

# AUTOMATED BIOBANKING

## *the next big step for biorespositories*

As a significant proportion of the many newly established national, regional and disease-specific biobanks or biorespositories contemplate how they will enable enhanced sample integrity, tracking and audit trail, there has never been a more opportune time to consider biobanking automation. With the anticipated availability of several new  $-80^{\circ}\text{C}$  off-the-shelf modular automated storage systems, that can be expanded as capacity grows, biorespositories finally have a reasonable alternative to those ad hoc clusters of  $-80^{\circ}\text{C}$  freezers. When considered with the new developments in automation-compatible plastic tubes with integral 2D bar codes and LIMS software systems, the automation of biosample tracking and complete inventory control can now be realistically achieved. In this article we examine how a sample of biobanks responded to a recent survey on automation and review a growing set of tools and technologies that will facilitate automated biobanking.

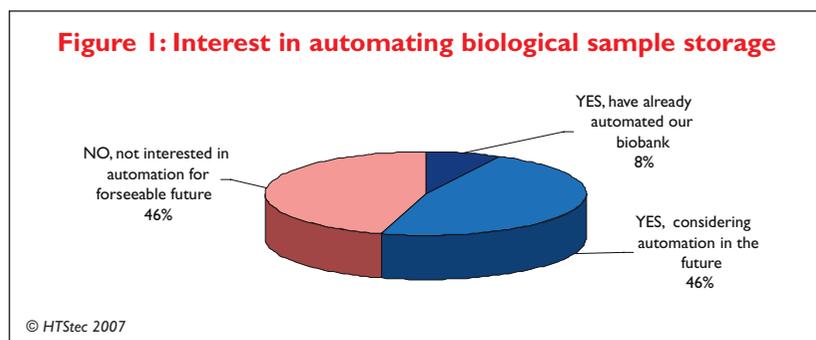
The past decade has seen significant demand in the pharmaceutical and biotech industry for automated storage and retrieval systems for compound management, although in recent years the number of new installations of very large core systems has reached a plateau. Recently, interest in smaller, more compact stores and those that facilitate automated storage below  $-20^{\circ}\text{C}$  has been increasing, the latter driven mainly by those groups who plan to store large numbers of biological samples. The incidence of these biostores, often referred to as biobanks or biorespositories, seems to be rapidly growing, with many national, regional and disease specific (eg

cancer) facilities being established. The function of these stores is quite diverse ranging from storage of frozen cell aliquots intended for primary pharmaceutical screening; to tissue biopsies for some diseases; to patient DNA samples; to whole population studies, with multiple aliquots of fractionated blood and urine samples stored. Some of these facilities (eg UK Biobank) have been extensively planned with automation enabled at the outset to facilitate the intended large storage capacity and desired retrieval rates<sup>1</sup>, others are currently based around an ad hoc collection of deep-cooled freezers and still rely on manual retrieval. In either case the role of automation in enabling the processing,

**By Dr John Comley**

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**Figure 1: Interest in automating biological sample storage**

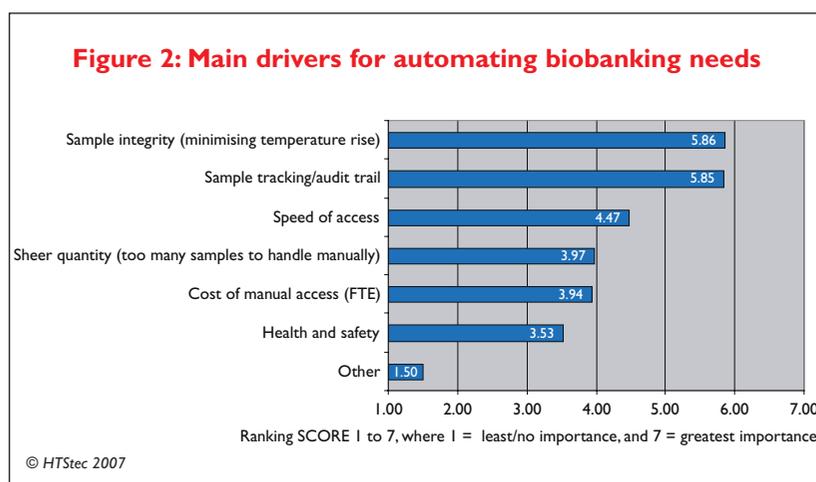


fractionating and transfer of samples to storage; their rapid retrieval on demand; their subsequent tracking and audit trail; is increasingly becoming an important consideration. This increased interest in automated biobanking was one of the reasons HTStec was commissioned to investigate this area and resulted in the publication of HTStec's Automated Biobanking Trends report in December 2006.

### The growing need for automated biobanking

Only 8% of the biobanks and biospositories contacted in HTStec's industry-wide survey have already automated biological sample storage (Figure 1). 46% indicated they had no foreseeable future requirement for automation, leaving a further 46% who envisage having to automate their biological sample storage needs at or below -20°C in the next five years.

**Figure 2: Main drivers for automating biobanking needs**



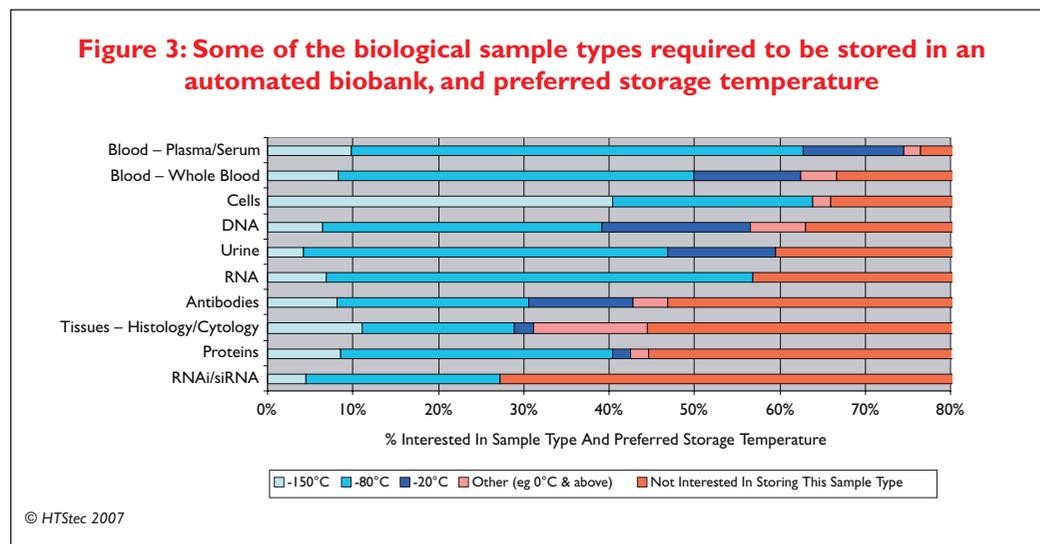
### What is driving biobanking automation?

