Brochure

QIAGEN Bioinformatics Clinical Portfolio Overview

A comprehensive suite of solutions for the entire test continuum from development to commercial implementation

Sample to Insight

Genomic knowledge base and software solutions for powering clinical insights

The most advanced suite of products, services, and platform capabilities to deliver insights from clinical genomics

QIAGEN is a global leader in the development and delivery of commercial-grade, enterprise software solutions for implementation of genomics in research and clinical applications. These solutions have been developed under highly rigorous commercial design practices and are supported by a global organization of engineers, application scientists, and professional service consultants. The breadth of QIAGEN's bioinformatics products, services, and support capabilities can accelerate any healthcare institution to establish a personalized medicine capability with genomic-guided clinical decision support.

QIAGEN's software solutions have been designed to support genomics laboratories in efficiently scaling test volume, data, and menus across a broad range of NGS applications and platforms. The solutions are powered by QIAGEN's industry-leading, proprietary, and continually curated Knowledge Base, enabling laboratories to interpret and report test results with an up-to-date and vast source of scientific and clinical information.

QIAGEN has more than two decades of expertise in:

1. Commercial-grade bioinformatics development with products and services in active use by tens of thousands of researchers, geneticists, and clinicians worldwide
2. Bioinformatics software platforms, quality standards, and business processes for software construction, knowledge curation, and large-scale variant analytics
3. Technology agnosticism enabling the full range of NGS assay platforms used by genomic labs
4. Robust performance and secure scalability to grow genomic NGS test volumes
5. Global services and support for genomic labs and healthcare systems

Figure 1. QIAGEN's extensive experience allows genomics testing laboratories to adopt NGS capabilities and achieve efficiencies across the discovery-to-testing continuum.

The Curated QIAGEN Knowledge Base: A Unique Platform Capability

QIAGEN's proprietary, continually curated Knowledge Base has a long and trusted reputation as the most advanced and broadly used database of biological and clinical findings in the life sciences industry. Based on the industry-leading Ingenuity® Knowledge Base, acquired by QIAGEN in 2013, the QIAGEN Knowledge Base has a proven track record in delivering tremendous efficiencies for rapid analysis of genomic data and for driving insights from patient test results.

This Knowledge Base delivers important features for testing laboratories that require rapid determination of relevant biomarkers for evaluating a target patient population. QIAGEN's capability for sourcing and curating clinical and biological findings is unrivaled in the industry. The products and services built on top of the QIAGEN Knowledge Base provide clinical geneticists with a scalable solution for staying current with the dynamic nature of external information from numerous sources, such as primary literature, drug labels, professional guidelines, clinical cases, disease pathways, clinical phenotypes, clinical trials, and third-party databases including HGMD®. Indeed, the accelerating rate of information generation, driven by genomics, has created significant challenges for any testing laboratory to provide accurate interpretations to physicians with the evidence necessary for effective genomic-guided clinical decision support in patient care.

Demonstrated value of the QIAGEN Knowledge Base - up to 33% reduction in VUS

Other clinical decision support products annotate variants using sources such as HGMD and ClinVar, but they lack curated content from the primary literature. This burdens users with the time-consuming task of searching articles and curating their own papers to fully classify variants. This is especially problematic for workflows that incorporate ACMG guidelines for variant interpretation, since these guidelines require information that public sources can't provide — examples include co-segregation data, de novo

