PROCEDURE

Metro South Health Research Biorepositories – Facility, Equipment, Storage and Security

PR2017/103
Version No. 2.0

PURPOSE

An efficient Metro South Health research biorepository has many particular design elements which ensures the safe keeping of the material stored, supports the equipment employed and provides a safe and effective working environment for personnel. This procedure describes requirements for facility, equipment, storage and security when operating a research biorepository in Metro South Health.

OUTCOME

Whilst research biorepositories must be operated in accordance with the Metro South Health 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 Metro South Health employees who have established or propose to establish a research biorepository and/or collect biospecimens for storage purposes from patients/participants
- all persons external to Metro South Health who propose to collect biospecimens from Metro South Health patients/participants and/or access biospecimens collected from Metro South Health patients/participants
- researchers who propose to access biospecimens stored within a Metro South Health research biorepository
- all personnel involved in all aspects of research biorepositories and biospecimen collections in Metro South Health.

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 Metro South Health Research Management and Research Biorepository procedures.

KEY PRINCIPLES

The following key principles guide Metro South Health research biorepositories in assessing their requirements for facility, equipment, storage and security. The way in which individual Metro South Health research biorepositories put these principles into operation may be scaled in relation to the research biorepository's size of operations.

- Research biorepository facility, equipment and storage requirements are dependent on the types of material being stored, the required storage and handling conditions, the projected retention periods, projected growth of the biospecimen numbers, and the projected use of the materials.

- A Custodian and/or director must ensure sufficient space is available to accommodate the material planned for initial, future and backup storage and provide for the safe movement of people, equipment and biospecimens, as needed or as required by law and/or other regulatory agencies.
- Research biorepositories should aim to have dedicated facilities where possible that are not shared with other activities however it is acknowledged that this may not always be possible in some circumstances. Sufficient air conditioning must be provided for air circulation and to maintain conditions to prevent excess freezer wear and early failure.
- Research biorepositories require a constant source of electrical power. Given that all commercial power will fail at some time, a backup power system is required. Such a system should have the capacity to run for sufficient time to allow the restoration of power supply (typically 48–72 hours) and must be regularly tested.
- Research biorepositories must be equipped with a system that adequately limits access to appropriate staff and protects against physical intrusion. In principle, only persons assigned to the research biorepository operation should have access to the material, and all materials added to or withdrawn should be documented.
- Biospecimens must be stored in a stabilised state. In selecting the biospecimens' storage temperature, Custodians must consider the types of biospecimen, the anticipated length of storage, the biomolecules of interest and whether goals include preserving viable cells. Some other conditions should be considered such as humidity level and light etc.
- Adequate, fit for purpose equipment must be available to allow for the safe and ergonomic deposit and retrieval of individual samples from fridges and freezers etc. Examples of this equipment might be (but not limited to) a mobile table/platform, cold resistant gloves, adequate eye/face protection. Please see Section 1.0 Facility below for more information.
- Automated security alarm systems must be in place to continuously monitor the function of storage equipment and should have the capability to warn resource personnel when equipment failure has occurred. Backup equipment, such as an alternative power source, should be set to activate automatically when necessary and should be tested regularly.
- Alternate cooling sources also might be needed in some cases. Written Standard Operating Procedures (SOPs) that are tested on a routine basis must be in place to respond to freezer failures, weather emergencies, and other disaster recovery/emergency situations.
- Biospecimens must be stored in a secure location with limited access only by authorised personnel.

LEGISLATION OR OTHER AUTHORITY

Legislation

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

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
- Organisation for Economic Co-operation and Development (OECD): Best Practice Guidelines for Biological Resource Centres
- World Health Organisation (WHO): Common Minimum Technical Standards and Protocols for Biological Resource Centres Dedicated to Cancer Research

Metro South Health policies, procedures, manuals and frameworks

- Metro South Health Research Management Policy (PL2017/55)
- Procurement Policy (PL2015/44)
- Risk Management Policy (PL2013/06)
- Integrated Risk Management Framework
- Risk Assessment Tool

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 Metro South Health research biorepositories.

