

Streamlining Drug Discovery and Development



Sample & Assay Technologies

Introducing QIAGEN's sample and assay technologies

QIAGEN is the market and technology leader in sample and assay technologies and, in this brochure, we show you how you can access these technologies. We aim to enable you to achieve breakthroughs in drug and vaccine development that will, in turn, advance our shared goal of improving healthcare and disease prevention worldwide. With QIAGEN as your trusted provider, the challenges of researching, developing, and commercializing safer and more targeted medicines, and companion diagnostics for those medicines, will be met with greater success and efficiency.

This brochure describes phases of the drug development process and demonstrates how QIAGEN's sample and assay technologies fit perfectly into the workflow (Figure 1), from early drug discovery to safety assessment and preclinical studies.

QIAGEN® solutions facilitate your demanding research needs by providing:

- Fully integrated product and instrument systems for biological sample analysis
- Low-, medium-, and high-throughput automated solutions
- Customized solutions to meet your specific program goals
- Global service and R&D support
- 100% satisfaction guarantee
- Freedom to operate without reach-through claims

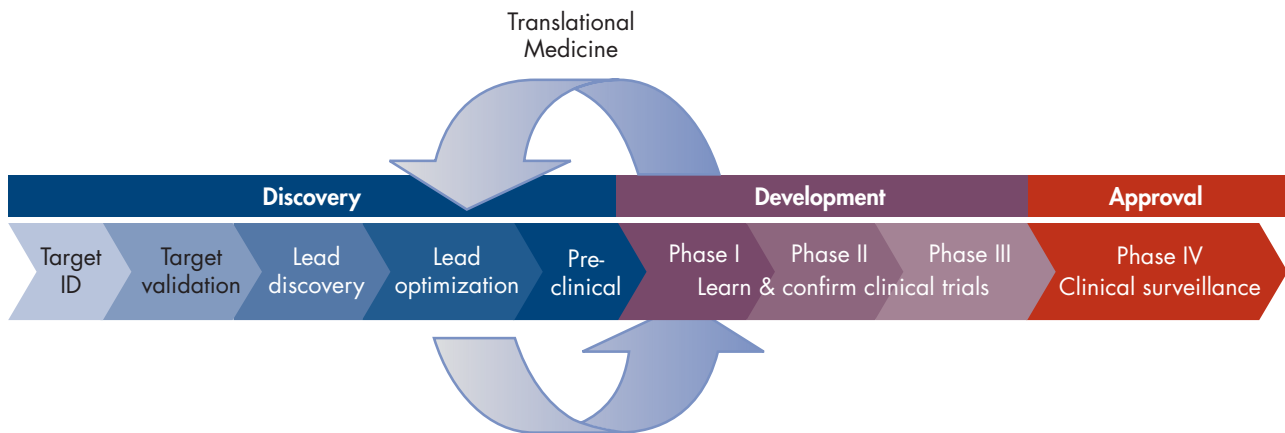


Figure 1. The drug and vaccine discovery and development workflow. QIAGEN sample and assay technologies address the goals of standardization and efficiency across the value chain while providing the flexibility required for translational medicine and “learn and confirm” clinical trials.



Target identification — the identification of biological targets involved in disease etiology which can be effectively targeted by a therapeutic compound. In the post-genomic era, molecular biology techniques are central to the target identification process. QIAGEN's portfolio of genomic, transcriptomic, and proteomic technologies facilitate the identification of biomarkers and corresponding genes. By enabling establishment of standardized techniques, QIAGEN solutions accelerate the target identification workflow and speed to discovery.

Sample collection and stabilization

Appropriate sample handling is a fundamental process in your research. From the start, you can rely on QIAGEN systems for immediate sample stabilization and storage, ensuring the quality of results downstream. The PAXgene™ Blood RNA System is the gold standard for stabilization of whole blood at the point of collection and subsequent RNA purification. To stabilize DNA, RNA, and protein in tissue samples, use Allprotect Tissue Reagent for long-term storage without freezing.

Sample preparation

For genomic, transcriptomic, or proteomic analysis, mutational studies, or cloning, high-quality sample prep is a critical initial step. Trusted kits, including QIAGEN Plasmid Kits, and QIAamp®, RNeasy®, miRNeasy, DNeasy®, and QIAprep® Kits for nucleic acid purification, as well as Qproteome™ Kits for protein sample preparation, ensure your experiments are based on the highest quality starting material. Find out more at www.qiagen.com/Overview/Sample.