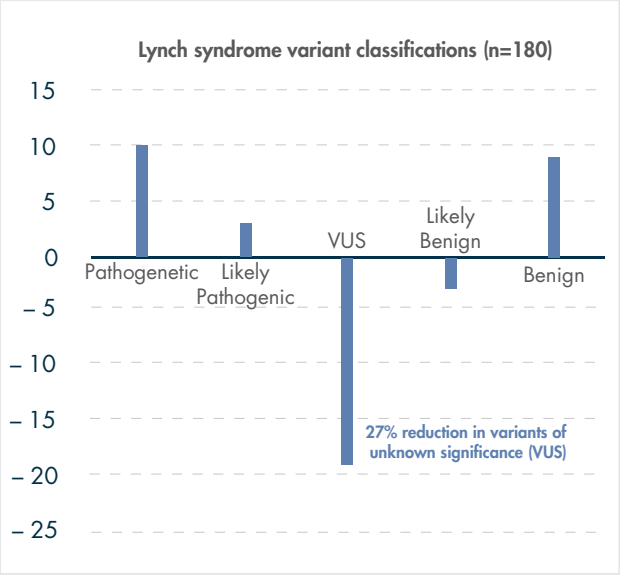


Figure 2. Variant classifications for Lynch Syndrome using QCI Interpret with and without QIAGEN curated primary literature. Data is represented as the difference between variant classifications with QIAGEN content minus variant classifications without QIAGEN content (i.e. public data sources only).

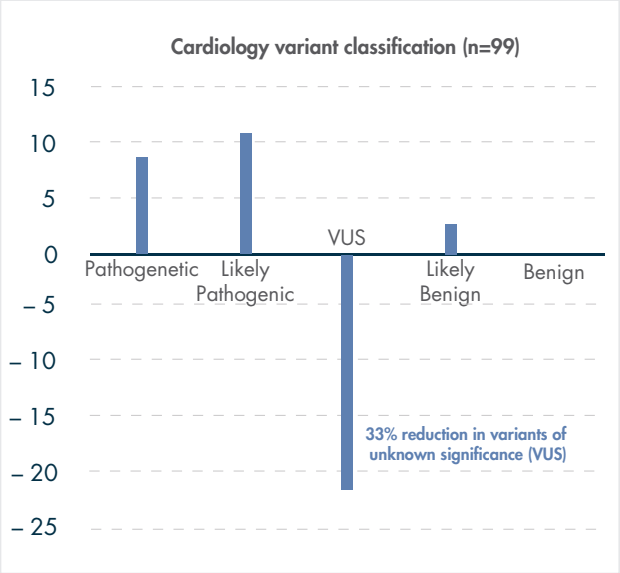


Figure 3. Variant classifications for cardiology disease using QCI Interpret with and without QIAGEN curated primary literature. Data is represented as the difference between variant classifications with QIAGEN content minus variant classifications without QIAGEN content (i.e. public data sources only).

status, co-occurrence with other pathogenic variants, functional study data, and case-control study data.

To demonstrate the challenge of interpreting variants without using peer-reviewed literature, we classified 279 randomly selected variants associated with Lynch syndrome (n=180) (Figure 2) or Cardiology diseases (n=99) (Figure 3) using QCI Interpret with and without content from the curated primary literature. The number of variants classified as having unknown significance (VUS) based on ACMG guidelines was 27-33% lower in the datasets interpreted with primary literature than in the datasets relying only on public sources. That significantly increased the number of variants with clinically meaningful classifications (pathogenic, benign, likely pathogenic, and likely benign).

Content Development

QIAGEN's Knowledge Base enables highly efficient determination of biomarkers that are relevant for specific patient populations. QIAGEN partners extensively with drug and test developers with its Knowledge Base to determine the genetic constituents of pathways and mechanisms of action related to diseases. Use of the Knowledge Base mitigates risk and allows testing laboratories to rapidly expand their test menu roadmap for new disease indications. This process is integrated with QIAGEN's NGS panel development services for design and delivery of custom panels. QIAGEN also provides custom curation services to mine the Knowledge Base for highly specialized diseases areas and clinical use cases.

Clinical Development

Following content development, QIAGEN's Biomedical Genomics Workbench & Biomedical Genomics Sever Solution and Ingenuity Variant Analysis are highly specialized software solutions that allow testing laboratories to rapidly evaluate and iterate variant calling and interpretation pipelines during analytical development of a particular assay. These products are based on industry-leading product portfolios from CLC bio and Ingenuity Systems, both acquired by QIAGEN in 2013. Now fully integrated into a QIAGEN sample-to-insight workflow, these products enable best-in-class clinical test development for labs interested in expanding their personalized medicine test offerings.

