

# Personalized Medicine

## Issues affecting adoption of personalized medicine

### Introduction

*Personalized medicine offers a new paradigm for the development of drugs and the practice of medicine. While the potential benefits of personalized medicine include development of drugs that are safer and more effective for specific disease populations, such benefits cannot be realized until certain obstacles to adoption are removed. Obstacles in public policy include uncertain regulatory requirements, insufficient insurance reimbursement for diagnostic tests linked to pre-emptive care, incomplete legal protections to prevent genetic discrimination, the lack of a comprehensive healthcare information technology system, and a medical education system that has not taught physicians how to incorporate personalized medicine diagnostics or pharmacogenomics into their practices. A supportive public policy environment would address each of these issues, and provide incentives to reinforce emerging business models that accelerate the co-development of drugs and diagnostic tests. Understanding all of these key factors – from obstacles to incentives – is a necessary step in determining how to apply resources to influence the direction of personalized medicine and its progress.*

### Genetic privacy and non-discrimination

Key issues:

- Federal and state laws provide only a patchwork of protection against misuse of genetic information.
- The Genetic Information Nondiscrimination Act would fill gaps in current laws protecting genetic information (e.g., HIPAA), but it has not yet been passed by Congress.
- Surveys indicate that the public may be inhibited from full participation in personalized medicine research or clinical care, unless full genetic privacy protections are put into place.

Currently, federal and state laws offer only a patchwork of protection against the misuse of genetic information (Council for Responsible Genetics 2004). A number of key acts of federal legislation provide the foundation for the protection of medical and genetic information in the United States, including the *Privacy Act* of 1974 (5 U.S.C. § 552a), the *Electronic Communications Privacy Act (EPCA)* of 1986 (18 U.S.C. §§ 2510-2521, 2701-2710), the *Americans with Disabilities Act (ADA)* of 1990 (42 U.S.C. § 12101 et seq.), and the *Health Insurance Portability and Accountability Act (HIPAA)* of 1996 (42 U.S.C. § 1320d et seq.) The latter strikes a balance between facilitating exchange of medical records among healthcare providers and public health officials, and the need to ensure privacy of personal medical information. HIPAA rules filled some gaps in protections against discrimination by shielding workers from unauthorized disclosure of their medical information to employers. However, insurers may still request genetic information, or require genetic tests of policy applicants. Enforcement of HIPAA rules is also fairly weak, relying solely on administrative action.

The *Genetic Information Nondiscrimination Act (GINA)* of 2005 would explicitly prohibit employers and health insurers from discriminating against individuals on the basis of their genetic risk factors, thus filling certain gaps in HIPAA privacy protections. As of March 2007, GINA had not been enacted: a Senate version (S.306) was passed by a unanimous 98 to 0 vote in the U.S. Senate in 2005, as well as in the 110<sup>th</sup> session (S.358), and a House of Representatives bill (H.R.493) is in committee.

**State legislation.** In the absence of uniform federal regulations around genetics privacy and discrimination, many states have established their own regulations, resulting in an uneven landscape of protection, which works against the adoption of personalized medicine.

Several surveys have been conducted to gauge public opinion around the use and protection of genetic information (White *et al* 2003; Womak 2005; JHU 2004; VCU 2001). The surveys revealed that more than two thirds of the public is concerned about potential misuse of genetic information. About one third of the public say that, if unresolved by legal protections, genetic privacy concerns might prevent them from making use of genetic tests or participating in genetic research.

PMC believes that all genetic information, including family history, deserves strong and enforceable protections against misuse in health insurance and employment, and PMC supports passage of the Genetic Information Nondiscrimination Act. The benefits of personalized medicine can only be fully realized when the fear of genetic discrimination, and its actual practice, are eliminated from the healthcare system.

### **Healthcare worker attitudes, awareness and education**

Key issues:

- Physicians and other healthcare providers are “gatekeepers,” making many of the decisions related to using personalized medicine products and approaches.
- Current healthcare workforce generally does not have the training to administer personalized medicine.
- Medical school curricula have not incorporated personalized medicine concepts and tools.

Physicians and other healthcare providers will have to administer or advise on the application of a growing number of molecular and genetic tests and pharmacogenomic drugs, make treatment decisions based on more predictive evidence and estimations of risk, utilize information systems for managing patient care, and deal with new ethical and legal issues that arise from molecular and genetic testing. However, a survey conducted by the National Cancer Institute on physician use of genetic testing (Wideroff *et al.* 2003) suggested that the healthcare workforce, primarily physicians, does not have the training or confidence to administer personalized medicine.

Medical education curricula have generally not incorporated personalized medicine concepts (including genetics, genomics and pharmacogenomics). Only a few comprehensive genomic education programs exist worldwide. These include programs at the University of California San Francisco, Harvard Medical School, and Duke University (Abrahams *et al.* 2005). Despite these pioneering efforts, the current availability of genetics training for physicians does not meet the anticipated need and the current educational infrastructure would have to be updated in order to facilitate adoption of personalized medicine. Non-physician specialists, including nurses, pharmacists, and genetic counselors may also require updated educational and certification programs in genetics and personalized medicine.

