Standardizing Biosample Management:

Why Use Collection Kits?

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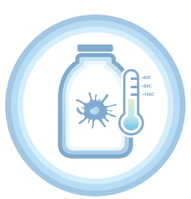
Fisher BioServices

this "eBook"

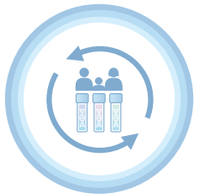
Biobanking & Biorepository

Cell Therapy Solutions



Clinical Trial Kit Production

Laboratory Processing



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About the Author

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Mr. Hixon has been at Fisher BioServices for 23 years, and has extensive experience in biorepository services, regulatory compliance, clinical trial support, and laboratory procedures. He oversees contract operations, develops and implements standard operating procedures (SOPs) in accordance with current good manufacturing procedures (cGMP), coordinates with QA/QC staff, and provides technical expertise on stem cell and cellular therapy products, including transitioning cellular therapies from clinical trials to the commercial marketplace. Mr. Hixon is a subject matter expert in clinical trial services, and creates trial-related manuals and forms, designs custom collection kits, designs labels, generates status reports, and oversees project implementation.

Ian E. Sutherland, MS, Area Director of Resource Planning

Mr. Sutherland oversees all clinical component inventory, batch record execution, kit production, and product distribution for Fisher BioServices' Production and Distribution Department. He has more than 20 years of experience in pharmaceutical manufacturing and the management of supply chains and related data.

Overview

Introduction

Whether you are conducting a phase 3 clinical trial of a new therapy or looking for biomarkers, you will need to collect samples, and that leads to a number of questions. How do you collect the samples in such a way as to preserve their usefulness—maintain molecular integrity—for your specific (or unknown) downstream analyses and assays? How many samples will be needed, how many "collectors" will be involved, and how many locations? How long do the samples have to be preserved, and how will they be stored? And how will you manage the data?

Here are some basics to help with planning sample collection and to help make the process as cost-effective as possible.

1 It's All About Controlling Variability

It's All About Controlling Variability

Biospecimen-based research depends on controlling pre-analytical variability, maintaining sample integrity, and on annotating the samples with the appropriate data. Collection kits not only assist in controlling variability, but can also serve as an ideal starting point for data collection.

Kits allow you to standardize the components used for collection, a major factor in controlling pre-analytical variability. Instructions for specimen collection, whether the sample is tissue excised during surgery or blood drawn into a tube, can be included to ensure best practices and any special requirements are followed. The supplies and instructions for shipping the specimens and processing them at the lab can be included as well, which further reduces variability.

2 Why Assemble Supplies Into Kits?

Why Assemble Supplies Into Kits?

Given that many basic items such as tubes and swabs can be shipped in bulk to clinical sites, why use kits? There are advantages and disadvantages to both scenarios.

Advantages to designing and assembling collection kits:

- Kits can include the return shipping supplies and air bills that specify the courier service, delivery time at the lab, and instructions regarding packing the samples. This ensures that samples arrive on time and in the correct condition to maintain their integrity.
- Kits allow better management of complexity, such as visit-specific sample collection schedules that involve unique supplies, collection of different patient samples at different time points, and specimen collection by field phlebotomists, whose "office" is an automobile and who work in unpredictable environments (patients homes).
- Kits help site staff better manage timed collections—everything is ready to go.
- Kits allow for differences in site capabilities.
- Supplies that are sealed in a box or bag are far less likely to be used for other purposes.
- Items can be pre-labeled with barcodes or Quick Response (QR) codes to link the sample to the patient.
- Kits allow features such as custom-molded foam forms to protect fragile items.
- Kit boxes can be printed with identifying logos and other information.

+Advantages

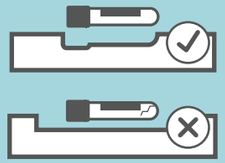
+ Return shipping supplies & airbills

+ Management of complexity

+ Everything is ready to go

+ Printed with identifying logos and other information

+ Pre-labeled with barcodes or QR codes



+ Custom-molded foam forms to protect fragile items

Why Assemble Supplies Into Kits?