Production Testing

Production testing is the implementation of validated tests, variant calling pipelines, and clinical interpretation workflows under a certified production environment to build reports for requesting physicians. The subsequent interpretation and reporting of test results can be fraught with the need for pathologists, clinical geneticists, and variant analysts to access highly disparate data sources to ensure they are citing the most relevant evidence for variant scoring and classification. The QIAGEN Clinical Insight (QCI™) workflow addresses this by facilitating evidence-based clinical decision making through best-in-class interpretation of variant data.

QCI, powered by the QIAGEN Knowledge Base, delivers scalable decision support for NGS tests. Variants are queried against the QIAGEN Knowledge Base to identify and score all relevant sources of evidence from literature, databases, drug labels, clinical trials, and clinical cases to allow for automated scoring of variants according to a customizable set of classification logic rules.

The QCI approach makes it easy for labs to implement diagnostic and treatment guidelines recommended by professional societies (such as the ACMG guidelines) and apply these rules to the automatic classification of diagnostic test results through the most comprehensive database of clinical genetics evidence. QCI is a highly configurable solution that makes it possible for testing laboratories to integrate their proprietary know-how and experience with disease genetics

to edit scoring rules and to customize report configuration for optimal relevance to their requirements.

Operational Efficiencies Achieved with QCI Interpret

Through a collaborative project with a leading genomic testing company, we performed an analysis of time allocation of internal clinical geneticists and variant scientists across the various functional areas. We determined that the activities for these stakeholders are allocated across:

1. Literature curation
2. Variant interpretation
3. Secondary review
4. QA and compliance
5. Meta-analysis
6. Test menu expansion

We compared their allocation of time across these activities when performed internally with manual and internal approaches and after implementation of QCI. Prior to implementation of QCI, the stakeholders allocated approximately 80% of their time to literature curation and variant interpretation (50% and 30%, respectively) (Figure 4). This massive consumption of time detracted from essential activities that are necessary for the long-term commercial viability of the testing laboratory and for reviewing test results with critical or equivocal findings.

The commercial viability of a testing laboratory is largely dependent on the ability of its stakeholders to identify new variants and content for expansion of test content and menu. This is achieved by allocation of resources to meta-analysis of prior test results and investigation of new indications for business expansion.

Stakeholders allocated 10% of their time for secondary review of test results with equivocal or critical findings.

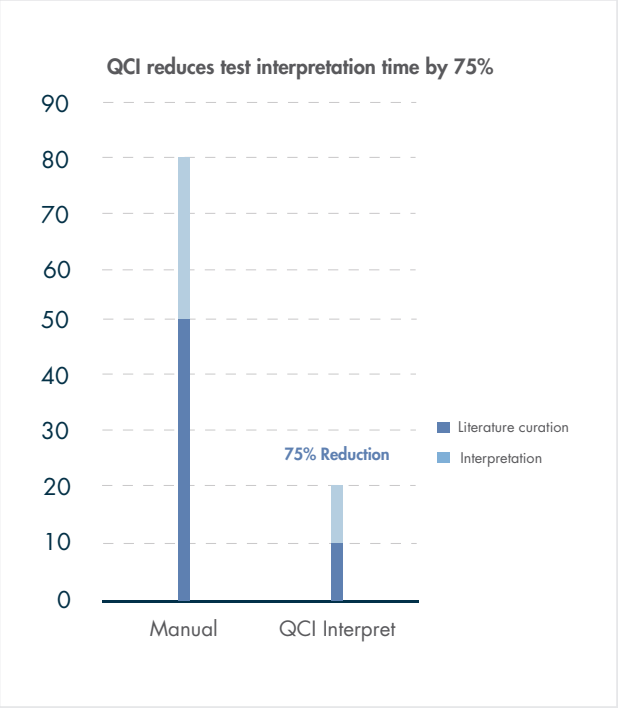


Figure 4. Time-savings for literature curation and interpretation using QCI Interpret.

