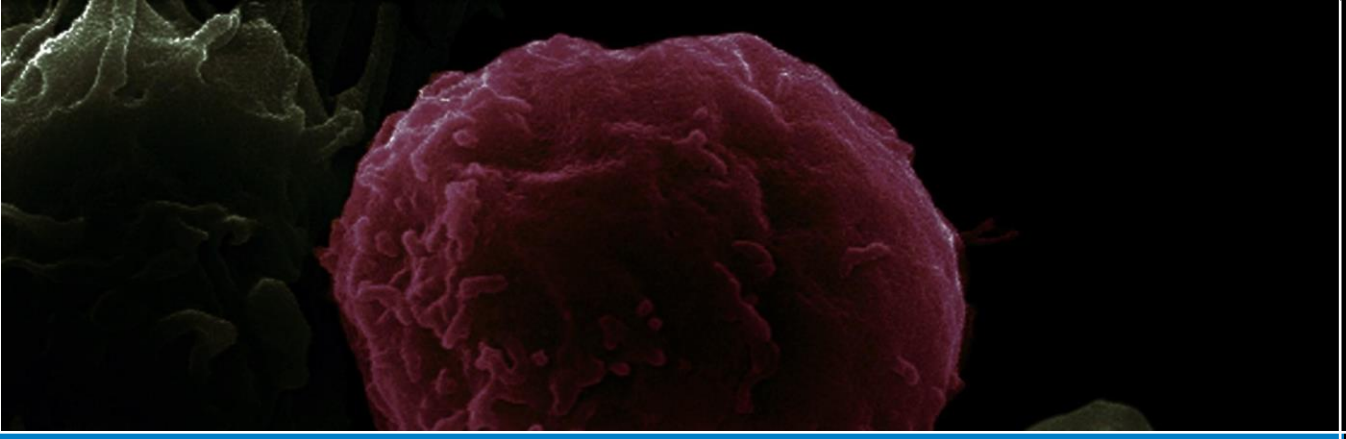

Sample Chaos in Oncology Clinical Trials

Challenges and opportunities for generating scientific and operational insights

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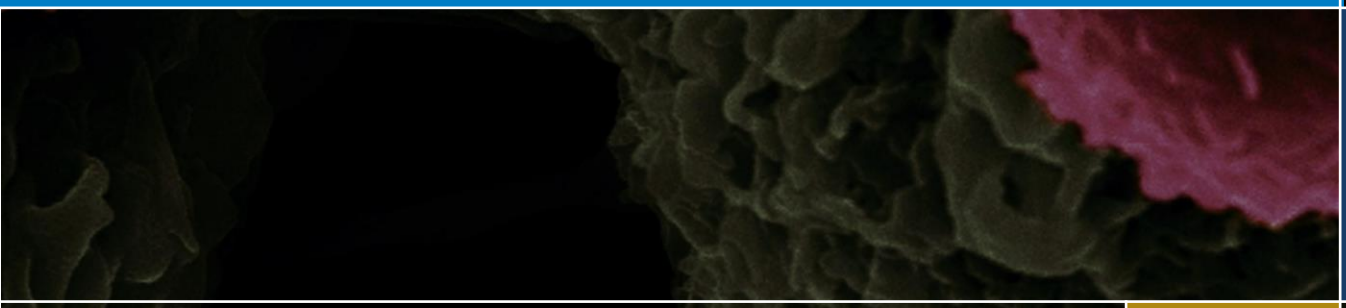

