DNAnexus®

Powering the Future of Diagnostics:

QSRs & GxP Compliance for Partnering with Pharma & Beyond

As pharmaceutical companies are incorporating companion diagnostics as part of their regulated submission, they are also partnering with diagnostics companies to incorporate their tests as critical steps in drug development and clinical trials. Increasingly, pharma are developing more targeted therapies and treatments, and need access to tools that can help them stratify patients for clinical trials. Next-generation sequencing-based assays and panels are now used in oncology to select patient candidates for participation in clinical trials focused on various cancer subtypes as well as for assessing prognosis and likelihood of recurrence. As a result, pharma needs diagnostic partners that can provide access to large quantities of clinco-genomic data that can be used for their regulated processes.

Diagnostic partners bring value by having their tests marked as companion diagnostics to targeted treatments as this also provides a path to approval by the relevant regulatory authority (e.g. FDA, MHRA, EMA, etc). For example, tests from Myriad Genetics are approved in the US as companion diagnostics to olaparib, a treatment for breast, ovarian, pancreatic, and metastatic castrate resistant prostate cancers. Diagnostic partners can generate additional value to pharmaceutical companies by quickly identifying candidates that meet the selection criteria for their trials, are most likely to benefit from treatment and minimal adverse events — speeding the time for achieving "database lock" on information accrual for preparing regulatory submissions.

Working with pharmaceutical companies as a customer brings new challenges. Pharma takes on significant risk by sharing with third-party partners, using processes and protocols that they have no control over. Compliance with Quality System Regulations (QSRs) — also known as a GxP compliance — is critical to operating in this heavily regulated environment. Pharma companies and their diagnostic partners are required to meet these QSRs. Understanding and adhering to QSRs is crucial for diagnostics companies to ensure that their data and accompanying tests meet the quality regulations that pharma needs to file for regulatory approval of their drugs. This compliance extends from the wet lab test processes through the supporting informatics infrastructure that diagnostics companies use to capture, analyze and store the genomic data collected in a consistent and reproducible manner.

1 What is QSR quality & GxP?

The FDA's quality system regulation (QSR) as defined by 21 CFR § 820 states that manufacturers shall establish and follow a quality system to help ensure their products consistently meet applicable requirements and specifications. In this context, "manufacturing" means the processing of samples from the wet lab through analysis and integration into the clinical decision support system. GxP is an abbreviation of supporting guidelines focusing on cGMP (current Good Manufacturing Practices), cGLP (current Good Laboratory Practices), cGCP (current Good Clinical Practices), etc. Newer guidelines, such as Software as a Medical Device (SaMD) and applicability of AI/ML to the software that interprets data streams follows the general approach of the QSRs and the GxP guidelines. Similar guidelines appear in the ICH documentation.

These guidelines can be summarized under the Quality by Design (QbD) elements:

Context - pertains to the metadata or contextual information required to understand the data, including structured information that describes, explains or otherwise makes it easier to retrieve, use or manage data.

Traceability - ensuring that all the processes and objects managed by these processes are documented to establish their provenance and documented state at all times. Traceability processes provide a mechanism to reconstruct and recreate every object and managing process.

Accountability - creating an auditable record describing every action traceable object trail throughout the regulated processes.

Data Integrity - described as "...the degree to which data are complete, consistent, accurate, trustworthy, reliable and that these characteristics of the data are maintained throughout the data lifecycle. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate."

Data Governance - addresses the data ownership and accountability throughout the lifecycle, and considers the design, operation and monitoring of processes and systems to comply with the principles of data integrity including control over intentional and unintentional changes to data.

A range of compliance guidelines fall under the GxP umbrella, but there are three that are important for diagnostics companies seeking to partner with the pharma industry. Keep in mind, any data or records stored electronically must comply with 21 CFR § 11 (Annex 11), including the requisite requirement for Computer System Validation and described in the following FDA Guidance document.

Current Good Clinical Practices (cGCP)

Good Clinical Practices refer to practices that ensure the quality and protection of data collected from human subjects. These practices set minimum standards for conducting clinical trials using human subjects that test the safety and efficacy of drugs, diagnostics, and medical devices. They ensure that clinical trials are conducted in ways that protect the subjects' rights, safety, and well being while generating reproducible and scientific valid results.

