WHITE PAPER

De-risk Your Biospecimen Data by Turning Your Static Lab Manuals into Software-Guided Workflows

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SLOPE

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Executive Summary

As precision medicine demands more complex study designs, static lab manuals and traditional methods for biospecimen management become incredibly convoluted and subject to frequent changes due to protocol amendments and other study modifications. This can create risks downstream, as the interpretation of these paper-based and PDF-based documents are susceptible to accidental oversights that impact lab kit management, as well as the handling of patient samples and sample data. The more frequent and the more pronounced study amendments become, the harder it can be for sites to stay compliant. This white paper sheds light on the lab manual's current role in sample management, the inherent pitfalls of traditional approaches, and the ways in which sponsors can leverage technological innovations to standardize research site practices, optimize compliance across all of their trials, and gain real-time access to critical biospecimen data along the way.

How Are Complex Study Designs Hindering Traditional Lab Manuals?

Complicated specimen management schemes have proliferated in response to innovations in precision medicine. Personalized approaches to patient care require specialty assays, a greater body of diverse data, and specific conditions that dictate when and how a patient can be enrolled, tested, and treated. These tailored approaches to clinical research are as exciting as they are necessary for scientific advancement, but their implications for study execution should be considered — especially when it comes to site compliance.

These nuances in study design yield complex lab kits with more visits and containers, complicated requisition forms, and intricate instructions for when to pull certain kits or when to collect certain patient samples. Once all of the biospecimens for a patient visit are collected, site staff face the daunting task of methodically processing specimens, transferring them to the appropriate return containers, storing and packaging them at the right temperatures, and ensuring that they are sent to the right labs at the right times.

When a study requires sites to manage several kits, supplies, stipulations, and shipping destinations, the lab manual becomes incredibly dense. Even if sampling instructions are clearly defined, the interpretation of these details is tedious, prone to error, and subject to variability based on individual site processes. Clinicians may accidentally overlook important information pertaining to sample collection, processing, shipping, and storage. This is compounded by the fact that research sites are oftentimes juggling responsibilities across multiple studies, sponsors, labs, and patients simultaneously.

In addition to executing on the instructions in the lab manual, clinicians must also juggle the documentation of several data points. Using the requisition form, internal paperwork, and spreadsheets, clinicians are expected to meticulously document administrative details, collection dates and times, chain-of-custody checks, and other records that make up the sample audit trail. These manual processes are not only prone to oversight and error — the data must also eventually make its way through disjointed clinical systems, including EDC and LIMS. The entry of this data is often manual, disparate, and delayed, so sponsors may lack visibility to this information for weeks — even months.

Under traditional methods, sponsors face greater challenges with data reconciliation, as the use of disconnected systems introduces a greater number of discrepancies that must be addressed. Research sites also must sift through disjointed, paper-based records when addressing queries and sample-related investigations, putting critical lab results and other downstream lab processes on hold until the queries are resolved. This has the potential to intensify the patient burden and put patient enrollment and retention at risk.

Study amendments further complicate the utilization of the lab manual. When sponsors update their protocols or any study plans, these changes are subsequently implemented in an updated version of the lab manual. Site staff are tasked with keeping track of these modifications, which may impact the kits on hand, biospecimen collections, shipping destinations, and shipping frequencies.

What Are the Risks That Stem from Using Static Lab Manuals?

Using paper- and PDF-based lab manuals comes with inherent risks, and those risks are amplified by an intricate study design. With more variables at play that directly impact sample management, site processes that were once sufficient are now buckling under the pressure of the demanding trial paradigms that dominate the modern clinical research landscape.

Risks are inevitable in any operation, but it's important to highlight the preventable vulnerabilities that emerge as a direct consequence of working with static lab manuals.

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Protocol deviations

Let's face it — humans make mistakes, especially when they are juggling multiple tasks and priorities at once. When clinicians read through a lab manual — especially when they are in a hurry — they are at risk of committing an accidental oversight that can result in a protocol deviation and sample mishandling. The downstream effects for the patient and the study's overall integrity can be detrimental, with consequences spanning from a lack of data integrity, to difficulties with patient attrition.