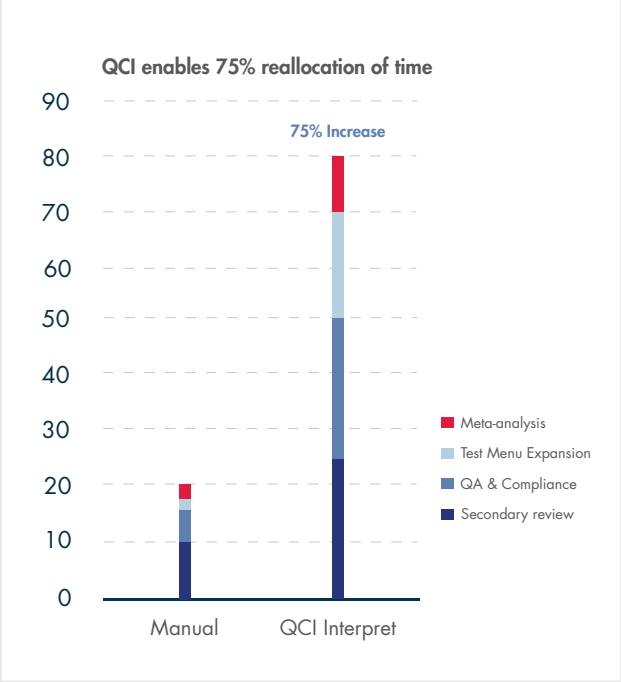


Figure 5. Reallocation of time using QCI Interpret.

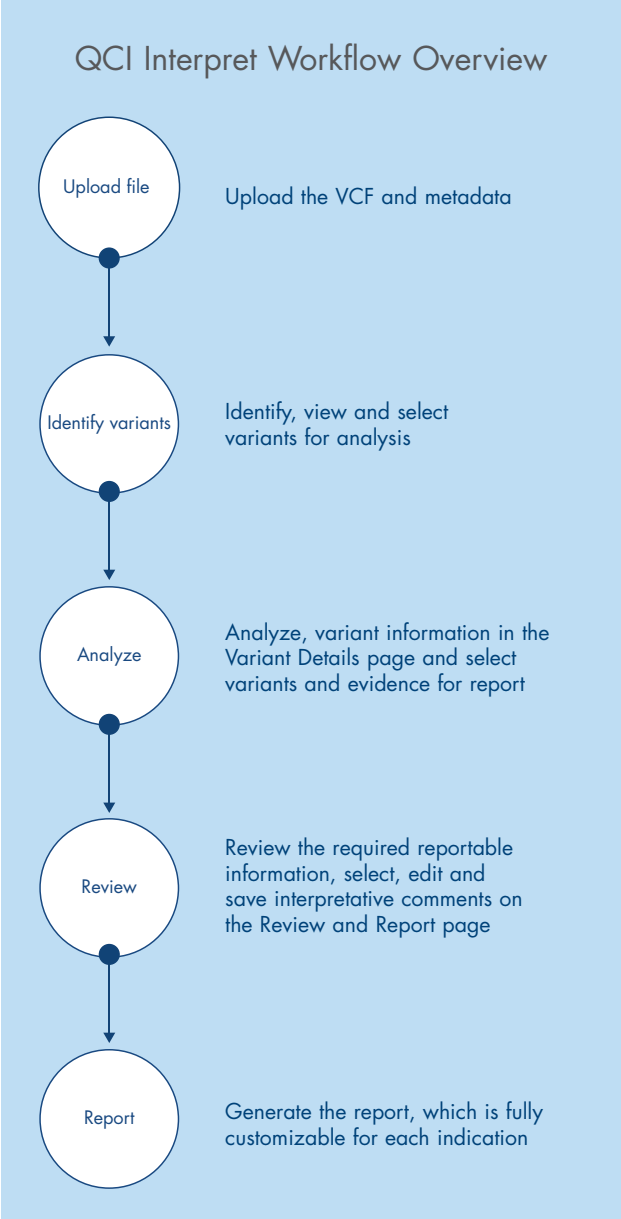
Equivocal test results are often due to sample insufficiency, analytical errors, or the detection of rare findings. Conversely, critical findings that have major clinical implications for patients also require secondary review for unequivocal ascertainment of accuracy. Many times, these samples require additional validation testing with separate test modalities or re-analysis.