Centres for Health 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 Metro South Health Research Biorepository Governance Framework.

Metro South Health Research Biorepository Strategic Oversight Committee

Provide clarification and assistance in facility, equipment, storage and security requirements for the collection of biospecimens for each research biorepository.

Custodian/Principal Investigator – responsible officer

Ensure the research biorepository's facility, equipment, storage & security arrangements are in compliance with the Metro South Health Research Biorepository Governance Framework and appropriate for the type of biospecimens collected.

Research biorepository manager

Maintain and monitor all facility, equipment, storage and security requirements on behalf of the research biorepository and report any matters which require action to the Custodian.

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 Metro South Health patients/participants are performed in accordance with the Metro South Health Research Biorepository Governance Framework and applicable SOPs.

SUPPORTING DOCUMENTS

Attachment 1 - Application

Attachment 2 - Maintenance and Calibration Requirements for Equipment Commonly Used in Research Biorepositories

Attachment 3 - Facility, Equipment, Storage and Security Checklist

DEFINITIONS

See the Metro South Health Research Biorepositories Glossary

PROCEDURE - FACILITY, EQUIPMENT, STORAGE AND SECURITY

STEP 1: Facility identification

The Custodian must ensure the Metro South Health research biorepository is housed in an appropriate facility which considers heating, ventilation, air conditioning, lighting and backup power requirements.

STEP 2: Equipment identification

The Custodian must identify required equipment and storage equipment requirements prior to establishing a research biorepository in Metro South Health. Please see Establishment of a Research Biorepository Procedure (PR2017/100) for more information.

Storage vessels should be stable under planned storage conditions. Biospecimen containers should be chosen with analytical goals in mind and evaluated prior to use to ensure that contamination or chemical leaching into the biospecimen does not occur. Vial size and number should be suitable for typical aliquots and anticipated investigator uses. Optimal volume and type of containers may prevent sample loss and minimise the costs of collection, storage, and retrieval.

Screw-cap cryovials may be used for long-term, low-temperature storage; glass vials or vials with popup tops are unsuitable for long-term storage. Snap-frozen biospecimens should be wrapped in aluminium foil or placed in commercial storage containers to minimise desiccation. Labelling and printing systems should be chosen for stability under the long-term storage conditions appropriate for the biospecimen. Face shields and appropriate gloves should be worn for worker protection.

STEP 3: Procurement of equipment

Prior to purchasing or procuring equipment, including storage equipment, the Custodian must consult with the Metro South Health Research Biorepository Strategic Oversight Committee to investigate the potential to house samples in current storage facilities. If the Custodian is supported in purchasing a new piece of equipment Metro South Health procurement policies and processes apply (Procurement Policy PL2015/44).

STEP 4: Maintenance, repair and replacement

Research biorepository managers must monitor and plan for equipment maintenance, repair, calibration and replacement. The Custodian and research biorepository manager are responsible for all equipment which is housed within a research biorepository or as part of a biospecimen collection.

Before new equipment is purchased, if it is unable to be repaired or replaced, the Custodian must contact the Metro South Health Research Biorepository Strategic Oversight Committee to ascertain if alternative storage arrangements can be accommodated within pre-existing equipment and facilities.

STEP 5: Security systems

The Custodian and research biorepository manager must ensure appropriate security systems are implemented including:

- restriction and monitoring of access
- intrusion detection systems
- biosecurity measures
- response alarms

Security systems must be monitored and alarms responded to twenty-four hours per day, seven days per week.

STEP 6: Backup

Adequate backup capacity for low-temperature units must be maintained. Please see Emergency Preparedness and Work Health and Safety Procedure (PR2017/108) for more information.

STEP 7: Self-audit, review and compliance

Utilise Attachment 3 - Facility, Equipment, Storage and Security Checklist to aid in self-auditing, review and compliance.

