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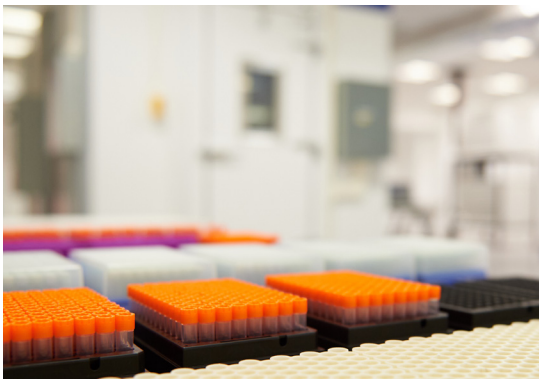
Case Study

NIHR – National Biosample Centre Maximizes Flexibility, Accuracy, and Productivity with Centralized Biosample Management

The NIHR - National Biosample Centre is the U.K.'s largest facility providing services to research involving human volunteers and includes substantial capacity for storing biological samples. This case study outlines the facility's organization and goals, and details how the centre applies the industry's latest solutions for centralized biosample storage and management.

Background

The United Kingdom's NIHR - National Biosample Centre (NIHR - NBC) opened its main site at Milton Keynes in Buckinghamshire, about 50 miles northwest of London, late in 2014. Funded by the National Institute of Health Research (NIHR) it's the nation's new centre for biomedical services.



The NIHR - NBC builds on the experience and infrastructure developed in the recruitment and enhancement phase of the prospective cohort study of the U.K. Biobank. (This large-scale initiative recruited and collected biosamples — blood, urine, and saliva — from 500,000 adults.) The new NIHR - NBC Milton Keynes complex aims to provide a high-quality, high-capacity, cost-effective service for researchers across the academic and industrial biomedical community. It serves investigators engaged in studies that include collection, processing, storage, and analysis of biological samples from volunteers and patients.

As Dr. Tim Peakman, CEO of UK Biocentre (the organization that runs NIHR - NBC) states: "This is an exciting initiative. The aim is to improve health research infrastructure so that researchers can focus on the important stuff — their research."

Goals

U. K. Biocentre planners intended their facility to echo the earlier Biobank project in utilizing large-scale automation; centralized biosample collection and storage; and effective quality management processes. These enable the centre to offer an important collection of core services to the biomedical research community. Services would include:

- Advice on sample collection
- Reception of biological samples
- Automated processing and aliquoting
- Storage (automated and manual)
- Picking supplies from storage for supply to researchers or for downstream processing
- High-throughput, high-quality nucleic acid extraction from a variety of tissues

The centre would help dramatically reduce start-up times, risks, costs, and management burdens for academics and industrial partners. With study speed and quality thus improved, scientists could instead focus on study design and data analysis.

The facility is an HTA-licensed and ISO 9001 certified centre.

Strategic Planning for Storage Automation

NIHR - NBC planners identified several key characteristics that their automated biostorage systems should emphasize.

Environmental control was critical. In manual storage and management, samples might be exposed to wide temperature variations during handling, often with dire consequences for sample quality and study results. By contrast, the centre sought an automated solution that would maximize sample integrity, keeping samples at a consistent low temperature. Samples and infrastructure must remain frost-free, to prevent obscuring of bar code information. And it should protect "innocent" samples from rising toward ambient temperature while adjacent samples were being stored or retrieved.

Also, automated systems offered speed — a desirable quality in a centralized facility designed to store millions of samples. But even more important, automation ensured accuracy. Studies show that manual handling suffers as much as a 10% error rate in picking randomly distributed samples. (When picking a case group, for example, this significantly increases false positive rates.) By contrast, a good automated system can achieve 100% *accuracy*. So the storage solution should allow accurate and responsive sample retrieval, for provision/sharing with researchers. This also enables the centre's downstream processing

options such as high-throughput DNA and RNA extraction.

Another important consideration: *flexibility.* Instead of standardizing on a single type of storage container, the NIHR - NBC storage hardware and software should be able to handle a large number of different sample containers and consumables received from a wide variety of researchers.

Ideally, the centre's automated storage capabilities would be utilized mostly for collections that required a reasonable percentage of *continuing sample retrieval.* Planners estimate that automated storage makes the best sense for collections retrieving at least 5% of their total samples each year.

Also, NIHR - NBC will become self-funding. So its storage solution should be as *economical* as possible, to minimize the cost premium of automated over simple manual freezer storage.

Selecting a Storage Automation Partner

The process for procuring U.K. Biocentre's storage automation supplier was comprehensive, and fully transparent. To be considered a vendor had to have a well-regarded system that fulfilled a number of technical requirements.

The chosen supplier: Brooks Life Science Systems.

"Brooks won against a whole series of criteria," said Dr. Peakman. "They had a good, credible system with a number of performance characteristics we needed.

"Several other suppliers also had good systems. Amongst the various assessment criteria, Brooks also had a senior management and technical team with a high degree of commitment and partnership. This proved to be invaluable as the project moved forward."

The Storage Automation Solution

Primary biostorage technologies implemented at NIHR - NBC site in Milton Keynes consist of six BioStore™ II QuadBank systems, made by Brooks Life Science Systems. Each of these large units — 40.6 feet by 14.7 feet by 9.1 feet (12.4 meters by 4.5 meters by 2.8 meters) — maintains samples at -80° C. Possible capacity between them: approximately 19 million biosample tubes. At NIHR - NBC, these units will handle the great majority of samples held in the facility.