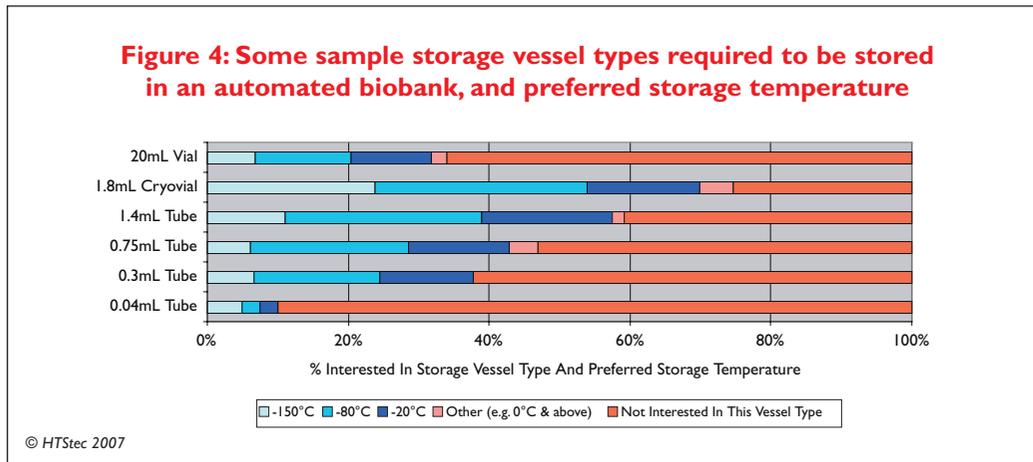
The most important drivers for automating biobanking needs were sample integrity (minimising temperature rise) and sample tracking/audit trail. Other drivers were of much less importance. These include in descending order: speed of access; sheer quantity (too many samples to handle manually); cost of manual access (FTE); and health and safety issues (Figure 2).

### Sample types and storage vessels

Some of the types of biological samples that respondents were interested in storing in an automated biobank and their preferred storage temperature for

**Figure 3: Some of the biological sample types required to be stored in an automated biobank, and preferred storage temperature**





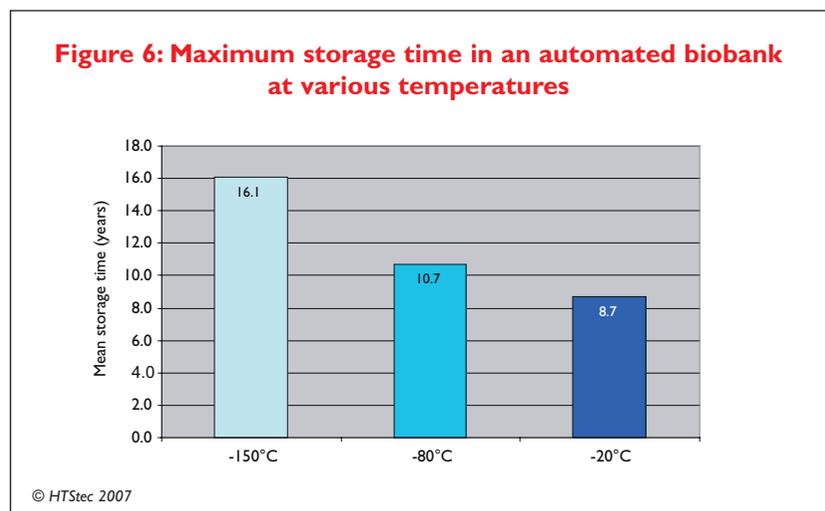
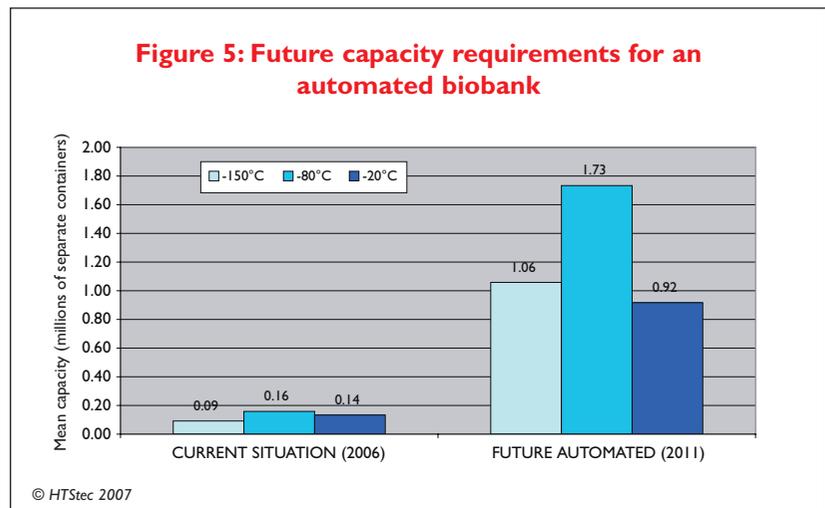
these sample types are given in Figure 3. Overall greatest interest was shown in storing blood plasma/serum, then whole blood, then cells, with least interest in RNAi/sRNA. The preferred storage temperature for most biological sample types was -80°C, with -150°C being only the preferred storage temperature for cells. The types of sample storage vessels that respondents were interested in using in an automated biobank and their preferred storage temperature for these vessel types are given in Figure 4. Greatest interest was shown for 1.8mL cryovial, 1.4mL tube and 0.75mL tube, with -80°C as the most desired storage temperature for these vessels.

**Store capacity and duration of storage**

The average current capacity requirements for respondents' existing biobanks were estimated to be around 0.1 million containers at all temperatures (-20°C, -80°C and -150°C). These capacities are expected to grow significantly, by at least 10-fold, with the availability of an automated biobank in the next five years, with greatest future automated capacity anticipated at -80°C (Figure 5). The average maximum sample storage times required in an automated biobank were: 1) 8.7 years at -20°C; 2) 10.7 years at -80°C; and 3) 16.1 years at -150°C (Figure 6). This data suggests that storage at -150°C may be viewed as more of a long term practice.