Disadvantages of using a pre-assembled kit:

- If a component is lost, damaged, or past expiration date, the entire kit may have to be discarded.

Advantages to simply stocking supplies in bulk:

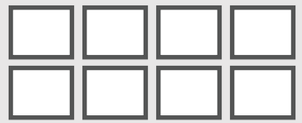
- Depending on the study and supplies, a bulk supply chain may take less time to set up.
- If an item is damaged, another is always available.
- Some supplies are so standard and well-stocked (needles, butterfly sets, gauze, bandages, tourniquets, etc.) that kits are simply not needed.

The downside of using bulk supplies:

- Managing bulk supplies requires more experienced site personnel.
- Bulk supplies can require significantly more storage space.
- Standardization is lost.
- Having to compile individual items for collection, labeling, packaging, and shipping of specimens adds time and complexity to the collection process, potentially reducing compliance with best practices.

-Disadvantages

- Require more experienced site personnel

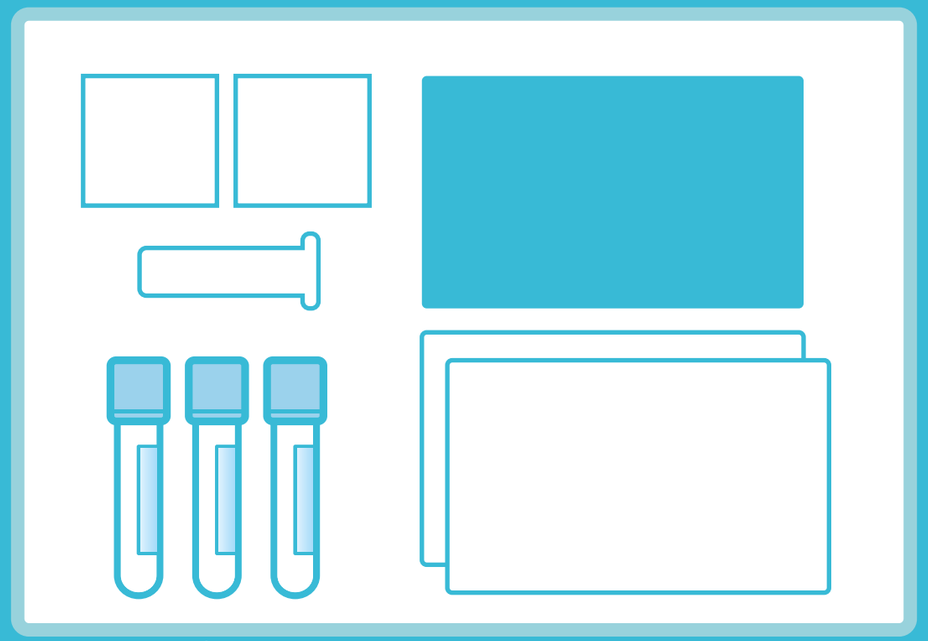


- More storage space

- Adds time and complexity to the colleciton process

Why Assemble Supplies Into Kits?

Provide limited bulk supplies as back-up to the kits



Assemble the pre-labeled collection tubes

The combination approach:

Fisher BioServices often provides a combination of both kits and bulk supplies. For example, we:

- Assemble the pre-labeled collection tubes, cryovials, and transport tubes in the kit, but
- Provide the phlebotomy supplies (vacutainer holders, needles, alcohol swabs, bandages, and others) in bulk or
- Provide limited bulk supplies as back-up to the kits, in case less common components are damaged.

Kits vs. bulk supplies and the clinical site:

- Clinical sites that are experienced with clinical trials and other research processes may be set up to manage bulk supplies.
- The flip side of this is that a busy site may have several trials in progress, and it may prove difficult for them to separate each trial and collection protocol.
- Sites with less experience may not have study management systems in place, and sending kits will reduce their risk.

