Introduction

In his January 20, 2015 State of the Union address, President Obama brought to the nation's attention the promise of personalized medicine when he announced the Precision Medicine Initiative (the "PMI"). In announcing this initiative during his address, which was to be funded with $215 million in the President's 2016 budget, the President gave many in the nation their first hint of the tremendous benefits to be gained by physicians being better able to tailor medical treatments to individual patients. This focus on the unique attributes of each patient – the patient's environment, lifestyle, and, most notably, genetic characteristics – allow targeted therapies to be deployed that are more likely to be efficacious, less likely to lead to adverse side effects, and, in many circumstances, more cost-effective for both the patient and society at large than current approaches to many different illnesses.

The PMI is a far-reaching multi-disciplinary effort to foster the development of personalized medicine. Funds for the PMI were allocated to different government agencies as follows: (1) the National Institutes of Health (the "NIH") to develop a national cohort that would facilitate understanding of and set the foundation for new ways of doing research; (2) the NIH Cancer Institute to identify genomic drivers in cancer and more effective approaches to therapy; (3) the FDA to advance development of high quality curated databases to support the regulatory structure needed to advance innovation in precision medicine; and (4) the Office of the National Coordinator for Health Information Technology for the development of interoperability standards to address privacy issues and enable the secure exchange of data across different systems. Perhaps the most ambitious aspect of the initiative is its call for the development of a one (1) million patient volunteer cohort, which would engage individuals as active partners in the undertaking and not just as patients or research subjects.

Personalized medicine, often referred to as "precision medicine," is the result of emerging technologies that allow scientists and physicians to build upon what has long been a focus on a patient's individual characteristics in diagnosing illness (e.g., the patient's family history, social history, prior medical history, and presenting symptoms). The development of genetic sequencing and the discovery and use of biomarkers has now given clinicians new tools to better diagnose patients and develop more targeted treatments. By way of example, before the advent of genetic sequencing, a clinical trial of a treatment for cancer might have demonstrated a twenty-five percent (25%) success rate, which, depending on the type of cancer and the other therapies available at the time, might have been viewed as a fairly good outcome. However, even with this degree of efficacy, every four (4) patients treated only one (1) patient would benefit from the medication. The other three (3) patients would receive no benefit and would also be subject to any adverse side effects of the treatment.

Today, genetic sequencing might reveal the subset of patients with a specific genetic mutation who would be most likely to respond to a particular treatment thereby allowing for a much higher success rate with a particular drug. In many situations, genetic sequencing will provide physicians with the necessary knowledge so that they will only prescribe a drug for those patients who are likely to respond and will be able to avoid treating others with a particular medication when that therapy is unlikely to be successful. This benefit is emblematic of one of the most significant characteristics of personalized medicine – what is commonly referred to as "the right treatment, for the right patient, at the right time."

Personalized medicine has been recognized as greatly improving patient outcomes. For instance, it has been reported that the 5-year survival rate for myelogenous leukemia doubled following the introduction of imatinib (a targeted therapeutic), the 5-year survival rate for colorectal cancer increased by fifteen percent (15%) following discovery of molecular receptors associated with tumor growth, and the hospitalization rate decreased by thirty percent (30%) when warfarin (otherwise known as Coumadin, a frequently used anticoagulant) was dosed based on a patient's genetic characteristics. The potential cost savings to the health care system by the adoption of personalized medicine are likewise projected to be dramatic. By way of example, it has been projected that the frequency of chemotherapy could be decreased by thirty-four percent (34%) in women with breast cancer if they all received genetic testing prior to treatment. Notwithstanding the clear benefits offered by personalized medicine, there are any number of legal and policy issues, including those related to approval of products by the FDA, intellectual property rights in genes and genetic information, and reimbursement of targeted therapies, that will need to be addressed for the full promise of personalized medicine to be realized.

FDA and the Regulatory Requirements for Personalized Medicine Products

When the Federal Food, Drug, and Cosmetic Act was passed in 1938, the term Personalized Medicine had not yet been coined. As result, the Food and Drug Administration's (FDA) oversight activities related to precision- or personalized medicine stem from FDA's role in regulating drugs, biologics and medical devices rather than from specific requirements for "personalized medicine" products. These oversight activities are centered in several different centers for Devices and Radiological Health (CDRH), the Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER).

