PROCEDURE

Metro South Health Research Biorepositories – Acquisition, Attainment and Recruitment

PR2017/102
Version No. 3.0

PURPOSE

Metro South Health (MSH) is committed to the highest standards and practices in the operation of tissue banks, biobanks, tumour banks and biospecimen collections ('research biorepositories') for research purposes. This procedure describes the processes for the acquisition, attainment and recruitment in the collection of biospecimens from MSH patients/participants.

OUTCOME

Whilst research biorepositories must be operated in accordance with the MSH Research Biorepository Governance Framework, principles may be adapted so that they are appropriate to the mission and goals of each research biorepository.

This procedure applies to all MSH or Queensland Health (QH) employees whose usual reporting line is through a MSH facility or service (including visiting medical officers, visiting health professionals, students and researchers) who operate or access, or who propose to establish or access, a research biorepository that includes biospecimens collected, processed or stored within MSH facilities.

Failure to comply with this procedure may amount to research misconduct on the part of the responsible individual. This procedure must be read in conjunction with other MSH Research Management and Research Biorepository procedures. Additionally, this procedure applies to the major business planning considerations that are applicable to research biorepositories in MSH.

KEY PRINCIPLES

The following key principles guide MSH employees in the acquisition, attainment and recruitment in the collection of biospecimens from MSH patients/participants. The way in which individual MSH research biorepositories put these principles into operation may be scaled in relation to the research biorepository's size of operations.

- The Custodian must determine the type of biospecimen to be collected that is best suited for a particular scientific investigation and the goals of the particular research effort supported.
- Material type, biospecimen source and downstream testing plans will influence decisions surrounding how biospecimens are collected and processed. Some material types are better suited for some types of analyses over others that may be less well-suited.
- Research biorepositories must also determine the most appropriate storage environment for the particular biospecimens it holds and ensure that the equipment and facilities are in place to support the storage of these biospecimens until they are needed.

- The Custodian, director and/or research biorepository manager must establish Standard Operating Procedures (SOPs) for the acquisition of new biospecimens and culling of collections (when biospecimens have fulfilled their original purpose or are no longer suitable for their intended purpose or if patients/participants request the withdrawal of their biospecimens) in accordance with the MSH Research Biorepository Governance Framework.
- Effective planning efforts should consider the sources of biospecimen acquisition to be sure that appropriate biospecimens are obtained for the defined scientific purpose (eg for human biospecimens examples could include surgical biospecimens or biospecimens obtained from autopsies). Decisions should be made early in the process to determine if any material types should be excluded from collection efforts.
- Research biorepositories must develop a clear understanding as to the identity and needs of the investigators and scientific clients it desires to serve. Whenever possible, efforts should be made to understand the downstream testing planned to ensure that the biospecimens being provided are collected and processed in a way to ensure the success of future research efforts.
- Participant recruitment should be carried out in a non-coercive and equitable manner that respects individual freedom of choice and consumable biospecimens used must be of a high standard.
- The Custodian must give careful consideration to any special issues related to the participation of vulnerable populations or groups, and their involvement should be subject to protective conditions in accordance with applicable law and ethical principles.

LEGISLATION OR OTHER AUTHORITY

Legislation

- *Hospital and Health Boards Act 2011 (Qld)*
- *Information Privacy Act 2009 (Qld)*
- *Human Rights Act 2019 (Qld)*
- *Public Health Act 2005 (Qld)*
- *Therapeutic Goods Act 1989 (Cth)*
- *Transplantation and Anatomy Act 1979 (Qld)*

To the extent an act or decision under this document may engage human rights under the *Human Rights Act 2019*, regard will be had to that Act in undertaking the act or making the decision. For further information on the *Human Rights Act 2019* see: https://www.qhrc.qld.gov.au/

Regulation

- Transplantation and Anatomy Regulation 2004 (Qld)

Statements, papers and guidelines

- International Society for Biological and Environmental Repositories (ISBER): Best Practices: Recommendations for Repositories Fourth Edition
- National Cancer Institute: Best Practices for Biospecimen Resources
- Medical Research Council: Use of Human Samples in Medical Research
- Organisation for Economic Co-operation and Development (OECD)
    - Best Practice Guidelines for Biological Resource Centres
    - Guidelines on Human Biobanks and Genetic Research Databases
- World Health Organisation (WHO): Common Minimum Technical Standards and Protocols for Biological Resource Centres Dedicated to Cancer Research