3 Getting to the Actual Kit Design

Getting to the Actual Kit Design

Kit design begins with the study design. A kit vendor should work with you to analyze the study protocol and estimate enrollment and/or other factors and then create a forecast of needed supplies. This should include timing of component orders to manage expiration dates, as well as the production and shipping schedule. Beyond the protocol and study, the kit vendor should also have extensive relationships with suppliers and be able to advise on what components are expensive, what substitutes may be available, what components can be cheaply custom-made, and what components will best preserve the target analyte.

Following a high level overview (will the kit be used at a clinical site, or by field staff, or visiting phlebotomists at patient's homes?), the protocol is then analyzed for the specifics:

- Number of sites?
- Number of participants/site?
- Number of visits/participant?
- Participant-specific and/or visit-specific kit needed?
- What samples will be collected at each visit?
- What supplies are needed for each sample?
- Labeling requirements?
- Need for post-collection shipping kits and air bills?
- Instructions for the clinical site staff or field phlebotomists?
- 2-, 3-, or 4-part collection/requisition forms?

Getting to the Actual Kit Design

Arranging the Components:

A kit may be as simple as a few tubes in a zip-lock bag. However, kits containing dozens of items are not unusual, and the more complex the kit, the more critical the layout. A good overall design will minimize the possibility of damage and loss of components and also help ensure use of the right item at the right time. This is where the experience of the kit designer counts most. The overall layout of the package can make a significant difference in the efficiency of your sample and data collection and also promote compliance with correct procedure.

Items should be secured to prevent displacement and damage during shipping and handling, and the components arranged so that clinical staff need only reach for the next available item as they follow instructions. Items needed for a specific task should be organized together, and sub-kits, if used, should also be placed in the order needed (consider shrink-wrapping sub-kits for security as well as clarity). Labels should be pre-applied and components easily and quickly identifiable; staff should not have to sort through a box or squint at a label to be sure they have the correct item. Any non-standard instructions or item should be incorporated into the overall design in a careful and step-by-step manner. Include extra labels in patient-specific kits, as small pieces of paper are easily misplaced.

It is not unusual for patient samples to go to different locations after collection. The shipping supplies—gel packs, labels, air bills, and related items—should be pre-labeled to the extent possible and packaged to minimize error. Leave no room for confusion as to what sample goes where.

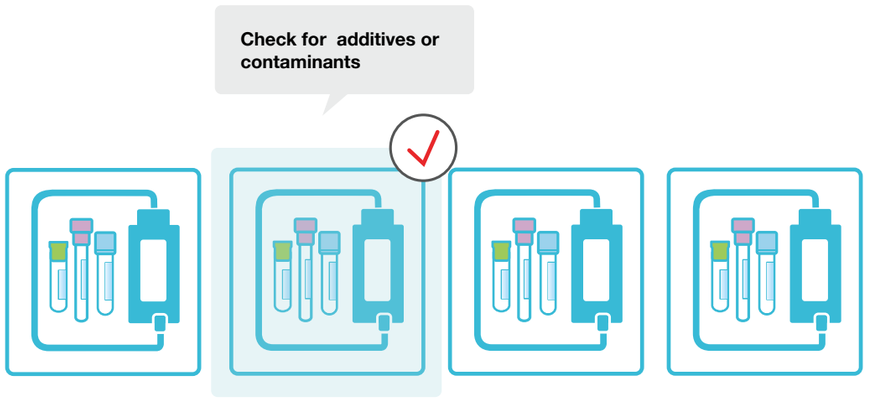
All of these considerations increase accuracy and efficiency, reduce errors, and help control variability. Most importantly, they also allow clinical staff to maintain their focus on the patient.

Getting to the Actual Kit Design

Component pre-screening:

Will potential downstream assays include testing for heavy metals or other contaminants? Many items used in sample collection kits can have additives or carry contaminants that can interfere with certain target analytes.