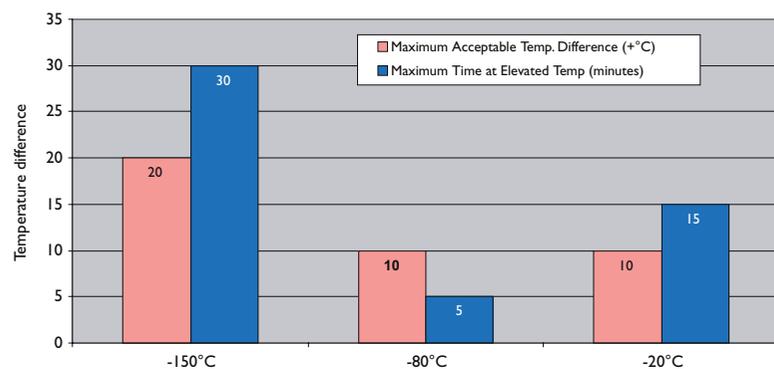
**Post-storage automated cherry (tube) picking**

One of the biggest issues in biobanking, owing to the biological fragility of the samples stored, is the permissible elevation (rise) of sample temperature during post storage cherry picking from the store or sorting within the store. Survey respondents were



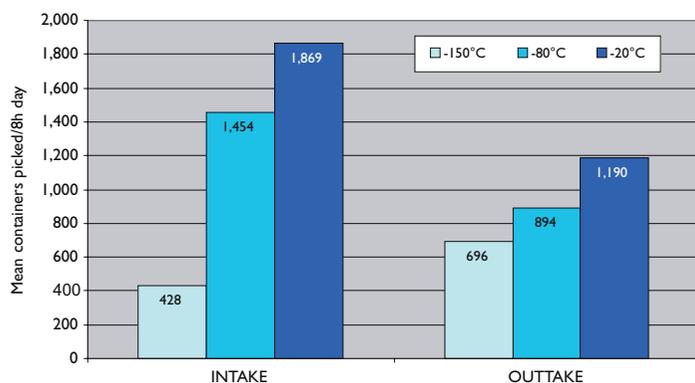
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**Figure 7: Acceptable temperature difference above storage temperature and maximum time at elevated temperature during post-storage cherry (tube) picking**



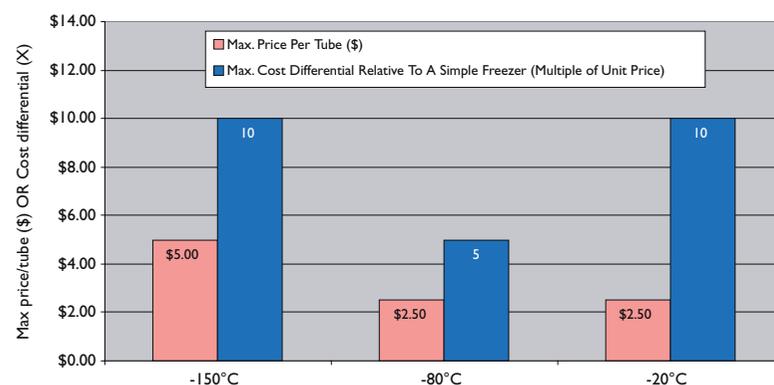
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**Figure 8: Cherry (tube) picking throughput requirements for an automated biobank**



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**Figure 9: Maximum price per tube and reasonable cost difference relative to a simple freezer for an automated biobank**



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asked for their opinion on the maximum acceptable temperature differences and maximum allowable time at that elevated temperature and the following averages obtained: 1) for -20°C storage +10°C elevation for 15 minutes; 2) for -80°C storage +10°C elevation for 5 minutes; and 3) for -150°C storage +20°C elevation for 30 minutes (Figure 7). The average cherry picking throughput requirements for an automated biobank are presented in Figure 8. This throughput was specified for both intake and outtake. It is important to note that intake is often linked with the required up front sample fractionation and these processes will limit the rate at which a large biobank can be populated with samples. The intake and outtake respondents wanted per 8 hour day were as follows: 1) for -20°C storage 1,869 tubes intake and 1,190 tubes outtake; 2) for -80°C storage 1,454 tubes intake and 894 tubes outtake; and 3) for -150°C storage 428 tubes intake and 696 tubes outtake.

### What is acceptable pricing for biosample automation?

Survey respondents were asked about their pain points, ie the price above which the automation of biological sample storage becomes financially unattractive compared to manual storage in stand-alone freezers, which is the current situation for most respondents. The maximum price per tube stored and reasonable cost differential relative to a simple (standalone) freezer for an automated biobank were found to be: 1) for -20°C storage a maximum of \$2.50/tube and 10x cost differential; 2) for -80°C storage a maximum of \$2.50/tube and 5x cost differential; and 3) for -150°C storage a maximum of \$5.00/tube and 10x cost differential (Figure 9).

### Biobanking vendor update

Having sought the opinion of potential end users of automated biobanking, it is interesting now to review what vendors are offering or developing to meet these needs. Table 1 summarizes the products offered by the key vendors supporting automated biobanking. The details of the individual product offerings are discussed below.

The Secure Robotized Sample Vault (SRSV) from deCODE Genetics ([www.decode.com/biorepository](http://www.decode.com/biorepository)) is a fully automatic, highly flexible sample storage solution for biological samples. As the first such system ever designed and built it boasts a six-year flawless 24/7/365 track record of operation with millions of sample transactions without any sample errors or robot failures. Offering

**Table 1:** Vendors supporting automated biobanking

VENDOR	AUTOMATED BIOBANKING STORAGE SOLUTIONS AT:				AUTOMATED BIOBANKING SAMPLE PREP	AUTOMATION-COMPATIBLE PLASTICWARE FOR BIOBANKING	LIMS SOFTWARE FOR BIOBANKING
	AMBIENT	-20°C	-80°C	-150°C			
deCODE Genetics		✓	✓				
GenVault	✓					✓	
Hamilton		✓			✓		
LabVantage							✓
MatriCal		✓		✓			
Micronic						✓	
Nexus Biosystems	✓	✓	✓				
Qiagen					✓		
REMP		✓	✓			✓	
RTS Life Science		✓	✓		✓		
The Automation Partnership		✓	✓			✓	
Thermo Scientific		✓	✓			✓	✓
Titian Software							✓

total flexibility in tube sizes from sub-mL to 50mL and even beyond, the system has a carrying capacity from a few hundred thousand up to 5,000,000 samples. Several different vial sizes can be stored in the same system and even SBS footprint trays. Storing and retrieving 1000s of samples each day, the Sample Vault relies on tried and tested industrial robots for uninterrupted operation. The input/output buffer area can hold various types of tray formats, including standard SBS footprint trays. Residing in a refrigerated heavily insulated room, supported by redundant compressors and power supplies the shelving units holding the storage trays can be kept at temperatures from ambient to -80°C. Designed to maintain sample integrity by uniform storing conditions the system also offers complete audit log on all actions and sample history as well as administrative control over samples with high security chain-of-custody sample restriction access (Figure 10).

