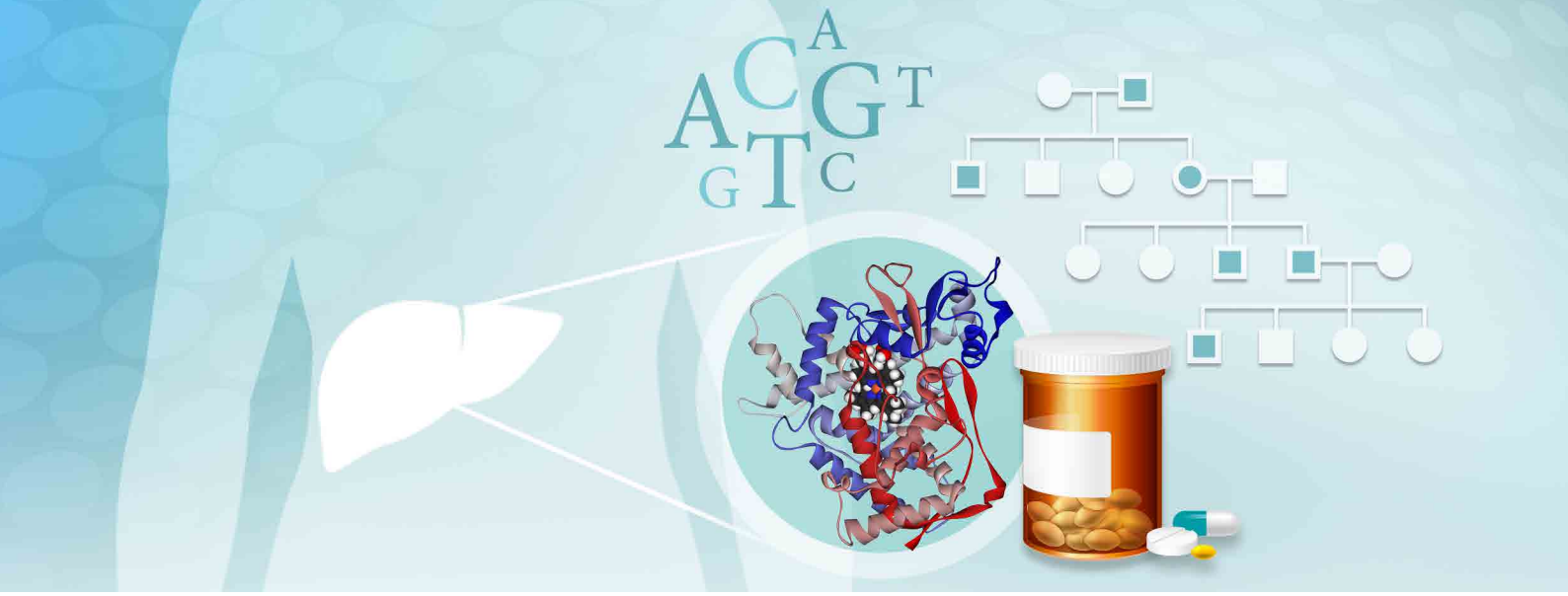


How to succeed in pharmacogenomics

What the experts are saying

Increasing understanding of the genetic basis of an individual's response to drugs, including how and how quickly a drug is metabolized (pharmacodynamics and pharmacokinetics), has opened the door to an increasingly personalized approach to drug prescription. A notable example is the genes that code for the cytochrome P450 family of enzymes, associated with individual variations in drug metabolism.[1] By identifying drugs most likely to benefit a patient, assessing likely dose response, potentially avoiding adverse reactions and reducing unnecessary use of drugs, pharmacogenomics testing (PgX) can help optimize treatment and reduce costs associated with complications or inappropriate utilization. As research demonstrating its clinical utility and associated health economics benefit continues to accumulate[3,4] and with the trend toward value-based healthcare, PgX is on the path to becoming standard of care. Already, more than 150 FDA-approved drugs include pharmacogenomics information in their labeling.[5] This demand for PgX presents an opportunity to clinical labs, many of which have successfully launched PgX services over the last two or three years and enjoyed robust growth.

The following is based on insights gleaned from an expert panel of lab directors and consultants at leading labs as they discussed industry trends, best practices and guidance for labs looking to tap into the opportunities in PgX.

