing potential new drug targets. All of this is beginning to lead to novel approaches in drug discovery, an individualized application of drug therapy, and new insights into disease prevention.[1]

In drug therapy today, the approach is to treat large patient populations as groups, irrespective of the potential for individual, genetically based differences in drug response. In contrast, pharmacogenomics may help focus effective therapy on smaller patient subpopulations that, although demonstrating the same disease phenotype, are characterized by distinct genetic profiles. Whether this approach will result in better, cost-effective treatment is still unclear.[1]

Genes are segments of DNA that are found in all human cells, and they can influence a person's response to medications. DNA is essentially a key part of our interactive chemical operating system in the body, instructing the body how to behave and interact on a cellular level. A basic gene can have many different forms and chemical messengers. It is those interactions that also affect drug activity in the body.

For instance, consider genetic variation in codeine metabolism. Roughly 5% of the population do not catalyze codeine to morphine; for that reason, codeine is ineffective because it provides no pain relief. Codeine converts to morphine using the CYP 2D6 enzyme. However, genetic variation in this enzyme can result in too little or too much enzymatic action, resulting in non-conversion or too little absorption (hence no therapeutic effect). For example, a patient may have a genetic variation

that makes the drug stay in the body longer than normal, causing serious adverse effects, or another person might have a variation that makes the medication less potent. Researchers and clinicians are trying to identify and then record as many genetic variations as possible. When a variation is identified, scientists might be able to match it up with a response to a particular medication and then develop a personalized approach to medicine.[2]

Pharmacogenomics, for example, is demonstrating benefit for a variety of conditions. One common example requiring the use of various medications that have numerous toxic effects is breast cancer. Today, oncologists can choose a medication, such as trastuzumab (Herceptin, Genentech) based on standard drug therapy and dosing guidelines for that disease. They can also consider such factors as a patient's weight, age, and medical history and the reactions of other blood relatives to the same drug.

Despite all of that, no one knows how an individual will react to a specific medication. A patient may experience terrible side effects or none at all. The medication might put the breast cancer into remission, or it might have no effect. Consequently, an individual may have to return many times for a dosage adjustment or to be switched to another drug. This is how medication choices generally work today—it is often a matter of trial and error—which, regrettably, can result in side effects great enough to cause death, serious irreversible conditions, and costly hospitalizations.

Pharmacogenomics offers the promise of speeding up this process while optimizing outcomes. Before a breast cancer patient takes a single dose of medication, for instance, a blood test would be done to see which genetic variations are present. The test may show a genetic variation that is likely to adversely affect how that patient will respond. In such a case, the physician can skip that drug and prescribe a different one, or the dose can be altered to match the patient's genetic profile.[2]

To exploit these opportunities in genetic medicine, novel technologies must be developed, legal and ethical questions must be clarified, health care professionals must be educated, and the public must be informed about the implications of genetic testing in drug therapy and disease management.[1]

The field of pharmacogenomics is promising. In fact, a handful of tests are already commercially available that can detect some of these genetic variations and predict how a person is likely to respond to certain drugs, and many more are under study. However, pharmacogenomics is not yet widely used; we need to know more to determine just what pharmacogenomics can offer.

Although current uses are limited, pharmacogenomics has the potential to offer many benefits on a broader scale within the next several years. Some of the most important benefits include:

1. **Better medication selection.** Each year, thousands of Americans die from adverse reactions to medications, and more than two million people are hospitalized. Although drugs generally undergo rigorous reviews and testing processes before they are approved for sale, there is often no way to predict how a certain individual will react to a specific agent. Even if a medication appears safe for most people, some patients may experience a toxic reaction because of variations in their genes. Pharmacogenomics may be able to predict those who are likely to have a bad reaction to a drug before they ever take it and those who will be likely to respond successfully.

2. **Safer dosing options.** Following FDA approval and clinical trial requirements, the dosage of a medication either is a standard one-size-fits-all dose, or it is based on key factors such as liver or kidney function, weight, and age. These parameters might not be sufficient, however. A standard dose may prove toxic to one person and not another because of a genetic variation. Using pharmacogenomics, doctors can avoid this problem by predicting the optimal dose to use, not just which medication is right for an individual patient.

3. **Improvements in drug development.** Pharmaceutical companies must often spend years conducting research on and clinical trials of a new drug before it goes to market. Diagnostic and device firms, along with pharmaceutical companies, typically have to test a product in many people to ensure that it is safe and effective. Pharmacogenomics may help these companies focus their testing. As an example, if a company knows ahead of time that someone has a genetic variation that will cause an adverse reaction to a drug or that will make a drug ineffective, those patients can be excluded from the clinical trial. This may speed up the clinical trial process and target the specific population that can be helped by any one medication.