Each of these centers applies specific sets of regulations implementing different statutory authorities to different products. Thus, the personalized medicine effort at FDA has required significant coordination, which has not always been easy. In 2009, FDA created a Personalized Medicine Staff within the Office of In Vitro Diagnostic Device Evaluation and Safety to address the unique issues for diagnostics used in personalized medicine and to coordinate regulatory oversight between the devices and drugs/biologics centers to try and provide consistency and timeliness in regulatory decision-making for these products. There is also a multidisciplinary Genomics Evaluation Team for Safety (GETS) and the FDA Genomics Working Group, which is tasked with developing systems to deal with regulatory submissions including high-throughput sequencing data.

Coordinating the testing, preparation and submission of the paired products can be challenging, especially when two companies have partnered to bring the two components to the market. A further challenge is that FDA's review of each component is generally handled by a different center. In Guidance entitled "In Vitro Companion Diagnostic Devices", FDA has recommended contemporaneous development of a drug and its corresponding diagnostic device. If the device and its test results are essential for the drug's safety and efficacy, FDA will not approve the therapeutic or use of the product with the device if FDA has not also approved/cleared the device itself. However, FDA retains discretion to approve a drug for use with a companion device, even if FDA has not yet approved/cleared the device. In this situation, FDA would approve/clear the device
subsequently, and then the therapeutic sponsors can revise relevant product labeling accordingly.

While the goal of individually tailoring medicines for individual patients carries the promise of great benefits, significant FDA challenges remain. The standards for FDA approval have not changed for personalized medicine products, and, in fact, the complexities associated with obtaining approvals for such products are often greater than those for traditional products. Early communication with the Agency can help applicants understand how any challenges can be addressed and overcome.

Property Rights and Personalized Medicine

It was expected that genomic medicine and technology would lead to new advances in the delivery of health care. Indeed, when the Human Genome Project was launched in 1990 to sequence the complete set of DNA in the human body, one of the project’s stated goals was to understand the genetic factors in human disease, paving the way for new strategies for their diagnosis, treatment and prevention. These discoveries are key to personalized medicine as they allow tailored therapies and medical strategies based on an individual’s genome. The impact of advances in genomic medicine and its application to diagnosis and treatment has not, however, been limited to new treatments and tests – it also has impacted over twenty years of U.S. patent practice by challenging what can, and cannot, be the subject of a United States patent.

A patent is a property right issued by a government to one or more inventors. In the United States, a patent allows the patent holder to prevent others from making, using, importing, offering for sale or selling the patented technology. However, not every discovery is patentable; only discoveries that meet the criteria of novelty, non-obviousness, and utility may be a patent. The utility requirement ensures that the invention is useful and is of a class for which the patent office is authorized to grant patents. It has been the U.S. Supreme Court’s recent interpretation of this utility requirement (or more specifically what is patent-eligible) that has modified whether discoveries that relate to personalized medicine can be patented.

Medical diagnostics are key tools of many personalized therapies. Diagnostic methods can provide a physician with useful if not critical information to treat a patient. For decades, diagnostic methods that link a genetic characteristic to a treatment option were routinely held to be patentable in the United States, provided that the methods were novel and non-obvious. However, the Supreme Court changed this paradigm in their decision Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S.Ct. 1289, 1296 (2012). In Mayo, the Court ruled that predicting the use of a product that the person is taking from the presence of a genetic variant in an individual’s genome is not patent-eligible under the patent laws, nor is it patent-eligible to claim a diagnostic test based on the presence of a genetic variant in an individual’s genome because the claim is not transformative,” a test that has been applied by the courts to determine whether a claim is patent-eligible or not. The Court held that the diagnostic use of the information obtained from the test is not transformative because it is merely an attempt to apply natural规律 in a routine, well-understood, non-inventive context.

Developers of personalized medicine products need to have a clear business plan from the earliest stages in order to be sure they have the necessary data to present to payers. One year after limiting the scope of diagnostic method patents, the U.S. Supreme Court addressed the question whether isolated human genes are patent-eligible. In Ass’n. for Molecular Pathology v. Myriad Genetics, Inc., 133 S.Ct. 2107 (2013), a unanimous U.S. Supreme Court removed from patent-eligibility isolated, naturally occurring genes and gene fragments – a class of discoveries that has been an important driver of the biotechnology industry for the last few decades. Myriad sold a genetic test that confirms the presence of a BRCA1 or BRCA2 gene mutation that are responsible for the majority of hereditary breast and ovarian cancers. Myriad had exclusive rights to provide the test in the United States by virtue of at least seven patents assigned or exclusively licensed from the University of Utah. The patent rights covered the genes as isolated from the human body, synthetic, or man-made genes, fragments of the genes, and use of the genes to perform screens and diagnostic tests. The Supreme Court held, however, that the patent rights to unmodified whole genes and gene fragments were invalid for claiming a product of nature. In the holding of Mayo has since been extended to any isolated, naturally occurring and unmodified product of nature such as proteins, antibodies and plant extracts.