Amplification

Whether you are performing quantitative or qualitative analysis, benefit from QIAGEN's expertise in amplification enzyme technology and one of the widest portfolios currently available for PCR and RT-PCR. If you face the challenge of limiting nucleic acid quantity, whole genome and whole transcriptome amplification enable immortalization of DNA and RNA for real-time PCR analysis. For advanced amplification solutions, visit www.qiagen.com/PCR and www.qiagen.com/WGA.

Sequencing

QIAGEN sample technologies that help in your sequencing experiments include QIAprep Kits for plasmid purification, QIAquick® Kits for PCR purification, and DyeEx® Kits for dye-terminator removal. Alternatively, why not take advantage of our years of experience in handling nucleic acids? QIAGEN Sequencing Services range from single sequencing reads to cDNA sequencing, or sequencing of complete genomes.

Gene expression

For efficient gene expression analysis, achievement of accurate real-time PCR with minimum time and effort is a priority. QIAGEN's QuantiFast® Kits help you reach your goal using innovative fast real-time PCR technology for detection with SYBR® Green or sequence-specific probes. For more information, go to www.qiagen.com/geneXpression.

miRNA

Misregulation of microRNA (miRNA) expression is associated with several diseases, including cancers. To support you in this exciting new field of research, innovative miRNeasy and miScript technologies enable purification and detection of human, mouse, and rat miRNA. Find out more at www.qiagen.com/miRNA.

Epigenetics

DNA methylation is of interest in many areas of research, including cancer, DNA repair, cell cycle control, and developmental biology. QIAGEN's epigenetics portfolio covers every step of epigenetics research, from DNA purification to bisulfite conversion and PCR analysis. See www.qiagen.com/goto/epigenetics.

RNAi screening

High-throughput RNAi screens targeting specific gene families, druggable genomes, or whole genomes are invaluable for the identification of genes involved in disease processes and pathways. QIAGEN's expertise encompasses an advanced design algorithm, highly flexible siRNA sets, comprehensively validated controls, and exceptionally effective siRNA transfection. Find out more at www.qiagen.com/siRNA.

Protein purification and detection

A major problem when working with proteins, especially low-abundance proteins, is the sheer complexity of the proteome. To meet this challenge, QIAGEN has developed the Qproteome range of kits for standardized and reproducible protein fractionation and depletion without the need for specialized equipment. If you prefer to use a mass spectrometry approach, QIAGEN's Sample Preparation on Chip (SPOC®) technology delivers high-sensitivity MS analysis, see www.qiagen.com/maldiprep.

Automation

Standardization of operating procedures is an important objective as part of good laboratory practice. QIAGEN automated systems are designed and built for ease of use, process standardization, and reliability. All our systems give high performance, fast results without the need for optimization, and free up your time. The award-winning QIAcube®, which processes up to 12 samples per run, automates multiple QIAGEN spin-column purification procedures. Automated systems that process samples in 96-well format are also available and are preinstalled with optimized protocols for sample preparation, sequencing, genotyping, and gene expression applications.



Target validation — proving that DNA, RNA, or a protein molecule is directly involved in a disease process and is a suitable target for development of a new therapeutic drug. Pharmaceutical industry experts agree that drug target validation is the most critical challenge facing pharmaceutical companies. Given the vast number of potential drug targets that genomics has delivered, it has become crucial to pinpoint those most likely to be amenable to therapeutic intervention. QIAGEN's key sample and assay technologies facilitate detailed studies of individual gene targets.

Gene regulation

Expression analysis of target genes in disease and healthy tissue is a standard part of target validation strategy. When used in combination with RNAi, miRNA, and DNA methylation techniques, many exciting possibilities open up for research into the causes and effects of disease. QIAGEN offers a variety of solutions for gene regulation analysis that have been extensively validated and standardized in combination, so you can be sure that the entire workflow is running optimally.

Knockdown confirmation

Analysis at the RNA or protein level allows validation of gene silencing and pathway disruption. If you require a rapid, high-throughput workflow, FastLane™ Kits eliminate the need for RNA purification, allowing real-time RT-PCR directly from cell lysates (www.qiagen.com/FastLane) . To effectively analyze low-abundance proteins, Qproteome Kits provide a simplified approach to fractionation and depletion, see www.qiagen.com/protein .