WHAT IS THE PROMISE? PHARMACODIAGNOSTICS AND THE MARKET IN 2011 AND BEYOND

Pharmacodiagnostics (theranostics) is considered the pathway to what has been termed "personalized medicine"—the use of molecular analysis to achieve optimal medical outcomes in the management of disease or a patient's predisposition to disease. As such, PM promises to bring about a new standard of health care, with the potential to accelerate clinical trials, achieve better outcomes, and satisfy patients.

About 0.1% of the 3 billion bases of DNA differ from person to person. These polymorphisms and the methods of using them can assist with designing clinical trials and epidemiological studies, and they serve as links to human disease and drug response. A natural next step, from bench research to clinical practice, is to move to PM and theranostics—the marriage between diagnostics and therapeutics—commonly referred to as companion diagnostics.

In recent years, our knowledge of the genome, proteome, and metabolic pathways has increased exponentially, given improvements in research techniques and the population of databases. The field of theranostics thus allows health care practitioners to use detailed information about a patient's genotype and to monitor the individual's therapeutic regimen and assess the patient's response to it. If there is a test to predict adverse reactions or resistance to a drug or to target patient selection for a clinical trial, the risk of clinical failure drops tremendously. It would seem that developing a drug based on genetic information might also shorten the time needed for this process, which today takes about 12 years, according to many industry sources, including the FDA.

More importantly, fewer dollars should be required from research and development (R&D) to the clinic, then on to the

market. Various R&D manufacturing firms and clinical research organizations, including the National Institutes of Health (NIH), are exploring how theranostic applications can be applied to simplify the drug-selection process for clinical testing, to refine clinical testing, and to develop more focused clinical trials that provide enhanced knowledge of a drug or biologic medication in humans within shorter time frames. In addition to the decreased time and expense needed to produce new medications, more precise prescriptions, monitoring, and management, thanks to PM, offer opportunities for reduced costs throughout the health care system.

Given the continual rising costs of health care in the U.S., increasing patients' out-of-pocket contributions for health care, as well as the recognition of genetic variations and heterogeneity of disease, we should realize that these factors inevitably necessitate individualized therapeutic decisions. The number of serious adverse drug events reported to the FDA more than doubled between 1998 and 2005. Periodically, prescription drugs, including biologics, are pulled from the market because of serious safety problems. Recent examples include rofecoxib (Vioxx, Merck), valdecoxib (Bextra, Pfizer), and natalizumab (Tysabri, Elan). These highlight the importance of public health safety and illustrate the need for improved systems to better manage the risks associated with use of all categories of regulated prescription drugs.

A handful of so-called theranostic products on the market have already led to successful treatment outcomes for patients with cancer and HIV infection. Still, the number of such commercialized products today is low. Examples include:

- Dako's Hercep genotyping test for trastuzumab.
- Myriad's *BRCA1/BRCA2* test to determine breast and ovarian cancer risk.
- Roche's AmpliChip CYP 450 Test, which predicts a patient's response to various therapies.
- Monogram's Trofile Co-Receptor Tropism Assay for HIV infection.
- Bayer's Trugene genotyping HIV tests.

Other examples of theranostic products in development are:

- DNAPrint Genomics' Statinome, designed to measure the likelihood of developing myalgia as an adverse response to the commonly prescribed statins such as atorvastatin (Lipitor, Pfizer) and simvastatin (Zocor, Merck).
- DermTech's noninvasive skin test for melanoma.

Theranostics and PM have the potential to transform the medical industry and the overall approach to health care. For the first time in the history of the U.S., the largest proportion of the population is older than 65 years of age. Clearly, widespread adoption of theranostics has the potential to eliminate unnecessary treatment that would be ineffective or even dangerous, and the end result would be major drug cost savings for patients and the entire health care industry.[3]

Although theranostics is not expected to be inexpensive, the offsetting cost reductions in other areas of health care resource utilization may be very significant in addition to the enhanced therapeutic outcomes and patient satisfaction with the health care system.

