Pharmacogenomics (PGx) is often considered “the great new wave” in medicine, promising better, safer, and more affordable healthcare. Yet its adoption and widespread use in the clinic is up against some tremendous challenges. This report considers:

- Drivers of PGx
- Applications of PGx in drug development
- Industry experiences with PGx and lessons learned
- Type of evidence needed to establish clinical utility
- Challenges to moving PGx forward
- Survey results and expert views on utilization of PGx

Unlocking the enormous potential of pharmacogenomics
Overview

Pharmacogenomics: Delivering on the Promise explores the PGx realm of personalized medicine, analyzing current R&D and market trends related to the use of genetic information to predict how well patients will respond to certain drugs.

PGx is an extremely difficult business, one for which there are no easy answers. Even companies manufacturing and marketing already successful PGx 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.

Not the least of the challenges facing PGx is scientific. Separating a consistent, predictive association between a SNP or other genetic marker and a drug response phenotype from all the other variables that play into drug response can be next to impossible. 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. Pharmacogenomics: Delivering on the Promise considers prospective versus retrospective clinical trial design and when, if ever, the FDA might allow the latter for regulatory decision-making purposes.

Moreover, validating an association in a carefully controlled clinical setting is different than knowing whether or not that association is truly clinically useful. 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. Varying opinions raise questions about the nature of the evidence necessary for establishing the clinical utility of PGx tests. We consider the growing skepticism about the universal nature of the randomized controlled trial (RCT) gold standard and the usefulness of non-RCT experimental designs with respect to genetic testing.

Challenges examined include economic, reimbursement, regulatory, technological, and those related to a lack of physician education and awareness of pharmacogenetic testing. Overcoming these challenges could enable physicians to engage in smart PGx prescribing, leading to increased efficacy and reduced adverse drug reactions. PGx also has important applications in drug development, both with new drugs or new indications and as a way to “rescue” failed drugs; these various uses of PGx are explored in detail. Pharmacogenomics: Delivering on the Promise also includes comprehensive interviews with experts in the field and results from a qualitative survey of individuals involved with PGx.

Table: Will your company or lab be expanding its PGx-based research or development efforts in the near future?

<table>
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<th>Response</th>
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<tr>
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<td>Yes, substantially</td>
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<tr>
<td>No, our focus in that area will remain the same</td>
<td>6</td>
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<tr>
<td>No, our focus in that area will be decreasing</td>
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Source: Insight Pharma Reports

About the Author: Leslie A. Pray, PhD, biologist and author, has written extensively on a range of biotech and pharmaceutical industry, public health policy, genetic and epigenetic, infectious disease, and higher education issues for The National Academy of Sciences, the American Association for the Advancement of Science, the American Chemical Society, the Immune Disease Institute, The Scientist, The Chronicle of Higher Education, and others. She also wrote Epigenetics: Technologies, Applications, and the Commercial Landscape, a previous Insight Pharma Report (http://www.insightpharmareports.com/reports_report.aspx?id=72344&r=555). She received her doctorate in population genetics from the University of Vermont. An elected member of Sigma Xi, she has been the recipient of numerous scientific research awards.

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Survey Exhibits

Please classify your organization.
What disease area does your company, or lab, focus on?
When did your company or lab become involved with pharmacogenomics? (Or, if the sole focus of your organization is pharmacogenomics, when was your organization founded)?
About what percentage of your company or lab’s research and/or development efforts revolve around pharmacogenomics?
Will your company or lab be expanding its pharmacogenomics-based research or development efforts in the near future?
What is your or your organization’s chief application of pharmacogenomics?
If you (or your organization) are involved with discovering or analyzing gene-drug response associations, which theoretical approach do you take?
If your company, organization, or laboratory is involved with the development, manufacturing, or marketing of a pharmacogenomics-based product or service, which of the following business models best describes your company?
Have you been involved in any way and at any stage, from basic research through marketing, with a pharmacogenomics-based product (either drug or test) that is currently on the market?

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If your company or organization is involved with drug development, how often does your company or organization collect pharmacogenomic information during clinical development?

Is genotyping done because preclinical or other evidence suggests that it should be done, or is it done for a broad range of genes and not necessarily for any particular reason?

Is genotyping done in-house, or is it outsourced?

Which of the following genotypes have been used?

At what stage of development is pharmacogenomic information collected?

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