PROCEDURE DETAILS

Procedure Number
PR2017/103

Procedure Name
Metro South Health Research Biorepositories - Facility, Equipment, Storage and Security Procedure

Policy Reference
PL2017/53
Metro South Health Research Biorepositories Policy

Supersedes
Version 1.0

Procedure Author
Erica Wright, Project Manager, Research Development, Centres for Health Research, Metro South Health

Portfolio Executive Director
Professor Timothy Geraghty, Chair, Centres for Health Research, Metro South Health

Approving Officer
Dr Michael Cleary, Executive Director, PAH-QEII Health Network, Metro South Health

Approving Date
02 July 2018

Effective From
02 July 2018

Date of Last Review
05 July 2018

Date of Next Review
02 July 2021 (within the next 3 years)

ATTACHMENT 1 - Application

1.0 Facility

A Metro South Health research biorepository's infrastructure depends upon the types of biospecimens being stored, the required storage conditions, the projected retention periods and the projected use of the materials. It is the responsibility of the entity which comprises the research biorepository to provide an environment that is conducive to handling micro-organisms, for example, free from contamination.

1.1 Heating, ventilation and air conditioning

1.1.1 Temperature and humidity

In most research biorepositories it is critical to maintain ambient temperature within defined limits. Sufficient heating capacity must be provided to prevent the freezing of water in drain lines. Likewise, sufficient air conditioning must be provided to prevent excess load on the compressor systems of mechanical freezers and refrigerators that may result in excess wear and early failure. Humidity level restrictions may need to be considered when storing at ambient conditions.

For optimal life of the mechanical refrigeration equipment, research biorepository ambient temperatures must be monitored and maintained at a temperature that is within manufacturer's specifications. This is particularly critical for rooms containing multiple mechanical units.

1.1.2 Air flow and circulation

Sufficient air circulation must be provided to prevent excess moisture and condensation. Excess humidity can lead to fungal growth if left unchecked, which may affect biospecimen integrity and cause health problems for staff. Sufficient space for air circulation is required especially in areas where freezers and refrigerators are employed to prevent excess heat accumulation which may negatively affect compressor function.

Adequate ventilation and monitoring are also critical in research biorepositories where liquid nitrogen (LN_2) and dry ice are used to ensure that sufficient oxygen levels are maintained. Similarly, when services are performed in which potentially harmful vapours are generated (eg formaldehyde) the ventilation system should ensure that personnel are protected and that regional and national standards for the removal of specific harmful vapours are met.

Rooms that contain LN_2 tanks must be equipped with appropriate air flow systems coupled to an oxygen level alarm system to avoid the accumulation of N2 in case of leakage. It is recommended that appropriate monitoring devices (eg oxygen and CO2 monitors) and exhaust systems are installed within areas where there is the potential for a low oxygen level to develop or harmful vapours to accumulate.

1.2.3 Environmental monitoring systems

Acceptable temperature ranges must be determined for any biospecimen storage equipment that is designated for operation at a particular temperature before the equipment is put into service. Temperature ranges allow for normal operating variations and provide some variation for warming when the material is accessed. It is important to understand that temperature probes measure the temperature where the probes are located; therefore different locations in the equipment might exhibit different temperatures depending on the size and age of the unit as well as other factors.

Also note, freezers and refrigerators that are full will likely display temperature readings that are different from readings taken when the equipment is empty. Once placed in service, daily and continuous monitoring practices and systems must be used for evaluating the performance of all fixed temperature storage units. Storage units with defined environmental conditions must have temperature-monitoring devices that can be visually inspected on a regular basis (eg a chart recorder or unit controller display).

In addition to regular temperature monitoring activities performed by research biorepository staff, an automatic temperature monitoring system must be utilised that continually monitors temperatures of all critical equipment and other important parameters, creates logs, generates audit trails and generates alarms to notify personnel trained in emergency preparedness to respond. An option to have an audible alarm for those individuals physically present in the research biorepository can be beneficial as well.

The alarm notification system must call or page the individual 'on call' (or should activate the 'on call' list) rather than simply providing passive notification (eg provide computer generated notification which is monitored by staff). This call should continue down the list of contacts until it is acknowledged.

