Veridix

Global Trace

Do you know where your Biospecimens are?

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White Paper

The Case for Centralized Inventory Management of Clinical Trial Specimens

For several decades, broadcasters in the US ran a public service announcement on late-night news programs asking viewers: “Do you know where your children are?” To borrow on that long-running catch phrase, we might ask:

Do you know where your biospecimens are?

Biospecimens are, of course, an essential part of trials in which immune responses are surrogates for clinical efficacy or in which the mechanism of action is being studied. They, therefore, should be treated as a precious commodity and managed with great care until they are no longer sufficient or approved for testing. Yet, tracking biospecimens manually as they move through a complex network of clinical trial sites, repositories, and central laboratories is inefficient and error prone. And, electronic data capture (EDC) systems, which typically reply on case report forms (CRFs) to record the collection and shipment of biospecimens, are inadequate for this purpose for a multitude of reasons. The answer lies in having a purpose-built, automated system for managing and tracking biospecimens throughout the trial ecosystem.

Here, we explain when software- such as Veridix GlobalTrace – is needed to track biospecimens; demonstrate the risks and inefficiencies of not using such a tool; and show how GlobalTrace works to

Provide visibility

Deliver efficiencies

Maintain sample integrity

Protect the chain of custody

Improve data quality

When a Purpose-Built Specimen Management System is recommended

› Not every clinical trial that involves laboratory testing needs to be supported with specialized software to track bio-samples and expedite their handling. This is the case when clinical laboratory specimens are sent to a local laboratory and then depleted in the testing process. Local clinical laboratories, which don't have to be blinded, have their own existing inventory systems for labeling and receiving samples, and this is sufficient in such trials.

However, there are several types of protocols and testing situations in which a system capable of recording the history of each specimen from the moment it is collected until its final disposition is essential to smooth operations. We recommend deploying a centralized inventory tracking system for biospecimens when:

- Research assays will be conducted and used as surrogate endpoints or biomarkers, or where the trial is designed to study a drug's mechanism of action
- Specimens will be shipped from clinical trial sites to a repository before being shipped to laboratories
- The volume of specimens is great. A vaccine study with multiple immune parameters, for example, can involve dozens of separate batch shipments for laboratory testing
- Specimens will be banked for future use
- Biological samples require special handling or prompt testing, depending on automated communications to ensure that the specimen's arrival is anticipated at each step of its journey
- The study will require multiple "picklists" of samples for testing and the selection criteria require evaluating clinical characteristics or study outcomes data in the EDC

In studies that fit this description, there are various points at which it is critical for sponsors and those involved in handling biospecimens to know the whereabouts and disposition of each sample and its derivatives. Real-time visibility is called for when:

Subsets of samples are to be tested – for example, one aliquot per blood draw that generated multiple aliquots, for a sentinel cohort, or dose escalation study	It is desirable to test repeated samples on the same subject in a single batch	It is necessary to track the residual volume of specimens and from that, to determine when it is no longer sufficient to allow for further testing
Shipping manifests do not match the samples physically received at a location	Temperature-sensitive samples are being shipped between locations	When samples are pulled for use in more than one trial or years later for future research

The Challenges of Manual Tracking and Disparate Inventory Systems

› Although electronic data capture (EDC) systems can record sampling data, many do not recognize that specimens can be created by pooling or aliquoting. Nor do they track specimen lineage. Sponsors that attempt to rely on the EDC, their partners' separate inventory systems, and manual processes quickly discover how difficult it is to:

- Answer queries. Queries as to the location or status of a sample can involve multiple phone calls and collecting reports from every entity in the process. And when specimens are lost, gaps in the specimen history, tracking, and inventory information may make it impossible to trace and recover them.
- Reconcile data on transfers between repositories and labs, and between labs and the data center. Completing this work manually is both slow and error prone. Often, any discrepancies between the clinical and laboratory data are discovered after the window of opportunity for further sample collection has closed.
- Select aliquots from picklists. When clinical data in the EDC and sample data are not integrated in real time, it can complicate sample selection, and in the worst case, the wrong samples can be pulled.
- Preserve samples at the required temperature. A lack of communication between sites and repositories and laboratories can result in precious samples being left to thaw on the loading dock if the receiving entity wasn't properly notified of the shipment.
- Access samples in the future. Without knowing the current disposition of samples, it can be impossible to know the feasibility of accessing samples in the future for additional testing.

