# THE RIGHT MEDICINE FOR THE RIGHT PATIENT

BY DENISE MYSHKO

**ON THE EVE OF THE 50TH ANNIVERSARY OF PUBLICATION OF THE DOUBLE-HELIX DNA, PHARMACEUTICAL RESEARCHERS ARE EMBRACING PHARMACOGENOMICS AS A WAY TO DISCOVER AND TEST NEW MEDICINES THAT COULD LEAD TO AN ENTIRELY NEW WAY OF TREATING DISEASE.**

The one-drug-fits-all approach to medicine is soon expected to be a thing of the past, thanks to the emergence of pharmacogenomics. Since 1953 when James Watson and Francis Crick published the DNA structure, much has been learned about the human genome.

Fifty years later, a new scientific leap is unfolding. The initial map of the human genome two years ago, coupled with existing and emerging genomics technologies, will create a greater understanding of how disease develops and lead to better ways to study and evaluate new medicines. The completed map of the genome is expected to be finished in April, and the National Human Genome Research Institute plans a month-long celebration.

These advances, however, will require the entire healthcare community to change how it views medical treatment to make "personalized medicine" the standard of care. To start, patients will first receive a diagnostic test to evaluate their own genetic profile. Genotyping will help physicians determine which drugs are likely to provide the best therapeutic option for a particular patient with a particular set of genetic variances, as well as the best dose for that patient.

The DNA sequence from one individual to another is 99.9% identical; only 0.1% difference in sequence accounts for all genetic variations. It is this genetic variation that plays a role in whether a person has a higher or lower risk for getting particular diseases. Single-gene differences in individuals account for some traits and diseases, such as cystic fibrosis and sickle cell disease. More complex interrelationships among multiple genes and the environment are responsible for many common diseases, such as diabetes, cancer, stroke, Alzheimer's disease, Parkinson's disease, depression, alcoholism, heart disease, arthritis, and asthma. This 0.1% variation also can affect how a person responds to a drug. The study of how an individual's genetic makeup shapes the body's response to drugs is called pharmacogenomics. The term comes from the words pharmacology and genomics and combines traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins, and single nucleotide polymorphisms (SNPs).

The term pharmacogenetics and pharmacogenomics have in the past been used interchangeably, but more recently have taken on two distinct meanings (see box on next page).

"This research is evolving," says Chris Chamberlain, M.D., Ph.D., medical genetics expert, genetics and integrated medicine, Roche Products Ltd. "We use the term pharmacogenetics to be the study of DNA variation as it relates to changes in drug response at the patient-care level. Pharmacogenomics are

the tools that pharma companies use to determine the response to those differences."

## THE PROMISE

In the short term, pharmacogenomics offers pharmaceutical and biotechnology companies an opportunity to discover products that target specific patient populations based on individual genetic differences, determine which patients, based on these differences, will or won't respond to a particular product, and even to customize chemicals to address this difference. These drugs are likely to have fewer side effects since companies will have a better understanding of drug toxicity.

The hope is that additional drugs can be developed that work like Genentech's Herceptin and Novartis's Gleevec. Although not developed with genomic technologies, they are examples of the types of products that pharmacogenomics can yield.

Herceptin was approved in 1998 as a treatment for women with metastatic breast cancer who overexpress the HER2 (human epidermal growth factor receptor 2) protein. In the late 1980s, researchers at UCLA discovered that HER2 was overexpressed in about 25% to 30% of breast tumors and is associated with a more aggressive type of breast cancer and poor prognosis. The HER2 protein was first cloned by Genentech scientists and later a humanized antibody was developed to specifically target this genetic abnormality in certain breast tumors while limiting adverse events.

Gleevec was approved in the U.S. in May 2001 to treat chronic myeloid leukemia (CML). In CML, an abnormal chromosome (called the Philadelphia chromosome) produces the protein Bcr-Abl, a tyrosine kinase. In the case of leukemia, Bcr-Abl changes a genetic signal to overproduce white blood cells. In 1990, Novartis's research led to the discovery of Gleevec, the first Bcr-Abl inhibitor.

The expectation is that this research will lead to diagnostics that can help to determine variations in genes that lead to disease, as well as the individual responses to medications.

Different responses to the same drug could be caused by differences in the rate that the drug is metabolized by an enzyme. The receptor molecule to which the drug binds can have different affinities for the drug because of genes.