A 2008 OpEd article by Michael O. Leavitt, former Secretary of the Department of Human Health and Services, and Raju Kucherlapati, Professor of Genetics and Medicine at Harvard Medical School, discussed common scenarios in asthma and cancer diagnosis and treatment that relate to the evolution of PM.[4] The writers used examples of PM in practice, but the term personalized medicine reflects the growth of scientific understanding and medical tools that may help to custom-tailor care at a new level. Such tools can match treatments to individual genetic variations or may be able to differentiate between subtypes of disease—and that can take more of the guesswork out of medicine, making health care decisions more precise and effective, often at lower cost, they argue.

The opportunity of PM stems from advances in molecular biology, especially the explosion of new knowledge of the human genome. The tools of PM can help direct the right treatment to the right patient. The potential improvements in health as well as savings in health costs are vast, according to Leavitt and Kucherlapati.[4]

Likewise, a new definition of disease by patients and physicians alike needs to be more precise in order to improve health care for the individual. With PM, they argue, we can improve the current paradigm.[4] Over time, increased knowledge of genetics and molecular biology should also enable detection of disease before symptoms appear, making it possible to treat earlier and perhaps event pre-empt the disease, they state.[4]

As a prelude to the health reform debates in 2009, the writers also pointed out that PM, as transformative as it promises to be, cannot be implemented if it is going to result in a great increase in health care costs. However, they claim that the practice of PM can be an important part of achieving higher value in health care. They suggest that more accurate dosing, enabled by a relatively low-cost genetic test, might save as much as $1 billion per year while delivering higher-quality care and better health.[4]

WHEN WILL WE SEE PERSONALIZED MEDICINE AT THE LOCAL PHARMACY?

Prescription benefit management (PBM) companies have already implemented their plans to offer genetic testing as part of the prescription-filling process. Pharmacogenomic testing is being used commercially for some commonly prescribed drugs such as tamoxifen (Nolvadex, AstraZeneca) for cancer and warfarin (Coumadin, Bristol-Myers Squibb) to manage blood coagulation.

In the current procedure, a PBM company contracts with large drugstore networks. When prescriptions for some drugs arrive, the company contacts the physician to state that a genetic test is available, which may promote more appropriate prescribing of that medication. The patient may then be offered the genetic testing, but it wouldn't be required. A physician must still authorize the test, and in all likelihood a patient's decision will rest on whether or not the test is covered by insurance.

Supporters of this application of pharmacogenomics say that this procedure can improve patient safety, health outcomes, and decrease overall health care costs so that the right drugs will be given to the right patients. This strategy may also

provide an opportunity to advance the field of pharmacogenomics by collecting data on genetic testing results and drug effectiveness, including costs of therapy and avoiding adverse events.

Others are concerned about the privacy of genetic testing information and worry that the science of pharmacogenomics is premature. (Privacy will be discussed in Part 2 of this series.) Drug metabolism is based not only on our genetic makeup; it is also affected by many factors, such as epigenetics, exposure, body size, and age. In addition, because pharmacogenomics is a relatively new science, insurance companies might or might not pay for the cost of genetic testing.

KEY GAPS AND BARRIERS

The field of pharmacogenomics is still in its early stages. Millions of genetic variations may exist, and identifying them all could take many years—if it's even possible. In addition, how one person responds to a medication might not be determined by only one gene but, instead, by many genes interacting with each other. Combing through this complicated genetic map is expensive and time-consuming.

Some types of PM, based on the science of pharmacogenomics, are in use today—but on a limited basis. A few tests are available that can help predict likely responses or poor reactions to certain medications. For example, let us consider a woman with atrial fibrillation who receives the widely used anticoagulant drug warfarin. A genetic test costing approximately $350 is performed to look for variations in two specific genes that affect the body's metabolism and response to the drug. Combined with other factors, the test indicates a proper dosage range for this patient. Thus, with a test that considers the genetic profile, the patient avoids experiencing uncontrolled bleeding, life-threatening blood clots, or a risk of stroke that can accompany the use of this powerful drug.

Several other genetic tests are available:

1. **CYP 450 genotyping test**. A group of enzymes (known as CYP 450), as indicated earlier, is responsible for metabolizing more than 30 types of medications. The test can determine how quickly and effectively these agents are eliminated from the body. Depending on an individual's genetic makeup, the body might not break down the medication fast enough, instead allowing drug levels to accumulate, resulting in severe side effects. Conversely, a patient might have a genetic variation that causes the body to break down the medications too quickly before they have a chance to work. The CYP 450 test can be used to determine dosing and effects of specific antidepressant medications, anticoagulants such as warfarin, proton pump inhibitors, and a number of other agents.

