Elevating Effective Outcomes with Companion Diagnostics

Companion diagnostics (CDx) is a keystone for pharma to create more precise drug therapies as personalized medicine accelerates. Here's why a CDx central laboratory partner is necessary

The successful development and commercialization of personalized medicines often necessitate use of companion diagnostics (CDx).

Now more than ever, drug developers need an experienced global partner to advance CDx development, who understands how to navigate the technical, regulatory and commercialization nuances to enhance the chances of program success.

Additionally, there is a sharpening focus toward smaller populations treated with drugs for orphan indications and rare diseases, umbrella clinical trials where targeted drugs are used for multiple tumor mutations, and basket clinical trials where targeted drugs focus on multiple tumor indications.

The improvements that precision medicine brings to patient outcomes are increasingly being implemented in clinical practices worldwide. Companion diagnostics are assays that are required to be used before a specific therapy can be initiated. They are often co-developed alongside a therapeutic during its clinical development journey. Extensive testing in clinical trials is required, often in multiple sites across the globe.

CDx enables more effective development of personalized medicine by identifying likely patient responders based on efficacy and safety. The FDA released a guidance document ("In Vitro Companion Diagnostic Devices"), deeming essential that CDx needs to be considered early in drug development, and to plan for co-development of the product with a companion diagnostic.[1]

This is the junction where Q^2 Solutions enters and leads the journey through development. Q^2 Solutions has a venerable track record of successfully supporting drug developers and in-vitro diagnostic (IVD) companies in many global CDx programs, from the early stages of biomarker validation through clinical trials testing and commercialization.

CDx projects tend to be highly intricate, often necessitating involvement of an IVD company, a global central laboratory and pharmaceutical company. These projects tend to carry substantial cost and risk in their development. Q^2 Solutions expertly and deftly supports the traditional path of CDx development through its network of global laboratories by testing samples using IVD products.

Concurrently, as an alternative, a single-site premarket approval (ssPMA) model is increasingly considered within the industry under specific circumstances. Q^2 Solutions' CDx experts can direct co-development strategies towards the most appropriate route. Considerations include disease indication, complexity of assay, addressable market size in the post-approval setting, and ability and willingness to invest in an IVD CDx -- especially in the early stages of a clinical development program.

"As part of the CDx assay development strategy, it is good practice to review all technical, regulatory and clinical aspects with a line of sight towards the ultimate positioning of a reimbursable assay in the marketplace," says Alan Wookey, Global Head, Companion Diagnostics. "Many considerations will determine the best path. Using our experience, we review multiple strategies and provide recommendations for the right co-development approach, helping execute a strategy for a traditional IVD-led path to CDx development, or towards an ssPMA path that could be supported under our quality systems regulation (QSR) infrastructure"

Partnerships: The Key Difference

There is no room for error when during co-development from planning through execution. The right partnerships can significantly elevate success rates. Successful CDx development relies on effective partnerships between groups with the required expertise to optimize probability of success. Q^2 Solutions is flexible and responsive, employing numerous partnership models, each with embedded roles and responsibilities for the specific partners involved.

In Q^2 Solutions' experience, early set up of three-way partnerships between the central laboratory, pharmaceutical sponsor and IVD manufacturer provide a framework to allow open discussion to ensure all three parties are aligned for planning, conduct and execution. Those frameworks have allowed Q^2 Solutions to be successful in supporting several major approvals for several oncology indications from its global laboratory network.

Q^2 Solutions Capabilities

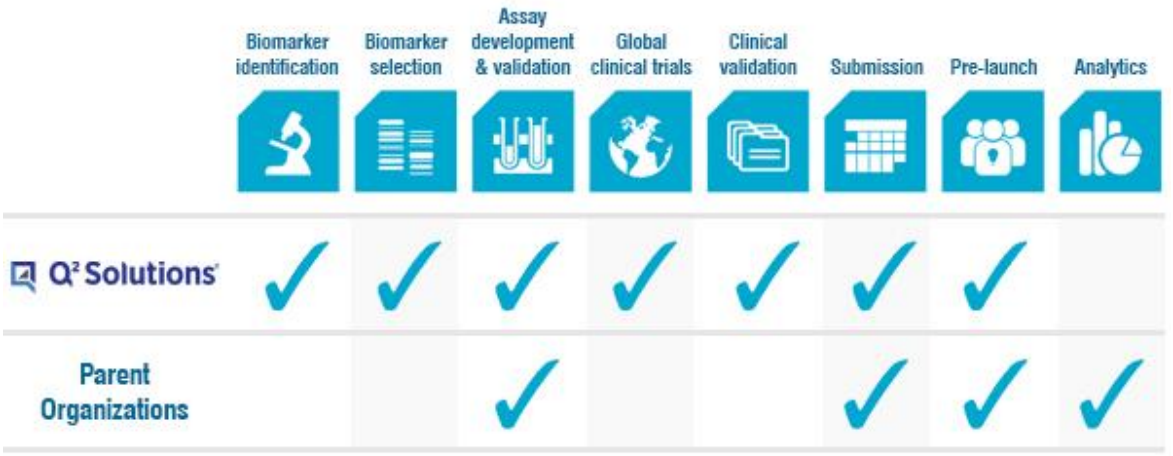
Q^2 Solutions is uniquely prepared to collaborate with the IVD partner and the pharma or biotech company, starting with early engagement, the drug development process and through to launch and commercialization.