Depending on the size of the research repository and number of staff available, more than one individual should be available at all times, in case the first individual is in a location where they cannot receive or respond to the notification. Alarm conditions should be responded to in a time frame that minimises the likelihood of damage to the stored material. Research biorepository management must assure that personnel with adequate training who can take corrective action should be available or reachable twenty-four hours per day; seven days per week.

One additional method for automated temperature monitoring involves the connection of thermocouple wires from the 'dry' temperature contacts to the building security system. The wires may be run from one freezer to the next to minimise the number of wires and the length of wire needed. The alarm point for these probes should be set a few degrees higher than the alarm point of the automatic monitoring system. An alarm obtained through this type of backup system will not indicate which unit is in alarm, but will provide additional backup if a failure occurs in the monitoring system.

Visual inspection of equipment temperatures must be performed regularly (at least three (3) times a week) and a record kept of the temperatures observed. Temperature records must be verified by supervisors on a monthly basis. In addition to monitoring the current equipment conditions, regular recording and review of temperatures provides a way to spot trends which may provide an indication of degraded performance or incipient failure.

Temperatures must be monitored during extended periods of freezer access to ensure that safe temperature ranges are not exceeded. Attention should be given to the fact that warming may not be immediately reversed by closing the freezer or refrigerator.

When possible, a temperature profile of the freezer or refrigerator must be performed prior to its initial use so that warm and cold spots that could be problematic for material storage can be identified.

In Metro South Health research biorepositories, where samples are stored in the vapour phase of liquid nitrogen (LN_2), staff must regularly employ a technique whereby a physical measurement of the LN_2 level is taken with a tool such as a dipstick to confirm the LN_2 level. Alternatively, probes may be placed at various levels in the freezer to monitor LN_2 levels (eg temperatures below minus 196ºC indicate that the probe is submerged in LN_2 and temperatures warmer than -196ºC indicate that the probes are in the vapour phase of the chamber). If a tool is used to measure liquid levels it should be treated with ethanol, bleach or other disinfectants for the purpose of disinfecting the tool before and after it is used.

Alarms must be tested on a regular basis (eg weekly or monthly) to ensure proper functioning and call-out to pagers and other notification devices used by staff that are ‘on call’. In research biorepositories that use an automated environmental monitoring system, periodic review of temperature profiles or trends should be employed to ensure consistency between the controller display values and the environmental monitoring system values. This practice will allow staff to proactively evaluate each unit’s performance and determine if any maintenance work is needed.

1.2 Lighting

1.2.1 General lighting

Lighting in a Metro South Health research biorepository must be sufficient to provide a safe working environment and to allow materials to be accurately put away and retrieved. The lighting levels required will depend on the particular spatial environment where the samples are stored, the type of activity that is being performed, the volume and biospecimen type, and the labelling/identification system employed.

Lighting may be both general and task, depending on the situation. General area lighting may be incandescent, fluorescent, metal halide or another appropriate source. Some research biorepositories may contain materials or biospecimens which are sensitive to light levels or to particular frequencies of light. Appropriate lighting should be planned for and used during the storage and handling of materials or biospecimens determined to have sensitivities to certain lighting conditions.

1.2.2 Task lighting

Task lighting may be necessary to have sufficient illumination for tightly packed materials, reading labels, or where overhead lighting is impaired. In situations where task lighting is employed, care should be taken that the lighting method does not adversely affect the sample integrity and the storage conditions. For example, the heat from incandescent lighting placed too close to stored material may cause a sample to thaw or partially thaw. Fluorescent lighting or another type of lighting that does not create a source of heat is recommended for use in task lighting near frozen materials.

1.2.3 Emergency lighting

In case of power loss, it is critical that emergency lighting be available to indicate exit routes from the research biorepository and to provide an illuminated, safe environment to aid in monitoring equipment and responding to the needs of the emergency. Emergency lighting must have battery backup support and should be tied to backup generators. It may be beneficial to use small night lights that plug into outlets that have a battery component for low level illumination. Research biorepositories should also have portable lighting (eg flashlights) on hand to use as focused light sources, as needed. Focused light sources can be essential during an emergency for use in equipment diagnosis and repair. Emergency lighting should be tested on a regular basis and batteries checked on an annual basis and replaced as needed as a part of the overall safety and maintenance SOPs.