Roche

"We are seeing a shift right now to value-based care. … There is definitely growth in that area because people managing risks for their patients recognize that improved medication management can really drive down the cost of care. In particular, one area of focus for us is improving polypharmacy management."
Kristine Ashcraft, CEO,
Genelex Corporation, Seattle, Washington

Changing economics

Despite growing evidence supporting its role in improving patient care and reducing costs, PgX suffered a setback in reimbursement when the Centers for Medicare & Medicaid Services (CMS) assigned coverage decisions to regional Medicare Administrative Contractors (MACs) in 2015, in effect rolling back coverage that was previously allowed. With the lack of a unified national policy, labs are required to seek reimbursement from individual MACs and meet varied sets of criteria, such as clinical utility studies and supporting statements of medical necessity from physicians. Overall, the longer-term outlook on PgX reimbursement is still favorable as evidence of its value continues to accumulate and awareness among physicians increases. And the emergence of accountable care organizations is adding a new payer to the traditional mix of Medicare and private insurance.

Working with physicians

"Physicians don't have time to research what a CYP2D6 poor metabolizer is, nor do they have time to read a 65-page report. … This means labs have to do the intellectual heavy lifting—the dry lab work—to make sure results are reported in a manner that is useful to physicians."
Bronwyn Ramey-Hartung, PhD, CEO,
Phoenix Lab Consulting, Louisville, Kentucky

"The point of ordering these tests is to manage medications. Then it's a matter of at what point do you order it. A lot of physicians are doing that proactively rather than wait until an initial prescription fails, and that is what we have to encourage through education. We also have to keep physicians updated about new genes that are added to our panels."
Tariq Adwan, PhD, Director of Research and Development,
Alpha Genomix Laboratories, Lawrenceville, Georgia

Cardiology, psychiatry, pain management and oncology are the clinical specialties most likely to order PgX. Primary care physicians are joining in, as they increasingly prescribe many of the same medications, especially to elderly patients, many of whom suffer from chronic diseases and receive multiple medications.

Communication with physicians is a top priority. To help physicians maximize the value of PgX, labs must provide them with an easy-to-read, actionable report that summarizes patient results and how the results translate into clinical decisions. Just as important is setting realistic expectations and guiding physicians on which patients are most likely to benefit from PgX.

Investments in physician education and having medical science liaisons on staff to provide ongoing consultation to physicians are important, especially as PgX expands into other clinical specialties and as physicians are called upon to provide statements of medical necessity to support reimbursement. And as genome sequencing and companion diagnostics drive new PgX applications, labs will find that investing in physician education can lay the groundwork for a successful relationship.

The operations perspective

Inside the lab, lab directors strive for quality of results and efficiency—getting high-quality PgX results to physician clients in a timely manner and being cost-efficient. Currently, an average turnaround time (TAT) of three to five days is satisfactory to physician clients and readily achievable by labs. However, reducing TAT is a factor as competition in PgX intensifies. And in some situations (e.g., when ordered by surgeons for perioperative pain management) a 24-hour TAT or better may be necessary.

Quality is paramount from multiple perspectives—patient care, liability, professionalism and the cost of repeat analysis.

In the drive for accurate, error-free results, disciplined quality control, adherence to guidelines and maintaining accreditation are a given, as are good practices such as proper care of reagents and attention to expiration dates.

"I think incorrect test results are certainly the biggest risk any clinical lab can have."
Weike Mo, PhD, FACB, Technical Director,
Molecular Testing Labs, Vancouver, Washington

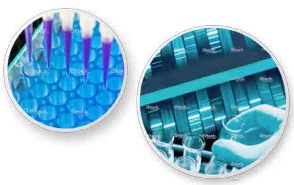
"One of the worst bottlenecks is repeat analysis, especially when faulty results are discovered after the fact. This can compromise credibility with physicians and is costly for labs that do not have the workflow or equipment in place for small-scale repeat analysis, such as a single SNP assay as opposed to an entire panel."
Bronwyn Ramey-Hartung, PhD, CEO,
Phoenix Lab Consulting, Louisville, Kentucky

Automating DNA extraction to achieve quality and efficiency

Without exception, lab directors point to automation as the way to reduce human error and to ensure more consistent processes and results. Automation also improves throughput, improves efficiency and helps expand capacity, especially important with the shortage of trained lab personnel.

The panel unanimously pointed to DNA extraction as perhaps the single most time-consuming and labor-intensive step and, from a quality perspective, the one that can benefit the most from automation. A high-quality DNA specimen will also reduce costly repeats.

A recent study comparing five automated DNA extraction platforms highlighted some workflow parameters to consider *Click here to access Study Summary.*[6] In addition to comparison studies like this, a thorough evaluation of available publications and studies can help guide selection of the platform most appropriate for specific lab requirements. Another valuable source of information, when selecting new extraction instrumentation, is the experience of other labs. For example, to see one Pharmacogenomics lab's experience performing buccal swab extractions with the MagNA Pure 96 system from Roche, click here.