MSH policies, procedures, manuals and frameworks

- Metro South Health Research Management Policy (PL2017/55)
- Risk Management Policy (PL2018/62)
- Risk Management Procedure (PR2018/97)

RESPONSIBILITIES

Executive Management

Ensure collaborative, harmonised, clear and detailed publicly available policies, procedures and SOPs are in place for the establishment and operation of all MSH research biorepositories.

Metro South Research

Support Custodians in the establishment and operation of a research biorepository through the provision of guidance and support when interpreting principles and provisions contained within the MSH Research Biorepository Governance Framework.

MSH Research Biorepository Strategic Oversight Committee

Provide guidance around acquisition, attainment and recruitment in the collection of biospecimens for each research biorepository.

Custodian/Principal Investigator – responsible officer

Ensure the research biorepository's processes for acquisitioning, procuring and recruiting patients/participants not only supports individual and institutional interests however also ensures that high quality biospecimens will be available for future research efforts.

Research biorepository manager

Write, revise and update organisational and administrative SOPs pertaining to the acquisition, attainment and recruitment in the collection of biospecimens from MSH patients/participants.

Laboratory technician/technologist assistant/clinical personnel

Research biorepository personnel must possess sufficient educational background, experience and training to assure that assigned tasks pertaining to the collection of biospecimens from MSH patients/participants are performed in accordance with the MSH Research Biorepository Governance Framework and applicable SOPs.

SUPPORTING DOCUMENTS

Attachment 1 - Application

Attachment 2 - Use of Existing Collections of Samples Flowchart

Attachment 3 - Minimum Data Set

Attachment 4 - Minimum Data Set Template

Attachment 5 - Australian Quarantine and Inspection Service (AQIS) Permit

DEFINITIONS

See the MSH Research Biorepositories Glossary

PROCEDURE - ACQUISITION, ATTAINMENT AND RECRUITMENT

STEP 1: Purpose of the MSH research biorepository

Through the operation of the research biorepository, the Custodian must consult with the MSH Research Biorepository Strategic Oversight Committee to ensure the collection suits organisational and individual researcher requirements.

STEP 2: Research biorepository services to be provided

In consultation with MSH Human Research Ethics Committee (HREC) and MSH Research Biorepository Strategic Oversight Committee the Custodian must ensure the services provided not only meets individual interests however has also considered organisational need.

STEP 3: Recruitment strategy

As part of the Research Protocol the Custodian and/or director must outline the recruitment strategy to be implemented in attaining biospecimens for the MSH research biorepository.

STEP 4: Acquisition

Custodians may acquire biospecimens from patients/participants within MSH and external to the Health Services. Where external tissue attainment occurs the HREC of the participating institution must have the MSH research biorepository's Participant Information and Consent Form (PICF) approved prior to collection.

PROCEDURE DETAILS

Procedure Number
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MSH Research Biorepositories –
Acquisition, Attainment and Recruitment Procedure

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MSH Research Biorepositories Policy

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05 July 2024 (within the next 3 years)

ATTACHMENT 1 - APPLICATION

1.0 Organisational considerations

When planning a research biorepository, it is important that the mission of the research biorepository be clearly defined. The mission must address the purpose of the research biorepository and the entities served by the collections obtained. The mission must be reviewed over time to ensure its appropriateness as conditions surrounding its implementation may change. A research biorepository's mission and purpose is outlined as part of the relevant Research Protocol.

The specific mission and goals of a biospecimen resource will influence the type of biospecimens collected. The biospecimens collected should be appropriate and feasible for the clinical setting, as well as appropriate for the downstream applications anticipated for the biospecimen. If tissue biospecimens are being collected, they should be reviewed histologically for accuracy by a qualified histopathologist; this is a requirement for some accrediting agencies

It is important that the equipment, facilities, staffing and funding for a research biorepository be established according to a structure that will support the mission and activities during the anticipated lifecycle of the research biorepository.