By the same token, adverse events may result from slow drug metabolism, resulting in excessive blood and tissue concentrations; presence of alternative metabolic enzyme that produces toxic metabolites; nonspecific action of the drug on alternative receptors (that have similar structure but different function), and interactions with environmental factors, such as other drugs or diet.

Roche Molecular Systems Inc., the diagnostics division of Roche, is currently working on a diagnostic test that can evaluate the CYP 2D6 and CYP 2C19 enzymes present in the liver that help to eliminate drugs from the body. The company plans to launch this product at the end of the first quarter of this year. Initially, the company plans to market the test to pharmaceutical companies and contract research organizations.

Eventually, Roche Molecular Systems plans to market this to physicians as a way to help them adjust drug doses.

"The two areas that we believe this particular set of polymorphisms will have the most relevance is in psychiatry and cardiovascular disease because of the large number of drugs used in those areas that are principally metabolized by the CYP 2D6 enzyme," says Walter Koch, Ph.D., director of the department of pharmacogenetics at Roche Molecular Systems.

Roche Molecular Systems is developing another test for the CYP 2C9 enzyme, which also is found in the liver.

"CYP 2C9 metabolizes a variety of drugs, but the one of principle interest is warfarin, which is used as an anticoagulant," Dr. Koch says. "About 10% to 11% of the population only has one functional copy, so these patients would have half the enzyme activity. About one in 200 people to one in 300 people lack that enzyme activity. In these patients, a normal dose of warfarin would lead to internal hemorrhaging. Because of this effect, warfarin is titrated very carefully and patients are monitored on an almost daily basis. If physicians knew at the outset the genotype of an individual, they could use it to adjust the dose of warfarin to a safer dose and reduce the risk of internal bleeding that can arise from inappropriately high levels of the drug."

Genotyping also can be used to improve the efficacy of some drugs, Dr. Koch says. He cites omeprazole (Prilosec), which is metabolized by CYP 2C19, as an example.

"In Asia, about one in five people lacks that enzyme," he says. "What's interesting is that those individuals who lack the enzyme actually have a more favorable response to the drug in treating peptic ulcers and healing *Helicobacter pylori* infections of the stomach than do the normal individuals. In this case, Asian normal metabolizers may be underdosed. Genotyping would allow for dosing up of the normal patients to allow for a more effective cure rate."

This use of diagnostic tests at the patient-care level would create customized or personalized treatment for patients.

"In my view, personalized medicine is a way to improve medical care through diagnostic tests, whether they be clinical laboratory blood tests, X-ray imaging, or physical examination," says Jeffrey Ross, M.D., VP of molecular medicine at Millennium Pharmaceuticals Inc. "When medicine and diagnostics are combined physicians have the most information possible to select the right therapy for the right patient at the right time and to achieve a more positive outcome."

From a patient's perspective, people would undergo a series of genotyping tests, says William Evans, Pharm.D., scientific director and clinical investigator in trials involving children with cancer, at St. Jude Children's Research Hospital.

"With today's technology, genotyping tests are done one at a time," Dr. Evans says. "In the future, through DNA chips and other technologies, we will be able to do thousands of tests at a time in an automated fashion. Physicians could test for a whole panel of genes. Instead of using a chart or algorithm to determine which drug to prescribe, physicians and pharmacists would be guided more precisely on which drug to use based on the genetic background of the patient."

### DEFINING A NEW ERA

Commonly the terms pharmacogenetics and pharmacogenomics are used interchangeably, but this has led to confusion. While there is no universal definition, there is an emerging agreement on the following:

**PHARMACOGENETICS**

- Relates to genetics, the study of inheritance of biological differences from generation to generation, and the resulting diversity in the population
- Relates to differential effects of a drug *in vivo* in different patients, dependent on the presence of inherited gene variants
- Assessed primarily by genetic (SNP) and genomic (expression) approaches
- A concept to provide more patient/disease-specfiic health
- One drug, many genomes
- Focus — patient variability

**PHARMACOGENOMICS**

- Relates to the study of the genome, the entirety of all genes in each cell
- Relates to differential effects of compounds — *in vivo* or *in vitro* — on gene expression, among the entirety of expressed genes
- Assessed by expression profiling
- A tool for compound selection/drug discovery
- Many drugs (i.e. early-stage compounds, one genome)
- Focus — compound variability

Source: F. Hoffmann-La Roche

This vision for personalized medicine, however, may not be realized for sometime, says Ashish Singh, VP at Bain & Company Inc. "When the costs of genotyping come down, when all of us can walk around with our own genetic profile in our pocket, when there are enough diagnostic tests available, and the physicians are trained in genotyping, then we will start to get to more personalized medicine."