Mutation detection

Detecting mutations in disease genes of patient sample collections can generate an enormous data set which is time-consuming and laborious to analyze. Save time and effort by outsourcing to QIAGEN's Mutation Detection Service which uses sequencing-based mutation detection to provide you with clear data focusing on relevant results.

Recombinant protein expression and purification

Validation of potential drug targets often requires detailed analysis of protein structure and function such as in binding studies with small molecules. This makes expression of recombinant protein necessary to produce milligram amounts of the target protein. Identify the optimal expression construct using the EasyXpress® System, purify His-tagged proteins with Ni-NTA matrices, and remove the His tag using the TAGZyme™ System, then start work with highly pure, native proteins.

Protein crystallography in structure-based drug design

The use of NMR and X-ray crystallography to understand precise protein interactions at the molecular level is becoming common practice in validation and in enabling lead discovery and optimization. QIAGEN solutions increase your chances of obtaining protein crystals using the world's largest selection of systematically ordered crystallization conditions, designed to save you time and protein. View the complete range of crystallization products at www.qiagen.com/goto/crystallization.

Automation

The QIACube and BioRobot® workstations ensure efficient sample preparation, which is critical for successful gene expression analysis. For DNA, RNA, and miRNA purification as well as sophisticated applications such as bisulfite conversion of methylated DNA, automated solutions standardize your research.

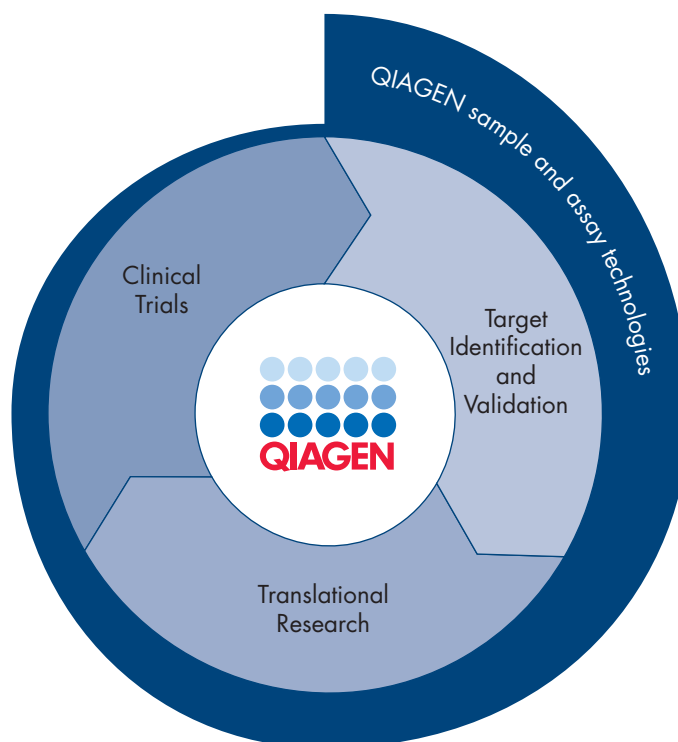


Figure 2. Multiple and varied sample and assay technologies. QIAGEN offers a wide range of diverse technologies for target identification and validation and translational research. For clinical trials, fewer, more-specialized and customized technologies are available.



Translational medicine — integrating basic R&D with drug discovery and early patient testing with clinical trials, for the purpose of making go-no-go decisions as soon as possible. Feedback to discovery enables refinement and reengineering of potential candidate drugs to ensure successful development.

Traditionally, new drugs were developed independently of the clinic, and safety testing and clinical trials often took place in isolation from research labs. Today, many therapeutic development programs use translational medicine to facilitate the interaction between basic research and clinical medicine. QIAGEN's sample and assay technologies enable genomic, transcriptomic, and proteomic research in a clinical setting by taking advantage of proprietary molecular diagnostics and knowledge of regulatory standards.

Safety assessment and toxicogenomics

Toxicogenomic analysis, such as transcriptional profiling, assesses the effect of a drug on living tissue and can predict unwanted side effects. QIAGEN's advanced technologies are ideally suited to support your toxicogenomics assays. For reliable expression analysis, you can maintain sample integrity, preserve true expression profiles, and ensure streamlined, efficient workflows using QIAGEN's complete solution for tissue management. For more information, visit www.qiagen.com/TissueManagement.