Reimbursement Concerns

Although personalized medicine can lead to better patient care outcomes and lower costs of care, reimbursement has been an area of continuing challenge for this industry sector. As the industry has matured and sales have increased, payers have begun to implement a more selective approach to coverage. In many cases, payers may also expect clinical evidence showing that the product works better than products that are already covered, or is specifically helpful in a particular clinical setting. As part of the coverage process, the manufacturer must be able to establish product safety, clinical efficacy, and for some payers, economic efficiency. In some cases, payers may also expect clinical evidence showing that the product works better than products that are already covered, or is specifically helpful in a particular clinical setting.

For therapeutic purposes, coverage generally requires that the product be approved by FDA for at least one use. For diagnostic testing, there currently is arguably more latitude for laboratory-developed tests (LDTs), although the FDA’s parameters require careful business planning and the regulatory landscape for LDTs is currently in flux. Other types of laboratory-developed tests, such as tests developed and offered by a hospital or other non-commercial entity, may be covered under the Hospital Insurance Program (Medicare). However, payers continue to manage the program by implementing the same criteria for a variety of reasons, including economic efficiency, appropriateness, and to control costs.

One of the most significant challenges faced by personalized medicine products is obtaining coverage for the product. Payers have become more selective in the products they will cover and have increased their scrutiny of product claims. Payers will consider a wide range of factors in determining whether to cover a product, including the product’s clinical benefits, cost-effectiveness, and whether the product is appropriate for the patient. Payers may also consider whether the product is already covered by a competitor or whether there is evidence that the product is more effective than existing therapies.

Conclusion

Personalized medicine promises to provide treatments tailored to the unique attributes of each individual patient that are more efficacious, less prone to side effects, and potentially less expensive than many of the therapies now available. However, before the benefits of personalized medicine can be fully realized, there are a number of challenges that must be addressed. The FDA must adopt and offer a path to regulatory approval that recognizes the issues unique to personalized medicine products, intellectual property issues can be protected by a patent. Retailers continue to incentivize development of new and innovative products while fostering collaboration and the sharing of information, and payers must adopt clearly articulated reimbursement policies that reflect the value provided by personalized tests and products.

Additional Resources

NOTE: Those interested in an in-depth exploration of the complex business issues, trends, and opportunities in personalized medicine may wish to check out the 4th Annual
Business of Personalized Medicine Summit, to be held in San Francisco on September 29, 2016. This one-day, one-of-a-kind thought leadership forum will bring together key executives with varying stakeholder perspectives to deliver insights and strategies for capitalizing on this challenging yet profitable market. For details, visit www.personalizedmedicinesummit.com.

1. The Case for Personalized Medicine (4th ed. 2014),
2. The Precision Medicine Initiative Cohort Program—Building a Research Foundation for 21st Century Medicine (Sept. 17, 2015),
3. FDA’s Role in the Precision Medicine Initiative,
http://www.fda.gov/ScienceResearch/SpecialTopics/PrecisionMedicine/default.htm (last visited June 13, 2016).
http://www.uspto.gov/blog/director/update_to_examiner_guidance_on
5. Donald Zuhn, Patentable Subject Matter Eligibility Guidance – Example on Screening for Gene Alterations, (June 9, 2016),
http://www.patentdocs.org/patentable-subject-matter/
6. Palmetto GBA, Molecular Diagnostic Program (MoIDX) Coverage, Coding, and Pricing Standards and Requirements (M00106) (Version 11.0, May 2016)

https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

A “biomarker” is “[a] biological molecule found in blood, other body fluids or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition.” See NCI Dictionary of Cancer Terms,

For a detailed explanation of Medicare’s coverage and reimbursement process, see Innovators’ Guide to Navigating Medicare, Version 3 (2015),