The Lifetime Management of Histology Samples with Mosaic

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The new century has seen a surge in the need for tissue and other biological samples, with new collections arising almost daily. There may be a need to accumulate samples that are directly linked to clinical trials, or to support genomic research and the development of personalised medicine. Or they may be in support of longer term objectives with samples collected speculatively for future research. The collection of samples is only part of the story however, and the research value of these collections will only be realised if several key factors in their management are correctly addressed.

From the very point of collection the integrity of the samples needs to be assured, and the provenance in terms of the donor (anonymised) information and disease state must be accurately recorded. For some collections the use of pre-labelled kits helps with the rapid stabilisation of the samples. For clinical trial sample collection the samples are typically taken at specific events against a planned schedule. Often the critical sample collection event is very distant to the storage and analysis facilities, placing further challenges to the management of the sample acquisition process.

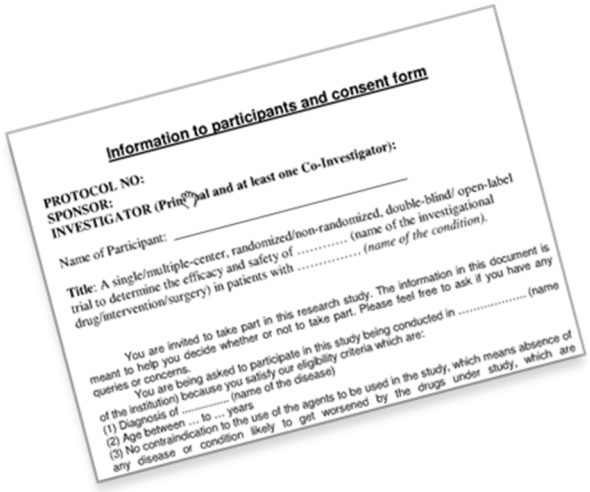
Methods of preservation vary by sample type and their expected end use. In some circumstances, preservatives may be used in place of, or in addition to physical stabilisation such as freezing or drying. There are numerous articles that describe a broad variety of techniques [1] involving reagents such as Formaldehyde, Carnoy's reagent and other reagent-free techniques including freeze-drying, air-drying[2], and even microwave heating[3]. The preservation technique and conditions will dictate the future usage (and usefulness) of the samples. The physical variety in tissue container types[4] from single vials, tissue blocks, to tissue microarrays determine the type of storage facility that can be used, and this can be a limiting factor when automated storage systems are considered.

Figure 1: A variety of storage container types may require segregation of collections.

The storage environment clearly has to be considered to match the preservation technique employed, with vapour and gaseous conditions monitored with temperature controlled from room temperature to the familiar 77°K 'LN2' environment. Positive and rapid identification of samples is typically achieved using optical barcodes and occasionally RFID tags.

Collections of samples are segregated physically or virtually to assist in the correct and efficient picking of the samples from storage. In the case of human biological samples, retrievals should only be made if the access is in accordance with the donor's stated consent.

However since there is little standardisation of consent forms[5] and, across different nations, a large variation in regulatory requirements[6] it is difficult to provide a common recording and validation mechanism to suit all cases.



Information to participants and consent form

PROTOCOL NO:
SPONSOR:
INVESTIGATOR (Principal and at least one Co-Investigator):

Name of Participant: _____

Title: A single/multiple-center, randomized/non-randomized, double-blind/ open-label trial to determine the efficacy and safety of ..... (name of the investigational drug/intervention/surgery) in patients with ..... *(name of the condition).*

You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study being conducted in ..... (name of the institution) because you satisfy our eligibility criteria which are:

(1) Diagnosis of ..... (name of the disease)
(2) Age between ... to .... years
(3) No contraindication to the use of the agents to be used in the study, which means absence of any disease or condition likely to get worsened by the drugs under study, which are

Figure 2: Sample consent forms are usually designed to suit the study, and often do not use common terminology, limiting the potential use of a sample.

