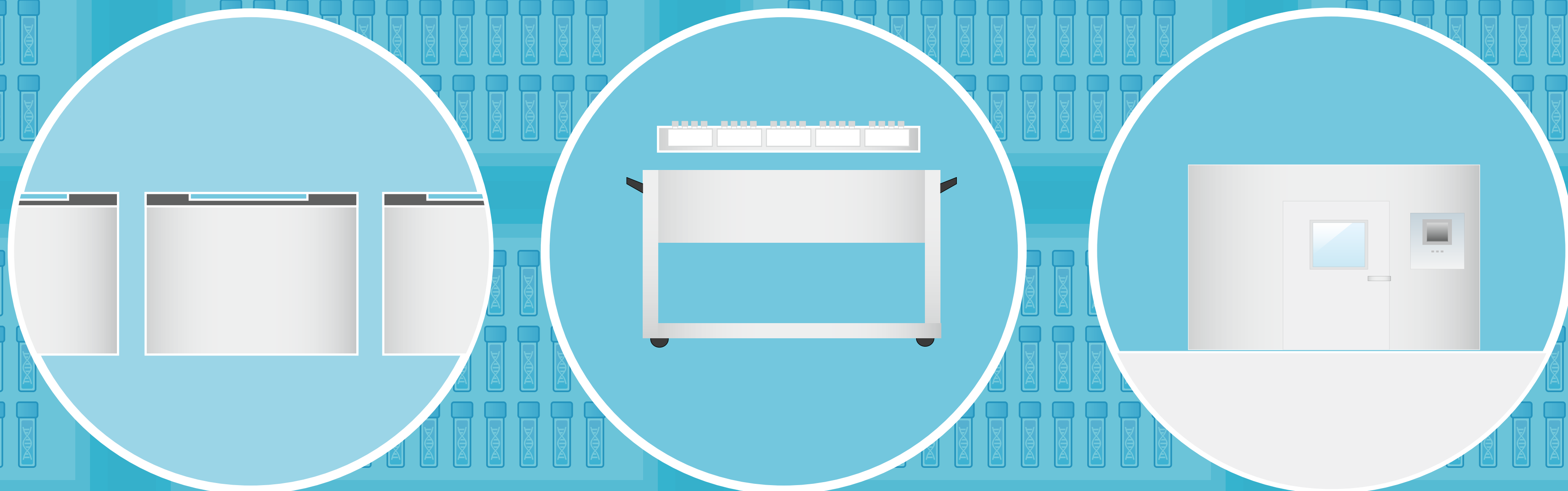
Extreme Biobanking:

How to Build and Operate a -80^{O}C Walk-In Freezer

By Sheri Gimigliano, MS & Debra Barnes, PhD



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About the Author

Sheri Gimigliano, MS

Debra Barnes, PhD

Sheri Gimigliano, MS

Ms. Gimigliano is a Project Director at Fisher BioServices and is responsible for all aspects of her operation, including facility layout, cold storage equipment selection and validation, budgeting, staff training, and other activities. She received her BS in Medical Technology from Slippery Rock University and her MS in Organizational Leadership from Geneva College. Ms. Gimigliano has extensive experience in the healthcare and biotechnology industries, and is co-inventor on a patent for the ChemoFx®, a drug response marker.

Debra Barnes, PhD

Dr. Barnes is Director of Government and Laboratory Services at Fisher BioServices. She has more than 25 years of research experience as well as 15 years of experience in directing and coordinating complex group projects and Federal programs. She is responsible for ensuring that client research programs are fully supported, and that the facilities, staff resources, and other aspects of our services meet contract requirements. Dr. Barnes has also served as a reviewer for the National Cancer Institute's Office of Biorepositories and Biospecimen Research (OBBR).

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Overview

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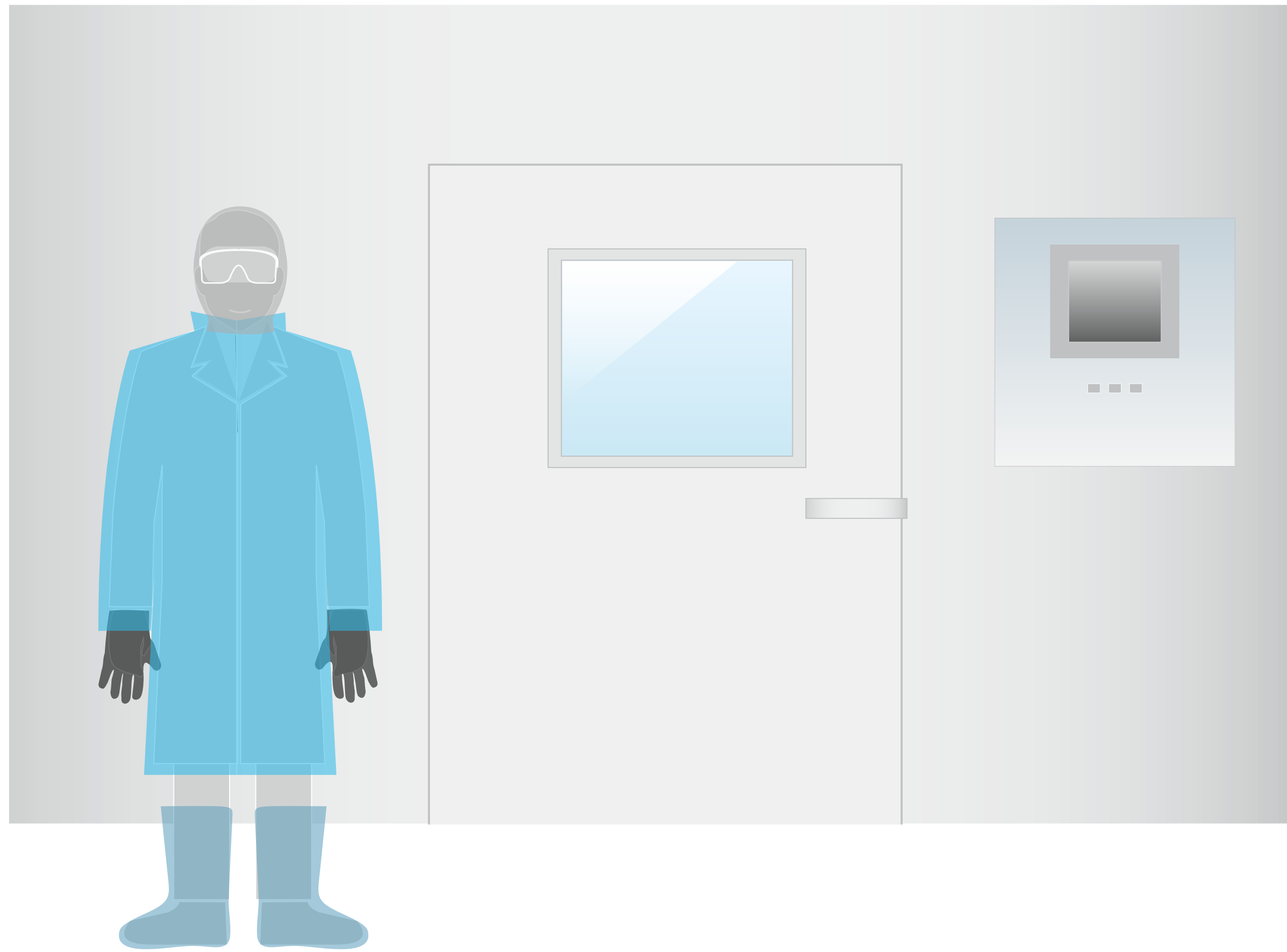
Introduction

Opening a door and walking into the equivalent of Antarctica takes preparation. Scientists studying climate can use instruments to measure extremely cold temperatures: NASA documented the lowest temperature on record, -93.2°C, in 2010 from a high ridge on the East Arctic ice sheet, using satellite data. But what if instruments won't do the job? What if your employees have to work in such an environment?