GenVault ([www.genvault.com](http://www.genvault.com)) offers an alternative to expensive cryogenic sample storage that can be fully integrated into any organisation's



**Figure 10:** From inside deCODE Genetics Sample Vault industrial robots can cherry-pick vials from storage trays and verify by barcode. Here shown picking 9mL vacutainers

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**Figure 11:** GenVault's Dynamic Archive is a room temperature fully automated storage and retrieval system, part of a fully integrated sample management system that includes software, hardware and consumables designed to save DNA, space and energy for any size sample collection



**Figure 12:** Hamilton Company's sample management units provide a one-vendor solution for completely automated bio-sample storage and processing in microtubes and/or microplates

workflow, costs less to operate, saves space and is better for the environment. This alternative includes: 1) a dry-state media with which to store biosamples, GenPlates; 2) a reliable, permanent and tamper-free labelling system, GenCode; 3) reagent kits for subsequent DNA recovery, GenSolve; 4) software to request or track individual biosamples and their information, GenConnect; 5) a secure method of physical storage for several hundred to a thousand samples in stand-alone benchtop storage units, Desktop Archive; and 6) completely automated storage and retrieval systems for tens to hundreds of thousands of samples which free lab workers and avoid human error, Dynamic Archive. Additionally, GenVault's sample management software GenConnect, now has the ability to manage samples in all formats, not just GenVault's hardware. GenConnect can be deployed at an individual level and grow to an enterprise-wide solution with no data migration and no additional software costs. This flexibility allows users to grow their collections over time, eliminate disparate databases and maintain centralised control over valuable resources. Further, GenConnect allows users to easily link their physical samples with clinical data for the easy generation of sample cohorts for genetic analysis. When linked to the Dynamic Archive for automated retrieval, GenConnect provides instant access to hundreds or thousands of samples in a secure transaction that may be accessible by multiple users across multiple locations (Figure 11).

Laboratories are increasingly automating biosample supply and storage, but combining automated storage and liquid handling platforms typically requires complex integration of systems from multiple vendors. **Hamilton** ([www.hamiltoncompany.com](http://www.hamiltoncompany.com)) is now integrating the Integrity storage devices with its STAR line of sample processing platforms to offer customers a seamless automation solution. Customers pressed to respond to an ever increasing number of orders with expanding levels of array complexity can now submit the requests to the automated system and generate the final output array without the need for manual handling. The modular design of standardised units provides a compact footprint that can be expanded on site as sample library size increases. The integration of the hardware and software provides complete transactions records for ID, tracking and security of each sample. The SQL Server database is directly accessible or may be linked to a LIMS. The system can assemble sample selections

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and deliver them immediately or keep the samples in the safe, inert environment of the Integrity store module until needed. This option is ideal to prepare sample collections overnight and have them available promptly the next day. Samples stored in standard microtubes and microplates may be replicated and/or reformatted into a wide variety of labware, without the need for proprietary, expensive plates. The replicate samples may be sealed and shipped to remote locations or may be directly assayed in the STAR module utilising one of many published and validated applications. Future system directions include development of  $-80^{\circ}\text{C}$  storage environments (Figure 12).

In the cutting-edge world of translational medicine, biospecimens serve as the basis for novel research and development of tomorrow's drugs and medical treatments. As a result, accurate, compliant and efficient management of these biospecimens is critical. LabVantage's Sapphire BioBanking Solution ([www.labvantage.com/products/biobanking](http://www.labvantage.com/products/biobanking)) is specifically designed to address the unique challenges of specimen collection and banking for pharmaceutical discovery and clinical operations, academic and biosciences research centres, medical institutions and contract research organisations. As an example, this biospecimen LIMS solution supports myeloma research throughout the Multiple Myeloma Research Consortium (MMRC) partner network and the MMRC has recently shared its insights into the implementation of LabVantage's Sapphire BioBanking Solution (see website). Specifically, the MMRC addresses the barriers to specimen management and data warehousing, including how to span the lifecycle of the specimen, address the needs of multiple end users, capture correlating clinical data, maintain flexibility and provide global visibility. Developed in conjunction with Millennium Pharmaceuticals, the Sapphire BioBanking Solution addresses the need for data capture, location management, chain-of-custody, handling assurance, and operational efficiency required to manage a biorepository at any organisation. Whether storing or tracking whole blood, tissue, cellular lysates, DNA, RNA, proteins, etc, Sapphire supports organisation-wide inventory control. Sapphire's thin-client, zero-footprint user interface provides global access and quick user acceptance. Moreover, its built-in Evergreen configuration tool enables organisations to tailor the solution to the needs of each laboratory's data capture, result management, storage and specimen handling requirements (Figure 13).