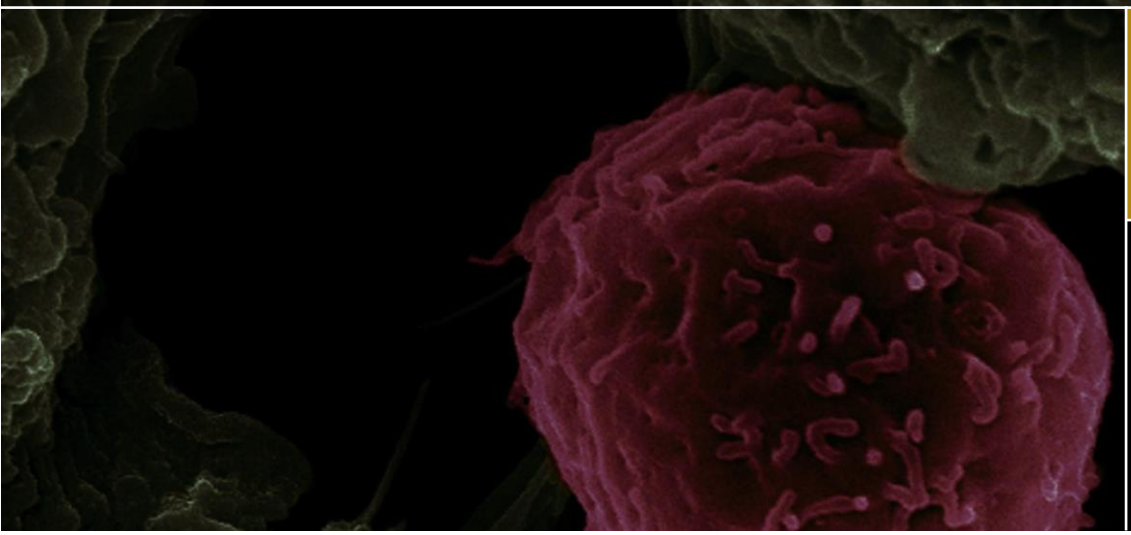

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Clinical sample chaos: Gaining centralized visibility into sample collection, processing, and storage status across siloed systems

Clinical samples in modern, biomarker-informed oncology trials traverse a complex path, with data located in multiple systems, most of which are not "sponsor-centric." Clinical operations and translational science teams lack visibility into questions like:

- "Are we collecting the samples we expect and need?"
- "When will we have enough samples to trigger batch processing?"
- "Have these samples been properly consented?"

In this ebook, we explore the challenges of monitoring clinical sample status in biomarker-rich therapeutic areas, including oncology. We discuss how breaking down data silos can enable clinical and translational teams to streamline trial operations and generate actionable insights.

1. Centralizing PK, Clinical, and Exploratory Data to Advance Biomarker Operations and Translational Intelligence

The COVID-19 pandemic has forced clinical trial stakeholders to rethink the paradigm as sponsors adapt to site restrictions, remote monitoring, and updated regulatory guidance.

This is especially true in precision oncology programs, which have developed global footprints in order to reach targeted patient populations and rely on specialty labs running complex assays to assess safety, characterize patient response and drug MoA, and provide insights into efficacy.

In the absence of consistent and predictable in-person presence, how can sponsors maintain the timely visibility necessary to optimize operations of these complex trials?

One critical challenge is the chain of events that starts with sample collection at sites, follows sample movement to central and/or specialty labs, and culminates in assays being run to generate complex biological data for on-study and broader insight generation.

In many ways, this value chain highlights the critical links between trial operations, translational science, and clinical development (and is arguably at the heart of biomarker-centric development).

Yet, traditional clinical trial management systems like EDCs (covering patient data) or CTMS (covering document management, payments, and the like) are not well suited to delivering on-study visibility and actionable insights within this realm of translational studies.

Our team has identified three key areas that span site performance, sample availability, data availability, data quality, and translational intelligence that are critical to today's biomarker-centric clinical trials:

1. **Visibility into sample collection and processing:** including performance by sample type, cohort, and site; confirming the right samples to the right lab at the right time should be viewed on executive dashboards alongside KPIs like enrollment status
2. **Biomarker data availability and data quality:** sponsors make significant investment in generating biomarker data because of the depth of insight it can enable. It is critical to maintain insights into assay- and batch-specific performance throughout studies, as well as general data availability, to meet scientific objectives
3. **Delivering translational intelligence:** once integrated, effectively analyzing the millions of data points to distill key insights across operations, science, and beyond, leveraging dashboards and tools that deliver actionable intelligence. This spans on-study performance evaluation (e.g., dose escalation meetings), understanding MoA, and informing strategic development decisions more broadly.

Of course, much of the information necessary to deliver translational intelligence exists today – though it is dispersed across workstreams (e.g., sample, assay, translational, clinical, data management) and stakeholders (e.g., CROs, sites, labs, sponsors) and systems (e.g., EDC, CTMS, LIMS). As a result, attaining visibility is a laborious, manual, and ad hoc exercise diverting attention from gaining insights from the collected data. Along with the current challenges facing the industry, there is an opportunity to integrate and centralize data, enabling sponsors to overcome the roadblocks to unlock transformative insights.