Research biospecimens are commonly stored at -80°C, but this usually occurs inside mechanical reach-in freezers that result in minor, transient exposure of workers to the extreme cold. However, if the freezer is the size of a large room, then employees must be specially equipped and protected. How do you protect workers handling research materials in an environment that has to be maintained at a temperature that is typical of winter in Antarctica? The first step is to team with an organization that is already expert in safely managing materials at ultra-low temperatures.



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1 About Ultra-Low Storage Systems

About Ultra-Low Storage Systems

The cost of storing biospecimens at ultra cold temperatures (-80°C) is one of the most significant operational expenditures of a biorepository and affects the long-term sustainability of biobanks. Storage at ultra-low temperatures has relied predominantly on mechanical freezers, which have storage capacities ranging from 25 to 32 ft^3, and will hold 23,000 to 47,000 cryovials, depending on their size. While these freezers may work well in smaller facilities where sample collections are limited, some aspects of these freezers can be problematic in the operation of larger, more complex biobanks.

- These freezers typically include high stage and low stage compressors with a single condenser that may be susceptible to failure if ambient temperatures rise (ultra-low freezers using a free piston Stirling engine do not have compressors, but these are relatively new and to date few of these freezers are in use at biorepositories or biobanks).

- Although mechanical ultra-low freezers have become more energy-efficient and offer greater storage capacity for a given footprint, these units still represent a high energy cost.

- Mechanical freezers have a useful life of from 7 to 15 years, after which they must be replaced and/or compressors rebuilt.

- The condensers release heat directly into the surrounding space, resulting in a need for excess HVAC capacity, especially in warmer weather, which adds to energy costs.

- The expelled heat needs a minimum amount of space to efficiently dissipate, or the mechanical freezers will not function properly and may fail. This requirement creates the need for a larger footprint (for better air circulation) and fewer ultra-low units can be installed in a facility, compared with the number of -20°C freezers or refrigerators.

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About Ultra-Low Storage Systems

An alternative to stand-alone mechanical freezers is a walk-in freezer. Large, walk-in storage environments allow for space-efficient biospecimen storage in flexible configurations. These units may last a very long time with appropriate preventive maintenance and occasional replacement of the compressors, and can operate over extended years while exhibiting narrow windows of temperature fluctuation (+/- 5°C). Walk-in freezers are cooled by mechanical refrigeration units, but provide an advantageous ratio of storage space per compressor.

However, walk-in freezers assume that staff members are working inside the freezer, and for this reason, walk-in freezers are typically designed for products maintained at -20°C. A temperature of -20°C is mechanically easier to maintain and brief exposure to -20°C is safe when personnel are provided with the proper protection. However, exposure to -80°C is dangerous even for a very brief time, which normally renders ultra-low walk-in units impractical.

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About Ultra-Low Storage Systems

The other alternative to mechanical freezers, and specifically ultra-low freezers, is the automated, high-capacity, high-density, ultra-low temperature biospecimen storage unit. These units reduce the facility space needed per sample, reduce energy consumption, and consequently offer important opportunities for reducing overall operational costs. The automated storage unit typically has a robotic arm that functions at -20°C, while the samples are stored in a separate -80°C area. Because storage and retrieval of the vials is performed by these robotic arms, they are suitable for active inventory and also prevent exposure of staff members to cold temperatures.

However, one potential disadvantage of these units is the need for a uniform vial size; research collections that include a variety of samples in varying containers are challenging for these units to accommodate. The robotic arms may not work with all vial types and it may be necessary to determine which cryovial is optimally suited for storage in a particular unit. Another disadvantage is their initial cost, ongoing maintenance, and potential problems with reliability.

2

Why Construct a Walk-In -80°C Freezer?

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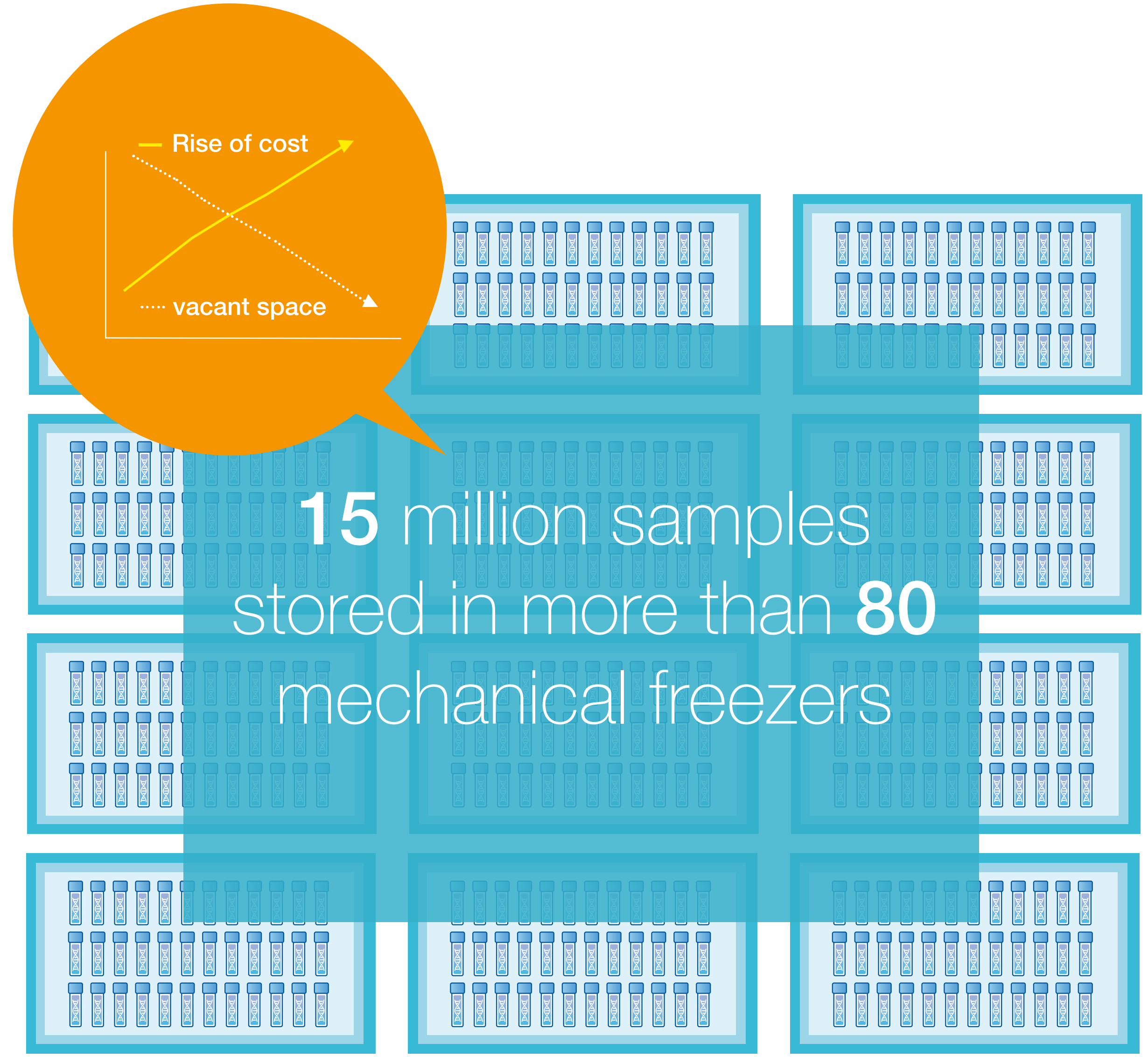
Fisher BioServices operates a biorepository facility for a client with more than 15 million samples, a large proportion of which was initially stored at ultra-low temperatures in more than 80 mechanical freezers. The maintenance and energy cost of these freezers, as well as the cost of replacing the aging units, was rising. In addition, the facility housing these specimens was nearing capacity. Automated ultra-low storage was considered, but the client's inventory consisted of a variety of vial sizes, and the client questioned the reliability of automated units. At the client's request, Fisher BioServices assisted in the design and construction of a 2,500 ft^3 walk-in, ultra-low (-80°C) freezer that provided high-density, high-energy efficiency storage for approximately 40 percent of the client's inventory.