A Day in the Life of a Biospecimen not Supported by a Centralized Inventory System

› To understand the need for an automated system to track biospecimens, it is helpful to appreciate what can go wrong as specimens are handled in the course of a typical trial. Where are the risks? What is the worst that can happen? To illustrate this, let's trace the path of a biological sample, pointing out the opportunities for errors and delays along the way- situations that waste time and resources and even jeopardize the data quality...

A specimen is collected from a trial participant at a trial site – anything amiss at this stage could affect the ability to analyze study data later on.

STEP 1

- The site fails to prepare the required number of aliquots from the specimen, limiting the data available for analysis.
- The specimen is mislabeled, which renders it unusable and limits the data available as the sample is usually irreplaceable.
- The child's specimen is not linked properly to the parent's specimen, so any subsequent aliquots will be missing key details and information needed to complete the analysis.
- The site discovers an error with the specimen attributes, but can't correct it after the specimen has shipped.
- The site can't blind those downstream to the subject/visit, leading to assessment bias, which could color the conclusions drawn and alter study results.

The specimen is shipped to the repository for storage.

STEP 2

- The physical sample isn't listed on the shipping manifest that is packed with the shipment, creating confusion downstream about what was to be included.
- The site doesn't notify the repository that the shipment has been sent, so no one at the repository is prepared to receive it.

The repository receives the shipment.

STEP 3

- The sample experiences a temperature excursion because the repository didn't know it was coming and allowed it to sit on the loading dock in inadequate temperatures.
- The sample received does not match the shipment manifest, causing confusion and requiring reconciliation.
- The sample received can't be linked to data in the clinical trial management system. With absent identifying information and instructions, such samples go to waste.

The sample is selected for testing and shipped to a laboratory.

STEP 4

- The repository pulls the wrong sample for testing, resulting in missing or duplicate results.

The laboratory receives the sample shipment and sends the assay results to the CRO.

STEP 5

- Results are missing and require research to discover what went wrong. This may require analyzing the testing workflow again. Additional samples from the subject may not be available.
- Results are duplicated, requiring research to identify the correct result.

A sample is needed in a future study.

STEP 6

- The information on the Consent Agreement is wrong, making it impossible to have an accurate inventory of what is legally usable.
- There is no Consent Agreement on record, rendering the sample unusable and limiting research opportunities.
- Consent records are kept manually, which is burdensome for site staff and error prone, and errors require reconciliation.

This illustrates a “terrible, horrible, no-good, very bad day” in the life of a biospecimen, and, admittedly, it is unlikely that every one of these problems exist with a single sample. Yet, over the course of a study the risk is very high that many of these issues will arise again and again. At any point in the process, queries about the status/location of a sample or test results must necessarily be addressed through a very inefficient process that involves the clinic, the laboratory, and the biorepository. It thus takes a very long time for queries to be resolved, wasting resources, delaying database lock, and potentially, eliminating some participants from the trial.

A Model Biospecimen Workflow, Aided by Technology

› Regardless of the number of sites and their locations, a best-in-class system such as GlobalTrace maintains a central inventory of biospecimens and records the history of each specimen from the moment it is collected until it is no longer available. This system automates steps in the process, embeds quality control checks into the system, and offers visibility into samples across the clinical ecosystem.

STEP 01

A specimens is collected from a trial participant at the site and recorded in GlobalTrace

- The specimen is labeled with a unique barcode.
- The label is scanned and entered as part of a batch into the system which applies logic/quality.
- control checks to prevent duplicate bar codes Lab staff enter the specimen attributes and clinical information into the system.
- A link is established in the system between the unique barcode and the specimen attributes so that any derivative samples (i.e., subsequent aliquots) can be traced back to the original sample and thereby linked to the relevant clinical information.
- The lab staff select from drop-down menus to enter details such as the protocol, the subject ID, visit number, specimen type, and purpose (including consent for future use).

STEP 02

The specimens is shipped to the repository for storage

- The site generates a shipment record in the system and selects from among pre-defined destinations and carriers.
- The system links to carrier websites so that the shipment can be tracked with a single click.
- The system creates an electronic shipping manifest. An email with an attachment of the manifest is automatically sent to the sending site, the receiving site, and the contract research organization (CRO). This serves to alert those receiving the sample so that they can prepare for timely processing.

STEP 03

The repository receives the shipment and performs reconciliation.