SOPs must be created, enforced and reviewed on a regular basis concerning biospecimen access, handling, culling and for the termination of the research biorepository. Please see Establishment of a Research Biorepository Procedure (PR2017/100) for further information.

Numerous successful scientific results have emerged from research projects using shared biospecimens samples and data. Uniform information infrastructure for research biorepositories will facilitate the discovery of underutilised research biorepository samples in MSH. To achieve this recommended MSH Minimum Data Set has been established (Attachment 3). The aim of the MSH Minimum Data Set is to facilitate data discovery through harmonisation of data elements describing a research biorepository at the aggregate level.

As many collections within MSH and across Queensland possess large sample cohorts that are underutilised, a Minimum Data Set would help pave the way for networking on a national and international level, resulting in time and cost savings and faster emergence of new scientific results. Research biorepositories may accept collections of scientific value that cannot meet the full Minimum Data Set (MDS). If this is the case the research biorepository must disclose which items of the Minimum Data Set are missing. A process for defining the Minimum Data Set and Recommended Data Set for a collection may be established before the collection is constituted, see Attachment 3 and 4.

1.1 Pre-analytic and analytic variables

A variety of factors may affect biospecimen quality and research results; these may be divided into two (2) general categories designated "pre-analytic factors" and "analytic factors". Pre-analytic factors refer to collection, processing and storage variations that influence biospecimen integrity prior to its removal from the human research patient/participant and carry through to the point at which a biospecimen is ready for testing. Analytic factors refer to those variations that affect performance of a particular testing process.

1.2 Pre-analytic factors

Pre-analytic variables may be divided into three general areas:

- The physiology of the human research patient/participant prior to biospecimen collection.
- Biospecimen collection practices.
- Biospecimen handling practices prior to their inclusion in downstream testing.

1.2.1 Physiology of the human research patient/participant

Research has demonstrated that analyte levels may be affected by a variety of factors such as the overall health of the human research patient/participant, the type of anaesthesia used, food and beverages consumed prior to biospecimen collection, the medication status of the patient/participant, and the time of day at which the biospecimen was collected. Additionally, the menstrual cycle in females may affect some downstream analyses. Efforts should be made to collect and record information pertaining to these factors to decrease or adjust for the variability of these contributing factors. The issue of medications is particularly important since many over-the-counter medicines may not be remembered as such by the patient/participant (eg antacids, non-steroidal anti-inflammatory medications).

1.2.2 Uniformity in biospecimen collection practices

The methods used to remove and collect biospecimen from human research patients/participants may influence the quality of the biospecimen collected. Significant research has indicated that during surgical removal of biospecimen the amount of time following the cessation of blood flow to an organ can affect both levels and molecular profiles of target analytes. The biospecimen should be preserved as quickly as possible after removal from the patient/participant (eg appropriately sized tissue sections snap frozen and/or placed into ten percent phosphate-buffered formalin, as appropriate). In recent years alternative fixatives have been developed and validated, such as PaxGene Tissue®, which allows for the preservation of tissue for molecular analysis as well as histological analysis. As appropriate, consideration should be given to the use of newer preservation methods.

Expected as well as unforeseen future uses of biospecimen should be considered when deciding on preservation methods. When biospecimens are collected from research patients/participants, the organ site at which the biospecimen is removed (tumour or non-tumour, as well as location within the tumour), any anaesthetic being used, warm ischemia time (the length of time the specimen is only partially perfused due to vessel ligation during surgery, before complete removal), any stabilising agents used to preserve the biospecimen following its removal, the type of fixatives used and the length of time the tissues are exposed to fixatives, any further processing, and the temperature at which biospecimen are maintained following collection, as well as duration (ie cold ischemia time) may all affect molecular stability and degradation.

Prior to the collection or removal of biospecimen, a plan should be in place to allow for the appropriate annotation of the biospecimen. This annotation should include information about the human research patient/participant, and timing of collection and processing activities (eg the type of clearing agent, the type and temperature of paraffin used to process the biospecimen etc). This data should be maintained in a database that can be linked to the biospecimen at all times. Details about particular biospecimen collection, processing, and storage procedures can be important supporting information for scientific publications on research utilising the biospecimen.