## THE WAY FORWARD

According to report by IBM Business Consulting Services, "Pharma 2010: The Threshold of Innovation," pharmaceutical companies eventually will sell "targeted treatment solutions," that will include diagnostic tests, drugs, monitoring devices, and support services.

"Herceptin probably is the closest thing we have to this today, although it doesn't have the monitoring and the support services," says Sam Barnett, Ed.D., Americas lead partner for the Pharmaceutical and Life Sciences practice at IBM Business Consulting Services. "Wrapping support services around products should provide the added benefits of improving patient compliance."

This, the IBM report says, will lead to a new business model for the industry. Modeling, simulation, and high-performance computing, together with some Phase II trials will provide regulators with enough information to be able to grant "conditional approval" to products, followed by continued "in-life testing."

"The simulations provide a very high level of predictability as to ultimately what we may find within the clinical trial," says Terri Cooper, Ph.D., partner in the Global Pharmaceutical and Life Sciences Practice at IBM Business Consulting Services. "We've done quite a few retrospective analyses using data that would have been available before a product went to Phase III clinical trials. These were products for which the clinical program had been stopped. We've simulated the outcomes and found that if companies had done the same type of simulation they would have recognized the problems earlier on and would have either completely revamped the Phase III program or made the decision to cancel the program before Phase III."

In addition to a new approach to research, Mr. Singh notes this research will require some changes in how the industry does business.

"There is an uncertainty right now as to how the business model is going to be different from the blockbuster model that exists today," he says. "Frankly, more and more big pharma companies are coming to the realization that today's model is not sustainable. They are finding that blockbusters are much harder to produce and harder to market."

## THE MARKET

Some analysts have suggested that the pharma industry is starting to shy away from pharmacogenetic/pharmacogenomic research. But a closer look shows that the industry remains committed. GlaxoSmithKline, Roche, Pfizer, Schering-Plough, as well as other companies such as Millennium, CuraGen, and Vertex continue to pursue genetics and genomics either internally or through collaborations.

"There were many large investments in the late 1990s and 2000, both in genomics deals as well as in technology infrastructure investments that didn't yield the expected results," says Michael P. McKenna, Ph.D., VP of collaborative research at CuraGen Corp.

He says there is a de-emphasis on the technology, with the focus now on the real-world applications of these technologies.

The study of pharmacogenomics is growing, according to a January 2003 report from Front Line Strategic Consulting. In 2003, Front Line estimates the market will be $670 million, and by 2008, the market is estimated to be $1.66 billion.

Multiple factors will influence this growth, including the availability of SNP databases; reduced cost of development; more patient support; a greater number of gene association studies; improved drug recovery (recalls); and greater support by healthcare providers.

Mr. Singh says there are several opportunities for the industry. The first is a potential savings in research and development spending.

"Pharmacogenomics has the potential to cut R&D costs significantly — by as much as 25% to 50%," he says. "There is some significant savings to be had up-front because companies will know the patient population. They don't have to do huge trials. They don't have to show safety for the entire population. So trial sizes can be reduced, cutting down on recruitment time."

IBM's report determined that development costs could be reduced to as little as $200 million per drug, from the current average of $800 million.

Secondly, Mr. Singh says, there is opportunity for increased sales as compliance with treatment regimens increase. "One of the biggest inefficiencies in our system today is that people stop taking drugs because they are not as effective or there are side effects," he says. "This will start to go away and compliance numbers will go up dramatically."

## APPLICATION IN DRUG DEVELOPMENT

Millennium has incorporated pharmacogenomics into its development programs. Dr. Ross says the company has woven this research into the fabric of the discovery and development for all its drug candidates. The company's management believes so strongly in the personalized medicine concept, that every product, including those in very early development, will include a written pharmacogenomics strategy.

One example is Velcade, the company's product for the treatment of relapsed and refractory multiple myeloma. In January, a NDA for Velcade was submitted to the FDA. Dr. Ross says that while pharmacogenomic data were submitted to regulatory authorities, they were not part of the approval application for Velcade.

Dr. Ross says while the genomic information was not used to guide ongoing trials, it may be used for future trials.