QIAGEN assay technologies

In preclinical and clinical development, the availability of straightforward solutions for complex requirements aids clinicians and researchers alike. QIAGEN assay technologies, such as QIAplex Panels for medium-density, multiplex RT-PCR detection of pathogens and RUO and CE-marked *artus*[®] Kits for quantitative RT-PCR for infectious disease testing provide clear-cut, efficient procedures and reliable results.

QIAGEN Genomic Services

For your special projects and specific individual requirements, turn to QIAGEN Genomic Services for a tailored solution. Partnership for assay development, assay validation, and companion diagnostics are all provided with complete flexibility and confidentiality. You can outsource your experiment to our expert scientific team and request customized solutions (page 11).

Automation

Following sample collection, you can automate purification of nucleic acids and proteins for use in subsequent assays using QIAGEN automated systems. The QIAcube automates proven QIAGEN spin kits while the new QIASymphony® SP — which uses proven magnetic particle technology — sets a new milestone in automated sample technologies (www.qiagen.com/MyQIAcube and www.qiagen.com/goto/QIASymphony). For high-throughput applications, the BioRobot MDx workstation purifies nucleic acids for use in applications such as gene expression analysis and genotyping. In Europe, the BioRobot MDx DSP purifies viral nucleic acids from 96 human samples for in vitro diagnostic use. If you prefer to store purified DNA prior to analysis, QIAsafe™ Plates and Tubes provide convenient room temperature storage.

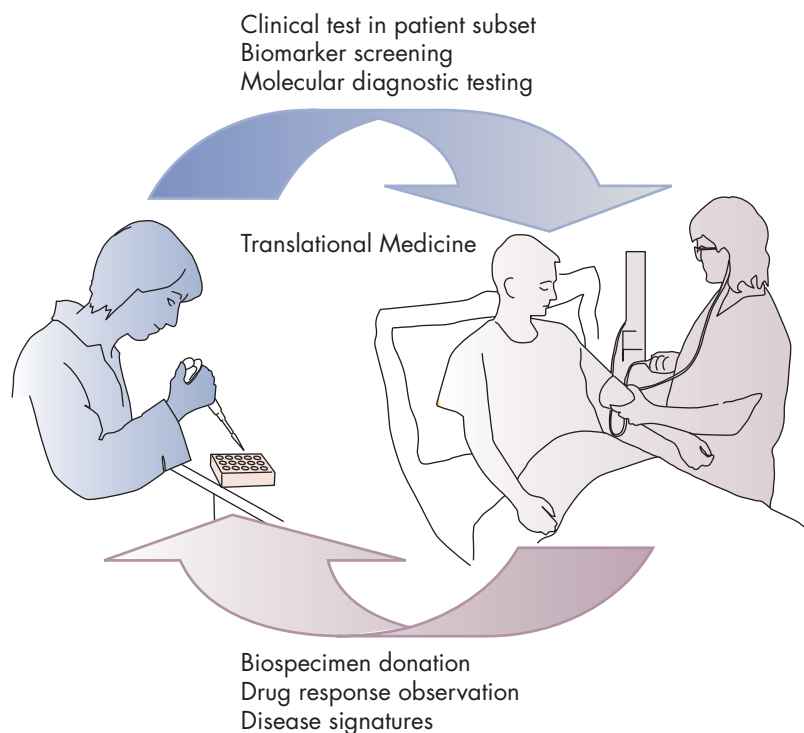


Figure 3. The “bench to bedside” approach. Translational medicine focuses on moving results from basic research into clinical practice, and also on feedback in the other direction.



Clinical trials — evaluating the effectiveness and safety of therapies by monitoring their effects on large groups of individuals. They can be undertaken using a stratified patient population to eliminate nonresponders, minimize adverse reactions, and ensure appropriate dosage.

QIAGEN sample management technologies enable purification of DNA, RNA, and protein from patient samples. Our innovative assay technologies enable rapid, specific and yet complex analysis of analytes in easy-to-use formats, ideal for the clinical environment.

Patient stratification

Using genomic biomarkers, it is possible to identify individuals who will respond to a therapeutic agent. Designing clinical trials to use a responsive patient pool can reduce the overall cost of development and speed up the approval process by eliminating the inefficiency of testing in nonresponsive individuals (Figure 4). QIAGEN is uniquely positioned to facilitate patient stratification through the development and use of genotyping and gene expression assays. QuantiTect® and QuantiFast technology platforms enable singleplex and multiplex analysis without the need for optimization. These technologies are fully licensed allowing transfer of research-based assays to the clinic.