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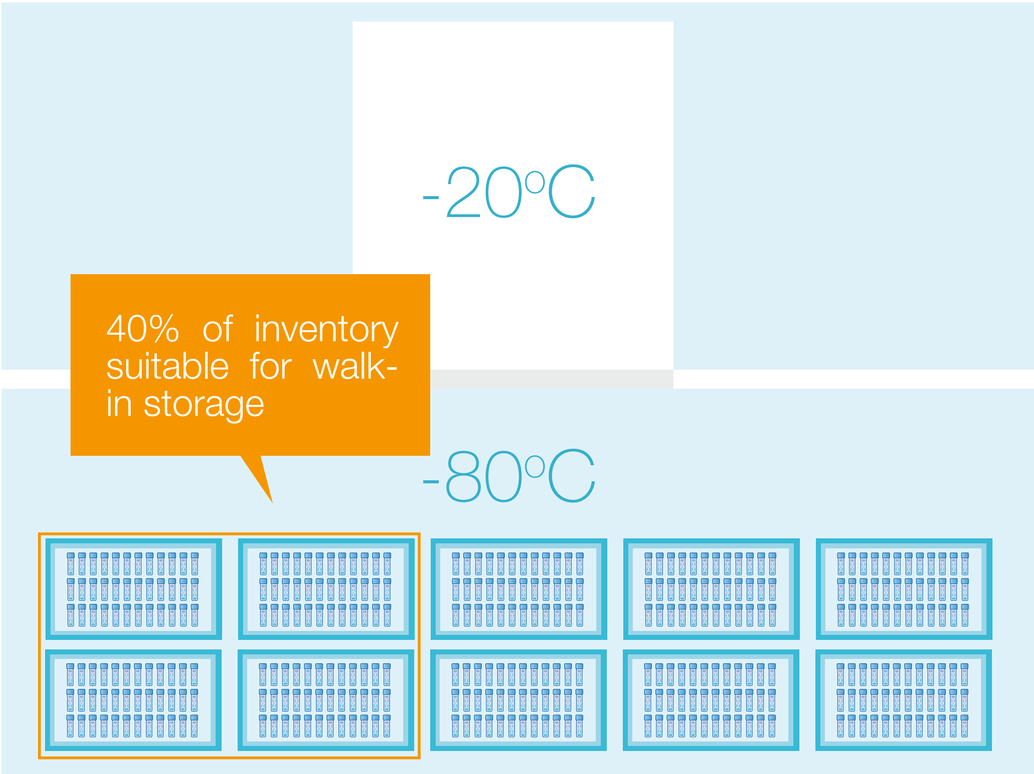
Why Construct a Walk-In -80°C Freezer?

Because the client could identify such a large proportion of inventory that was primarily archival, it was determined that automation/robotics was not cost-effective. However, without robotic components to move samples in and out of the unit, repository staff would on occasion have to enter the unit, and Fisher BioServices, as part of assisting in the design and construction of the unit, also created and implemented a number of processes and designed some specialized equipment and software tools for the safe and efficient management of the specialized storage unit.



Walk-in freezers are generally used for storing materials at temperatures of -20°C and warmer. Fisher BioServices has built and uses walk-in storage at both -20°C and at -40°C, and has the processes and personal protective equipment (PPE) in place to allow employees to enter these walk-in freezers and spend a brief amount of time conducting the necessary inventory activities. However, devising a safe means for staff to work in a -80°C environment presented unique challenges.

One way of managing this issue was to design the freezer, to the extent possible, specifically for safe access by employees. To accomplish this, the unit was constructed with an ante-chamber and a central interior corridor that are maintained at -20°C. The -20°C environment allows safe access by properly equipped repository staff members while at the same time protecting the -80°C storage areas, consisting of reach-in bays containing “dresser drawers,” from temperature shock. The ante-chamber and corridor doors were designed with windows that allow a full view of the interior, so that staff members working inside could be observed by an exterior “spotter” for safety.