The hope is that once Velcade is available, a diagnostic test will be developed using the gathered genomic data that can aid physicians in determining which patients would receive the most benefit from Velcade, Dr. Ross notes. Millennium is not developing such a test, he says, but is open to pursing potential partnership with a diagnostic company.

Roche also has undertaken a number of initiatives to develop targeted therapeutics. The Roche Center for Medical Genomics aims to apply genetic and genomic technologies to understand the molecular pathology of major human disease.

# Pharmacogenomics Timeline

**1960s.** Scientists identify deficiency in enzymes that explained adverse effects of drugs.

**MID-TO-LATE 1980s.** GenBank transfers administration to the National Institutes of Health's National Center for Biotechnology Information (NCBI).

**1988.** The National Research Council calls for a scale-up phased approach to the Human Genome Project and endorses $200 million a year.

**1990.** Stephen Altshul at NCBI publishes BLAST, a DNA sequence search engine that becomes the standard for online gene searching.

**1990-1992.** The Human Genome Project is initiated and sequence information begins to increase exponentially.

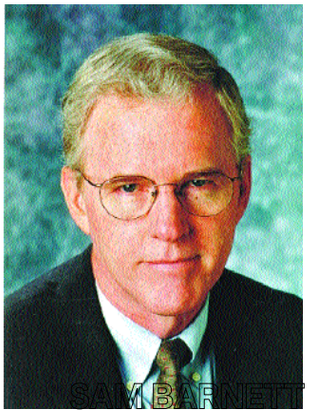
Source: Front Line Strategic Consulting Inc.'s January 2003 report on pharmacogenomics. For more information, visit frontlinesmc.com.


MITCHELL MARTIN

▼ IF PHYSICIANS KNEW AT THE OUTSET THE GENOTYPE OF AN INDIVIDUAL, THEY COULD USE IT TO ADJUST THE DOSE TO A SAFER LEVEL AND REDUCE RISKS.


WALTER KOCH

◀ WITH ADVANCES IN TECHNOLOGY GENOTYPING, IT'S POSSIBLE TO DO MOLECULAR EPIDEMIOLOGY TO TRY TO GET A BETTER PICTURE OF THE MOLECULAR BASIS OF COMPLEX DISORDERS.


SAM BARNETT

▲ HERCEPTIN PROBABLY IS THE CLOSEST THING WE HAVE TODAY, ALTHOUGH IT DOESN'T HAVE THE MONITORING AND THE SUPPORT SERVICES. PHARMA COMPANIES WILL BE ABLE TO WRAP SUPPORT SERVICES AROUND THEIR PRODUCTS AND GET MUCH HIGHER COMPLIANCE.


TERRI COOPER

▼ WHEN THE COSTS OF GENOTYPING COME DOWN, WHEN ALL OF US CAN WALK AROUND WITH OUR OWN GENETIC PROFILE IN OUR POCKET, WHEN THERE ARE ENOUGH DIAGNOSTIC TESTS AVAILABLE, AND THE PHYSICIANS ARE TRAINED IN GENOTYPING, THEN WE WILL START TO GET TO MORE PERSONALIZED MEDICINE.


ASHISH SINGH

◀ WE'VE DONE QUITE A FEW RETROSPECTIVE ANALYSES USING DATA THAT WOULD HAVE BEEN AVAILABLE BEFORE A PRODUCT WENT TO PHASE III CLINICAL TRIALS. THESE WERE PRODUCTS FOR WHICH THE CLINICAL PROGRAM HAD BEEN STOPPED. WE'VE SIMULATED THE OUTCOMES AND FOUND THAT IF COMPANIES HAD DONE THE SAME TYPE OF SIMULATION THEY WOULD HAVE RECOGNIZED THE PROBLEMS EARLIER ON.


MIKE MCKENNA

▲ THERE IS A CERTAIN DEGREE OF LEARNING THAT HAS TO TAKE PLACE SO THAT COMPANIES CAN DETERMINE WHERE THESE TECHNOLOGIES PLAY A ROLE IN DRUG DEVELOPMENT. WHEN THIS LEARNING CURVE IS COMBINED WITH THE GENERAL ECONOMIC MALAISE IN THE INDUSTRY AND THE DOWNTURN IN THE STOCK MARKET, INVESTORS ARE MORE CONSERVATIVE.