All partners should be engaged as early as possible. "Constant communication between all partners, including regulatory authorities where feasible, is critical," Wookey emphasizes. "Early engagement with our experts can help circumvent issues during clinical development and provide a clear direction for commercial/post approval assay testing. Early in the co-development process, our experts lead discussions on key topics, such as assay validation versus its intended use and the regulatory paths to enable approval."

In working with Q² Solutions, risks associated with cost, feasibility and timelines are identified and mitigated as early as possible. It is important to identify clear roles and responsibilities are identified for all parties during the execution of the clinical trials, emphasizing deliverables, timelines and the escalation process. All parties should identify critical tasks, discuss potential risks, and ensure collective signing off on agreements and on any ulterior modifications under change control. Initial results generated with clinical trial samples must be reviewed jointly by subject matter experts from all parties to be clear on the performance of the assay, so that course corrections can be made early.

To develop a clinically and commercially viable CDx strategy, partners need to ensure that the assay is reduced to practice. Real-world feasibility, platform, sample type and collection, pre-analytics (including shipment and stability), throughput, and the percentage of test repeats and generation of unambiguous results all need to be considered in the context of multiple jurisdictions. Assay robustness and clinical utility should be assured using clear, actionable medical value cutoffs. Lab commercialization implications must be considered with respect to reimbursement, education, and asymmetry in revenue between the IVD manufacturer and the drug developers.

Q² Solutions works with IVD companies that provide developed assays tested at its central labs (qualified by the IVD partner companies), following a verification of assay performance. In addition, following installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ), utilizing a central laboratory that has been previously qualified allows the process to be streamlined through a site initiation visit, proficiency training and study start-up. Q² Solutions utilizes on-site and dedicated principal investigators and study coordinators to assure compliance to the testing and regulatory requirements, as well as operational excellence through the delivery of data to clinical sites and study sponsors.



Seamless Global Coordination

According to Wookey, global solutions are increasingly needed because of the advancements in clinical development in China and the challenging regulatory conditions on sample import and export. Q^2 Solutions has supported CDx assays for 12 years, and continually advances its capabilities -- technology, bioinformatics, regulatory compliance, clinical and commercialization aspects. Q^2 Solutions has extensive companion diagnostics experience across the world, including APAC, China, EMEA and US, and we have generated lab data supporting multiple successful CDx submissions and more than 150 CDx clinical trials engagements.

With an extensive instrument footprint in laboratories throughout the world, Q^2 Solutions can expediently service CDx requests utilizing a range of technologies: immunohistochemistry (IHC), fluorescence in situ hybridization (FISH) next generation sequencing (NGS), and quantitative polymerase chain reaction (PCR).

Wookey explains, “Most clinical development programs require testing to occur in sites across the globe, and we have harmonized CDx SOPs in our sites. Our on-site pathologists are trained across indications by the IVD company for IHC cut-off evaluations, and we dedicate CDx study coordinators and both regional and local project managers on every CDx study. Also, all pathologists are Q^2 Solutions employees.”

Region	AP- IHC I/O (PDL1)	AP-IHC Other	FISH / ISH	Molecular NGS	Molecular Other	Other Protein
APAC	✓	✓	✓		✓	✓
China	✓	✓	✓	✓	✓	
EMEA	✓	✓	✓		✓	✓
US	✓	✓	✓	✓	✓	✓

Conclusion

Predictive medicine utilizing companion diagnostics is commonplace within oncology clinical development. Careful alignment of the technical, regulatory, clinical and commercialization factors is required to enhance the success of obtaining approval and market adoption of CDx assays. With extensive experience, Q² Solutions has the appropriate structure and attributes and indeed the global experience to help deliver successful CDx programs.

(1) FDA Guidance Document: “In Vitro Companion Diagnostic Devices” August 2014; Docket # FDA-2011-D-0215 issued by Center for Devices and Radiological Health

Written by Alan Wookey for Outsourcing Pharma. September 2020.