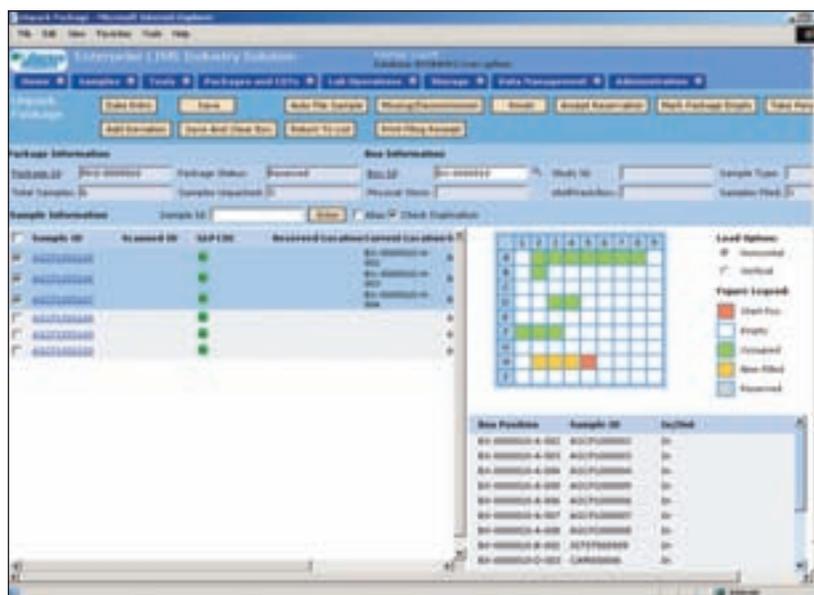


Figure 13: Screenshot of LabVantage's Sapphire BioBanking LIMS Solution

The NitroStore is a new stand-alone integrated automatic sample storage and retrieval system from MatriCal ([www.matrical.com](http://www.matrical.com)). The NitroStore is based on MatriCal's MatriStore/MiniStore platform, but it now enables storage of biological samples under ultra-cold storage conditions. Temperatures within each module of the system can be controlled from ambient down to  $-150^{\circ}\text{C}$ . The  $-150^{\circ}\text{C}$  module enables storage of samples below the glass transition phase of water which is critical for long term storage of biologics including mammalian or bacterial cells, clinical



Figure 14: MatriCal's NitroStore

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**Figure 15**  
Micronic biobanking Starter  
Pack for automated 2D coded  
sample storage



tissue samples, proteins, etc. Media storage includes plates, tubes and cryovials. The system design is modular and expandable starting with 79,200 x 1.4mL tubes or 33,600 x 2mL cryovial tubes. All robotic operations occur at  $-20^{\circ}\text{C}$ . Oxygen sensors ensure environmental safety. The design of the NitroStore platform has presented special challenges for protecting the robotics for storing and retrieving samples within the ultra-cold storage module. A new elevator and cherry picking robotics module (patent pending) have been developed to ensure reliable operation. This is the first system of its kind that allows you to stage modules next to each other, control the temperature of each module independently, change the module temperature at will, change sample types 'on the fly', allows easy integration with ancillary equipment, and is fully automated. Based on many years of MatriCal experience working with proteins and cells, as well as conversations with our pharmaceutical and academic partners, MatriCal has developed a cryo-storage system that is not only highly flexible but can also grow with customers' needs (Figure 14).

The collection and storage of millions of clinical samples throughout the world every year for research and diagnostic purposes has driven the

industry to build and maintain biobanks and biorepositories. However, the emergence of regulations on how to establish, maintain and use biobanks has necessitated that organisations put in place traceable regimes for sample collection and storage. Micronic BV ([www.micronic.com](http://www.micronic.com)) has recently been selected by Biobank projects in Germany, the Netherlands and the UK to supply a range of 2D and non-coded sample storage tubes and racks to improve their sample traceability and logistics. Having worked with a growing number of leading biobanking projects around the world Micronic has put together a specialist Starter Pack that contains everything needed to start using 2D coded sample storage tubes enabling laboratory workers to ensure a secure sample logistics system and eliminate the costly possibility of false sample identities. Each biobanking Starter Pack contains an easy-to-use tube scanner, operating software and a case of screw top tube, at a substantial saving over buying the products individually. Micronic screw top tubes, available in 0.5ml and 1.1ml sizes, provide laboratories with high integrity storage and easy retrieval of precious samples down to liquid nitrogen temperatures. Incorporating a novel 'single turn' screw cap mechanism ensures that accessing samples is a simple and rapid process. A unique 2D code on the bottom of each tube provides an

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**Figure 16:** NEXUS Universal BioStore for automated -80°C storage and retrieval



**Figure 17:** The Qiagen Autopure LS enables walk away purification of highly stable DNA ready for use or archiving

easy and unambiguous means of storing and identifying samples. The internal 'V' shape of each Micronic screw top tube ensures the lowest possible dead volume and maximum sample recovery. Standard microplate footprint racks designed to hold 96 individual tubes optimises valuable freezer space and ensures automation compatibility (Figure 15).

NEXUS Biosystems ([www.nexusbio.com](http://www.nexusbio.com)) is introducing a new line of biobanking systems that complement its successful family of 'Universal Store' sample and retrieval systems. This next generation biosample management system allows the user to select a desired level of -80°C and -20°C sample storage, automated cherry picking, sample input/output, and controlled thawing options from NEXUS' proven line of Universal Store sample handling systems. As user sample storage and sample workstation requirements expand, future storage chambers and workstations can be added without disturbing the integrity of the existing stored samples. -80°C, -20°C and room temperature storage chambers can all be easily interconnected and expanded while at the same time sharing the use of the existing and/or future sample handling workstations. Freeze/thaw cycles are eliminated as all frozen sample transfer and cherry picking operations are performed at -20°C. The deep-cooled -80°C samples are physically separated from the -20°C workstation environment by proprietary NEXUS 'Cool-Transition' storage technology. NEXUS' proven and easy to use Universal Store software is fully implemented in the Universal BioStores with security protection, audit trail and web-based alert messaging built in. Compared to the typical method of storing biological samples in clusters of -80°C freezers, the Universal BioStore is designed to automate in a single store the storage of deep-cooled sample collections that require varying levels of sample retrieval, high sample storage integrity, freeze/thaw avoidance, multiple temperature storage, and high quality sample tracking all at an affordable price (Figure 16).

Qiagen ([www.qiagen.com](http://www.qiagen.com)) recently launched a Biomedical Tissue Management and Biobanking System which comprises a chain of integrated products to standardise all steps of the workflow that starts with archived or prospectively collected tissue and blood and ends with data analysis. This ensures comparability and reproducibility of data in clinical case-controlled and population-based studies, facilitating biomarker discovery and, ultimately, the development of diagnostics and therapeutics. A key

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**Figure 18:** REMP's new Sample Safe store (left), showing an open I/O drawer for the tube racks and the user touchscreen interface (right)



piece of Qiagen automation is the Autopure LS workstation, the most recent version being completed this year for the biobanking community is designed for fully automated purification of genomic DNA from a broad range of sample types and sizes (including up to 10ml blood samples). Purified DNA that is free of inhibitors of downstream applications and other contaminants potentially resulting in DNA degradation is a prerequisite for long-term DNA archiving. In addition, sensitive downstream applications demand use of DNA of the highest quality and molecular weight. The Autopure LS, in combination with proven Autopure Puregene chemistries, enables purifica-

tion of highly stable DNA well suited for archiving. Results of stringent quality testing in what is believed to be the longest ongoing stability test demonstrated that DNA purified using the Puregene chemistry (like that used on the Autopure LS) and stored for at least 15 years shows no signs of degradation (Figure 17).

