# Automated storage and retrieval at –80 °C: Managing and documenting specimen security, integrity, and accessibility

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The University of Virginia Medical Automation Research Center (MARC, Charlottesville, VA) began its basic research program in hypertension (high blood pressure) in 1984. In order to perform research on a polygenic disease, such as hypertension, it is necessary to use samples from many individuals, as well as a wide range of cell types. Managing these samples over 18 years is a daunting task.

### *Challenges of sample management in a research laboratory*

The hypertension research program at MARC typically employs five full-time investigators. Each investigator is involved in independent experiments involving molecular cloning, cell culture, and protein analysis. Thus, each investigator is currently assigned a section of the existing upright freezer in which to store his or her research products. The responsibility of each investigator is to hand-enter the contents of each container to be stored in the freezer into his or her laboratory notebook. Specimens are normally stored in 5-in.-square cardboard freezer boxes. A hand-written label on each tube is supposed to match information that may be found in the laboratory notebook. Each 5-in.-square box should also contain a label that indicates the name of the investigator who is responsible for the contents of the box and the date it was first used. As investigators leave the laboratory, they should leave a well-documented legacy of molecular tools including transfection plasmids, purified proteins, and transformed cells. Furthermore, as each investigator begins to fill up his or her assigned freezer space, useless or outdated material should be discarded.

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The management of research freezer inventory is a time-consuming and error-prone task. Unfortunately, specimens often accumulate in the freezer with unreadable labels and partially filled freezer boxes, and these containers end up in various locations throughout the freezer. The large number of students and research fellows who have worked in the hypertension research laboratory leave behind specimens that are poorly labeled and thus no longer of use to the research group. The storage and retrieval of individual specimens, plus research products from a variety of sources, frequently results in sample mix-ups, misplacement of storage containers, and exposure of specimens and valuable reagents to excessively long periods of time at less than optimal temperatures. To find frozen material, investigators often have to search through the freezer for the correct box, which has often been moved by others looking for their boxes.

In the author's laboratory, an estimated 50% of the space is used, since the remainder is wasted as a result of partially filled freezer boxes; frost buildup, which prevents insertion of boxes; and old boxes that are useless since the labels are not decipherable by the currently employed members of the laboratory. Lost samples and products account for thousands of dollars of lost material and opportunity each year.

### *Solving sample management problems*

In order to provide a method for laboratory scientists to systematically organize specimens, the MARC has worked with **BIOPHILE, Inc.** (Charlottesville, VA) to develop an automated storage and retrieval system that consists of hardware and software designed to maintain a failsafe sample inventory system. The initial BIOPHILE freezer concept was developed by Sean Graves, Jim Gunderson, and Robin Felder of the MARC to meet the needs of a working research laboratory. An engineering partner was selected to help realize the design and fabrication of the alpha and beta prototypes (**Sparton,** DeLeon Springs, FL). Robotic hardware was built into a commercially available laboratory freezer (**Kendro Technologies, Inc.,** Ashville, NC) in order to conform to the space issues found in most biotechnology laboratories. The BIOPHILE provides rapid (26-sec) storage and retrieval of up to 960 standard size microplates (*Figure 1*).

### *Standardizing on the microplate format*

The use of the microplate standard was vital to pro-


**Figure 1** *The BIOPHILE can be easily operated by laboratory personnel to store and retrieve approx. 1000 microplates per unit. A touch panel on the door allows secure access to the contents. Multiple users may therefore share the same unit.*

vide maximum storage capacity and minimize the chance for wasting space. Fortunately, the microplate has become a popular format for performing experiments as well as for storing reagents and specimens. The standard dimension of a microplate facilitates its use in a variety of instruments and laboratory robots designed around this standard. With the advent of the BIOPHILE freezer, the microplate has become the ideal container for long-term use in the –80 °C freezer. Microplates should have a common footprint consisting of a length of 127.76 mm ± 0.25 mm (5.0299 in. ± 0.0098 in.) and a width 85.48 mm ± 0.25 mm (3.3654 in. ± 0.0098 in.) with corner radii of 3.18 mm ± 1.6 mm (0.1252 in. ± 0.0630 in.) to the outside (Society for Biomolecular Screening Standard, www.sbsonline.org/disgrps/platestd/details.html).

### *Selecting a proper storage temperature*

The choice of temperature for the storage of biological material is not obvious. Some material, such as pure DNA, will survive long periods at 4 °C in buffer solutions. However, for archival storage, DNA is best kept at –40 °C. Proteins, on the other hand, have been shown to degrade at –40 °C. Thus, –80 °C is the best temperature for the long-term storage of proteins and the short-term storage of living cells. Chemical li-

braries have also been shown to retain the highest percentage of expected activity when they are stored at –80 °C, and when the specimens were frozen and only thawed once prior to use.