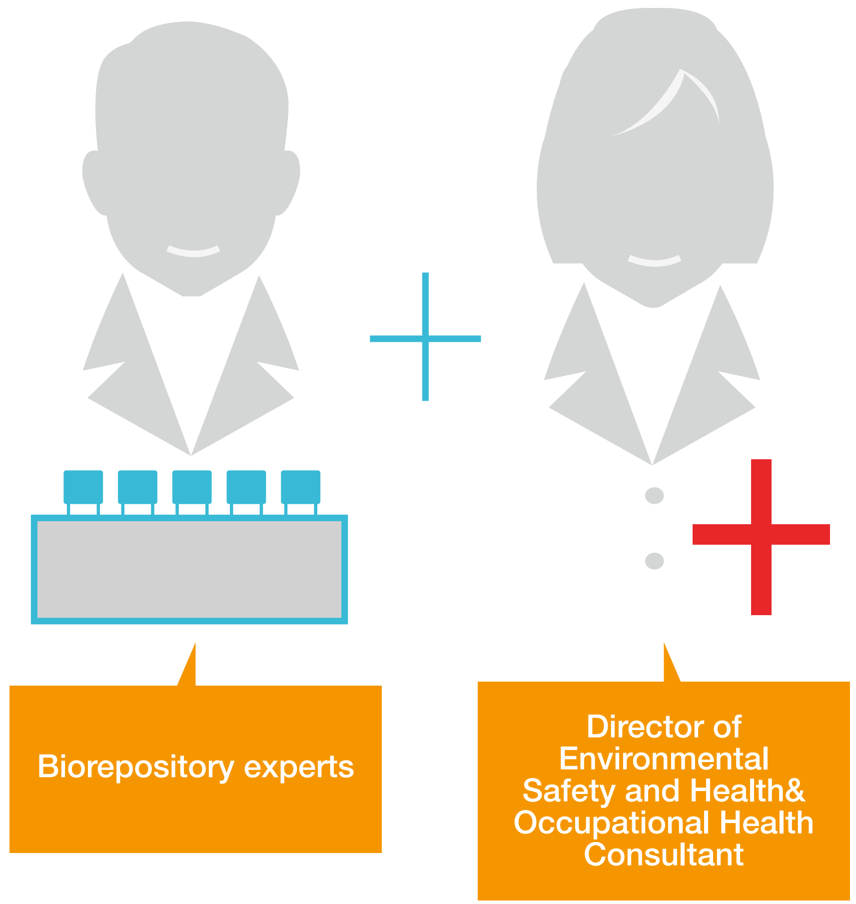
Fisher BioServices has procedures and PPE for working in a -20 environment. However, in this case, the employees are in a -20°C environment and opening doors into a -80°C bay. When the door is opened, some volume of -80°C air spills into the corridor—the amount depends on how full the bay is—and further lowers the temperature. For this reason, employees have to be protected against some exposure to -80°C, even though the corridor is maintained at -20°C.

3 Equipping the Staff for Access

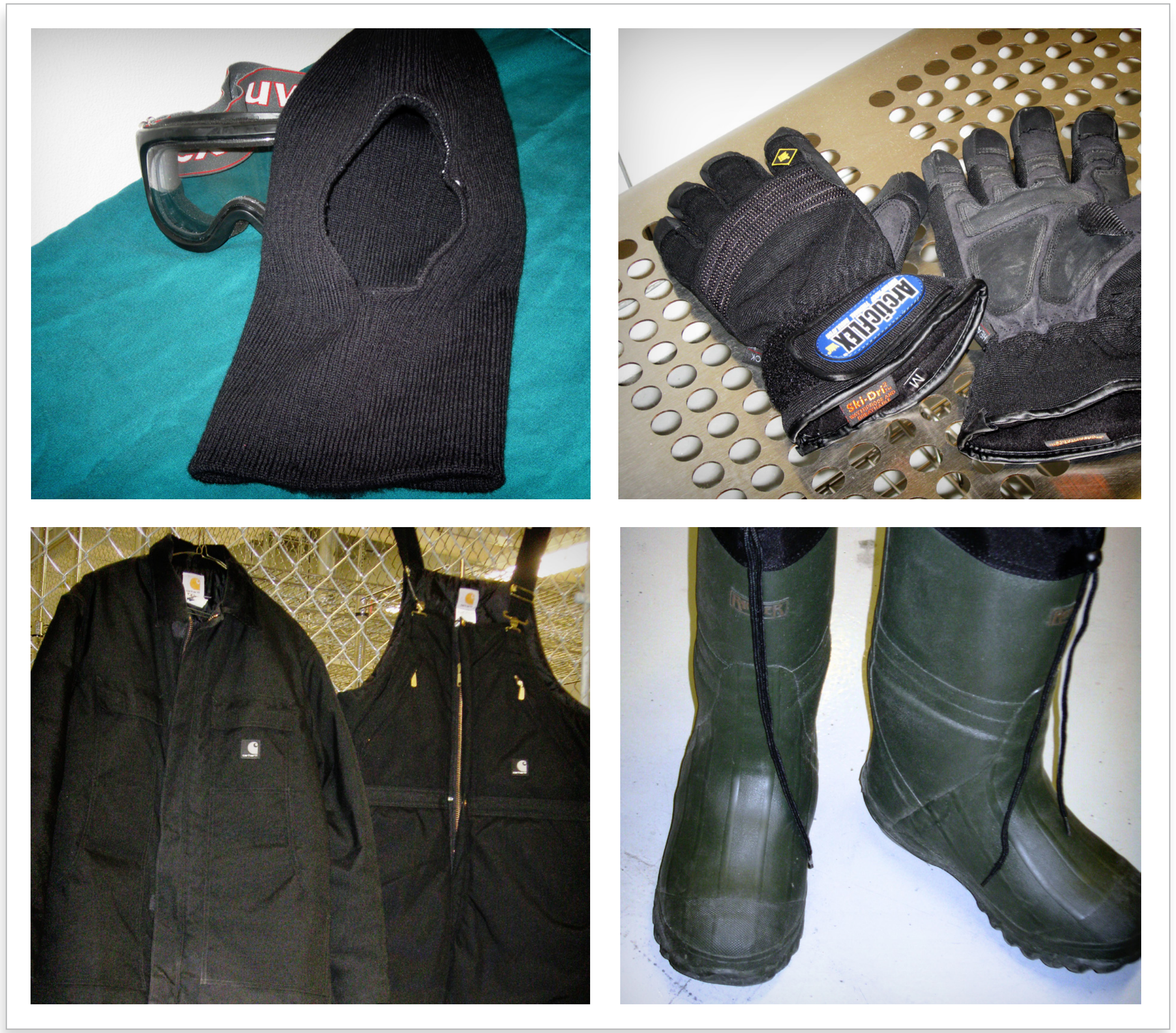
Equipping the Staff for Access

Fisher BioServices' biorepository experts collaborated with the company's Director of Environmental Safety and Health, the company's Occupational Health Consultant, and used data on arctic and similar environments as a reference for preparing the safety criteria. One result of this research is that employees require medical clearance before beginning training and work in the -80°C unit.

Once criteria were defined, a market search was conducted and a manufacturer of clothing and PPE that was rated for the temperature and time criteria was located. The process and procedures for entering and working in the unit were defined and documented in a Standard Operating Procedure that addresses cross contamination, inspection for damage and quarantine of the items for repair if needed, and other considerations.



Equipping the Staff for Access



The PPE consists of insulated boots, thermal overalls, thermal jacket, gloves with thermal liners, hat/face mask, and goggles. One employee enters the environment while a second observes from outside the unit for safety. Even with PPE, at the temperatures inside the freezer, the technician's ears, fingers and toes will start to tingle within only a few minutes. More critically, the technician's nasal passages begin to swell shut. Employees typically spend only about five minutes in the walk-in at a time; eight minutes is considered to be the maximum. Once the technician has left the walk-in freezer, an hour is needed for a full return to normal, and should the unit be accessed again in a short time, the technicians switch places.

However, access to the freezer is limited by the freezer itself, and not by staff safety considerations. The -80°C compartments of the walk-in freezer are very briefly exposed to the air in the corridor when samples are pulled, and access to the compartments must be limited to prevent temperature excursions. The need for temperature control inside the freezer, rather than human factors, is what limits the amount of inventory activity that can be performed in a day.