Patient sample handling

Clinical trials demand highly efficient sample handling. PAXgene Blood RNA Tubes and Kits offer a complete preanalytical solution for blood from collection and stabilization through to purification of high-quality RNA. If working with tissues, Allprotect Tissue Reagent immediately stabilizes DNA, RNA, and protein for refrigerated storage.

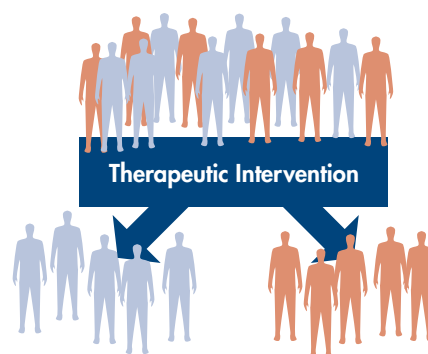


Figure 4. Patient stratification improves efficiency. Defining responsive subsets of patients improves the efficiency and outcome of clinical trials.

Genetic analysis

Genetic analysis enhances understanding of the results of clinical trials. Quantitative, real-time PCR is the preferred method due to its speed and reliability. Whether you perform singleplex or multiplex expression analysis using SYBR Green or sequence-specific probes, QIAGEN provides optimized solutions for all real-time cyclers.

For pathogen detection, select QIAplex Panels which deliver multiplex detection of respiratory pathogens or staphylococcus species and can be combined with detection on the LiquiChip® 200 Workstation.

Patient screening

Molecular profiling of patients allows conclusive identification of disease, stage, and severity. QIAGEN provides complete solutions for sample collection, nucleic acid purification, pathogen detection, and genetic testing. The broad range of IVD-CE-marked solutions enables manual or automated sample processing in combination with PCR-based HLA typing and infectious disease testing. QIAGEN is one of only a few companies with a worldwide PCR license for diagnostics. Discover more at www.qiagen.com/MDX.

Automation

The innovative QIASymphony SP uses optimized protocols and cutting-edge magnetic-particle technology to deliver automated purification of highly pure nucleic acids and proteins from a wide range of sample materials, setting new standards in automated sample preparation for clinical and biomedical research.

The CE-IVD-marked BioRobot MDx DSP offers higher throughput processing of 96 samples in less than 2.5 hours. Compliance with EU Directive 98/79/EC on in vitro medical devices makes validation and quality control fast and easy. The nature of the system streamlines integration into diagnostic workflows.

QIAGEN Genomic Services

QIAGEN Genomic Services cater for special projects and individual requirements. You can outsource your experiment to our expert scientific team and request customized solutions to suit your requirements. View the full range of services at www.qiagen.com/Products/Sequencing . Services include:

- Single-read sequencing
- siRNA hairpin run
- *De novo* and verification sequencing
- Mutation detection
- DNA purification
- Bioinformatics
- Whole genome amplification
- Custom siRNA Sets
- Plasmid preparation
- Other large-volume projects

Customization of solutions

For high-volume projects, QIAGEN offers kits and reagents customized to fit your requirements.

Examples of customized solutions QIAGEN has provided include:

- Bulk PCR reagents in quality-controlled, homogeneous lots for quantification of gene expression by real-time RT-PCR, eliminating regulatory compliance concerns.
- Consistent supply of high-quality enzyme in bulk for His-tag removal in development of novel therapeutics, removing the need for lot-to-lot validation and facilitating regulatory compliance.
- QIAGEN anion-exchange resin and buffers in quality-controlled, homogeneous lots have been supplied to numerous preclinical and clinical trials worldwide and have provided reliable results in gene therapy and DNA vaccine applications.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

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The BioRobot MDx DSP system is not available in all countries; please inquire. TAGZyme technology is licensed under U.S. Patent No. 5,691,169, U.S. Patent No. 5,783,413, and E.U. Patent No. 00759931B1. siRNA technology licensed to QIAGEN is covered by various patent applications, owned by the Massachusetts Institute of Technology, the Carnegie Institute of Washington, Alnylam Corporation, and others.

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Certain specific embodiments of the process of multiplex PCR may be covered by patents of third parties in certain countries and may require a license.

Qproteome GlycoArray Analysis technology is subject to the proprietary rights of Procognia Ltd and sold under license.

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