2. **Thiopurine methyltransferase test.** An enzyme called thiopurine methyltransferase (TPMT) breaks down a chemotherapy drug called thiopurine, which is used to treat some leukemias and autoimmune disorders. Some people have genetic variations that prevent them from producing this enzyme. As a result, thiopurine levels can build up in the body, leading to severe toxic reactions. A blood test can be used to check for this variation before treatment begins, resulting in better dosing guidelines for clinicians.

3. **UGT1A1 TA repeat genotype test.** This test is used to detect a variation in a gene that affects the UGT1A1 enzyme. This enzyme determines how the body breaks down irinotecan (Camptosar, Pfizer), a chemotherapy drug for treating colorectal cancer. In patients with a deficiency of this enzyme, the medication can build up to toxic levels, possibly causing suppression of the bone marrow, infection, and even death. Doctors can test for this genetic variation before treatment starts and then customize the dosage to prevent a toxic buildup of the drug. Alternatively, if a patient has normal levels of the UGT1A1 enzyme, the test may help to ensure that the dosage of irinotecan won't be lower than necessary.

4. **Dihydropyrimidine dehydrogenase test.** The medication 5-fluorouracil (5-FU), along with its related compounds, is one of the most commonly used chemotherapy agents. Some people have a genetic variation that results in a decrease in the dihydropyrimidine dehydrogenase enzyme, which is responsible for breaking down 5-FU. As a result of this deficiency, some people may experience severe or even fatal reactions to 5-FU. Knowing ahead of time which patients have this deficiency can help doctors tailor the dosage to prevent a dangerous adverse reaction.

In the future, pharmacogenomics could have an expanding role in the practice of medicine. Regardless of the promise of PM, pharmacogenomic testing is not yet widely available and it remains an uncertain science. Despite periodic news reports and other sources of information proclaiming that pharmacogenomics or other types of PM can already offer revolutionary results today, it is hoped that this will be the case in the future.

CONCLUSION

In this article, our first in this series on PM, we've explored and reviewed concepts to better inform, educate, and provide a sense of direction for health care decision-makers in the near future. Understanding the history, definitions, and various contemporary marketplace activities can assist in making the necessary plans or decisions to incorporate PM in hospitals, health plans, or health benefit strategies and coverage.

Unlike PM, conventional drug therapy typically considers large patient populations to be relatively homogeneous (the one-drug-fits-all approach). Only recently have genetically based differences in response to a single-drug or multiple-drug treatment been adopted and accepted. The 20th century brought us a broad arsenal of therapies against all major diseases of the time: infections, cardiovascular disease, cancer, and mental disorders. However, although drug therapy continues to treat disease, it has often failed and has caused substantial adverse or unintended effects. Moreover, the worldwide use of drugs in the 21st century has revealed substantial and documented interindividual differences in therapeutic response. Any given drug can be therapeutic in some individuals but ineffective in others, and some individuals experience adverse drug effects whereas others are unaffected.

Diagnostic and drug research today seeks genomic and molecular-level targeting of cells, tissues, and organs. Often, distinct submolecular mechanisms underlie intended therapeutic and unintended adverse effects that may hold the potential to optimize or, in some cases, revolutionize medical therapeutics.

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PM also offers an opportunity to enhance the value of currently approved drugs with limited market share because of significant toxicity or limited efficacy, enabling prescribers to identify patients for whom they can be both effective and safe. Such recognition of interindividual differences in drug response is an essential step toward optimizing therapy. Many times we have already seen that the marriage of drug-related diagnostics can provide better utilization parameters for new products as well as improve safety profiles or efficacy of older chemically based medications.

Overall, we can hope that PM will drive all stakeholders toward earlier and more efficient decision-making on a wide variety of medical care choices. Such decision-making and subsequent utilization of health care resources, ideally, will require redesigning systems of treatment and payment in the U.S. and at a more rapid pace than has been seen to date.

Individualizing drug therapy raises a number of issues with enormous practical consequences that will be explored further in this series. The dynamic complexity of the human genome, multigenic disease origins, and involvement of numerous genes in drug response impede effective, routine clinical application.

Many of the identified elements being evaluated for change in the health care system have been visible or active at various times over the previous 60 years. In this second decade of the 21st century, health care will be reframed and designed for at least the next decade. PM provides a kinetic energy to foster change in the health care system.

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ADDITIONAL RESOURCES

American Clinical Laboratory Association. Results for Life: Lab Testing: Better Health for Improved Outcomes. Available at www.labresultsforlife.org.