"Automation is good for reducing human error and getting more consistent results and in a shorter time. This is especially important in DNA extraction, the critical first step."
Weike Mo, PhD, FACB, Technical Director,
Molecular Testing Labs, Vancouver, Washington

"Ultimately, the quality of DNA extraction is really the main determinant of how well testing is going to be done downstream. … It typically boils down to DNA quality."
Tariq Adwan, PhD, Director of Research and Development,
Alpha Genomix Laboratories, Lawrenceville, Georgia

"As we look toward expanding our testing capabilities and wanting to be ready for an influx of samples, we look for ways to improve throughput. DNA extraction is one example where automation really makes sense."
Bradley A. Moss, President,
Patients Choice Laboratories, Indianapolis, Indiana

"Some PgX labs start off using an RUO instrument for extraction, such as the MagMax, only to realize later that the instrument is not GMP-compliant or IVD-labeled, nor does it have the basic contamination control safeguards needed for routine clinical work."
Liz Thompson, COO,
Clinical Lab Consulting, LLC, Portland, Oregon

"IVD-labeled devices can provide the best capabilities in sample tracking and audit trails."
Bronwyn Ramey-Hartung, PhD, CEO,
Phoenix Lab Consulting, Louisville, Kentucky

Risk management in a rapidly evolving field

PgX today runs the gamut from FDA-approved, kit-based IVDs to laboratory-developed tests (LDTs). There are limited commercially available plug-and-play systems and limited standardization. This puts the responsibility on labs to integrate instrumentation and reagent offerings from multiple vendors and to design, optimize and validate the workflow to meet quality and efficiency goals.

Proven technology platforms are cited by some lab directors as a way to reduce the unknown in ensuring quality results and, indirectly, regulatory concerns. Instrumentation that is IVD-labeled is strongly preferred, although other factors such as compatibility with current lab workflow are also important. FDA approval also plays an important role in companion diagnostics, where PgX is integral to approval of a therapy and regulatory clearance is a key consideration as early as the clinical trial phase.

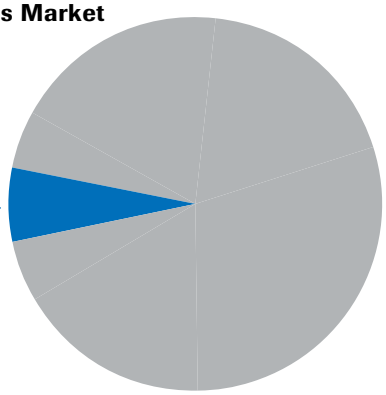
Reimbursement risk continues to be a challenge in PgX. Labs must, first and foremost, make sure that the tests they offer deliver actionable results and have demonstrated medical necessity. Published studies and guidelines are a starting point, but labs must be prepared to work with physicians to demonstrate clinical utility of the lab's offering.

U.S. Molecular Diagnostics Market

Sector	2012 Estimate	2013 Estimate	2014 Estimate	2015 Estimate	CAGR 2012-2015
Pharmacogenomics	**0.43**	**0.49**	**0.56**	**0.65**	**15%**
TOTAL	**7.5**	**7.8**	**8.5**	**9.4**	**8%**

Market estimate are in billions (U.S. dollar)
CAGR=compound annual grow rate

U.S. Molecular Diagnostics Market
2015 Total=$9.4 billion

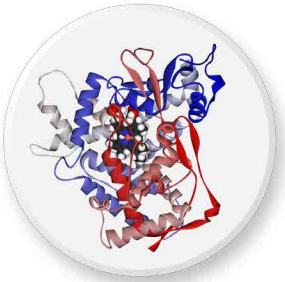


Source: G2 Intelligence, *U.S. Molecular Diagnostic and Genomic Testing 2013 – 2015: Laboratory Industry Analysis, Trends, and Forecasts*, © 2013 Kennedy Information, LLC

Getting started

Success in the PgX space requires a combination of good science (a clinically relevant test menu, reliable and actionable results), close communication with physicians, and good business, founded on a viable reimbursement strategy and a solid operating plan.

For labs that are just getting started, one effective approach to build the business may be to look for a fit with the existing client base. For example, toxicology labs may find that they can leverage the testing needs of existing clients who have a patient population that can benefit from PgX. In any case, all three components—the science and technology, operational infrastructure and reimbursement—must be part of an integrated business plan.



"Be sure you understand the reimbursement landscape. And have a team and a plan in place to prove the clinical utility of your offering.
Kristine Ashcraft, CEO,
Genelex Corporation, Seattle, Washington

"Build a team out before you do anything. Get the scientists in place, get all the guidelines, make sure you're compliant and your science is right. That's first and foremost. And you can do that with the right people."
Bradley A. Moss, President,
Patients Choice Laboratories, Indianapolis, Indiana

"Make smart decisions on technology and make sure the workflow is suited to expertise within the lab. For labs that can afford it, I advise upstream automation for DNA extraction."
Bronwyn Ramey-Hartung, PhD, CEO, Phoenix Lab Consulting, Louisville, Kentucky

Looking ahead

Ongoing discoveries and advancing technologies continue to create opportunities for expanding PgX services. Keeping abreast of scientific advances in a highly competitive field is a given. Lab directors speak of the need to continue to update existing panels by adding new genes or introducing new, clinically actionable tests. Many are excited about the promise of genome sequencing and anticipate adding DNA sequencing to their menu.