2. From Translational Teams to Clinical Operations: The Cross-Functional Impact of a Fragmented Clinical Sample Data Ecosystem

Clinical samples are moving across an increasing number of physical/virtual locations and data is delivered in an expanding array of file formats as clinical trials become increasingly more complex and data rich (report).

Biospecimens are analyzed using a variety of assay technologies, each generating its own set of reportables, quality control metrics and data/file formats. Data is delivered through multiple, disconnected pipelines (Figure 1).

This complexity creates obstacles for many functional groups within sponsor organizations:

- Clinical/Biomarker Operations: need visibility into site-level performance, need to know where all samples are in the sample lifecycle (transit, processing, storage) at a given point in time and identify gaps in sample collections
- Translational Research: need early visibility into sample quality, visibility into project data availability to inform study decisions – for example, they need to know how many participants have pre- and post-treatment samples for data forecast generation
- Data Management: need to quickly identify discrepancies and manage queries
- Office of the CIO: needs visibility into entire data ecosystem to ensure that significant investments in biomarker assay lab data are realized

Figure 1. Disparate, Disconnected Sample Journeys and Data Streams

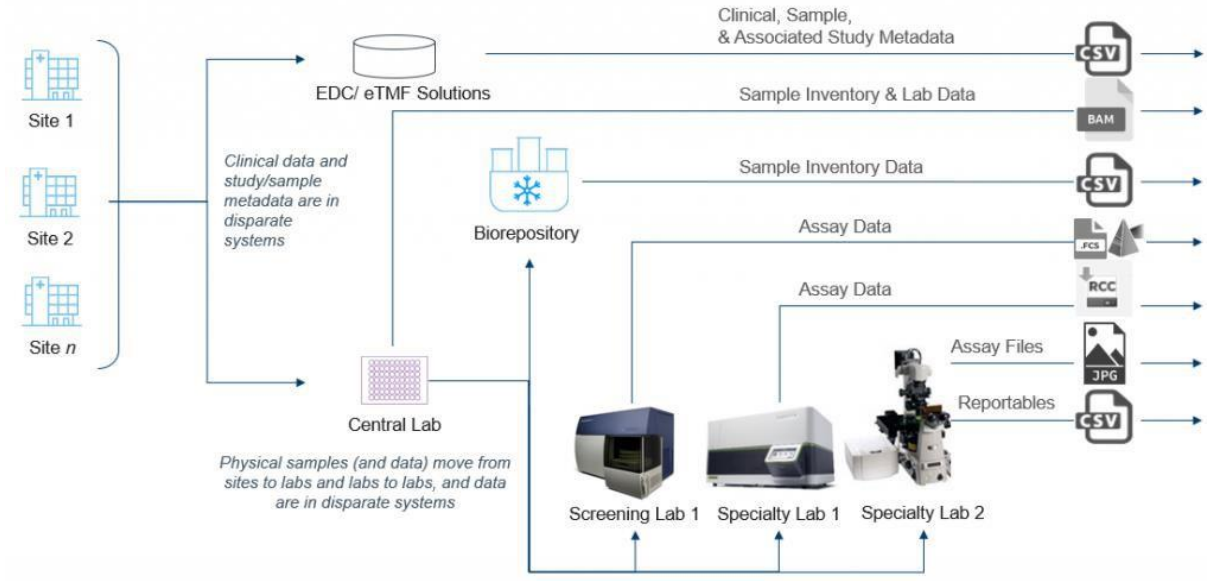

Figure 1. Each of the distributed physical locations playing a role in a clinical trial has its own underlying source system. Results data and ancillary information (such as images) are shared with the sponsor, but typically via disparate file formats and data pipelines.

3. Connecting LIMS to a Master Sample Inventory to Provide Sponsor-Centric Visibility for Biomarker Clinical Operations

Complex biospecimen operations are inherent in modern clinical trials. For recent protocols, biospecimen collections are designed to be broad and to enable flexible selection from the variety of biomarker assay technologies that are available. Biomarker clinical operations are critical to realizing the potential of biomarker data generation plans.

Multiple Labs, Multiple LIMS; Lack of Sponsor-Centric Visibility

Given the expanding footprint of sites, labs, and biorepositories, there is no sole source where sponsors can find information on biospecimens and get insights into the whereabouts of a given specimen within its complex journey across sites, labs, and biorepositories.

In this chapter, we explore the relationship between "lab-centric" and "sponsor-centric" sample inventory reporting, and how connecting these inventories can keep data generation on track.