Laboratory tests detect strep throat, diabetes, heart disease, allergies, cervical cancer, lead poisoning, HIV infection, kidney ailments, and West Nile Virus—and that's just a start. The most important job lab tests do is to provide information, the single most important thing that physicians and patients need to bring disease under control. "Results for Life" tells the story of why that matters in patients' lives.

Personalized Medicine E-Symposium (archived). Available at: www.pharmacogenomicsociety.org.

Hosted by the International Society of Pharmacogenomics, the symposium enables scientists, government officials, regulators, drug manufacturers, and medical professionals worldwide to share their knowledge about personalized medicine. Webcasting technology is accessible to listeners with a computer, a sound card, and an Internet connection.

FDA Unveils Critical Path Opportunities List Outlining Blueprint to Modernizing Medical Product Development by 2010. March 16, 2006. Available at: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108619.htm.

The Department of Health and Human Services (DHHS) and the FDA released an initial list of priority research projects that could advance innovation in medical products. The announcement of the Critical Path Opportunities List signals the next major step in FDA's Critical Path Initiative, aimed at modernizing medical product development, so new medical discoveries are brought to patients more rapidly and at a lower cost. The Opportunities List outlines an initial 76 projects to bridge the gap between the quick pace of new biomedical discoveries and the slower pace at which those discoveries are currently developed into therapies.

Guidance for Industry and FDA Staff. Pharmacogenomics Tests and Genetic Tests for Heritable Markers. June 19, 2007; draft guidance issued on February 9, 2006. Available at: www.fda.gov/downloads/Medical Devices/DeviceRegulationandGuidance/GuidanceDocuments/ucm 071075.pdf.

Health Information Technology Leadership Panel: Final Report. Lewin Group. Available at: www.hhs.gov/healthit/HITFinalReport.pdf.

The panel was convened to examine the importance of investing in health information technology, particularly regarding the roles of government and the private sector in its widespread implementation. Panel members were executives in widely recognized companies that purchase substantial levels of health care for their employees.

Evaluation of Genomic Applications in Practice and Prevention (EGAPP). Available at: www.egappreviews.org.

This three-year model project by the Centers for Disease Control and Prevention (CDC) is now under way. The goal is to establish and test a systematic, evidence-based process for evaluating genetic tests or other applications of genomic technology that are in transition from research to practice and to disseminate that information to health care providers, consumers, and other important stakeholders.

Genomics at FDA: *Guidances, Concept Papers, and MaPPs [Manual of Policies and Procedures].* Available at: www.fda.gov/Drugs/Science Research/ResearchAreas/Pharmacogenetics/ucm083374.htm.

Information on activities at the FDA related to incorporating genomics into the regulatory process is provided.

Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS). Office of Biotechnology Activities. Available at: http://oba.od.nih.gov/SACGHS/sacghs_ home.html.

The DHHS established SACGHS to serve as a public forum for deliberations on the broad range of human health and societal issues raised by the development and use of *genetic technologies and, as warranted, to provide advice on these matters.*

Pharmacogenetics Research Network, National Institute of General Medical Science. Available at: www.nigms.nih.gov/Initiatives/PGRN.

The network is a nationwide collaboration of scientists who are studying the effect of genes on people's responses to a wide variety of medications.

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Understanding Health Information Privacy. Available at: www.hhs.gov/ocr/privacy/hipaa/understanding/index.html.

The HIPAA Privacy Rule provides federal protections for personal health information and gives patients an array of rights with respect to that information. The rule also permits the disclosure of personal health information needed for patient care and other important purposes. The Security Rule specifies safeguards to ensure the confidentiality, integrity, and availability of electronic protected health information.

Chisholm R. What is Personalized Medicine? 2010 Science in Society. Available at: http://scienceinsociety.northwestern.edu/content/articles/2008/what-is-personalized-medicine?gclid=clatmksg_aecfufm5qodbhzifg.

Northwestern University's Center for Genetic Medicine offers one of the only dual-degree programs available in genetic counseling and medical humanities and bioethics. Available at: www.cgm.northwestern.edu/cgm/Academics/Graduate-Program-in-Genetic-Counseling.

The Impact of Personalized Medicine Today. HealthLeaders Media, April 30, 2010. Available at: www.healthleadersmedia.com/content/led-250352/The-Impact-of-Personalized-Medicine-Today-60k.

This report looks at how progressive health systems, researchers, and physicians are working together to bring the practical benefits of personalized medicine to health care delivery. ■