Increasingly, labs are looking to scientific collaborations and participation in industry groups such as the Association of Molecular Pathology, American Association of Clinical Chemistry, American Society of Human Genetics and Clinical Pharmacogenetics Implementation Consortium as important sources of new ideas that can drive the PgX field and expand the lab's services.

Expertise beyond traditional lab medicine will also be critical to the future of PgX. For example, increasingly complex drug regimens demand more participation by the pharmacist in patient care. Another significant growth area is data analysis. In the short term, this means translating test data to actionable results for physicians. On the horizon and a growing opportunity is the use of informatics to maximize a patient's PgX profile over the patient's lifetime and not just for the immediate need. Perhaps a pharmacogenomics profile for everyone is in the not-too-distant future.

"Ideally, the PGx profile is reevaluated in the context of the entire drug regimen every time a medication decision is made. That way, whether a physician is prescribing at the office or a patient is purchasing over-the-counter, the safest drug and doses based on current evidence can be selected."
Kristin Ashcraft, CEO,
Genelex Corporation, Seattle, Washington

Panel participants

Tariq Adwan, PhD, Director of Research and Development, Alpha Genomix Laboratories, graduated with honors from Misericordia University with a BS in biology and chemistry. He received his PhD from the University of Colorado's program of Cell Biology, Stem Cells and Development, where he also did his postdoctoral fellowship. His research focused on understanding the molecular mechanism underlying salivary gland dysfunction in head and neck cancer patients. Dr. Adwan is a co-author on a number of peer-reviewed publications and has been invited to present his work at scientific meetings, including the Federation of American Societies for Experimental Biology Conference on Lipid Mediated Signaling in Cancer.

Kristine Ashcraft, CEO, Genelex Corporation, defines the company's overall strategy, vision and place in the pharmacogenetics industry. She is responsible for business development, product design, market share and internal systems, in addition to being the primary liaison for governmental agencies, clients and partners. Prior to joining Genelex, Ms. Ashcraft worked in sales management at an insurance provider and served in management roles in the nonprofit sector. She obtained her MBA in entrepreneurship, graduating magna cum laude from the Franklin W. Olin Graduate School of Business at Babson College, and BS in molecular biology from the University of New Haven.

Weike Mo, PhD, FACB, Technical Director, Molecular Testing Labs, has built and managed both multidisciplinary R&D and clinical testing teams. His experience includes assay development for clinical diagnostics (molecular genetics, ELISA/EIA and LC-MS/MS) and implementation of a lab automation system for a genetics lab that performs more than 20,000 PCR reactions daily and a toxicology lab that tests 40,000 urine drugs daily. He received his PhD in cell and development biology from Oregon Health and Sciences University and BS in biotechnology from Tsinghua University, Beijing, China.

Bradley A. Moss, President, Patients Choice Laboratories, oversees business development, health economics, strategic partnerships and related activities within the company. Previously, he served as the Chief Business Officer for SeKayi Management, a $10M healthcare management organization, where he oversaw three subsidiaries managing more than 500,000 patients in four states. Prior to that, he was National Director of Sales for DailyMed Pharmacy, a subsidiary of Arcadia Resources, Inc. Mr. Moss received his BS from Eastern Illinois University and his MBA from the University of Illinois.

Bronwyn Ramey-Hartung, PhD, CEO, Phoenix Laboratory Consulting, has more than 15 years of laboratory experience in academic and clinical laboratories, where her work focused on molecular genetics assay design, validation and troubleshooting, as well as raw data analysis, phenotype interpretation and reporting. Her pharmacogenetic specialties include CYP450 haplotyping and copy number analysis. Dr. Ramey-Hartung also has experience in the development and quality systems management of LIMS, translational reporting and medical device software. She received her PhD in microbiology and biochemistry from Indiana University Bloomington and BS in biology from Trinity University.

Liz Thompson, MB (ASCP), COO, Clinical Lab Consulting, LLC, came to CLC from a large molecular diagnostics laboratory, where she managed the Laboratory Quality Assurance Department for Molecular Genetics, Toxicology and Infectious Disease. Her previous experience includes managing an HLA laboratory that focused on tissue typing for bone marrow transplant patients. She was published in Tissue Antigens and Human Immunology during this time. Liz graduated in 2006 with a BA in biology from Lewis & Clark.

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