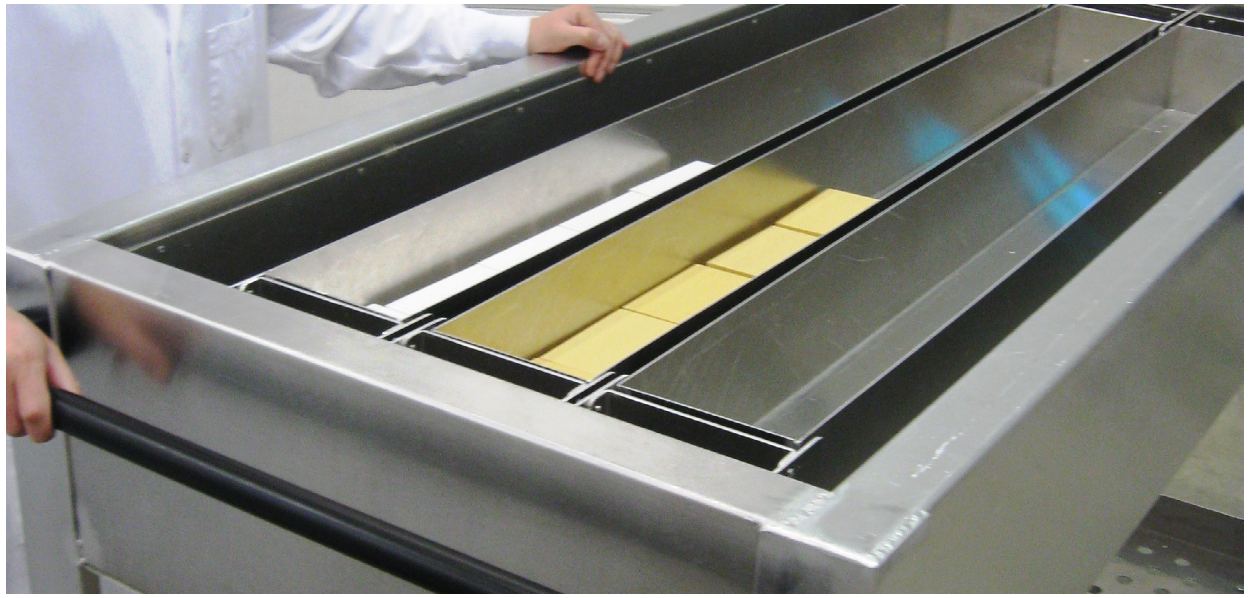
4 Maximizing Technician Time

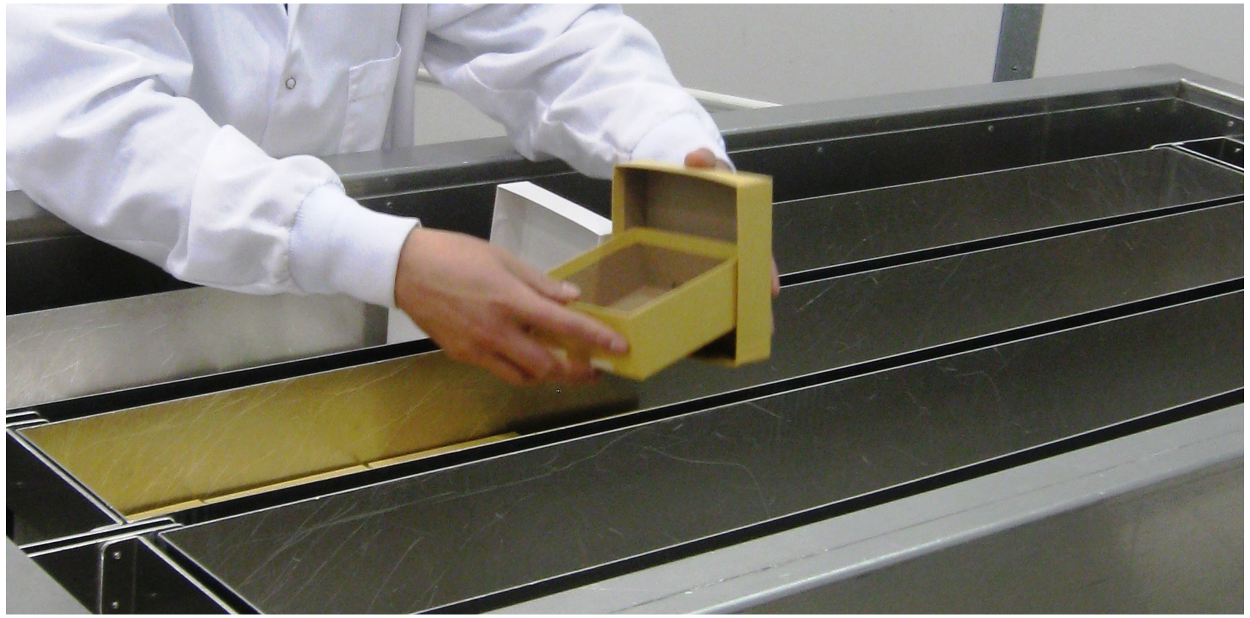
Maximizing Technician Time

Given the time limits for performing tasks within the freezer, placing and pulling samples from inventory had to be conducted at maximum efficiency. This was particularly the case when the unit began operation. When empty, the amount of -80°C air spilling into the corridor was at the maximum, placing the most severe restrictions on staff time in the unit while trying to transfer the maximum possible amount of material. In response, Fisher BioServices devised a system that optimized efficient transfer of samples from the mechanical freezers into the walk-in while protecting them from temperature excursion and minimizing staff exposure to ultra-cold temperatures.

The selected inventory consisted of millions of samples in 34,260 standard 2” and 3” boxes, distributed among dozens of chest and upright ultralow freezers. The high-density walk-in unit was organized into reach-in bays, with each bay containing a number of “dressers” of 70 drawers of two sizes, specifically manufactured to accommodate the client sample containers. Each drawer could hold 10 cryoboxes (5.25 x 5.25) or a number of SBS formatted racks. The transfer of more than 34,000 boxes required a process for both a high volume of work as well as the highest level of efficiency.

A number of approaches to pull, transport, and stage specimen boxes to the space were tried, and analysis of the various approaches took into consideration specimen temperature control, ergonomics, and efficiency of movement, and the variations in final location within the walk-in unit.





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5 Creating the Right Tools

Creating the Right Tools

The typical process for handling samples at ultra-low temperatures is to keep them resting on dry ice. However, this allows partial exposure to ambient air as well as potential cross-contamination between the sample and dry ice.

Our biorepository staff members analyzed several strategies for pulling and transferring specimens into the unit, which led to innovations in the design of the company dry ice carts. These custom-built carts hold a specific volume of dry ice and the basin holding the dry ice is insulated, reducing the rate of sublimation of the dry ice. Once the cart basin is filled with the prescribed amount of dry ice, an insulated bin or sleeve is then submerged in the dry ice to a specific depth.

By using a submerged container, Fisher BioServices eliminated both direct contact with and cross-contamination between the sample and the dry ice, and also created a heat sink for better temperature compliance. The walls of the submerged container are the correct height to retain a blanket of cold air on top of the materials, and are notched to allow repository staff to quickly and easily move materials in and out of the bin. This was tested, validated, and shown to provide both tighter temperature control, and maintenance at temperatures on average 12°C colder than the typical process. In addition, the sleeves/bins allowed a significant reduction in the amount of dry ice consumed and reduced staff exposure to CO_2.

