IQVIA LABORATORIES

Companion Diagnostics Expertise

Introduction

A companion diagnostic (CDx) is a medical device, often an in vitro diagnostic device, that is a companion to a therapeutic drug, providing essential information for the safe and effective use of the corresponding drug or biological product.

Companion Diagnostics (CDx) can enable personalized medicine, or precision medicine, by identifying likely responders based on efficacy or safety. Guidance released from the FDA in 2014 urges developers of therapeutic products to consider CDx earlier in the drug development, and to plan for co-development of a therapeutic (Rx) with a Companion Diagnostic.[1] The objective of that guidance is to foster relationships that will result in faster access for patients to promising new treatments.

IQVIA Laboratories has been able to successfully support drug developers in many of these clinical development programs globally from the early stages of biomarker testing through clinical trials testing to commercialization.

Managing complexities — delivering targeted therapeutics with CDx

Drug manufacturers are aware that companion diagnostic tests can greatly increase the clinical success of drugs by delivering their targeted therapeutics to a subpopulation of patients that has been carefully identi ed. As a diagnostic assay is part of a patient trial investigation, diagnostic device clinical trials are two trials in one, often co-development studies — a patient trial and a diagnostic device trial, or a trial on the instrumentation and/or reagents. This adds intricacies for the clinical trial laboratory advancing a study through analytical and clinical validation, regulatory approval, and market launch to enable optimal market uptake and commercial success of CDx/Rx combination. For instance:

- A principal investigator is needed for the diagnostic device part of the trial
- Patient samples from the drug trial are used as part of the CDx/IVD (in vitro diagnostic) portion of the trial
- CDx IVDs are typically classified by the FDA as Class III diagnostic devices, facing the highest regulatory hurdles
- Additional regulations may impact the trial depending on the geographical location of the testing or where the recruited patients are based. For example, in the EU, IVDR regulations could apply

We have the scientific, regulatory and technical expertise and global reach to deliver successful CDx trial execution

180 clinical studies

conducted with an intended CDx use

[1] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf

From early engagement to launch and commercialization

We provide holistic CDx offerings, including validation, verification, clinical trial testing, regulatory services, and commercialization guidance. Data generated from clinical trial sample testing in CDx studies is typically used for inclusion/exclusion or to stratify across treatment arms. This data is then provided to the IVD company to support their submission, including a CDx assay submission. Our laboratories are CAP-accredited and CLIA-certified, and our EU laboratory is certified to ISO 13485.

As part of the larger IQVIA CRO, IQVIA laboratories have access to analytical tools that can be applied to identify patients for clinical trials and clinical sites. Specifically for oncology studies, these tools help identify clinical sites that consistently provide high-quality formalin-fixed paraffin-embedded tumor tissue.

Across the CDx life cycle we are able to tailor our offerings to meet the needs of the particular study, beginning with advisory services for development, trial enrollment and commercialization and reimbursement planning. Beyond the feasibility phase, we work with our partners around assay development, laboratory and clinical validation through scale-up, leveraging our global footprint of laboratories and complementary services, for IVD, single site pre-market approval (ssPMA), and inter-lab reproducibility (ILR) studies. We have collaborated over many years with IVD partners, structuring 3-4 way multiparty deals. For an ssPMA route, we can manage the assay design control elements and FDA submission responsibilities, allowing for successful premarket approval.

We have the right relationships to ensure proper access to GMP reagent manufacturers. Our advisory services provide consultation on global implementation of CDx commercial strategies. And, we partner with our parent company's leading commercial laboratory to offer a global commercial solution.

	BIOMARKET IDENTIFICATION	BIOMARKER SELECTION	ASSAY DEVELOPMENT AND VALIDATION	GLOBAL CLINICAL TRIALS	CLINICAL VALIDATION	SUBMISSION	PRE-LAUNCH	ANALYTICS
IQVIA LABORATORIES	✓	✓	✓	✓	✓	✓	✓	
PARENT ORGANIZATIONS			✓			✓	✓	✓

Scientific expertise

- Our global central laboratories have laboratory directors and Principal Investigators that specialize in specific CDx disciplines: **Anatomic Pathology,** Immunohistochemistry, Molecular, NGS and more recently **Flow Cytometry**
- Our CDx services include in-house global Anatomic Pathologists who have been trained and proficient to report out IHC results. Capabilities in FISH and ISH with specific immuno-oncology capabilities for tumor infiltrating lymphocytes (TIL) measurement are available globally
- We have a comprehensive suite of **genomics services** and expertise to help design and deliver CDx using **Next Generation Sequencing** (NGS) for applications such as **tumor mutational burden** (TMB) and expression profiling. Most of our Genomic capabilities have been replicated at our Beijing, China facility.