▼ WE VIEW PHARMACOGENOMICS AS A WAY TO IMPROVE THE EFFICACY AND SAFETY AND UTILITY OF OUR THERAPEUTIC OFFERINGS. OUR DRIVER IS TO UNDERSTAND MORE ABOUT OUR DRUGS, TO UNDERSTAND HOW THEY WORK, AND TO UNDERSTAND THE DISEASES THAT THEY TREAT. WE WANT TO APPLY DIAGNOSTIC TECHNOLOGY TO HELP PHYSICIANS AND PRESCRIBERS MAKE THE APPROPRIATE DECISIONS.


CHRIS CHAMBERLAIN

**1997.** Abbott and Genset agree on co-development of a SNP map and its application in developing and marketing diagnostic systems. The deal is considered to be the beginning of the pharmacogenomics era.

**1999.** The SNP Consortium begins to create a public SNP database. It is initiated by the NIH and a number of private pharmaceutical companies.

**2000.** The Human Genome Project presents its preliminary results that each individual could have fewer than 30,000 genes.

**2001.** The U.S. Patent and Trademark Office releases newest gene patent guidelines.

Additionally, people who participate in Roche clinical trials on the safety or efficacy of a new medicine may be asked to consider giving an additional blood sample for genetics research. Roche stores these samples so that research can be conducted to analyze DNA, proteins, and other chemical components.

"With advances in genotyping, it's possible to do molecular epidemiology to try to get a better picture of the molecular basis of complex disorders," says Mitchell Martin, Ph.D., research leader in bioinformatics, genetics, and genomics and head of the Joint Program in Applied Genomics, Type 2 Diabetes initiative, at Roche.

Dr. Martin says Roche is working with Partners Health Care in Boston, which is developing an integrated healthcare delivery system, to identify patients from their large patient population who would like to participant in genetic association studies in type 2 diabetes. The companies plan to recruit between 1,000 and 3,000 patients and begin genotyping this year.

"We will take genes that we believe are involved in type 2 diabetes and try to determine which ones are more associated with the disease compared with genes from nondiabetics," Dr. Martin says.

Roche Molecular Systems has been working with Affymetrix, a developer of genomics tools, to develop microarray-based products. One such product is a genotyping test, to be launched by the second quarter of this year, that analyzes the CYP 2D6 and CYP 2C19 enzymes, which are involved in the metabolization of cardiovascular and psychiatric drugs. Roche and Affymetrix have several other agreements to develop and market genotyping tests as well as resequencing applications for a wide range of diseases, including cancer, osteoporosis, and infectious and inflammatory diseases.

Microarray technology represents a growing market. The current U.S. market potential for microarray technology is about $1 billion, according to a February 2003 report by Kalorama Information. By 2010, the total market potential for analytical microarrays in the U.S. is expected to reach $5.3 billion.

DNA/gene microarrays are one segment of this market and, according to Kalorama, represent the largest part of the analytical microchip market. Between 2000 to 2005, the U.S. DNA/gene microarray products market is expected to grow at a compound annual rate of 20%, expanding the total market almost 2.5-fold, from about $322 million to $800 million. Between 2005 to 2010, the compound annual growth is expected to slow somewhat, to 11.8%.

## THE KEY CHALLENGES

Despite the potential for pharmacogenomics, there are many obstacles. As people become more knowledgeable about these technologies, there will likely be a change in standards. "This is a moving target in that standards that are within ethical norms today may not be in five years," Dr. Martin says.

The scale of the pharmacogenomics research makes bioinformatics especially challenging. "There needs to be an informatics infrastructure to manage the data and then we can try to mine the data for patterns to look for interesting targets as markers," Dr. Martin says. "At Roche, we've developed an integrated informatics infrastructure to look at large data sets and genotype data and gene expression data and proteomics with the express purpose of looking for diagnostic markers and therapeutic targets and for integrating the data."

Several initiatives have been developed that

## Benefits of Pharmacogenomics

**MORE POWERFUL MEDICINES:** Pharmaceutical companies will be able to create drugs based on the proteins, enzymes, and RNA molecules associated with genes and diseases. This will facilitate drug discovery and allow drug makers to produce a therapy more targeted to specific diseases. This accuracy not only will maximize therapeutic effects but also decrease damage to nearby healthy cells.