1.2.3 Biospecimen handling procedures

Every attempt should be made to optimise the handling of biospecimen to minimise molecular changes that may result from the processing activities, most critically by reducing cold ischemia time (the time the biospecimen spends after complete removal from the patient/participant but before being placed into fixative). Other critical factors include the temperature and timing of biospecimen processing, the size and volume of the biospecimen that will be stored for future use, and the number of aliquots to be prepared from each biospecimen. Multiple small aliquots allow for analysis or experimentation on one biospecimen, while minimising freeze-thaw degradation of other stored samples. When samples are stored in a frozen state, the rate at which they are cooled to the storage temperature can influence the rate at which molecular degradation occurs, and subsequent freeze-thaw cycles can further degrade the molecular integrity of the biospecimen.

1.3 Analytic factors

When pre-analytical variables are introduced they lead to differences in the performance of a particular assay. To minimise errors in assay reproducibility, the following considerations should be applied:

- Use of validated assays, where possible.
- Use of SOPs in which the technical staff are well-trained.
- Lot uniformity of reagents.
- Inclusion of appropriate type and number of quality control (reference) samples.
- Randomisation, when possible.
- Standardised methods for documenting and interpreting testing results.

1.4 Defining reference ranges

Aside from pre-analytic and analytic factors, research dictates that values for particular cellular analytes are more accurately represented by a normal biological range of values (or reference range), even among individuals characterised as ‘normal’ or ‘healthy’. Disease is defined as a distinct deviation from the range of normal variation, and diagnosis of disease depends on knowing the scope of boundaries of normal variation. Where possible, efforts should be made to characterise reference ranges for the analyte of interest in the biospecimen of interest to ensure the likelihood of accurately detecting any deviation from the reference range.

1.5 Unique identifier

Each biospecimen should have a unique identifier or combination of identifiers that are firmly affixed to the container, clearly and legibly marked, and able to endure storage conditions. All other relevant information should be tied to this identifier, bearing in mind research patient/participant confidentiality, security, and informed consent provisions. Inventory systems should relate the presence of each aliquot to its position in a specific box, freezer, refrigerator, or shelf.

Consideration should be given to the location of biospecimen within storage containers to allow for the most efficient strategies for subsequent retrieval (ie by research project and by material type within studies) as appropriate. Please see Collection, Processing, Handling and Retrieval Procedure (PR2017/104) for more information.

2.0 Determination of services to be provided

Custodians and directors of a research biorepository must determine which services are to be provided and ensure that the appropriate infrastructure is in place to provide them in such a way as to ensure that high quality biospecimens will be available for future research efforts.

The infrastructure not only includes equipment and supplies but also the trained personnel to perform these services as needed. Services may include biospecimen collection, receipt into the research biorepository, processing, storage and distribution. Particular processing may be required not only for each biospecimen type but also may depend upon the state of the biospecimen received (eg fresh, frozen, fixed). Please see Operational Arrangements Procedure (PR2017/101) for further information.

There are a number of additional services that a research biorepository might provide in addition to the collection and storage of biospecimens. Examples of these include feasibility assessments to assist investigators with research project planning and proposal submissions, the provision of letters of support or the establishment of collaborative relationships with investigators, batching of samples and inclusion of quality control biospecimens for biospecimens destined to be sent to a laboratory for testing, histology services, micro-dissection, nucleic acids extraction and analysis etc. All services offered should be well-defined and included as part of the relevant Research Protocol. Please see MSH Research Management - Ethical and Scientific Review of Human Research Procedure (PR2017/113) for more information.

Custodians must also acknowledge the possibility that the purpose and scope of the research biorepository may evolve over its lifespan. For instance, scientific findings may show that the materials collected by the research biorepository are no longer suitable for its scientific purpose. An example would be where a research biorepository decides to collect samples for DNA isolation, but later determines that RNA is required to pursue its scientific objective. As the need for RNA was scientifically not foreseeable at the time of biospecimen collection, this is an example of a subsequent modification to the research biorepository's scope.