Most clinical trial sample and biomarker data are generated and stored in the laboratory information management systems (LIMS) of individual labs and biorepositories (Figure 2).

LIMS-based reporting provides sponsors with "lab-centric" information – for example, status of shipments to and from a given lab and specific assay results.

However, these individual LIMS-based reporting systems are siloed, and do not connect to other data sources, such as other LIMS, electronic data capture systems (EDCs), and informed consent forms (ICFs).

LIMS-based reporting does not pull in data from other systems or EDC. Depending on LIMS configuration, some, but not all, LIMS provide information on samples received versus samples expected.

Figure 2. LIMS-based Reporting Provides Limited Window of "Lab-Centric" Visibility

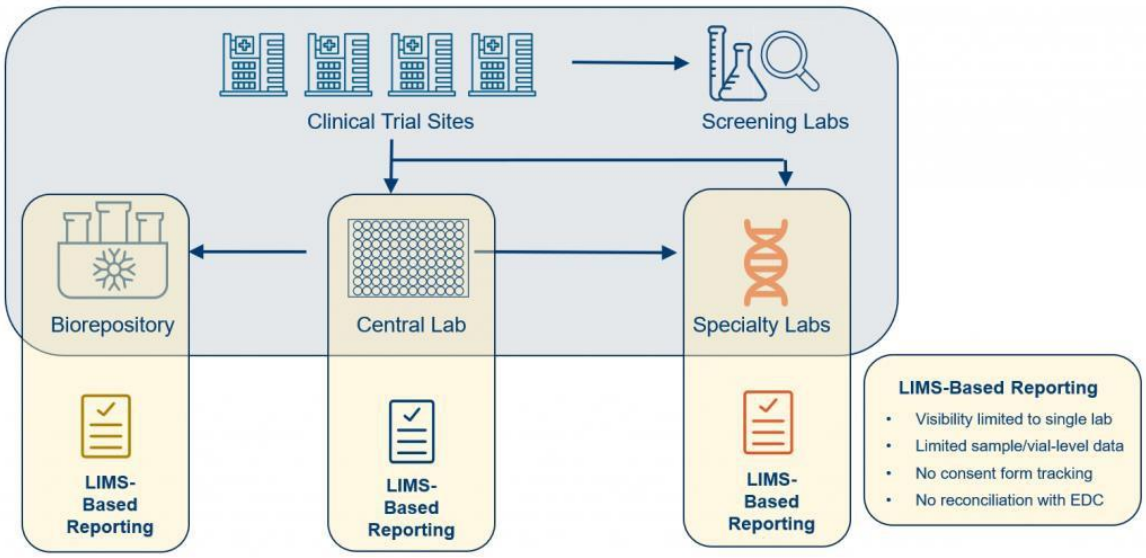

Figure 2. LIMS-based reporting is limited to providing a focused window into data from individual screening labs, biorepositories, and specialty labs performing specific biomarker assays.

Similarly, not all LIMS provide sponsors with insight into samples not collected per the protocol, samples collected out of the protocol, and future samples expected according to the protocol. Even when this information is provided, it applies to samples at a single laboratory, and sponsors often use manual processes to achieve visibility across labs.

Further, LIMS-based reporting has no sample reconciliation ability, and, with many LIMS, it is difficult to connect a sample/derivative to the correct version of the consent form.

LIMS-based reporting varies by laboratory and by system; custom, sponsor-centric reporting is likely to require custom programming, hindering the creation of bespoke summaries, key performance indicator reports (KPIs), and trend reports.

virtual Sample Inventory Management (vSIM) Delivers Sponsor-Centric Reporting

In contrast to LIMS, which are limited to providing focused information about samples processed by individual laboratories, QuartzBio has developed a virtual Sample Inventory Management (vSIM) platform that:

- Centralizes & harmonizes data across all sites, labs, storage facilities including 3rd party systems, plus all EDC sample collection data
- Identifies discrepancies across source systems
- Visibility on custom summaries, KPIs, trend reports
- Reports “Expected” vs. “Actual” by mapping subjects to collection groups defined by protocol version or informed consent version
- Provides context of protocol amendments, schedule changes, informed consent

By connecting trial data sources to a technology-enabled virtual Master Sample Inventory, QuartzBio enables operations teams to gain visibility into sample status across sample collection, processing, testing, and storage — including key questions like:

- Are we collecting the samples we expect (and need)?
- What samples were collected? Which of these samples have been processed? Which samples are in storage and can be tested?
- When do we have enough samples to trigger batch processing?
- Are samples consented for collection and assay testing?
- Are samples of sufficient quality for assay testing to generate reliable, high-quality data?
- What data has been generated on these samples? How many pre- / post-treatment data point pairs do we have?