**BETTER, SAFER DRUGS THE FIRST TIME:** Instead of the standard trial-and-error method of matching patients with the right drugs, doctors will be able to analyze a patient's genetic profile and prescribe the best available drug therapy from the beginning. Not only will this take the guesswork out of finding the right drug, it will speed recovery time and increase safety as the likelihood of adverse reactions is eliminated.

**MORE ACCURATE METHODS OF DETERMINING APPROPRIATE DRUG DOSAGES:** Current methods of basing dosages on weight and age will be replaced with dosages based on a person's genetics — how well the body processes the medicine and the time it takes to metabolize it. This will maximize the therapy's value and decrease the likelihood of overdose.

**ADVANCED SCREENING FOR DISEASE:** Knowing one's genetic code will allow a person to make adequate lifestyle and environmental changes at an early age so as to avoid or lessen the severity of a genetic disease. Likewise, advance knowledge of a particular disease susceptibility will allow careful monitoring, and treatments can be introduced at the most appropriate stage to maximize their therapy.

**BETTER VACCINES:** Vaccines made of genetic material, either DNA or RNA, promise all the benefits of existing vaccines without all the risks. They will activate the immune system but will be unable to cause infections. They will be inexpensive, stable, easy to store, and capable of being engineered to carry several strains of a pathogen at once.

**IMPROVEMENTS IN THE DRUG DISCOVERY AND APPROVAL PROCESS:** Pharmaceutical companies will be able to discover potential therapies more easily using genome targets. Previously failed drug candidates may be revived as they are matched with the niche population they serve. The drug approval process should be facilitated as trials are targeted for specific genetic population groups — providing greater degrees of success. The cost and risk of clinical trials will be reduced by targeting only those people capable of responding to a drug.

**DECREASE IN THE OVERALL COST OF HEALTHCARE:** Decreases in the number of adverse drug reactions, the number of failed drug trials, the time it takes to get a drug approved, the length of time patients are on medication, the number of medications patients must take to find an effective therapy, the effects of a disease on the body (through early detection), and an increase in the range of possible drug targets will promote a net decrease in the cost of healthcare.

SOURCE: HUMAN GENOME PROJECT. FOR MORE INFORMATION, VISIT ORNL.GOV/HGMIS/MEDICINE/PHARMA.HTML

aim to manage the amount of data generated by genomics research. One such project is PharmacoGenetic Knowledge Base (pharmgkb.org), a shared library for pharmacogenetics researchers created by Stanford University as part of a nationwide collaborative research effort funded by the National Institutes of Health.

Another project is The SNP Consortium (http://snp.cshl.org), a nonprofit foundation organized for the purpose of providing public genomic data. Its mission is to develop up to 300,000 SNPs and to make the information available to the public without intellectual property restrictions. Some of the companies involved in this project include: Novartis, Pfizer, GlaxoSmithKline, IBM, Aventis, Bristol-Myers Squibb, and Roche.

An SNP database has been developed by The National Institutes of Health. It is an independent database that will be integrated with other genomic data being collected by the National Center for Biotechnology Information.

## REGULATORY ISSUES

While the science is promising, the regulatory regime hasn't caught up, says David Beier, a partner in the law firm of Hogan & Hartson LLP. "Products such as Herceptin, where a diagnostic test is required before the product is administered, is a relatively new phenomenon and the FDA is going to need more experience," he says.

Mr. Singh agrees that the FDA will have to change how it reviews and approves diagnostics and therapeutics.

But, he says, the agency will have to address other issues as well, including what could be a higher volume of products that are likely to come before regulators in the future.

FDA officials acknowledge that they have limited experience with this research.

An article written last year by Janet Woodcock and LJ. Lesko, both of the FDA, in *The Pharmacogenomics Journal*, stated that the agency is aware that such tests leave many unanswered questions, including: What are the statistical requirements for pharmacogenetic and pharmacogenomics tests?; Will the label for that drug require a diagnostic test?; Will the agency require the drug sponsor to submit an application for a diagnostic test at the same time of approving the drug?; among others.

The same article stressed, however, that the FDA is preparing for more applications that contain pharmacogenetic information. The agency is assessing the education needs of reviewers and working with the industry to identify concerns and issues.

Mr. Beier suggests that the agency may have to make changes to guidelines and application requirements. "If the FDA doesn't change the clinical trial profile, then we could end up with trials that are as expensive and potentially more expensive especially if the number of study procedures per patient continues to go up," he says. ✦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

## Experts on this topic

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