Reliability and innovation made REMP ([www.remp.com](http://www.remp.com)) the global market leader for compound stores in drug discovery. Based on this experience REMP built the world's first automated large scale bio-sample repository which has been operational since March 2006 at Pfizer's Groton Kings Heights site. The next challenge was to develop a concept offering similar features as the Pfizer BioStore but compact in size. A key requirement was to ensure very stable storage conditions at either  $-80^{\circ}\text{C}$  or  $-20^{\circ}\text{C}$  to avoid damaging effects on biological samples caused by temperature fluctuations. Moreover, the new concept had to support increasing capacity needs of customers over years after initial installation. Now REMP is ready to introduce the Sample Safe store family as the ideal solution for the compact storage of biological samples or compounds. A key element for success in automating biospositories is the REMP Tube Technology. In order to minimise freeze-thaw cycles it has become good practice to store multiple aliquots of a sample in individual tubes instead of bulk volumes in one large container. REMP Tubes can individually be sealed for ideal long term storage or automatically be capped and decapped in a multi-access mode. This concept is sometimes

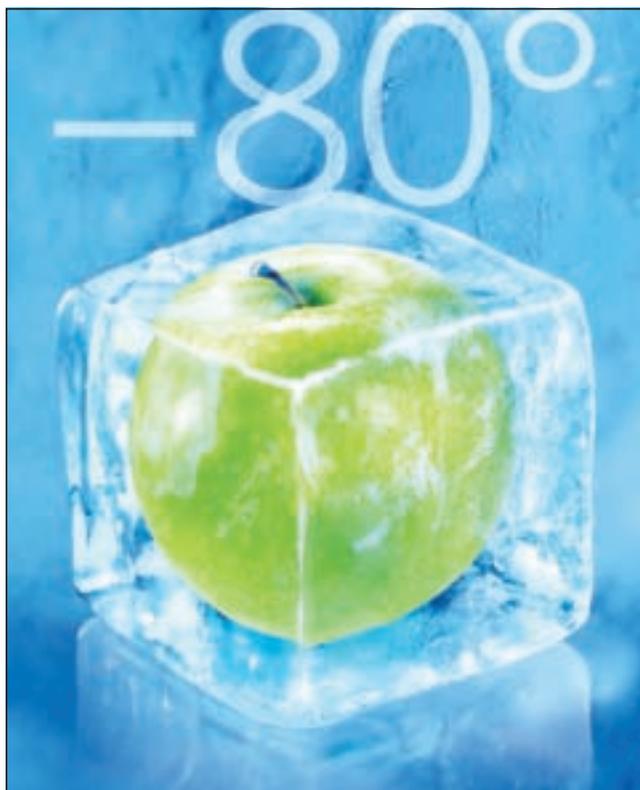


**Figure 19:** RTS Life Science's new  $-80^{\circ}\text{C}$  storage system for automated biobanking

applied to samples which show a more robust behaviour concerning temperature fluctuations such as DNA. The REMP Sample Administration Software (SAS) is designed to manage the processes in biobanking in an easy to use manner. Since REMP is part of the Tecan Group of companies customers can take advantage of smooth interfaces to Tecan sample processing workstations for steps such as blood fractionation, DNA extraction or even cell culturing ('Cellerity') systems to name just a few (Figure 18).

Sample security and integrity are key drivers for the automated storage of biological samples at  $-80^{\circ}\text{C}$ . With RTS Life Science's ([www.rtslifescience.com](http://www.rtslifescience.com)) SmaRTStore fulfilling the role of a medium-sized store operating at temperatures down to  $-20^{\circ}\text{C}$ , the next step in RTS's automated storage development strategy has been the introduction of a modular store capable of holding samples at temperatures of  $-80^{\circ}\text{C}$ . As a result, RTS has undertaken trials on the temperature gradient of samples removed from  $-80^{\circ}\text{C}$  and into  $-20^{\circ}\text{C}$ . Particularly for small volumes, this rise can be steep. The results of these trials have guided the design process, so that the temperature rise of both the picked and unpicked tubes is minimised. As always, RTS's guiding principle is to adopt the best existing technology where possible, integrating novel strategies where necessary. Therefore, this approach draws on standard refrigeration units for both  $-20^{\circ}\text{C}$  and  $-80^{\circ}\text{C}$  and also adopts SmaRTStore's flexible picking robot and airlock concepts. The resulting new  $-80^{\circ}\text{C}$  storage system has a modular construction, with elements of the floor structure borrowed from SmaRTStore, allowing quick installation without the need for special floor structures or strengthening. Entry level units can store 7,000 plates or 100,000 tubes and can be expanded in steps of 3,500 plates (or 50,000 tubes). The ingenuity of this product, which has yet to be launched, lies in the way it protects unpicked samples from the sample retrieval process. RTS's finely engineered solution is inherently robust, protecting samples, even if the  $-80^{\circ}\text{C}$  enclosure is exposed to the  $-20^{\circ}\text{C}$  picking environment (Figure 19).

The Automation Partnership (TAP) ([www.automationpartnership.com](http://www.automationpartnership.com)) has developed a new automated sample management technology called Polar, which has been adopted by The UK Biobank. In this application Polar will allow the storage, retrieval and full tracking of 10 million aliquots stored at  $-80^{\circ}\text{C}$  in individually 2D coded



REMP offers small, medium and large scale automated systems and stores to suit your needs without having to compromise on the quality of sample processing and storage.

## Sample Safe



The REMP Sample Safe™ is a compact, scalable, fully automated and easy to use storage solution that operates at temperatures down to  $-80^{\circ}\text{C}$ . It is supporting all SBS standard produced MTPs and DWPs. Combined with the unique, patented REMP Tube Technology™, it minimizes the degradation of valuable samples caused by freeze/thaw cycles significantly and helps to obtain highly reproducible data sets for your research. The REMP Sample Safe™ is designed to fit any lab and is able to grow with your storage needs.