Operations teams evaluating the QuartzBio solution often ask how the information provided by LIMS and other sample inventory systems fits with vSIM. Because vSIM is a platform-agnostic, lab-agnostic solution, any individual inventory system and LIMS can feed into vSIM to give biomarker operations teams the insights they need. Unlike individual LIMS, which are designed to track information on samples within an individual lab (“lab-centric” view), vSIM brings together information from all systems that are part of the study.

Only vSIM provides context of protocol amendments, schedule changes, and changes to informed consent tracking, and only vSIM consistently provides teams with visibility on custom summaries, KPIs, and trend reports.

A master sample inventory is most crucial because it enables discrepancy checks and site performance trend analysis across systems.

In addition to these capabilities, QuartzBio vSIM provides interactive, enhanced visualizations to enable rapid corrective actions.

4. Monitoring Consent Status With a Novel Virtual Repository

Sponsors are challenged to keep track of complex sample inventories, both on study and for samples collected as part of completed studies that might be later mined for translational research needs. We frequently hear that teams spend significant time manually cross-referencing spreadsheets of inventory data, to answer questions such as:

- "How many whole blood samples with a particular mutation do we have across all phase I studies?"
- "Can we report sample expiration status across all of our contracted biorepositories?"
- "When we identify a sample of interest, how can we confirm consent status?"

To address this challenge, many teams use QuartzBio's smart data aggregation/integration technology to rapidly generate a comprehensive virtual master sample inventory (MSI) across studies, vendors (central lab, specialty labs, data management CRO) and source systems (EDC, LIMS, assay data).

In this post, we focus on one specific element of complexity facing the "bedside to bench" paradigm: the fact that sample collections for the purpose of facilitating future translational research are based on optional, specific consent. This type of collection is advantageous to translational research teams, but it has a flip side:

Because not all samples are consented, every sample needs to be checked against consent given as consent is patient-centric.

Consent may further depend on a variety of factors, including protocol, consent version, consent expiration, location of the site (and applicable local consent requirements), and potential requirements for re-consent throughout the study.

Figure 3. QuartzBio Sample Consent Dashboard

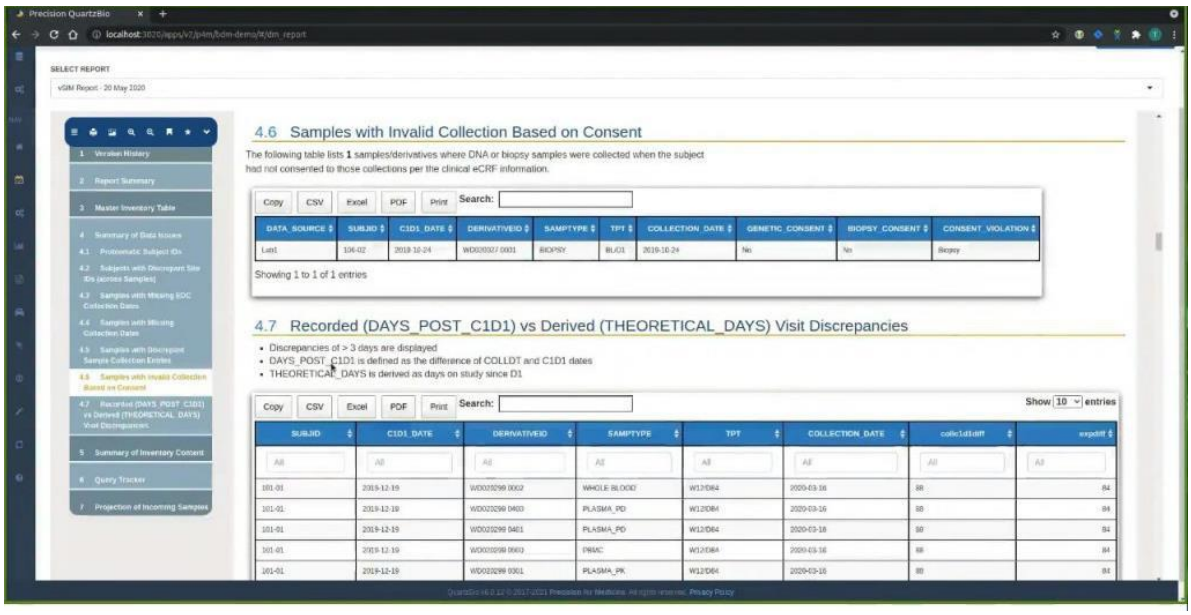

Figure 3. QuartzBio sample consent dashboard. This example shows a case in which a patient did not consent to optional DNA and biopsy sampling. However, a biopsy sample was taken and received, and thus was collected in violation of consent.