1.3 Flooring

Flooring surfaces used in research biorepositories must be appropriate for the equipment and refrigerants used in daily research biorepository activities. Flooring should be easy to clean and facilitate the movement of equipment when circumstances warrant. Special consideration must be given to the flooring in regions where LN_2 is used, as vinyl tile will crack and cause a hazard if LN_2 is spilled directly onto it. Research biorepositories should consider providing anti-fatigue mats for staff in areas where personnel stand for prolonged periods of time.

1.4 Backup power

1.4.1 Uninterruptible power supply

An Uninterruptible Power Supply (UPS), uninterruptible power source or sometimes called a ‘battery backup’ maintains a continuous supply of electric power to connected equipment when utility power is not available.

A UPS may be inserted between the source of power (typically commercial utility power) and the load it is protecting. When a power failure or abnormality occurs, the uninterruptible power supply will effectively switch from utility power to its own power source almost instantaneously.

Computer systems and electronic systems, such as environmental monitoring systems, safety systems (eg oxygen sensors, ventilations systems) or controllers for LN_2 freezers, should be protected by an uninterruptible power supply. Uninterruptible power supplies used in research biorepositories must be tested on an annual basis to ensure their proper backup capabilities.

1.4.2 Generators

The most common type of backup power is a motor generator. Generators have automatic controls that cause them to produce electricity when commercial power is interrupted.

A generator should have a fuel supply to run continuously for a minimum of forty-eight (48) hours and preferably a minimum of seventy-two (72) hours, with an ability to re-fill fuel storage supplies. Metro South Health research biorepositories that utilise generators must have an established plan for sources to replenish fuel supplies in case of an emergency. This plan should include lists of suppliers and backup suppliers committed to provide the fuel as needed. Research biorepositories should contact suppliers to be placed on a list as an entity that receives a quick response should an emergency situation arise.

1.4.3 Generator tests

To ensure the likelihood that backup power systems will function reliably when needed, they should be routinely tested to ensure that the system will start on demand and carry the required load. Load tests should be performed to ensure that the generator can function within specifications under full load. Additionally, for facilities that have bulk diesel storage, annual testing and filtering of the fuel should be performed to ensure that excessive water or bacterial build-up which can affect performance of the generators has not occurred.

The power generator system should be included in a frequent preventative maintenance plan, which includes weekly testing for automatic starting and power generation and load tested monthly. If load testing places sensitive equipment at risk, the generator should be tested less frequently. Those systems that have an automatic transfer switch should also be tested on a periodic basis (eg every six (6) months). Staging of the sequence of start-up of mechanical freezers and other systems should be considered to ensure sufficient downtime to allow the compressors to come to rest before restart.

1.4.4 Institutional emergency systems

Research biorepositories located in or associated with larger facilities (eg hospitals or universities) that automatically initiate backup power upon power interruption must link their freezers and other essential equipment into these emergency systems. The operational safety and testing must be performed by professional caretakers of the larger infrastructure (eg Metro South Health or the Translational Research Institute).

1.4.5 Construction and operation

Construction must respect the containment level appropriate for the risk group of the micro-organisms work with. If major building, renovation or repair work, or other work that is likely to compromise containment or clean conditions, is necessary in research biorepositories, normal activities should be suspended until the building renovation or repair work is completed.