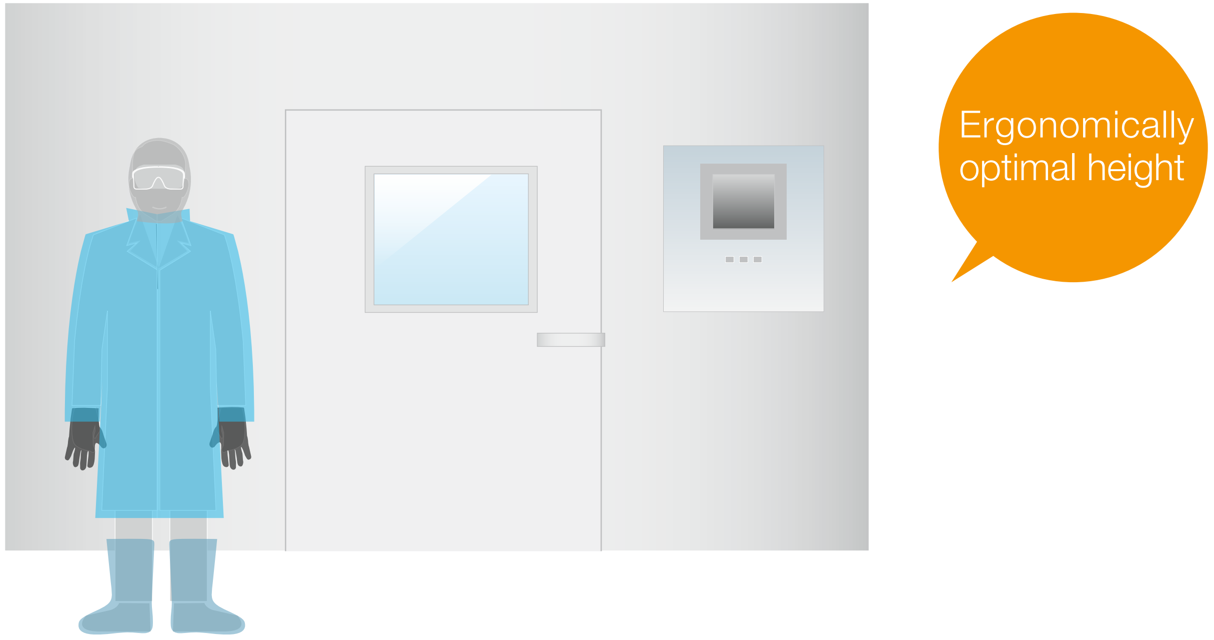
Creating the Right Tools

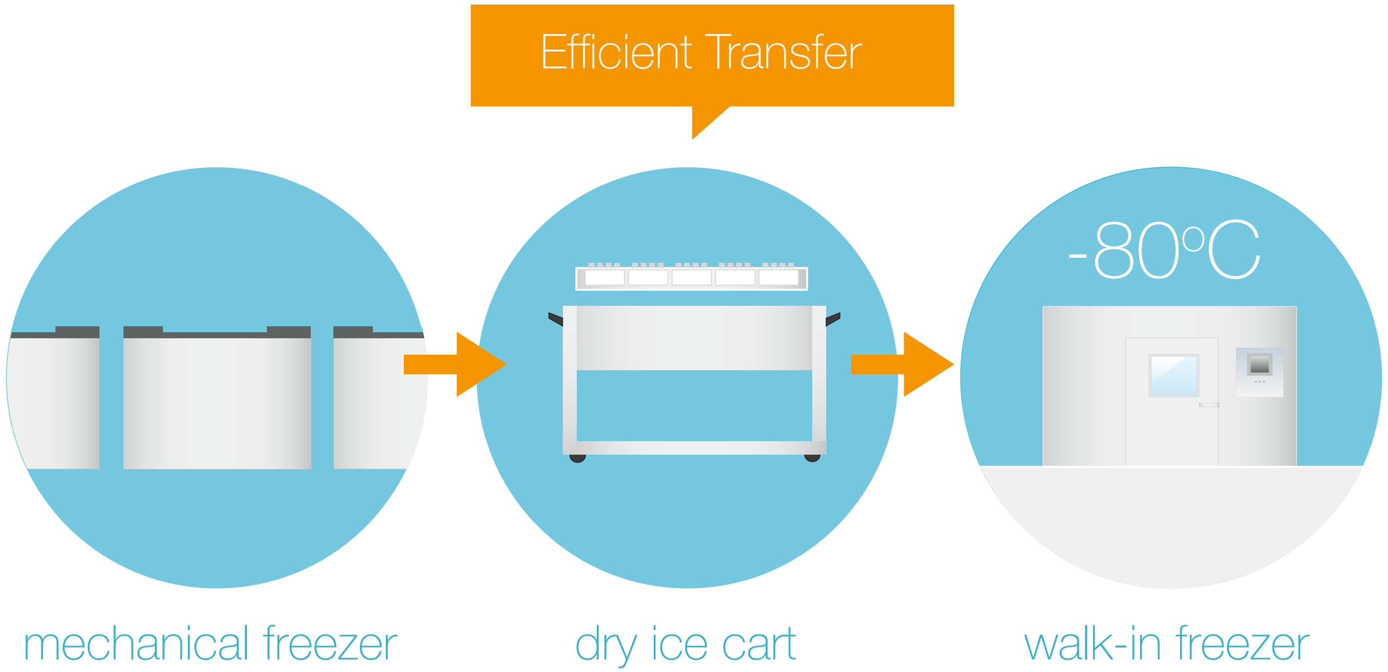
The carts were further designed so that the working surface is at an ergonomically optimal height, and the shelves beneath the working surface are cut in to allow leg room, so technicians can efficiently work while seated as well as while standing.

In the specific case of rapidly transferring the client's selected inventory from the mechanical freezers into the -80°C walk-in, Fisher BioServices configured the specialized dry ice carts with frames that fit the unit's compartment drawers. As with the standard-configured carts, the frame holds the walk-in unit drawers at the specific depth needed to create a heat sink and provide tighter temperature control.

Once the drawers were conditioned in their frames in the dry ice cart, the cryoboxes were pulled from their original location in the mechanical freezer, staged in the drawers, and moved to the walk-in. The technician team then transferred the drawers directly from the cart into the assigned compartment.

By staging the unit's drawers directly on the dry ice cart, the time needed for the transfer of three full drawers from one cart into the walk-in unit was decreased by two-thirds (from 15 to five seconds). This not only allowed efficient transfer of the materials but also minimized the time staff had to spend within the unit and prevented excursions within the freezer.





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6 Software Tools for Inventory Accuracy and Back-Filling

Software Tools for Inventory Accuracy and Back-Filling

Once the designated samples from a mechanical freezer were transferred into the walk-in, their location was updated in the electronic database using a Fisher BioServices-defined box movement software utility. This software tool displayed the old location and allowed technicians to scan in the new location and vial type in real time during the transfer of materials.