Options for in vitro diagnostic (IVD) or single site pre-market approval (ssPMA) paths

Our experts provide a exible approach, working in collaboration with our pharmaceutical company partners to choose the right regulatory pathway for optimized CDx commercialization via an IVD or ssPMA path

Option 1 — IVD

Traditional path:

- Most FDA approved CDx, e.g. HER2, PD-L1, EGFR
- IVD leads Regulatory and Commercialization Central Labs used for testing — Clinical trials or reproducibility studies

Option 2 — ssPMA

May be appropriate when:

- Defined geography
- Limited size of market
- Short timelines (between clinical phases)
- Big investment in IVD is risky
- Complex testing technology

Option 3 — Transfer ssPMA to IVD

Transfer occurs at some milestone, typically before design control:

- De-risks program for all stakeholders

Experience in CDx collaboration and partnering

We have many years of experience in collaborating with established and emerging IVD and life science partners in developing companion diagnostics for simplified multi-party engagements and seamless trial execution. As leaders in co-development, we develop strong partnerships and forge broad and deep relationships between pharmaceutical companies and the IVD CDx partners. Below is an example of a collaboration with NGS:

Case Study: NGS CDx

Situation

- Large pharma and RUO instrument provider (NGS) developing novel, second-generation CDx
- Complexity of data analysis, sophistication of assay platform, and challenges NGS-based CDx necessitated a lab with technical and analytical expertise

Solution

- Collaborative study planning and ongoing, direct communication with diagnostic partner for resource planning and assay-specific SOP development
- With pharma/Dx partners, IQVIA Laboratories developed processes and procedures for NGS diagnos- tics, including development of validated databases in support of the CDx trial and FDA submission

Results

- On-time delivery of quality data for ssPMA submission for a novel CDx assay
- Establishment of approved SOPs and best practices for pharma and Dx sponsor for ready implementation commercially as well as future studies

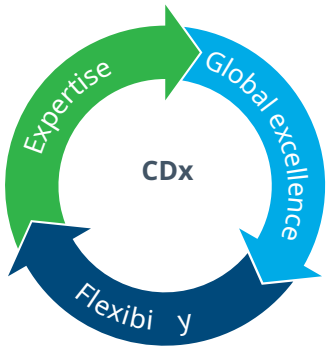
Integrated solutions for our clinical trial partners

With our global network of laboratories across US, Europe, China and Singapore, and experienced team of experts, we are uniquely positioned to provide successful companion diagnostics delivery.

Global delivery excellence

We leverage extensive scientific, clinical, regulatory and operational capabilities & expertise to manage the complexity of CDx trials on a global scale.

- Robust infrastructure with leading methods and processes around managing studies, site support, regulatory requirements, at each of our sites; China CDx experience
- Unique software solution for sample tracking through their lifecycle across the ecosystem of sites, labs, biorepositories, and other trial partners. BioFortis, a IQVIA Laboratories company, associates virtually any kind of data, using a powerful query tool to allow rapid identification of stored samples — with specific profiles for demographics, disease state, clinical outcomes, therapy, biomarker results, and other parameters, in addition to consent eligibility. Learn more about the true end-to-end sample tracking technology and services solution, and seamless integration with eConsent.
- Anatomic Pathology footprint in North America, Europe, Asia-Pacific and China
- Global commercial/clinical diagnostic testing — clinical trial technical and testing capabilities, including China
- Established governance model with oversight management for global delivery excellence, with a logistics and courier network to route samples. Regulatory compliance experts knowledgeable in U.S. and ex-U.S. regulations. Compliance across all sites from setup to data submission, delivering a harmonized and standardized infrastructure. Local



Proven companion diagnostics

Our strong scientific and technical expertise to allow us to execute on the technologies of today and tomorrow.

- **Commercial** — Extensive knowledge in CDx allows us to provide recommendations on multiple approaches for CDx commercialization
- **Scienti ic** — We use technologies such as NGS; our network includes global in-house AP services with onsite Anatomic Pathologists
- **Regulatory** — We have a thorough understanding of the CDx regulatory landscape on a global scale, and can define the assay characteristics to take for regulatory approval

As a leading clinical trials laboratory services organization, we have years of experience in companion diagnostics services. There are many factors to consider with companion diagnostics, and our solutions deliver the science, clinical, regulatory, and commercial expertise to support development of your companion diagnostic. Contact us to learn how we can help you.

CONTACT US
Toll free: +1 855.277.9929
Direct: +1 919.998.7000
International: +44 (0) 1506 814000
labs.iqvia.com

IQVIA LABORATORIES