PMC believes that extensive education will be required for practicing physicians, medical school students, and a range of healthcare professionals, to enable them to apply an ever-expanding set of molecular approaches for individualized care for their patients. Towards that end, PMC is collaborating with its member organizations that have expertise in genetics and education to develop a unique set of curricula.

### **IT implementation**

Key issues:

- Healthcare information technology (HIT) is needed to link patient information to genomic research, to enhance the discovery of new personalized therapies.
- Significant political will has gathered behind HIT, but adoption in hospitals and especially individual physician practices lag.
- System standards, financial incentives for small practices, and removal of IT investment barriers, are required to ensure widespread adoption of HIT.

Healthcare information technology (HIT) has a significant role in successful adoption of personalized medicine. Standardized data structures are necessary to characterize and record diseases by their molecular profiles, allowing physicians to coordinate and optimize individual patient care based on molecular and genomic information. Integrated health system networks can lead to better-tailored treatments as responses are compared between patients with similar conditions and genetics, long-term health and economic outcomes are calculated, and biomarker-disease associations are identified and validated by linking scientific and clinical research.

Unfortunately, the current state of medical information in the United States is far from adequate. Today, about 68% of hospitals have either fully (11%) or partially (57%) implemented electronic health records (EHRs) (AHA 2007). A survey by the Centers for Disease Control indicated that one-quarter of office-based physicians used fully or partially implemented EHRs in 2005, with most pegging their delays in adoption to the cost of purchasing and maintaining the systems. In order to encourage more even and standardized adoption among independent physicians, specialists, private hospitals, clinical laboratories, pharmacies and other healthcare providers, the federal government has begun to take on the role of providing support and incentives.

In 2004, the President issued Executive Order 133356 to “provide leadership for the development and nationwide implementation of an interoperable health information technology infrastructure to improve the quality and efficiency of health care.” The order established the position of a national coordinator for health IT reporting to the Secretary of HHS and called for the nationwide implementation of interoperable EHRs within 10 years. That action has set in motion several initiatives, including bipartisan Congressional legislation, which acknowledges the importance of, and supports the implementation of EHRs. Moving to full investment in healthcare IT and implementation, however, may require financial incentives, and the removal of certain barriers to adoption among hospitals and physician practices (e.g., addressing federal anti-kickback and physician self-referral laws), as well as guarantees of medical records privacy.

PMC actively supports the creation of a national health information network that enables the interoperable exchange of digital biomedical information securely between a diverse set of stakeholders in the healthcare ecosystem. This infrastructure should also take into account the unique needs of the basic, clinical and translational research community. PMC supports the examination of potential incentive structures to induce investment in HIT by all healthcare providers, from solo practitioners to large hospitals.

## Regulation

Key issues:

- Industry requires clear pharmaceutical/diagnostic co-development regulatory guidelines that will foster innovation in this space.
- All stakeholders need confidence in the process by which products are developed and regulated.
- Industry requires coordination and alignment amongst HHS agencies for regulating complex diagnostic applications.
- Industry supports a genetics specialty area within CLIA regulations.
- FDA requires more genomic data and input from industry (through voluntary submissions) to help develop new regulatory guidelines.

The regulatory climate in the United States has been favorable for personalized medicine, although currently regulations are in a formative state. The U.S. Food and Drug Administration (FDA) has demonstrated commitment to ensuring that regulation does not stand in the way of personalized medicine by developing guidance for voluntary pharmacogenetic data submissions (FDA March 2005); publishing a draft guidance for pharmacogenetic and other genetic tests, including microarrays (FDA 2006); publishing a concept paper for co-development of pharmacogenomic drugs and diagnostics (FDA April 2005);

establishing labeling regulations (21 CFR 201.57) that recognize the relationship between genotype and drug response; and establishing a precedent for microarray diagnostics regulation by approving the first such device for rapid genotyping of 29 CYP450 variants important for drug metabolism.

The industry is awaiting a definitive guidance on the co-development of pharmaceutical drugs and diagnostics. Business models for drugs and diagnostics have traditionally taken a path of separate development, but adaptation of business models to the new reality of linked development, and the diagnostic/drug products meant to benefit patients, will likely be delayed until greater clarity is achieved on what the FDA expects for combination product clinical trials and regulatory submission.

The diagnostics industry has expressed concern that two recently released guidances, the Draft Guidance for Industry, Clinical Laboratories, and FDA Staff on In Vitro Diagnostic Multivariate Index Assays and the Draft Guidance for Industry and FDA Staff for Commercially Distributed Analyte Specific Reagents (ASRs), might inhibit the development of tests profiling multiple biological entities, such as proteins or genes. Such tests are currently regulated under Clinical Laboratory Improvement Amendments (CLIA) provisions, which cover laboratory-developed or “home brew” tests that are provided not as a kit, but as a service offered by a clinical reference laboratory. In contrast to CLIA, the FDA regulatory pathway requires a careful pre-market review of not only its analytical accuracy, but also its clinical validity. While some manufacturers see the proposed regulation as potentially hindering development of new products that already have controls on analytical and clinical validity as well as clinical utility through market forces, others see the potential for new regulations to level the playing field and foster greater confidence (and reimbursement) for well-validated products.