QuartzBio's virtual Sample Inventory Management (vSIM) platform features a dashboard flagging all samples with invalid collection based on consent (Figure 3).

All instances where consent is potentially violated are reported out and flagged in the platform, which can also flag samples with consent expiration and provide insights into sample restrictions for future research for stored samples.

The ability to generate this information on an ongoing basis throughout the study allows for a significantly streamlined process.

Figure 4. Master Sample Inventory Dashboard

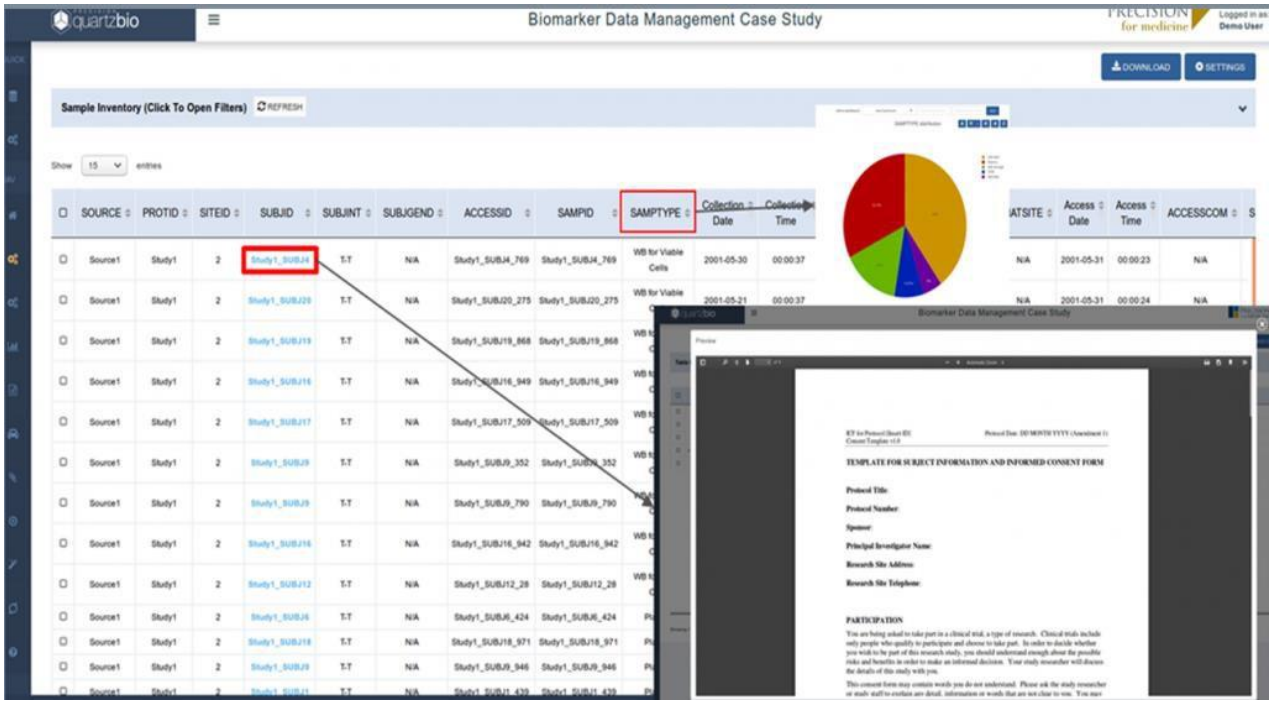

Figure 4. Master Sample Inventory Dashboard. Quickly report up-to-date sample status and location based on sample type, timepoint, testing status, treatment groups, site, consent, protocol revision, and other identifiers. Point-and-click access to underlying protocol information and ancillary files, such as PDFs.

Contact us to learn how virtual Sample Inventory Management can support your trial

quartz.bio/contact-us

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