### *Installing the freezer in a standard laboratory space*

One of the challenges of operating a research laboratory is optimizing the limited space available. The BIOPHILE has been designed around a standard laboratory freezer footprint so that it can be placed easily into any research laboratory, or a core facility that serves the needs of several investigators. The freezer fits into most elevators and through standard-sized laboratory access doors. The 79-in. height of the freezer will not violate height restrictions that are imposed in most laboratory facilities.

### *Maintaining sample security*

Security is an important issue for virtually every laboratory. The principal advantage of automation is the implementation of controlled access to the freezer. Access to the freezer is restricted to individuals who know the proper pass code. Furthermore, access to individual containers in the inventory inside the freezer may be protected by pass code as well. This feature prevents misplacement or misuse of valuable research material. The pass code can be administered by a selected individual who is provided with administrator privilege. From a research laboratory perspective, most laboratories wish to allow technologists, postdocs, and faculty to share resources, but not have access to each others' works in progress. However, there are certain shared resources that should be available in a catalog list to all investigators (such as plasmids).

### *Documenting sample history*

The BIOPHILE process allows complete documentation of sample history, from the time the sample container is first read in the airlock chamber, and each time the specimen is accessed. While this level of sample management is normally not pursued in research laboratories, there is increasing pressure with the advent of the Health Insurance Portability and Accountability Act (HIPAA) for investigators who deal with human subjects to keep better records. Thus, sample tracking in the BIOPHILE meets the most stringent information, operation, and production quality (IQ/OQ/PQ) validation standards. Fur-

**Figure 2** *The operation of the BIOPHILE relies on a patented airlock entry system, a microplate handling robot that can withstand the rigors of a –80 °C environment, and a high-density storage carousel.*

ther, database backup is provided both by internal nonvolatile memory as well as a ZIP drive system attached to the freezer's standard computer USB port.

### *Simplifying sample storage*

Operation of the freezer is simple and intuitive. A touch-screen computer has been built into the face of the freezer to allow touch-screen operation as well as access to a database listing specimen inventory (*Figure 2*). The door of the freezer remains locked and is never opened by any operators. Once the proper user identifier is entered into the computer, the plate is immediately inserted into the freezer by the robotics, dehydrated in an airlock chamber to a low relative humidity, and then automatically stored into the freezer carousel (*Figure 3*). When samples need to be retrieved, any microplate may be retrieved by the robot in less than 30 sec after a few simple keystrokes on the touch screen. A retrieved plate appears in the airlock tray ready for human access or access by robot.

### *Summary*

The benefits of the BIOPHILE process include a well-documented and retrievable freezer inventory, optimal space utilization by laboratory personnel, and more efficient utilization of employee time. It is imperative that an automated sample management process be accompanied by software that facilitates bar-

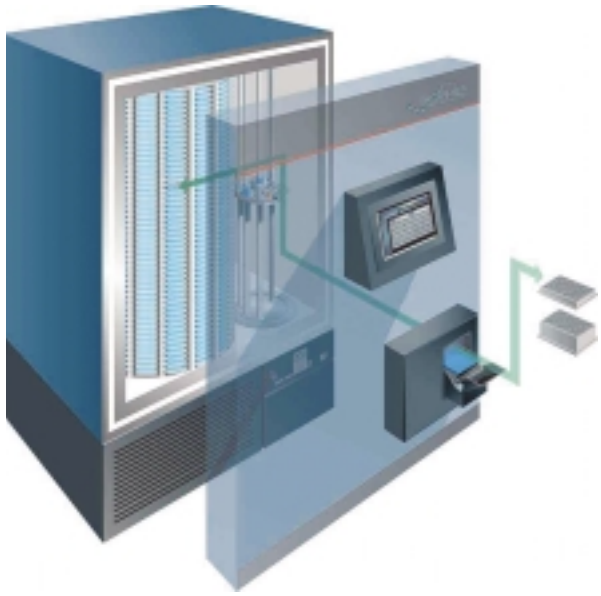

**Figure 3** *The BIOPHILE concept of specimen management is centered around a fully automated –80 °C storage cabinet that prevents specimen loss and damage from fluctuating temperatures. An entire corporate cold storage inventory system can be created around the BIOPHILE concept.*

code printing, inventory database management, and an intuitive and rapid search engine to facilitate sample location and retrieval.

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