Study delays and an increase in unplanned study expenses

Inefficient site operations translate into higher overhead costs. Site compliance issues can contribute to lapses in data integrity. Gaps in critical data can delay critical study milestones — including datalocks, regulatory submissions, dose escalations, necessary protocol amendments, and more — thereby significantly inflating study budgets by tens of thousands of dollars.

Data reconciliation challenges

Sample and data reconciliation is a normal part of clinical trial execution. But when the specimen audit trail is scattered across disjointed paperwork and spreadsheets, the process of piecing together the sample journey becomes a major and often impossible undertaking. A static lab manual provides site staff with a comprehensive overview of specimen management procedures, but it's not an interactive document that can prompt the reader to record data points or perform chain-of-custody checks, nor can it house any of this data in one centralized location. As a result, the reconciliation process often involves more time, effort, and back-and-forth with study stakeholders during the trial lifecycle.

Lack of visibility to the sample journey

Having real-time access to sample tracking data not only gives sponsors appropriate oversight of their trials — it also offers peace of mind and quick answers to sample-specific inquiries. But on most trials, the story of a sample is scattered across disconnected sources — including research sites, lab vendors, and clinical systems. As a result, sponsors have to spend more time performing sample-related investigations. This can be problematic when time is of the essence, such as when waiting for a critical patient result or trying to reconcile biospecimen data for a datalock.

Greater challenges in mitigating the impacts of staff turnover

Manual processes become problematic when site staff leave the organization, or are out on vacation or sick leave. When a clinician is expected to perform a patient visit for a study they've never supported before, or when a study coordinator is contacted about a lab query for a trial that is assigned to one of their colleagues, clinicians must haphazardly follow procedures in a lab manual that they aren't familiar with, or attempt to piece together data from disparate, paper-based sources. This creates an added challenge for site staff, many of whom are straining under the stress of high workload and turnover.

Deconstructing the Current Gaps in Sample Management Processes

In order to better understand the role that the lab manual plays in specimen management, it's important to examine the various steps involved in conducting a patient visit. By scrutinizing each stage of the sample journey — from its nascent state as an empty collection container in a lab kit, to its final state as a biospecimen that is ready for shipment and analysis — we can more accurately identify the gaps in conventional site practices as they relate to the utilization of the lab manual.

1

Pulling lab kit(s) and inventory for a patient visit

When a patient arrives for a visit, clinicians refer to the lab manual to determine the lab kit(s) and bulk supplies that are required for biospecimen collection, preparation, and shipment. Once all supplies have been identified, site staff search for the inventory in their facility. In many cases, study coordinators have to reference spreadsheets and sort through a mountain of lab kits from other studies, kitting vendors, and trial sponsors in order to locate the needed supplies for the visit. This step can be both time-consuming and risky without a proper inventory management system in place. Disorganized supplies and a lack of a centralized, digital system to keep track of on-hand inventory can result in lab kits and bulk supplies being lost, expired, or out of stock.

2

Sample collection

Once the inventory has been pulled from storage, site staff sort through all of the collection supplies in the lab kits. A nurse or study coordinator painstakingly flips through the lab manual to determine which biospecimens should be collected in accordance with the protocol. Even though there may be several collection containers in the kit, this does not mean that all of them are used. Many protocols contain predefined conditions that dictate when a patient sample should be collected. For example, a specific biomarker may only be collected at a patient's Cycle 1 Day 1 visit if the patient meets certain criteria. Perhaps the patient must be part of a certain demographic in order to merit the collection, or maybe the patient is required to have a certain test result at Screening in order to qualify for testing.

These stipulations can be easily overlooked and misinterpreted in a static lab manual, resulting in erroneous collections or critical collections being completely missed.