As samples are pulled from storage, the freeze-thaw cycles should be recorded as an indication of possible sample degradation [7]. The samples are prepared for analysis using a broad variety of techniques from simple staining through to sample coring and DNA extraction. There may be a need to record these preparation steps and the linkage between the created samples and the parent sample. The preparation steps might be performed on an automated instrument.

When sample analysis is performed, any results - which could be of specific study features or general quality data - are recorded against the samples. At the end of the analysis a record of sample disposal may be needed, and this is appended to the lifetime audit history of the sample.

How does Mosaic support the management of tissue and other biological samples?

Mosaic is a sample management system that has been deployed across more than 60 sites and provides sample inventory management for a broad range of sample types. Collections range in size from 20,000 to 200 million individual samples.

Mosaic provides a substance registration database and a sample inventory, allowing different sample descriptors to be configured, and allowing multiple containers with the same parent sample to share a common description of the sample. This can be used to record the collection event and the preservation technique used.

Figure 3: Mosaic substance registration separates the substance data from the container amounts and the specific properties for the substance are configurable from a large variety of data types

Different container types (single or arrays of samples) are easily defined in the Mosaic Configuration Editor, and the same module allows the user to define the correct storage locations where the container can be held. The storage temperature is also matched with the stated temperature held on the original sample information when allocating storage locations to items. All removals from sub-zero (Celsius) stores are recorded as potential thawing events.

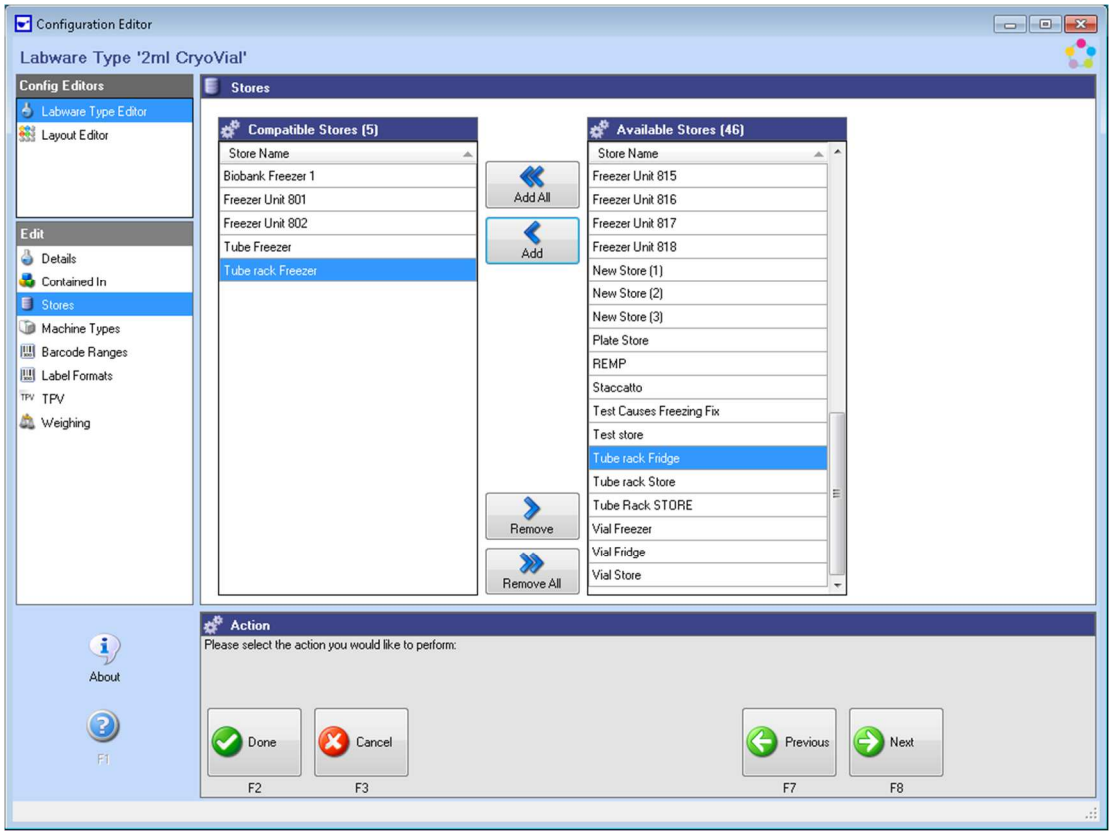


Figure 4: Mosaic provides a Configuration Editor for administrators to introduce new labware types and manage their usage, in this example where the new container type can be stored.