Additionally, the facility houses two SampleStore™ II 40-column systems, also from Brooks. Each of these midsize units — 18.0 feet by 7.8 feet by 8.5 feet (5.5 meters by 2.4 meters by 2.6 meters) — maintains samples at -20° C. Possible capacity among them all: approximately 2.4 million biosample tubes. At NIHR - NBC, these units for the most part will handle isolated DNA samples, which remain stable at relatively higher temperatures and thus don't require -80° C storage.

Finally, the facility also maintains manually accessed freezers at -80° C.

NIHR – NBC's centralized storage, as presently configured, should accommodate a total of more than 21 million samples. (Nominal capacities are based on the use of standard 1.2 mL tubes. Since the center can and does accept a wide variety of other containers, actual capacity will vary.) The facility includes space to expand if more storage is ever needed.

The Storage Solution in Action

Installation and commissioning of the automated storage systems occurred on an accelerated timeframe to meet the project's tight schedule. Preliminary designs began in March 2014, and the first Brooks automated systems were up and running in October 2014.

The centralized, automated sample storage and management system now in place at NIHR - NBC provides a number of key advantages, as detailed below.

Control

Centralized storage ensures consistent handling of the collection throughout the facility's life. It meets the centre's stringent demands for physical access security, environmental control, and ability to ensure precise tracking and handling of every sample at every point.

Flexibility

As a central repository, NIHR - NBC depends greatly on the innovative capabilities of its Brooks systems to handle multiple storage container types (including myriad sizes of tubes, plates, vials, boxes, and more) — all while maintaining optimal storage density. Samples from the widest possible range of researchers and collections can be stored and accessed with convenience and security, today and tomorrow.

Temperature stability

The centre's systems maintain temperature uniformity throughout the collection, for the duration of each sample's storage and

access. The systems ensure frost-free operation to eliminate errors in reading bar codes and/or interference with moving automated components. They provide protection of the innocents, so handling one sample won't compromise the temperature stability of adjacent samples. Finally, the systems enable staff to easily maintain accurate and complete documentation of sample temperature history for accreditation purposes.

Productivity

A facility using manual sample picking methods might be limited to pulling about 300 randomly distributed sample tubes in a single day from manual storage freezers. By contrast, NIHR - NBC s centralized, automated storage systems offer much greater productivity, with the capability to pick thousands of samples per day. For example, the SampleStore II system can pick 1241 tubes per hour from an SBS rack. (This assumes the unit encounters a 10% hit rate, so that 58 out of 576 tubes on each tray need to be picked before proceeding to the next rack.) Naturally, precise throughput totals depend on factors such as storage media type, temperature, exact storage location, and so on.

Energy Efficiency

Centralized, automated storage provides proven consumption advantages over trying to manage large collections using manual storage methods such as traditional upright electro-mechanically cooled freezers. For instance, each sizable automated enclosure possesses a large thermal mass that resists temperature excursions. Any efficiency calculation must consider two levels of energy expenditure: first to remove heat from storage spaces, and second to remove or manage heat from the entire building. For starters, estimates are that the QuadBank system alone can save up to 30% annually in energy costs versus conventional freezers.

Figure 1: BioStore II Quadbank -80° C automated store

Figure 2: SampleStore II -20° C automated store

Fewer Variables in the Cold Chain

With manual handling, samples are exposed to the risk of temperature excursions at almost every step. The improved cold chain management supplied by centralized, well-automated storage ensures enviromental stability, and lessens or eliminates any impacts to innocent samples throughout the collection.

Better, More Accurate Science

The NIHR - NBC's extensive use of high-precision automation not only guarantees sample integrity, it also ensures speed and accuracy of processing, plus efficient archiving and retrieval of samples. It lessens or eliminates tedious manual quality-control

checks, and minimizes the possibility of rework due to manual handling's high error rates. Finally, it helps prevent the misattribution of samples that can lead to false positives in cohort studies, or misdiagnoses in clinical settings. Results: higher-quality science and patient care.

Secure Sample Sharing

The storage automation systems' flexibility and precision offer greater opportunities for safe, efficient, secure sample sharing among researchers. When and if allowed by access protocols established by the originating researcher, samples requested by authorized investigators are accurately selected via a process that ensures sample donor anonymity. Overall collection utility is increased.

New Research Possibilities

Centralized, automated storage allows more researchers (when authorized) more access to more specimens — a wider population of specimens, all of which have been processed and stored under identical or complementary control protocols. It also provides the capacity to fulfill multiple requests for samples quickly and efficiently. Result: a proliferation of new research opportunities.

Conclusion

To date, the centre reports good initial progress in realizing many of its goals:

- Provision of important services to U. K. researchers
- Significant reductions in startup time and costs for biomedical studies
- Lowering of the cost threshold for collection of biological samples in studies
- Effective knowledge transfer among researchers
- Economies of scale — including capital, utilities, running costs, procurement and facilities
- Efficient utilization of critical research assets
- Energy savings (centre wide up to 60%) and associated reductions in carbon footprint

So far, the centre has also been well received by potential users. As Richard Archer, founding chair of the U.K. Regenerative Medicine Industry Group and originator of the concept of industrialization of biomedical processes, says, "The team at NIHR - NBC has applied the principles of industrialization to create a complete resource for biomedical science that, in my view, is unmatched in academia or industry anywhere in the world".

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