At the time of establishment of the research biorepository, the initiators may not be able to provide patients/participants with detailed information on future scientific and technological developments. However, they should make clear that continuous scientific and technological developments may necessitate adaptations/modifications of the research biorepository during the course of its existence. Please see MSH Research Management - Biospecimen Ethics and Participant Information and Consent Form Procedure (PR2017/115) for more information.

The research biorepository may also decide to not collect or maintain certain data, to not perform certain tests or to not allow certain types of analyses. The research biorepository should have a clearly articulated SOP about which specific types of data will not be collected and which specific types of tests will not be performed. For example, where applicable, the research biorepository could indicate that it will not carry out tests nor collect information about paternity, HIV/AIDS, or the use of illicit substances.

3.0 Models

The collection and storage of biospecimens may be performed in support of a variety of scientific endeavours. Biospecimens may be collected as a part of prospective or retrospective research projects and the method of procuring these biospecimens will depend on the availability of resources and the

particular scientific inquiry. There are several models for how biospecimens may be procured, stored and prepared for subsequent testing.

A MSH research biorepository may take advantage of a single approach or multiple approaches to achieve its scientific mission. Once a research biorepository is established in support of one model, it may be easier to expand the infrastructure to include other models as needed rather than to initiate a new research biorepository from the beginning. This approach prevents duplication of efforts and allows more efficient utilisation of resources. Regardless of the model employed, biospecimens should always be collected and processed according to the most current methods supported by scientific data and best practices, where possible.

4.0 Tissue attainment service

A MSH research biorepository that provides tissue attainment services, or request-based services, collects and processes biospecimens for specific requests on an 'as needed' basis. Principal Investigators and Custodians must state what biospecimens they are seeking and frequently supply the SOP for collection, handling and storage. The MSH research biorepository attempts to collect biospecimens specifically for that request and process them according to the investigator's specifications. A research biorepository based on this model may not require long-term storage if the biospecimens will be transferred to the requestor within a short time after they are collected. Researchers initiating requests may not be able to follow patients/participants over time and must wait until the desired biospecimen has been obtained before testing can be initiated.

5.0 Tissue banking service

Banking involves the storage of biospecimens in anticipation of current and future needs. Researchers seeking a particular type of sample can approach a research biorepository that has banked biospecimens to see if the desired samples are available among the existing collections, please see Attachment 2 for a flowchart on this process. Banked biospecimens may be received into the research biorepository through agreements with clinical sites and/or hospitals.

Biospecimens are subjected to identical processing procedures using pre-defined processes to ensure standardised practices. Data associated with banked biospecimens may be limited to what is available at the time of collection. One particular type of banking activity may be initiated by advocacy groups to advance research for a particular disease. Donors and families may direct hospitals and other clinical sites to send their biospecimens to these banks or biospecimens may be donated through biospecimen collection containers sent from the donor's residence (termed a donor's 'self-collected' biospecimen). Advocacy-oriented banks often have associated registries containing detailed clinical and follow-up information. Samples and information from family members may also be associated with these banks.

6.0 Population-based collections

Research biorepositories that store biospecimen collections obtained for defined research project purposes are typically collected and controlled by Principal Investigators. Decisions about which biospecimens and data are collected are typically made by an individual investigator or team of investigators as defined by the scientific goals of the research project.

Population-based collections are generally obtained and processed by trained field staff, clinical sites or hospitals according to best practices. A research biorepository of this type may be represented by a single laboratory or represent storage and processing capabilities for a large number of studies as a part of centralised research biorepository services. These research biorepositories may be operated by institutional staff or through contracted research biorepository services.

7.0 Virtual repositories

Virtual repositories are ones that either store virtual depictions of biospecimens stored and analysed elsewhere or that represent ‘clearinghouses’ for biospecimens stored in repositories located elsewhere. Virtual depictions allow for new scientific questions to be addressed using biospecimens that have already been processed (eg slides containing tissues prepared for immunohistochemical analysis).

Clearinghouses for physical biospecimens allow investigators to take advantage of biospecimens previously collected either through banking efforts or other collection activities. Information about available biospecimens is provided in the form of a searchable electronic inventory that can be used to identify the desired biospecimens. The repository provides contact information for a researcher to communicate directly with the research project’s Custodian to learn of access SOPs required for the actual sharing of biospecimens. This type of repository allows investigators to be connected with resources that are currently available rather than having to initiate new collection efforts that can be time consuming and costly.