Your vendor should be able to provide screening of each lot of the kit components for contaminants, store the approved supplies in a quarantined environment, track the supplies by lot, and generally ensure that samples are not contaminated by the containers and supplies used for collection. Many research organizations prefer to pre-screen kit components in-house or at an independent laboratory. Others do not, and these organizations should work with a vendor whose kit design personnel have the appropriate technical background and business relationships with independent specialized laboratories that can provide the needed screening.



FDA REQUIREMENT

- temperature control
- chain of custody
- GMP

Collection plus administration:

Management of a clinical trial can often be simplified by packaging the specimen collection supplies with the administration kit—the clinical agent and the items needed to administer the agent to the patient. To do this, you will need a vendor that is equipped to apply additional labels and/or replace the manufacturer's label, repackage items, generate a batch record, and comply with the applicable US Food and Drug Administration (FDA) requirements. If the clinical trial involves a vaccine or cell-based therapy that must be maintained within a specific temperature range, your kit vendor must also be equipped to provide qualified/validated shippers and on-board temperature data loggers.

Getting to the Actual Kit Design

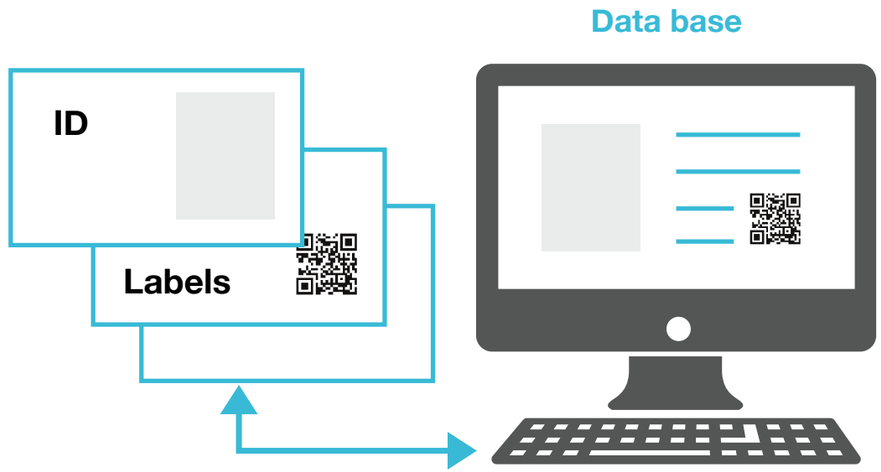
Labeling issues and opportunities:

If you are planning clinical trials, you may already have defined your patient labels, IDs, and other data and will simply provide the information for use in kit production. Ideally, your labels will include QR codes or barcodes to allow linking and tracking of every component of the kit with the patient. If you are not working with a contract research organization (CRO), consider using a vendor who can generate IDs, design and print barcoded labels, and provide randomization and other services.

Fisher BioServices created a custom program and database to manage this process, and if requested, we can generate and assign patient/sample identifiers and packaging. Once the IDs, labels and packaging are approved by the client, we print and apply labels as needed, and will also send IDs in a flat file to the clinical site to assign to enrollees and their corresponding collection kits. This includes labels with barcodes/QR codes and eye-readable information in multiple formats, on label stock that will withstand storage in liquid nitrogen if needed. IDs can be patient-specific, sequential, and comply with other client requirements; samples and data are all linked to the patient ID.

The demo:

Once an initial design is in place, ask for a demo kit for approval. Fisher BioServices' process is to design and build a demo kit and also generate a draft work instruction. The work instruction captures all critical information such as the project number, protocol number, clinical drug labeling and packaging criteria, a description of assembly and configuration requirements, label specifications, estimated number to be produced, estimated dates of production, and a listing of the components. We keep a copy of the approved demo kit on file with the work instructions to ensure uniformity and adherence to client requirements across production runs.



4 On to the Assembly Line

On to the Assembly Line

Two basic approaches to manufacturing kits are available: Assembling make-to-order, or assembling make-to-stock. Fisher BioServices uses both approaches, depending on client needs.

Make-to-Order Kits are not assembled until an order is received. These are generally patient-specific or visit-specific kits, and a lead time of several days is needed in order to assemble, label, and ship the kits.