Industry players have tried to address the issues around quality control for complex genetic tests by advocating for a genetics subspecialty within CLIA to ensure laboratories meet certain standards. Federal advisory committees have recommended such a step as far back as 1988. In 2000, the U.S. Department of Health and Human Services (HHS) published a Notice of Intent to propose a rule to create a genetic testing specialty, and in April 2006, the Centers for Medicare and Medicaid Services (CMS) placed the issuance of a proposed rule for a genetic testing specialty on its semi-annual regulatory agenda. According to the Personalized Medicine Coalition, the creation of a genetic testing specialty under CLIA would help ensure the accuracy and reliability of genetic tests, ensure personnel technical proficiency, increase the public’s trust in genetic testing and foster the promise of personalized medicine.

The PMC sees FDA’s proactive stance on personalized medicine as an important step towards creation of a clear regulatory environment for molecular diagnostic tests and related drugs. A definitive guidance on the co-development of drugs and diagnostic tests will ensure continued innovation and accelerate the translation of these products from the laboratory bench to the patient’s bedside.

The PMC also encourages the creation of a genetic testing specialty under CLIA, which would help ensure the accuracy and reliability of genetic tests, increase the public’s trust in genetic testing and encourage reimbursement by healthcare payers.

## **Reimbursement**

Key issues:

- Medicare and private insurers generally do not have policies to cover pre-emptive care.
- Insurers generally do not recognize contribution of collateral services (laboratory services, genetic counseling, etc.) for equitable coverage of personalized medicine.
- Insurers require more data on healthcare and economic outcomes for personalized medicine approaches to support reimbursement decisions.
- Regionally fragmented Medicare reimbursement policy hinders adoption of genetic tests.

- CPT coding system needs to be modernized to incorporate, fairly compensate, and encourage new technology and services.

Current reimbursement policies from Medicare and most private insurers fall short of what is needed to ensure patients have access to personalized therapies (reviewed in Secretary’s Advisory Committee on Genetics, Health, and Society 2005 report on “Coverage and reimbursement of genetic tests and services” SACGHS 2005). Personalized medicine challenges current assumptions made in coverage decisions. Compared to traditional diagnostics, certain imaging, molecular and genetic tests provide more precise information about future susceptibility to disease and response to pharmaceuticals. Insurers typically do not provide coverage for tests of disease susceptibility. There are also few policies that would consider a one-time test (such as a CYP450 test for drug metabolism) that provides data on a host of conditions or pharmacogenomic effects relevant to the patient’s entire lifetime of healthcare.

CMS states that, “tests for screening purposes that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury are not covered except as explicitly authorized by statute.” (Social Security Act sections 1862(a)(7) and 1862(a)(1)(A)). Such a policy leaves little room for the predictive screening and preventive treatment tools promised by personalized medicine.

A further hindrance to insurance coverage is that payers (and Medicare CPT codes) have not yet recognized the phalanx of providers and services required to ensure genetic tests are properly interpreted and used to the patient’s benefit. Treatment typically could require the services of the primary care provider or specialist, a laboratory specialist who conducts the test, a clinical geneticist to assist in developing a diagnosis and treatment strategy, and a genetic counselor to provide the patient with educational support and counseling on how to manage the genetic condition. Many of the services provided by these specialists are not eligible for reimbursement, or are undervalued under current payer policies.

Payers have stressed that prognostic tests (whether molecular, genetic, or based on some other technology) would have to be subjected to a rigorous assessment to determine their cost-effectiveness and impact on health outcomes in order to justify coverage. Unfortunately, there is little clinical data on health outcomes and cost-benefit for these tests and their associated treatments. Personalized medicine suffers from an inhibitory cycle of insufficient economic evidence, leading to under-use, which in turn restricts the supply of data for economic evaluation.

A fragmented Medicare reimbursement system creates challenges for personalized medicine. Coverage decisions in Medicare are comprised of a combination of national and local jurisdictions that are meant to permit regional flexibility in reimbursement options, but also create obstacles to establishing a uniform policy of coverage for certain technologies. For example, the currently available BRCA test for breast cancer susceptibility is covered in some Medicare regions but not others.

The PMC sees fair and equitable payment for diagnostic tests as having a direct impact on patient access to personalized medicine. Current coding and payment systems for these tests should be aligned with their technological, clinical and health economic impact. The establishment of outcomes evidence as a foundation for reimbursement should be a collaborative effort between public and private payers and product innovators.

The PMC supports the development of new uniform policies and legislation to expand payer coverage and reimbursement of predictive diagnostic tests and services focused on disease prevention and long-term patient and economic impact. Additionally, coverage decisions should be made through a timely and transparent process.

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