

# Executive Summary

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The goal of this report is to explore the pharmacogenomic (PGx) realm of personalized medicine and to qualitatively analyze current research, development, and market trends related to the use of genetic information to predict how well patients will respond to certain drugs. Pharmacogenomics is often referred to as a “revolution” or “the great new wave” in medicine—a future filled with promise not just for better, safer, and more affordable healthcare (*i.e.*, affordable for both consumers and third-party payers) but also, according to some, greater economic returns for drug makers. While there are in fact a handful of drugs on the market with genotype-based prescribing requirements, such as Herceptin, this next great wave has been slow to arrive.

The adoption and widespread use of PGx in the clinic is up against some tremendous challenges, not the least of which is scientific. Teasing apart a consistent, predictive association between a SNP or other genetic marker and a drug response phenotype from all the other countless variables that play into drug response can be next to impossible, even when such an association exists. Genes interact with each other, and they interact with the environment (*i.e.*, their cellular environment, which in turn is impacted by the external environment to which the body is exposed).

Once candidate associations are identified, knowing how to design clinical trials capable of teasing out these associations in the clinic and aligning those trials in preparation for regulatory review create another set of challenges. Most companies are only just becoming involved in doing this—utilizing a PGx strategy during drug development—and there is a lot of misinformation and confusion about how best to proceed.

Moreover, validating an association in a carefully controlled clinical setting is different than knowing whether or not that association is truly clinically useful. For example, do patients who respond well, or better, to a drug have improved long-term outcomes? Is their quality of life better? Does it make sense, from an economic standpoint, to utilize one drug over another based on what the genetic information reveals? Even for already successful PGx-based drugs (e.g., Herceptin), many of these questions remain unanswered. While, on the one hand, the success of Herceptin suggests that this lack of clarity is not reason enough *not* to pursue a PGx strategy, on the other hand, the risk of a product not being adopted as the standard of care (either by prescribers, payers, or patients) because of insufficient evidence regarding its “clinical utility” is clearly a disincentive.

What will be required to overcome these challenges? At a Cambridge Healthtech Institute (CHI) meeting in Montreal, Quebec, Canada, in November 2008, Christopher-Paul Milne, DVM, MPH, JD (Associate Director, Tufts Center for the Study of Drug Development, Tufts University, Boston, MA) said that more widespread, or accelerated, adoption of PGx will require a “change of heart ... and hand!” In other words, while there are a great number of practical problems that need to be solved, including how to operate a “small, specialized, science-driven, and smart” business strategy (as opposed to the “every market, model, and molecule exploited” strategy of tradition), there is also a fundamental philosophical problem that will need to be addressed: Instead of thinking “Let’s find something that will sell well,” industry needs to start thinking along the lines of “If it’s a good drug, we’ll find a way to sell it.” In an interview with Insight Pharma Reports, Wolfgang Sadée, PhD (Professor and Chair, Pharmacology, The Ohio State Medical Center, Columbus, OH) also discussed why this paradigm shift must occur before PGx can deliver on its promise. Milne and Sadée’s voices are just two of the many voices represented in this report.

Of course, overcoming these challenges and adopting a successful PGx business strategy requires more than a change of heart. Pharmacogenomics is an extremely difficult business, one for which there are no easy answers or magic bullets. Even companies manufacturing and marketing already successful pharmacogenomic drug-test combinations continue to face difficulties. This report examines how these and other companies have or are navigating through the scientific, statistical/experimental design, and “clinical utility” landscape of PGx. Much of the information in this report is based on the presentations and discussions that took place at that Montreal meeting, “Pharmacogenomics Now: Maximizing Benefits and Minimizing Risks,”

which was jointly sponsored by Genome Quebec, where more than 200 scientific and clinical research, industry, and government leaders in pharmacogenomics from across the world met to identify, discuss, and elaborate on the promise and challenges of pharmacogenomics. This report is also based on a partial review of the scientific literature, comprehensive interviews with experts in the field, and a qualitative survey of people with presumed involvement with pharmacogenomics.