For the timely collection of samples, Mosaic allows containers to be designated for specific collection purposes in advance of sample collection, or alternatively pre-barcoded containers can be associated with a sample and collection event at the time of collection. Container data can be imported into the system singly, via a webpage, or in batches via a flexible file import mechanism

The usage consent is recorded against the collected sample data, and this information can be subsequently checked against the sample requests. The original consent document can also be attached to the sample.

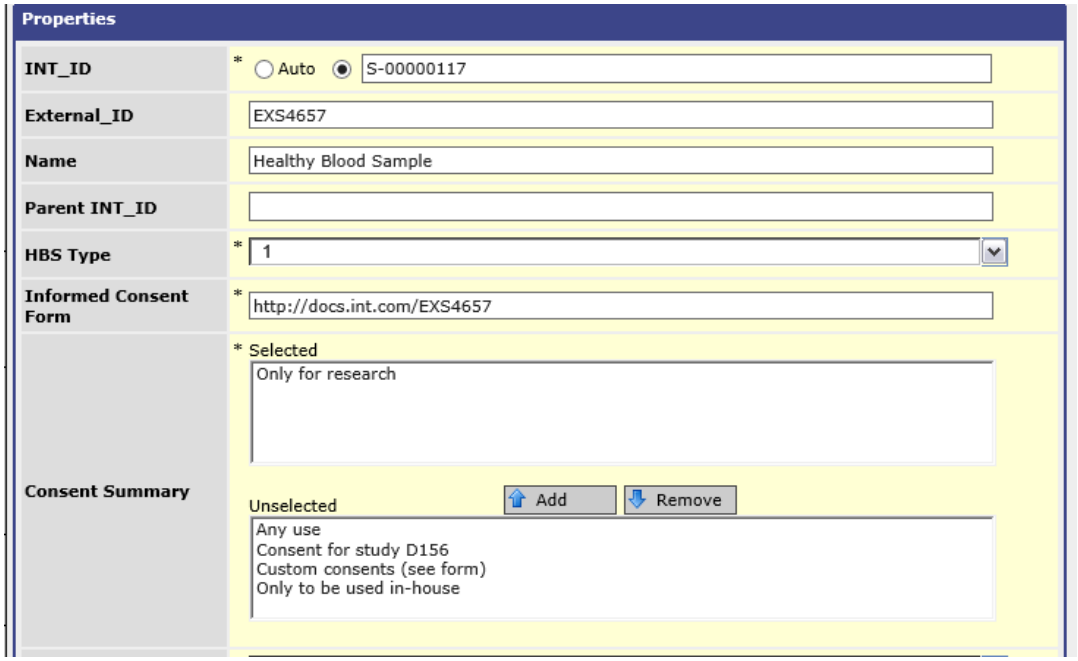


Figure 5: Donor consent is recorded on the substance information, and this can include a link to a scanned consent document. Consent can be edited at a later date, with all changes recorded in the substance audit trail

How can I find my samples?

The sample collection can be readily searched to find samples with specific criteria, and the search results can point the user to the sample containers and show their locations.

Searches can be saved for re-use, and the most recent searches can also be selected without having to re-enter the search criteria.