Make-to-Stock Kits are assembled in advance and either shipped to the study site for storage, or stored at the vendor facility and shipped out when ordered. Kits that are made and in stock can be usually be available on a very short time frame, including shipping overnight for next day delivery if needed. However, careful forecasting is needed to manage expiration dates, both for manufacturing purposes as well as ensuring the kits are not overstocked and allowed to expire at the study sites.

On to the Assembly Line

Optimizing expiration dates:

1. "Fresh" components (not always possible)

2. Just-in-time kit production

3. Minimize stop-lot dates (adds a management challenge)

Optimizing expiration dates:

From a study perspective, kits are only as good as the earliest expiration date, and the ideal scenario is to use items with maximum time to expiration. However, suppliers want to ship oldest stock first. It is possible to request the longest possible expiration date from suppliers of kit components vendors, but there are no guarantees. How do you optimize expiration dates and prevent the expense of replacing components or re-working kits?

Several options are available, including choosing just-in-time kit production. If you track enrollment and know when patient visits are scheduled, ordering and stocking a few kits at a time is the best way to manage expiration dates. Minimizing your batch production also helps, but adds expense as each production run involves performing line clearance and set-up.

Another option is to set stop-lot dates—the date by which a component cannot be included in a kit when it is manufactured—to a minimum. However, this results in kits with closer expiration dates and requires tighter management of kit inventory at the clinical site.

On to the Assembly Line

Placing your orders:

On-line systems for ordering kits allow study staff members to more easily manage the supply chain so they can better focus on research. These on-line systems can be primitive or sophisticated; look for capabilities that will help your study run more efficiently. For instance, will it allow:

- Management of approvals? Can you set limits and thresholds for individual study sites to prevent over-stocking and/or allow automatic approvals of orders?
- Prioritization of supply orders by the study principal investigator or the vendor project manager, in case of an emergency order by a site?
- Requesting specific shipping dates so that sites have their supplies when needed?
- Automatically generated notifications when kits ship?
- Other features? Many options exist that can help make sample collection more efficient.

Management of approvals

Prioritization of supply orders

Requesting specific shipping dates

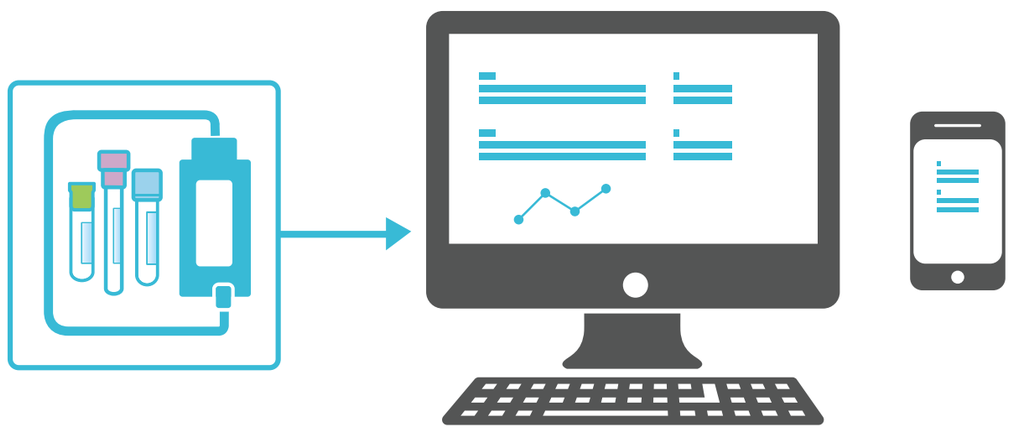
Automatically generated notifications

5 Beyond the Collection Kit: Integrated Sample/Data Management

Beyond the Collection Kit: Integrated Sample/Data Management

Designing and using collection kits is all about controlling variability and maintaining sample integrity from initial collection though final disposition, regardless of the downstream use of the specimen. However, with recent advances in IT and the onset of Big Data, collection kits now offer additional opportunities for fully integrating sample and data collection and management, particularly in cohort studies.