Once all of the mandatory biospecimens have been identified, clinicians must carefully follow the collection instructions that are prescribed in the lab manual. The procedures for each collection container require meticulous attention to detail; just one misread or overlooked step could threaten sample integrity. Downstream, these errors can harm the patient, who may be forced to repeat a visit or even drop out of a study.

As various biospecimens are collected from a patient, site staff across multiple departments must document several sample-related data points on the requisition form and in internal paperwork. Patient demographics — along with collection dates and times — must be accurately recorded in order to ensure seamless processing of biospecimens at the receiving lab. Under traditional site operations, the recording of these data points is often paper-based, manual, and fragmented.

3

Sample processing & storage

Once biospecimens are collected, they often must be processed immediately. As was the case for specimen collection, site staff must promptly follow the elaborate processing instructions in the lab manual for each biological sample, ensuring that they are centrifuged or fixed (if needed), transferred to the appropriate return containers, and stored at the correct temperatures. Additional data points are also recorded at this stage.

This step is particularly critical because it can have a major impact on sample integrity.

One mistake could be costly, resulting in a biospecimen being nonviable for analysis. For instance, if a specimen that should be frozen is placed in a refrigerator, or if a sample is transferred to the incorrect return container, then the lab may deem the patient sample unusable.

4

Sample shipping

Once processing is complete, site staff refer to the lab manual to determine shipping logistics — including sample destinations, courier details, shipping temperatures, which shippers to use for packaging biospecimens, blackout days, and shipping frequencies. On complex trials, this step can be complicated.

It is not uncommon for the shipping logistics of a singular patient visit to look something like this: Five biospecimens are shipping to *lab A* — two are shipping ambient on the day of collection, two are shipping frozen on the day of collection, and one is shipping frozen one week after collection. This same patient visit also has two biospecimens going to *lab B* frozen on the day of collection, and one biospecimen going to *lab C* refrigerated on the day of collection.

Considering all of the variables at play in this scenario, it's easy to see how site staff could ship a sample to the wrong location, forget to ship a sample one week after collection, or ship a sample in the wrong kind of shipper. A static lab manual usually provides research sites with the correct guidance, but important instructions can be easily overlooked.

5

Managing biospecimen data

The source sample data that was recorded during the sample collection, processing, and shipping steps — including patient demographic information, collection dates and times, and other administrative details — must be manually transcribed on requisition forms for lab processing, as well as in the EDC. Requisition forms are extremely error-prone, as site staff can easily transcribe the data incorrectly or otherwise leave a mandatory field blank. EDC are also subject to data entry, and oftentimes it can take weeks — or even months — for sites to enter data into the EDC. This data lag can cause headaches for sponsors, who need instant access to biospecimen data in order to make critical study decisions, perform sample-related investigations, and more.

Using Technology to Bring Lab Manuals to Life

Digital tools already exist that can turn a static manual into an interactive workflow that guides sample management activities at the site — enhancing compliance and unlocking real-time insights for sponsors along the way.

Use a centralized clinical trial platform to manage inventory

Successful biological sample management cannot occur without successful inventory management — after all, biospecimens can't be collected, processed, and shipped without the appropriate supplies on hand. Study coordinators often rely on paperwork and spreadsheets to keep track of inventory, but these outdated approaches to record-keeping make it more difficult to maintain continuity among site staff, locate supplies, track lab kit

expirations, and identify trends that inform resupply orders.

A clinical trial execution platform for managing inventory can significantly enhance a site's ability to monitor their supply use. Not only does this consolidate inventory data so that it's easily accessible and searchable, but it can eliminate the need for manually monitoring low inventory or supply expirations with automatic alerts.

Turn lab manual instructions into software-guided workflows

No need to decipher complex sampling instructions or reinvent the wheel during every patient visit — research sites can leverage technology to walk their personnel through every step of collection, processing, storage, and shipping. Site staff can use the lab manual to perform a one-time kit configuration setup using a digital specimen management platform; after that, sites never have to worry about sifting through a text-heavy lab manual again. All clinicians have to do is follow the predefined guardrails that were established during configuration as a clinical trial software guides users through every step of sample management.