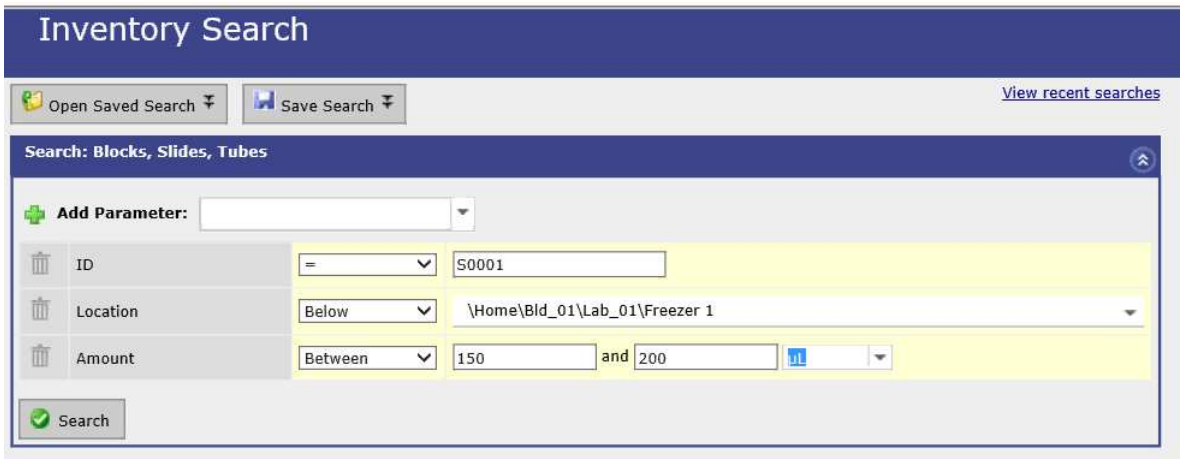


Figure 6: Mosaic Inventory search has smart searching capabilities with interpretation of the location hierarchy, Searches can be for labware or to find substance records

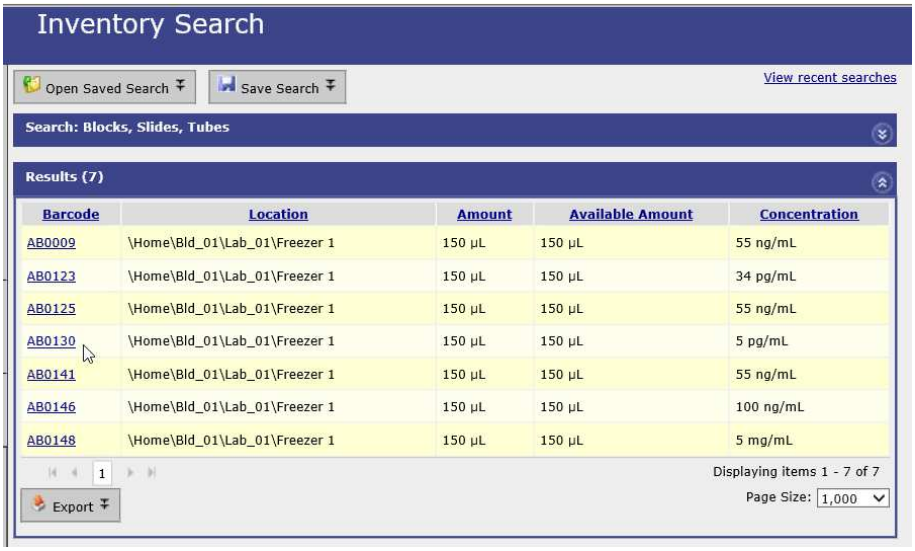


Figure 7: Search results (in this example) show a list of containers that match the criteria, so the user can decide to pick the samples or export the search results (to an internal List, a sample Order or as a 'CSV' file.)

Figure 8: Pick List in simple list form

When the sample is exported to a Picking List, it is added along with any other containers that need to be retrieved from the stores. The list of containers is editable, and the user can view the locations to pick from as either a simple list or a list with a graphic showing the position of the container on the freezer shelf.