The simplest collection kit, when labeled with a QR code and combined with mobile technology, can serve as the starting point for data collection as well as specimen collection. The participant ID, consent, biospecimen, assay results, and questionnaire responses can be linked via the QR code and immediately uploaded to the cloud. The savings in data management made possible by this emerging technology could dramatically reduce the cost of cohort studies that are the foundation of biomarker research. This process and technology will be outlined in a future eBook.



Another advantage to the use of kits: when combined with mobile technology, a well-designed kit provides structure for clinical staff in their time with study participants. The kit and software for the mobile device can help clinical staff walk participants step-by-step through consent, completing a questionnaire, drawing blood, and so on.

Additional Resources

When setting up a clinical trial or a longitudinal study, every decision revolving around sample management: collection, lab processing, storage, disssemination, and data management, is crucial to its success. For collection of clinical participants' biospecimens, one aspect that requires significant thought and planning is how the needed patient samples (e.g. whole blood, tissue) will be collected at the clinical sites. Sponsors, CROs, and clinical investigators must decide if they are going to provide their sites with the tubes and other supplies in bulk, or provide patient-specific or visit-specific collection kits.

Learn more about Bulk Supplies VS. Collection Kits

VIDEO BLOG

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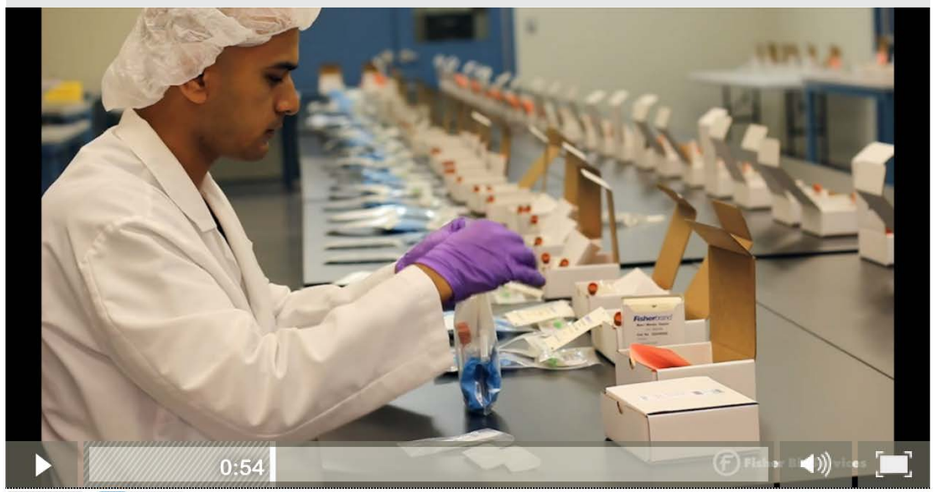
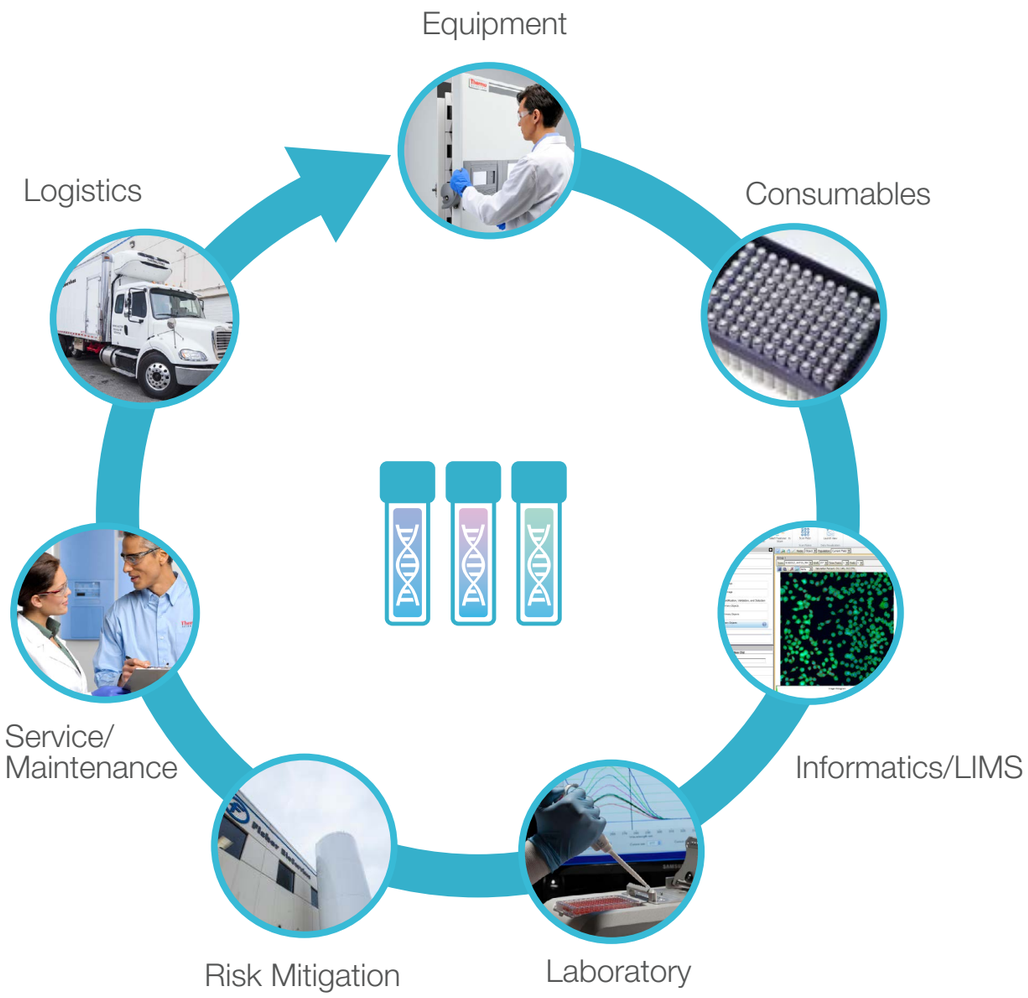