[www.remp.com](http://www.remp.com)

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sample management

## Compound Management



**Figure 20:** TAP Polar UK Biobank (right) showing the compartment access robot (large yellow structure) running down the middle. The blue-fronted ULT compartments are at the sides, with the vessel transfer station and loading buffer towards the rear, on the left beyond the ULT compartment. The compartment access robot with a compartment drawer open and a rack of microtubes being moved from storage on to a carrier tray held by the robot (left). In the foreground we see the work bed of the vessel transfer station where individual tubes or entire racks can be cherry picked for retrieval



microtubes, which can be picked out and collated for further research. The system consists of a set of Ultra Low Temperature (ULT)  $-80^{\circ}\text{C}$  compartments within a single high integrity outer enclosure which also contains the robots, vessel picking station and loading buffer. All the components inside the enclosure (except the ULT compartments) are held at  $-20^{\circ}\text{C}$ . Operators can load samples into the store and collect output from a loading hatch in an antechamber. The patented drawer access system allows all stored samples within the compartment to remain at  $-80^{\circ}\text{C}$  even during sustained robotic access and even in the event of a robot fault. TAP has developed and proven a unique refrigeration system for the ULT compartments based on liquid nitrogen, which offers considerable advantages in simplicity and reliability of operation, reduced infrastructure costs, and sample security. Polar can be provided with this technology, as for the UK Biobank, or with conventional cascade refrigeration. The modular nature of the storage compartments means that Polar can be configured for different end user requirements, for example to hold a variety of vessel types at temperatures between  $-20^{\circ}\text{C}$  and  $-80^{\circ}\text{C}$  within one store. Polar is designed to integrate easily with a variety of informatics systems including third-party LIMS, in-house inventory databases, or TAP's Concerto sample management software (Figure 20).

The Thermo Scientific ([www.thermofisher.com](http://www.thermofisher.com)) BioBank is an automated sample management module designed to safely store biological samples at  $-80^{\circ}\text{C}$  for a wide range of research applications such as cell based assays, bacterial clones, protein, DNA and RNA libraries. The BioBank holds thousands of samples in a range of configurations, including standard and deep well microtiter plates and cryotube racks. One BioBank module can store 984 standard microtiter plates, 510 half deep well plates and 354 full deep well plates or microtube racks. Unique to the BioBank is its patented rack design system that enables the location of the robotics in an ambient temperature, isolated from the ultra-low temperature that can cause mechanical failures. The often-observed frost build up on samples during their retrieval is negligible, due to a humidity-controlled enclosure ( $<5\%$  relative humidity). A special feature of the BioBank is its  $\text{CO}_2$  backup that protects samples up to 12 hours during power outages. The specific design of the BioBank as a stand-alone unit provides exceptional reliability for sample storage/retrieval and allows preventative maintenance without interfering with parts that would compromise sample integrity during long-term storage. An organisation which has implemented Thermo Scientific BioBank is the Harvard Medical School Institute

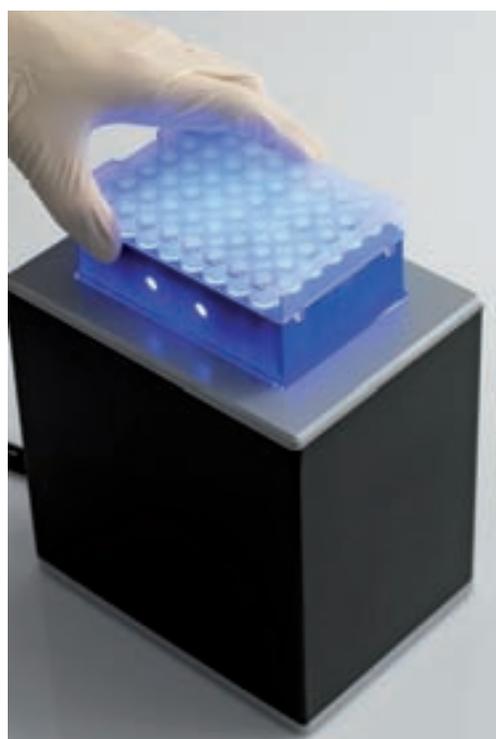
## Compound Management

for Proteomics ([http://dnaseq.med.harvard.edu/plasmid\\_repository.htm](http://dnaseq.med.harvard.edu/plasmid_repository.htm)). The institute offers a DNA Resource for plasmid repositories. With the utilisation of the BioBank and its BioBank Supervisor software, the system enables the organisation to distribute small and large sets of clones in a microtiter plate format arrayed to custom orders placed by researchers through the web. Thermo Scientific is also a leading provider of analytical instrumentation and laboratory information management systems (LIMS), and has implemented its Nautilus LIMS™ at the UK Biobank, the Hunt Biobank in Norway and the Singapore Tissue Network (Figure 21).

New products in the Thermo Scientific ([www.thermofisher.com](http://www.thermofisher.com)) line of 2D barcoded screwcap tubes include ABgene®, Matrix® and NUNC® tubes in volumes from 500µl to 12ml and supplied in automation-friendly, microplate footprint racks of 24, 48 or 96 tubes according to tube size. With tubes being used throughout the world in biobanks, including national centres in the UK and Norway, and with new tube sizes, materials and barcode reading technology continually being developed, Thermo Fisher Scientific is leading innovation in sample storage. The critical nature of biobank samples make permanently-attached 2D barcodes for secure sample tracking and chain of custody a superior choice over traditional labels,