A consolidation tool was then used to electronically eliminate the spaces vacated in the mechanical freezer. The system automatically moved the remaining specimens up and to the left in their virtual locations, and assigned the new locations in the database. The repository staff members then physically moved the specimens to the assigned location and performed a final verification for location accuracy. These tasks were performed in small increments during “down time” between receiving new client specimens, retrieving and shipping samples requested by investigators, and other repository tasks.

During the initial filling of the ultra-low walk-in freezer, 48 upright freezers and 33 chest freezers were emptied, resulting in a reduction of storage space by approximately 50 percent and a reduction in energy consumption by at least 50 percent for this part of the client collection.

7 Conclusion and Applications

Conclusion and Applications

The design and construction of a walk-in ultra-low freezer offers high-density storage and tremendous savings in energy, maintenance, and replacement costs compared to the equivalent storage space using mechanical -80°C freezers. This unit, which features a built-in liquid nitrogen system as well as redundant compressors and other risk mitigation strategies, is expected to return the cost of construction in operational savings within a two- to three-year period.

Non-automated, ultra-low walk-in freezers can be highly cost-effective in situations where the overall inventory activity is relatively low. They lack the expensive, complex robotics and can accommodate sample collections consisting of a variety of vial and container sizes. However, maintaining an internal temperature of -80°C, whether in a 25 ft^3 unit or a 25,000 ft^3 unit, requires that access to samples is limited to the capacity of the unit to maintain and recover correct temperatures when the door is opened. For this reason, maximizing efficiency in conducting inventory activities inside an ultra-low storage unit is critical; for a walk-in, maximizing efficiency is also critical to the protection of staff members.

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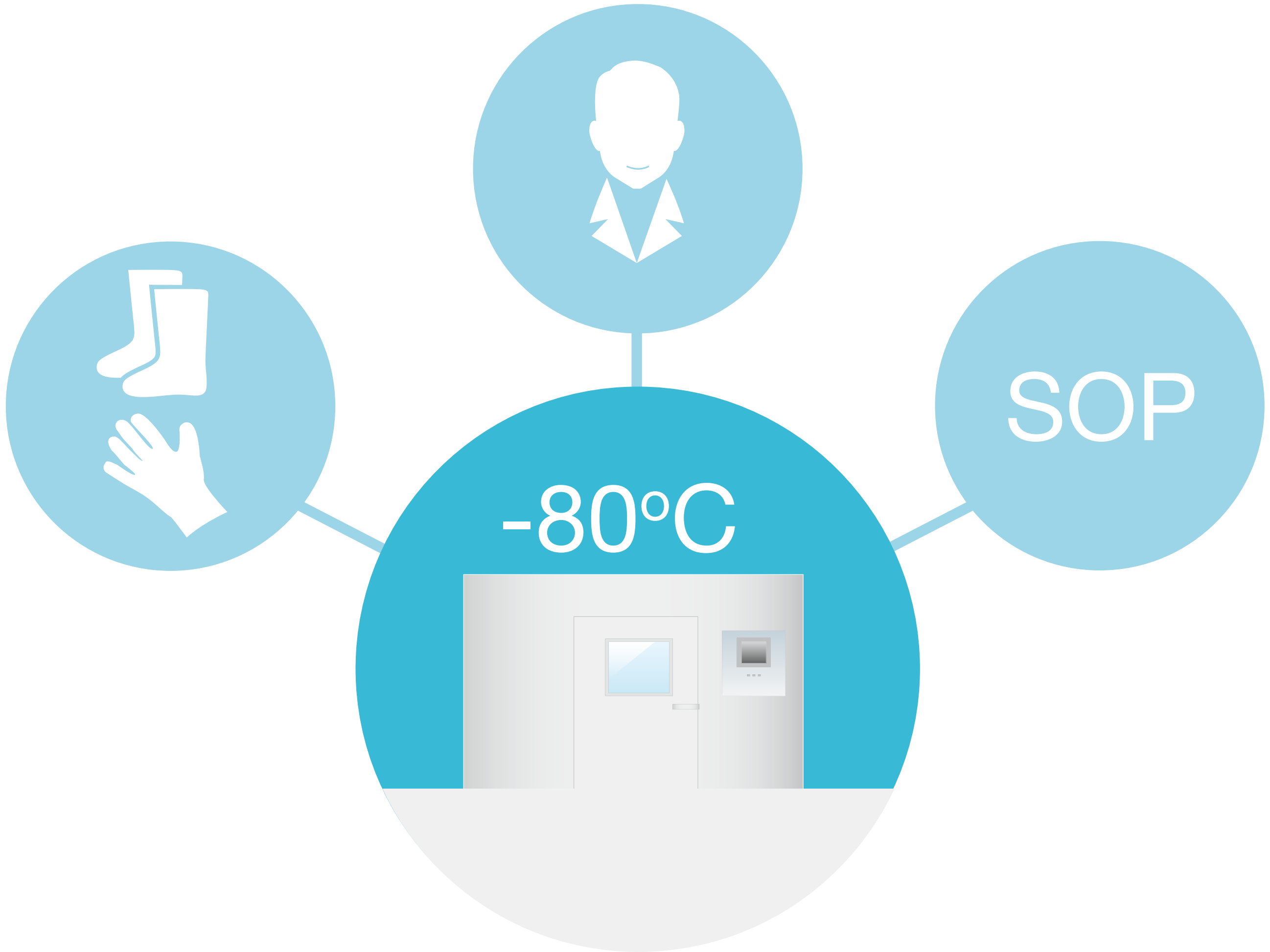
The successful management of these cold storage systems involves carefully considered maintenance and operating procedures (of the facility as well as the ultra-low freezer), correct PPE, staff training, and adherence to SOP, built on a foundation of established expertise in managing materials at -80°C.



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As a worldwide provider of biobanking and clinical trial sample management, Fisher BioServices can assist companies looking to store critical biological materials, biotherapeutics, manufacture sample collection kits, and process samples.

- Simple to complex sample collection kit design and production
- Sample processing, global biobanking, and data management
- Online access to inventory for data searching, requesting samples, and exporting reports