Use technology for real-time sample tracking

Traditional tools offer sponsors with limited visibility to the biospecimen journey from its origin at the site to various labs and biorepositories. Sponsors oftentimes must ask clinicians to provide them with a courier's tracking number to determine whether a biospecimen has reached its initial destination, but these details usually must be manually communicated during sample-related investigations. Even then, the post-shipment specimen audit trail can be limited — especially if patient samples are shipping to a third-party lab or biorepository after the site ships the samples to a central lab.

Digital solutions exist that can provide sponsors with full visibility to the sample journey. Having this information at their fingertips, study coordinators can improve their communication with sponsor stakeholders and vendor labs during sample reconciliation, while maintaining peace-of-mind that their patients' samples are being handled properly. If important patient results are delayed or canceled, having visibility into the sample journey can provide more context.

Streamline data reconciliation by integrating data capture into digital workflows

Specimen management encompasses more than just the physical collection and processing of a biospecimen — it also demands the meticulous collection of sample data, including collection dates and times, administrative questions, and sample chain-of-custody records.

Sponsors can reduce manual effort — as well as the amount of time and effort spent following up with research sites on query resolution and data reconciliation — by leveraging a clinical trial execution platform that automatically captures pertinent sample data in tandem with key specimen management steps. This capability not only ensures that all administrative data is collected in real time, but this data can be fed into other data sources, like an electronic data capture (EDC) system. The centralization and digitization of this information also equips sites to efficiently respond to queries and reduces the need for duplicate data entry, granting sponsors with real-time access to biospecimen data that requires less data reconciliation.

The Future of Sample Management: **Empowering Research Sites to Do Their Jobs Better — And Gaining Real-Time Access to Biospecimen Data in the Process**

Slope's clinical trial execution platform enables sponsors to help their research sites be more efficient and compliant on their trials. The platform's sample management solution dramatically improves day-to-day site operations by transforming static lab manuals into software-guided workflows that make it easier to collect, process, and ship biospecimens the right way during patient visits, while automatically capturing critical patient sample data. With Slope, sponsors are empowered to know the history of every specimen, spend less time reconciling data, and keep their research sites up to date with study-specific changes, so that they have improved access to the data they need in order to make critical study decisions.

Slope's clinical operations team uses the lab manual to configure guided workflows for all sites who are participating on the trial so that sponsors can empower their sites to be set up to perform study activities in Slope from Day 1. The software can also automatically roll out study amendments to sites as soon as they receive approval to perform study activities under the latest version of the protocol.

Slope's sample management tools streamline site processes into three simple steps:

1 Sample Collection

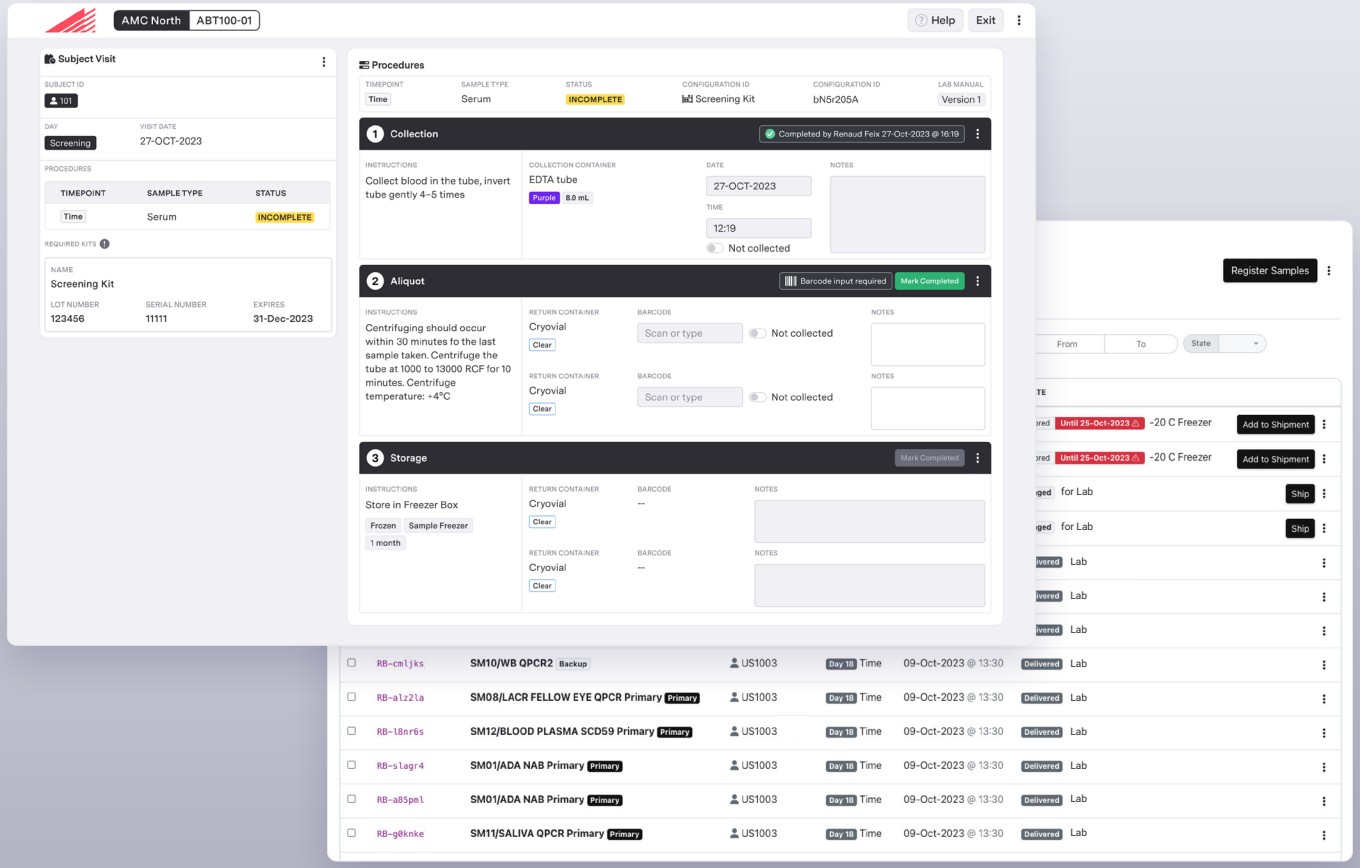
Sample collection facilitates accuracy and compliance by ensuring patient samples are collected in accordance with the lab manual.

- Maximize efficiency and compliance
- Interface enforces consistent capture of pertinent sample collection data
- Never miss a PK timepoint

2 Registration & Preparation

Sample registration and preparation walks site staff through the process of readying a specimen for analysis.

- Properly transfer biospecimens to appropriate return containers
- Intuitive, error-preventing aliquoting process
- Interface ensures samples are stored as prescribed in the lab manual



3 Sample Shipping

Sample shipping enables staff to build GCP-compliant shipments to destination labs.

- Get samples to the right places, at the right times
- Never ship on blackout days
- Actionable alerts ensure that batch shipments never fall through the cracks
- Integrations with couriers and carriers allow users to generate tracking numbers and print shipping labels directly from the platform

Request a demo of Slope's Biospecimen Lifecycle Software

SlopeClinical.com/request-demo

Slope is a global provider of biospecimen lifecycle software, data, and services for clinical trials. With a focus on tech-enabling the full biospecimen lifecycle, Slope offers expertise that empowers sponsors to make informed decisions using high-quality, real-time sample data. Slope has supported thousands of the most complex, sample-intensive trials worldwide and has been adopted by 79% of NCI-designated cancer centers. For more information, visit SlopeClinical.com