Overall, these stakeholders were able to expand their allocation of time by 75% toward these activities, including quality compliance and proficiency testing (Figure 5). The implementation of QCI allowed lab members to achieve tremendous efficiencies by reducing the time allocation for literature curation and variant interpretation. This enabled clinical geneticists and variant scientists to reallocate precious resources toward activities that will help them expand their business. Additionally, increasing efficiency made it possible for the laboratory to drastically scale its test interpretation and reporting throughput without incremental operating expenses.

Advanced Testing

Advanced testing of cases unresolved with routine panels often requires analyzing whole exomes or genomes to determine causative variants. Under these scenarios, test results can detect millions of variants that require extensive filtering against numerous criteria to reduce the variants to the critical few that are definitively implicated in disease causation. QIAGEN's Ingenuity Variant Analysis product uses the QIAGEN Knowledge Base for powerful filtering of specific pathways and phenotypes to enable mapping of variants to patients' phenotypic data. This highly flexible tool is compatible with QCI to allow for seamless analysis, interpretation, and reporting.

Our Hereditary Disease Solution is a highly flexible enterprise platform that enables genomic laboratories to solve more hereditary disease patient cases with superior accuracy and without bioinformatics expert knowledge required. The solution is for next-generation sequencing DNA applications and is powered by three elements: Biomedical Genomics Workbench and Biomedical Genomics Server Solution enable variant identification and filtering, QC reporting, and result validation/visualization, while Ingenuity Variant Analysis is used for data interpretation, filtering, and variant prioritization.



Professional Services

QIAGEN supports its solutions and customers with extensive professional service to ensure easy onboarding and operational integration into local environments and systems. QIAGEN's services cover training, customized API development for integration with local IT infrastructure, custom classification rule configuration for compliance with test reporting policies, configuration of sign-out credentials, integration of analytical criteria, and report configuration. Services are provided in local geographies and with redundant escalation procedures to avoid any interruption in operations and support.

QIAGEN, the Company

QIAGEN is a highly specialized global company with extensive expertise in molecular biology, genomics, molecular diagnostics, sample preparation, and systems integration, with more than 4,500 employees worldwide. The company has a trusted legacy in supporting customers across multiple market segments including government, academia, pharmaceutical and biotech companies, IVD manufacturers, agricultural biotech, and applied markets.

As the innovative market and technology leader, QIAGEN's mission is to create sample-to-insight technologies that provide access to valuable molecular insights from any biological sample. Through innovation and leadership, the company strives to make improvements in life possible by enabling customers to achieve outstanding success and breakthroughs in life sciences, applied testing, pharma, and molecular diagnostics.

Our commitment to the markets, customers and patients we serve drives our innovation and leadership in all areas where our sample-to-insight technologies are required. The exceptional talent, skill, and passion of our employees are key to QIAGEN's excellence, success, and value.

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QCI Interpret is an evidence-based decision support software intended as an aid in the interpretation of variants observed in genomic next-generation sequencing data. The software evaluates genomic variants in the context of published biomedical literature, professional association guidelines, publicly available databases, annotations, drug labels, and clinical-trials. Based on this evaluation, the software proposes a classification and bibliographic references to aid in the interpretation of observed variants. The software is NOT intended as a primary diagnostic tool by physicians or to be used as a substitute for professional healthcare advice. Each laboratory is responsible for ensuring compliance with applicable international, national, and local clinical laboratory regulations and other specific accreditations requirements.