- The repository scans the contents of the shipment, and the system automatically compares that to the electronic manifest and the repository either accepts or rejects the shipment.
- The repository reports any missing or damaged specimens to the clinical site staff through the system.
- The site clinical staff corrects and resends the electronic manifest.
- Once the reconciliation is complete, the specimen is recorded as transferred from the clinic's inventory to the repository's inventory.

STEP 04

The repository selects the sample for testing and ships it to the laboratory.

- The repository follows the picklist, placing the specific aliquots into a box that designates the required testing schema and is sent to the testing laboratory.
- The shipment process follows the same steps as in Step 2 above.

STEP 05

The shipment is received and reconciled by the testing laboratory.

- The process mirrors that in Step 3 above.

STEP 06

The laboratory uploads the assay results and integrates with the clinical database.

- The central laboratory reports the assay results via a secure data upload to a cloud platform such as Emmes' Advantage eClinical, where the data is linked to information on the subject.

STEP 07

The specimen inventory is maintained with reports available.

- The system retains information on individually identifiable specimens for ongoing clinical studies and historical archives.
- Whenever a specimen is entered, the current status and history of each specimen is automatically updated or otherwise modified for any reason.
- Attributes contained include: subject number, visit number, collection data, current and original site, specimen site and purpose, and status (available, in prep, sent, or not available).
- Users can review and select items from the inventory using various reports. Sites can retrieve these records, sorted and filtered by several parameters to facilitate management of assay results. They can also be exported for importation into specialized laboratory instrumentation.

The process of shipping, selecting, tracking, and reporting on biospecimens in significantly more efficient for all parties involved when activities are tracked in a centralized database and supported with automation. The kinds of delays and mistakes that can derail the flow of work as described in the first scenario are prevented.

The Use of Picklists

› When a laboratory assay result is a biomarker or surrogate for a clinical outcome, it is often more efficient to proceed by testing only a subset of specimens. This is the case when:

- The safety and immune response of a sentinel cohort must be evaluated before proceeding to fully enroll the study.
- The safety and response of the current dose level must be evaluated before escalating to the next dose level.
- Efficient nested case cohort or case control designs are used to establish correlates.
- Vaccine protection specimens are collected on all subjects but tested only on a random sample of controls.
- Subjects have granted consent for their samples to be retained and used in future research studies.

In these situations, statisticians develop a picklist to identify appropriate specimens to be assayed according to the sampling plan and method specified in the protocol.

Advantages of a Centralized Biospecimen Management System

› For trials that meet the criteria described above, a system such as GlobalTrace offers benefits that are appreciated at every step of a specimen's pathway over the course of a trial and that ultimately serve the sponsor through:

Efficiencies

The tool automates common tasks performed by specimen processors (such as barcode creation and batch scanning), eliminating the need to manually track and reconcile inventories, shipment manifests, and laboratory results.

Improved Quality

Having a comprehensive data repository with built-in quality checks reduces errors or omissions in specimen collection, labeling, and selection. It also eliminates discrepancies between clinical and laboratory records, and reduces errors or omissions in reporting laboratory results.

On-demand Visibility

The system provides visibility- in real time – to the whereabouts of individual specimens, the full history of transfers and use, specimen lineage, issue management, residual volume, and consent for future use. Search functions are available by specimen attribute, location, and, if used with Advantage EDC,by characteristics of the study and its participants. This integration with EDC ensures closed-loop tracking of specimens throughout their shelf life.

Protection of Perishables

The quality of precious samples is preserved through temperature tracking and alerts on incoming shipments.

By saving time at every step of the way in collecting, transferring, and tracking samples and by circumventing the need for a protracted reconciliation exercise prior to database lock, GlobalTrace successfully accelerates the trial timeline. And, by eliminating many opportunities for human error, the application helps ensure that all samples – and their assay results – are usable, improving data quality.

GlobalTrace has been designed to address the challenges inherent in overseeing the use of biospecimens is specific types of studies, and in those cases, it has proven invaluable in providing visibility, delivering efficiencies, maintaining sample integrity, preserving the chain of custody, and improving data quality. To learn more about Global Trace, visit www.veridix.com/global-trace

> "For our team here at Duke, GlobalTrace has been the most user-friendly specimen system we have used over the last 22 years of conducting clinical trials. GlobalTrace is easy to use, and a very intuitive system to organize and retrieve specimens easily. It is a simple system and, therein, lies its strength."
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> — Duke Vaccine and Trials Unit

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