8.0 Research project specific collections

The research biorepository must document its acquisition process defining the biospecimens to be maintained and the criteria on which the acceptance of new biospecimen offer to the collection is based. This process should balance capability, capacity with scientific and user’s needs. Project specific collections should only accept deposits of biospecimen that meets its acquisition criteria and fall into the groups of its specialist expertise.

9.0 Recruitment

The research biorepository’s Research Protocol must clearly describe the recruitment strategy and criteria for selecting patients/participants. The biospecimen received must have the following information:

- name (where one can be applied), or other identifier or cell culture description
- depositor’s name and address and depositors biospecimen number or other collection number(s), if deposited elsewhere
- source, substrate or host from which the biospecimen was isolated or derived (where identified) and date of isolation
- geographical origin of material (the minimum requirement is the country of origin or the furnisher of the source, substrate or host)
- growth media and conditions, cell preservation or storage conditions where known
- hazard information (eg in the form of a safety data sheet).

10.0 Acquisition

10.1 Standard Operating Procedures (SOPs) and documents

SOPs must be in place for receiving biospecimens into the research biorepository. All biospecimens provided to the research biorepository from outside sources must be confirmed and a record of the receipt should be maintained by the research biorepository.

Where external tissue attainment occurs the HREC of the participating institution must have the MSH research biorepository's PICF approved prior to collection.

Documentation must include the date and time the biospecimens were received, the tracking number assigned by the courier service, inspection of package and container for visible signs of damage, confirmation of the condition of the coolant used during biospecimen transport, confirmation that biospecimens received match those listed on the manifest, and documentation of all problems or discrepancies.

If data loggers are enclosed in shippers, they should be checked to determine if adverse temperature spikes have occurred. Template forms documenting the above activities should be available and this can be modified as may be necessary. This form should identify the person making the entries (name/signature/date). Any problems encountered with a shipment should be communicated to the sender to aid in the prevention of similar problems in the future. Note should be made of the stability of the cold chain for specimens shipped in the chilled, vitrified and frozen state.

10.2 PQ AQIS - permit to import quarantine material

All imports may be subject to quarantine inspection on arrival to Australia to determine compliance with the listed permit conditions and freedom from contamination. Imports not in compliance or not appropriately identified or packaged or labelled in accordance with the import conditions they represent may be subject to seizure, treatment, re-export or destruction at the importer's expense, please see Attachment 5 - Australian Quarantine and Inspection Service (AQIS) Permit.

11.0 Use of diagnostic samples/pathology archives surplus to clinical requirements

Samples of biospecimen removed during treatment (eg surgical procedures), or leftover after diagnostic testing, and those stored in pathology archives can be of considerable value for research, and other purposes (eg teaching). The value of these samples is further increased if they can be linked to information on the patients/participants (ie age, medical conditions, treatment and outcomes).

The primary purpose of diagnosis or treatment must always take precedence over any secondary purposes. Many patients/participants expect their samples to be used for maximum effect to benefit others; adopting the position that it is better the material should serve some useful purpose other than simply being disposed of.

If researchers require access to diagnostic archives without consent in place for research, this should be conducted within the legal framework provided for this purpose, respecting the confidentiality of the patients/participants and mitigating the risks of not being able to obtain consent. The flowchart in Attachment 2 provides information on making decisions related to the use of existing collections of samples including diagnostic/pathology archives. Engaging the public on the use of surplus material for research is important to improve transparency and trust between patients/participants and researchers.

It is good practice to ensure that patients/participants are informed that their samples may be used for research once all clinical requirements have been fulfilled, for example in a surgical consent form or by a clearly displayed notice to that effect.

One approach is to routinely ask patients/participants undergoing procedures whether they would consent for research use of any excess material. It should be clear to patients/participants that refusal to allow surplus material to be used for research will not affect their treatment in any way. It is acknowledged that many routinely collected diagnostic/pathology samples held to date will not have consent for research in place, and that the law permits research use without consent in certain circumstances.