Current Good Laboratory Practices (cGLP)

Good Laboratory Practices provide a set of rules and criteria for a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, reported and archived. For example, these practices might apply to a pharma company that is developing CRISPR-based therapeutic agents that do not involve human subjects. These guidelines describe the conditions under which these tests should be performed, evaluated, and reported, as well as the requirements for all procedures, equipment, and personnel.

Current Good Manufacturing Practices (cGMP)

Good Manufacturing Practices are put in place to ensure that manufacturers meet a minimum set of standards for the methods and infrastructure that they use to manufacture, process, and package products such as drugs, medical devices, and active pharmaceutical ingredients. The guidelines ensure that the facilities used to produce the drugs are properly maintained and meet standards for cleanliness, and that the equipment is properly calibrated. They also ensure that the production processes are consistent and reliable and that staff have the right qualifications and training.

Notice: We are seeing the FDA and other regulatory agencies leveraging cGMP practices to "manufacture" phenotypic (e.g. Real World Data and Real World Evidence) and genotypic information used in regulated processes.

.

2 Why DNAnexus?

Building a bioinformatics solution that complies with GxP guidelines can be daunting even for the most experienced diagnostics company. In order to collate and share large amounts of patient data with pharma, the data has to be captured, processed, and stored in a GxP compliant environment. Furthermore, diagnostic test processes and protocols also need to adhere to the same stringent regulatory standards used by pharma.

DNAnexus is a trusted bioinformatics partner that provides the expertise, process, and technology that diagnostic companies need to ensure that their offerings comply with GxP guidelines. We work with customers to understand their business needs, who their customer is, and the relevant regulatory requirements applicable to their use case and geographic location.

The DNAnexus platform provides a consistent experience for scientists to run their analyses in a way that achieves and maintains compliance with current regulations, standards, and industry frameworks. The DNAnexus team is fully trained with clear roles and responsibilities and we can provide full documentation of processes and procedures for regulatory submissions. With DNAnexus' support, diagnostics companies can develop and deploy their tests at scale in regulated environments.

Some other benefits of using DNAnexus for GxP are:

Ease of onboarding - Diagnostics customers can easily port their pipelines to 21 CFR § 11 (Annex 11) compliant environment, inheriting the computer system validation documentation provided by DNAnexus for both the DNAnexus Titan™ and DNAnexus Apollo™ products. The customer remains responsible for the computer system validation of their pipelines relevant to their regulated processes/systems.

Rapid time to sales - The level of effort to move a non-GxP pipeline to a GxP compliant pipeline is reduced to performing the pipeline validation. The engineering and performance is exactly the same as non-GxP environments, making the "tech transfer" into the regulated state very straightforward and predictable. This helps customers keep costs down and speed time to market.

Global reach - Quality System Regulations and GxP practices are similar across countries. This means that diagnostics companies that use DNAnexus will be compliant with country-specific regulations whether they are operating in the US, UK, Europe, or beyond.

Secure and protected environment - Data from tests and clinical trials have to be safely captured, stored, and processed. DNAnexus' platform meets the highest standards for security, privacy, and safety. Our customers can be confident that their intellectual property is safe and secure at all times even when working with partners across the globe.

Standardized analysis and reporting - The DNAnexus platform is built from the ground up to provide informatics infrastructure that reliably and consistently performs data analysis and generates detailed reports.

Audit support - Regulated industries are required to perform vendor assessments. At the very least, diagnostic companies will undergo a supplier audit. Diagnostic companies supporting pharmaceutical companies will also undergo separate Security and Quality audits. As the pharmaceutical company shares more risk with diagnostic companies, the degree of scrutiny increases. DNAnexus undergoes 50+ customer assessments and audits every year, not counting the ISO and FedRAMP security audits. Our expertise in regulatory compliance in the QSR space can be directly or indirectly leveraged to help customers pass their audits and demonstrate the risks are identified and effectively managed.

DNAnexus' approach simplifies QSR compliance for diagnostics companies, freeing them to focus on building and expanding the value of genetic tests rather than worrying about regulatory compliance. Connect with our team of experts to learn how DNAnexus can help your company build and support new partnerships globally, and reach out to discuss your specific QSR/GxP compliance needs by emailing us at **info@dnanexus.com.**