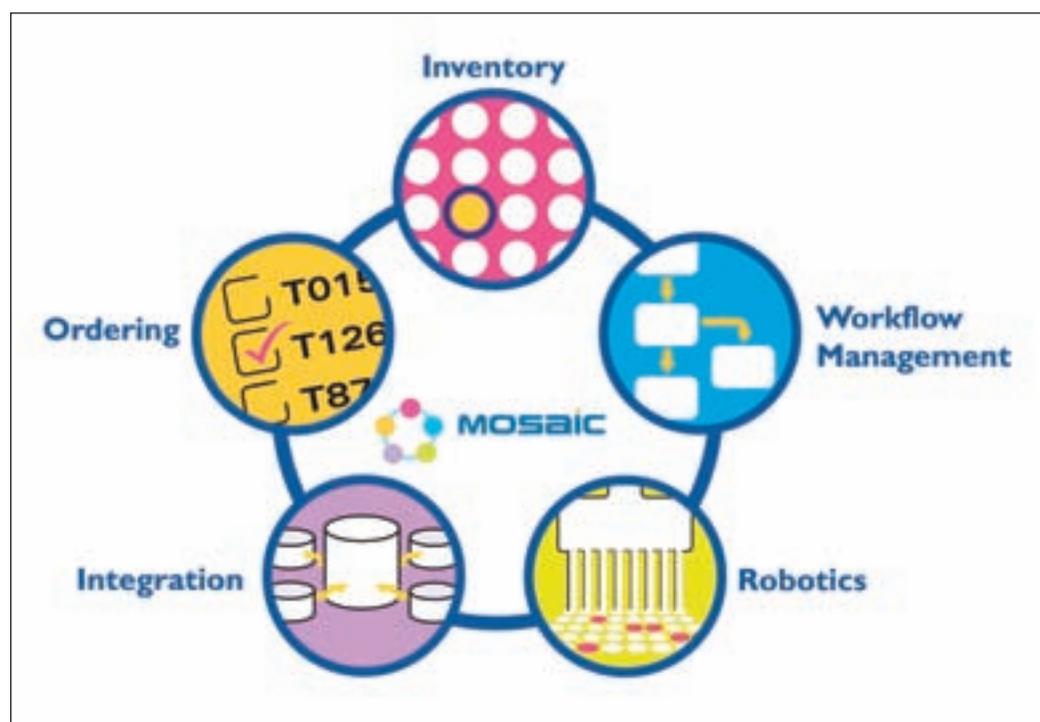
**Figure 21**  
The Thermo Scientific Biobank



**Figure 22**  
Thermo Scientific 0.5mL and 1.0mL NUNC Cryobank vials in NUNC flexible height aluminium rack (right), and SmartScan™ and ABgene® SmartScan™ 2D coded 2mL cryogenic vials (left)

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**Figure 23**  
Titian Software Mosaic's main  
module



which can fall off. Strict quality control, including use of class VI resins, clean-room moulding, guaranteed no duplicate codes, and code readability testing significantly enhance sample security. Long-term storage in biobanking is an important consideration when choosing consumables, and sample integrity is protected with tube compatibility from room temperature to the vapour phase of liquid nitrogen, and in selecting screwcap designs ranging from moulded-in gaskets or o-rings, to single-piece moulded caps. The compact, stackable nature of these dense tube rack formats saves storage space and caters to current and emerging biobanking processes, from the automation of whole blood storage in larger tubes to smaller volume storage of extracted DNA, by enabling existing automation to access familiar microplate footprint tubes. Couple this with 2D bottom-read barcodes, and sample processing increases dramatically from traditional side-read barcoding and 9x9 tube storage that is not easily automated (Figure 22).

**Titian Software** ([www.titian.co.uk](http://www.titian.co.uk)) is the industry leader in the supply of sample management software to Life Science companies. Six of the top 20 biopharma companies currently use Titian's Mosaic software suite. Mosaic manages the entire sample lifecycle including receipt, storage, preparation, modification, ordering, retrieval, dispatch and shipment. All interim stock logistic control,

full chain of custody and audit trail functionality, and a comprehensive library of software interfaces for automated storage and processing devices are also standard features of Mosaic. Mosaic is best known for its proven success in the world of compound management, but in fact Mosaic is entirely independent of sample type. The system tracks any form of biological sample including whole blood, serum, plasma, urine and tissue. From initial receipt and processing through sample delivery, Mosaic can track and orchestrate a variety of processes irrespective of sample type. Mosaic refers to all samples by means of a coded identifier. The level of linkage from this coded identifier to further data about the sample depends on the type of specimen and the requirements of the system and client. For example, in a compound management system Mosaic prevents unauthorised access to the molecular structure; in a biobanking system Mosaic prevents access to patient data. Future biobanking-related Mosaic developments include closer integration of blood fractionation automation and DNA extraction equipment, and the continued extension of Mosaic's range of integration modules to keep pace with developments in biobanking storage and retrieval systems. As well as software products, Titian offers consultancy services in requirements analysis, system design and functional specification, plus training and support (Figure 23).

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### Reference

I Peakman, T (2007). Implementing and operating large, complex capital projects in a research environment – the UK Biobank biosample processing and archiving facility. *DDW* 8(1): 51-61.

### Summary

What is evident from the vendor updates is that all these companies see automated biobanking as a significant growth prospect in the future and are investing heavily in new R&D. This is reflected in the fact that at least six different vendors are planning to offer in the very near future (or have already developed) -80°C storage automated solutions (deCODE Genetics, Nexus Biosystems, REMP, RTS Life Science, TAP and Thermo Scientific) and one -150°C storage system (MatriCal). Although many of these solutions are adaptations of their existing -20°C compound management stores and technology, the extended temperature capabilities (to -80°C or -150°C) and the implementation of deep-cooled buffer zone to minimise temperature changes during manipulation or picking, have presented special challenges for the robotics and have necessitated many novel engineering developments, eg protecting the unpicked -80°C samples from unwanted temperature rise during the sample retrieval process (RTS Life Science). Other systems (Thermo Scientific BioBank) rely on a unique rack design that enables the location of the robotics at ambient temperature, isolated from the ultra-low temperature that may cause mechanical failures. A key feature common to many of these new systems is their design as compact modular units that can be added to or expanded as the capacity needed grows in the future. Systems are supported by a rapidly expanding range of automation-compatible plastic tubes (Micronic, REMP and the Thermo Scientific line (ABgene, Matrix and NUNC brands)) with integral 2D bar codes, which together with LIMS software systems facilitate automation sample tracking and complete inventory control (BioVantage, Thermo Scientific and Titian Software). Furthermore, sample preparation tools are now being developed to standardise the workflow while archiving biospecimens that should lead to the enhanced purity and QC of the materials stored (Hamilton, Qiagen and RTS). Although the majority of the industry is focused on the cryogenic storage of aqueous-state biosamples, we should not ignore the dry-state media approach (GenVault) which provides a compelling alternative for the extraction, storage and distribution of patient DNA samples. In summary, we can justifiably conclude that there has never been a better time to take that big step forward and to automate biological sample storage. Organisations engaged in debating the alternatives strategies and offerings have available to them today a rapidly growing set of tools and technologies that will facilitate enhanced sample integrity, tracking and audit trail.

**DDW**

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