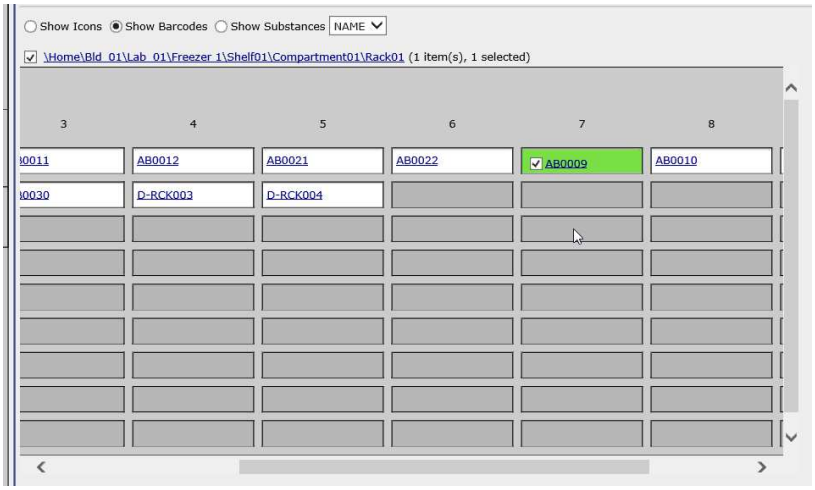


Figure 9: Pick List with location map form

Mosaic is available as a Freezer Management package where the user typically searches and retrieves the samples directly - a self-service model. In addition Mosaic can be provided to support a centralised service, where samples are requested, and those requests are fulfilled by the biobank staff. The Mosaic Ordering module is provided in this latter case, with the benefit of having a predefined and tracked preparation workflow, which permits (in many cases) the integration of automated instruments.

Where Mosaic Ordering is used, the system can validate the sample request for the assessment of the required amount of the sample, checking this against any usage restrictions for particular projects, and the recorded consent for the sample. In the case where a workflow is managed by Mosaic, there is an additional audit trail for the preparation steps. Analysis results and QC data can be uploaded and saved against the containers. In support of analysis, Mosaic can export container-maps to external analysis results systems in order to link results to the sample identity. All sample information on the container and the sample has a full audit trail, recording all movements, thawing events, dispensing events and QC data histories.

Mosaic is a highly configurable system, and can support a large variety of sample types and sample usage workflows. For further information on Mosaic please visit www.titian.co.uk or use the contact details shown below.

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Additional Reading:

1. "Critical steps in tissue processing in histopathology.", *Comanescu M, Annaratone L, D'Armento G, Cardos G, Sapino A, Bussolati G,* **Recent Pat DNA Gene Seq, 2012, Vol. 6, Page 22-32**
2. "Dry-state, room-temperature storage of DNA and RNA" – **Nature Methods 5th September 2008**
3. "A method of rapid fixation of large biopsy specimens using microwave irradiation.", *Leong AS, Duncis CG,* **Pathology, 1986, Vol. 18, Page 222-5**
4. "Effect of type of container, storage temperature and humidity on the biological activity of freeze-dried alkaline phosphatase." Ford AW, Dawson PJ. **Biologicals. 1994 Jun;22(2):191-7**
5. "Banking together. A unified model of informed consent for biobanking" Elena Salvaterra,.Lucilla Lecchi, Silvia Giovanelli, Barbara Butti, Maria Teresa Bardella, Pier Alberto Bertazzi, Silvano Bosari, Guido Coggi, Domenico A Coviello,Faustina Lalatta, Maurizio Moggio, Mario Nosotti, Alberto Zanella, and Paolo Rebulla - **EMBO Rep. 2008 April; 9(4): 307–313.**
6. "The International Harmonization of Human Tissue Regulation: Regulatory Control Over Human Tissue Use and Tissue Banking in Select Countries and the Current State of International Harmonization Efforts" Barbara Indech. **Food and Drug Law Journal Vol 55**
7. "Response of the cell membrane-cytoskeleton complex to osmotic and freeze/thaw stresses" Ragoonanan, Hubel, Aksan, **Cryobiology, Volume 61, Issue 3, December 2010**