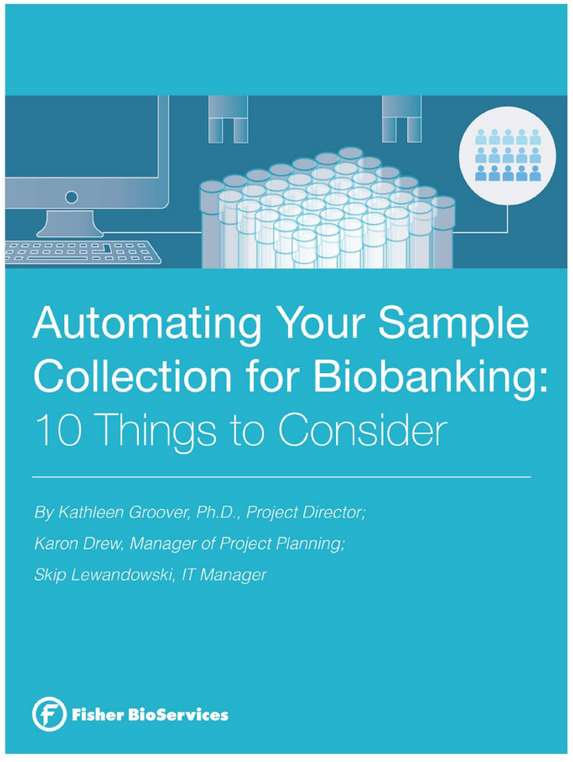
Additional Resources

Every phase of your sample lifecycle is critical to your risk mitigation strategy. Explore additional resources to learn how you can support every step of your biobanking workflow.

- Comprehensive Biobank Resources



Additional Resources



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