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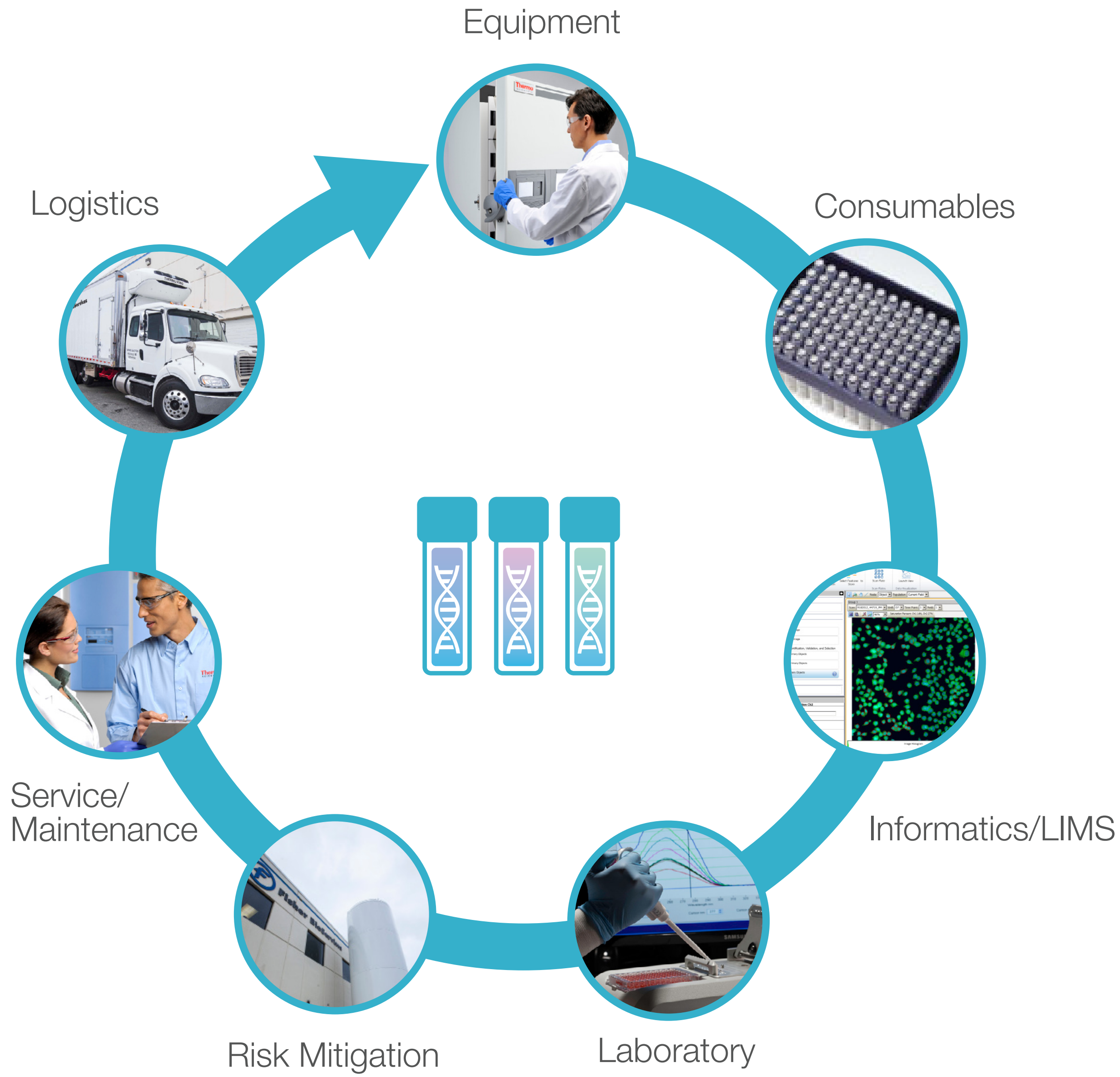
Additional Resources

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



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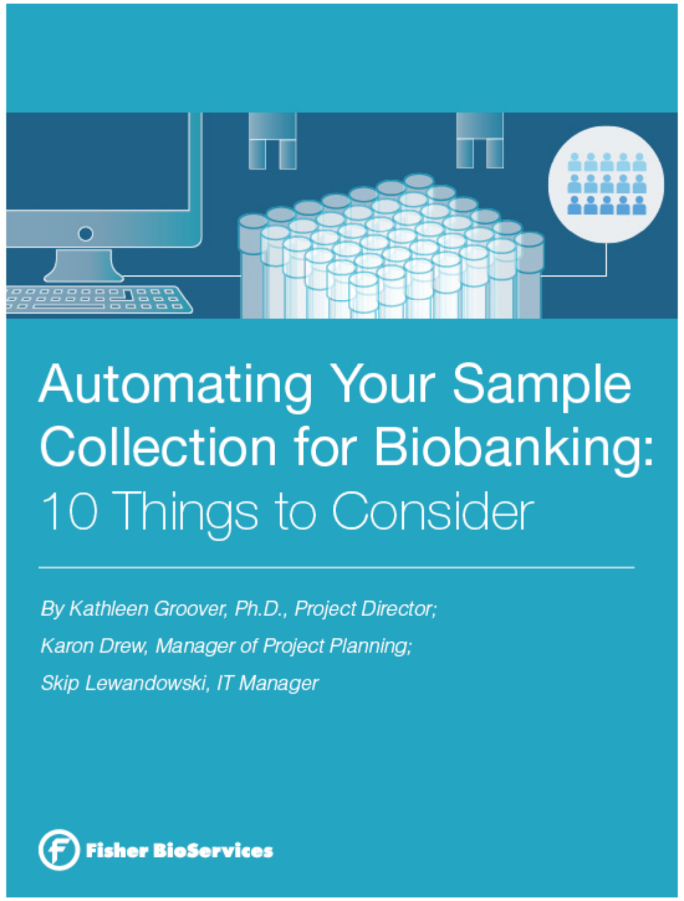

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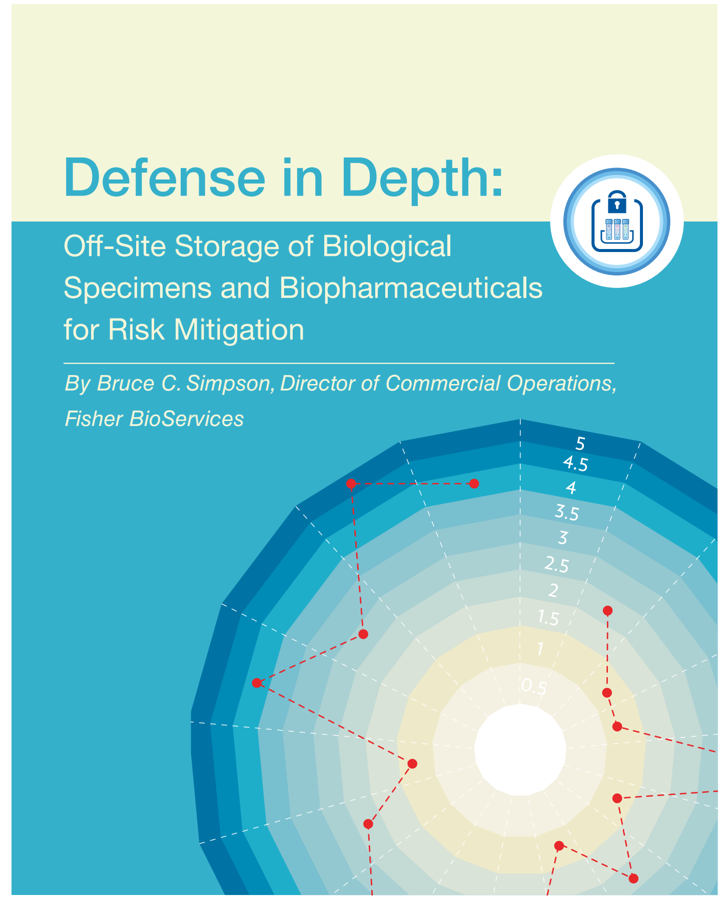

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