2.0 Equipment and storage conditions

The variety of storage systems available for biospecimen collections continues to expand as technologies advance. Storage equipment selections must be based on the type of biospecimens to be stored, the anticipated length of time the biospecimens will be stored, the intended use for the biospecimens and the resources available for purchasing the equipment. Also important are the size and physical design of the research biorepository and the number of biospecimens stored (as well as predictions for future growth in number of biospecimens stored). Some freezers and refrigerators now provide automated sample entry and retrieval components which may reduce long-term costs for the research biorepository. Often these larger systems are accompanied by increased initial costs which may be more than smaller research biorepositories can support. Equipment selections should take into consideration staffing requirements, quality issues, available resources and equipment support and maintenance. As costs for maintaining research biorepositories have continued to rise, every effort must be made to keep the costs for operating equipment to a minimum. Recent developments in energy-efficient equipment can generate significant savings on facility costs.

2.1 Liquid nitrogen freezers

The use of liquid nitrogen (LN_2) freezers for long-term biospecimen preservation is optimal for the storage of some types of biospecimens, provided that the critical temperature for storage of those materials is not exceeded. Cryogenic storage using LN_2 is an effective long-term storage platform because the extreme cold slows most chemical and physical reactions that cause biospecimens to deteriorate and because on-site LN_2 supplies reduce reliance on mechanical freezers that use electrical power.

While LN_2 storage has been traditionally reserved to containers that either hold LN_2 in the base of the freezer or which hold enough liquid for biospecimens that are submerged in LN_2, equipment is now available that allows for LN_2 to be used as a coolant to allow for storage temperatures in the -80°C range. This type of cooling may have the advantage of being able to cool biospecimens in the event of a power failure. A comprehensive assessment of available choices in equipment design needs to be made prior to making any new purchases.

2.2 Vapour or liquid storage

When considering storing in LN_2 vapour phase (≤ -150°C) vs submersion in liquid phase (-196°C), vapour phase storage is preferred because it provides sufficiently low temperatures to maintain samples below the Tg (Glass Transition Temperature; -132°C) while avoiding the safety hazards inherent in liquid phase storage. Many commercially available vials are penetrable by liquid nitrogen so vials selected for storage should be tested before they are used. Certain containers, like cryogenic straws, are hermetically sealed and specifically designed for the safe storage of biospecimens in the liquid phase of nitrogen.

2.3 Storage containers

LN_2 expands 700 to 800 times its original volume when brought to a gaseous phase at room temperature. This situation may produce an explosion hazard. Glass, metal and some plastic containers can explode if LN_2 is trapped inside the container when it is removed from the freezer. Any container used or stored at cryogenic temperatures must be rated for these temperatures.

2.4 Liquid nitrogen supply

Where LN_2 refrigeration is employed, an adequate supply of LN_2 must be maintained. For freezers filled from Dewars or supply tanks, a minimum three-day supply of LN_2 at normal usage and replenishment intervals should be maintained, with the assumption that a re-supply is readily available. Bulk supply systems should maintain at least three (3) days' working capacity. Bulk supplies should be checked for re-supply at least once a week. A telemetry system may be installed to allow suppliers to monitor liquid levels in real time to ensure stocks do not drop below agreed upon levels.

Bulk storage and piping systems require relief valves to prevent rupturing of the pipe and bulk tanks in the event of over-pressure. If relief valves trip unexpectedly, a person near a valve can be sprayed with either the cold gas or the liquid. More likely, in the event of a blockage or excessive pressure, several relief valves may vent nearly simultaneously. This can cause a 'whiteout' condition in a matter of a few seconds. Visibility can drop to near zero and oxygen levels in the area may become less than that necessary to sustain life. Under these circumstances personnel should evacuate immediately. For this reason, oxygen (O2) monitoring must be installed in any areas of the facility where bulk LN_2 is utilised. Daily LN_2 usage should be recorded either by monitoring the display levels or by manual means as excessive LN_2 usage can indicate problems with the vacuum component of the freezer.

2.5 Oxygen sensors

Because nitrogen displaces oxygen, care should be taken when LN_2 freezers are employed. The risk is inversely correlated with the size of the room. Oxygen level sensors must always be employed when LN_2 freezers are used in a research biorepository. Normal levels of oxygen in ambient air must be ~21%. Most installed oxygen sensor units have batteries or sensor cells that should be replaced and re-calibrated every few years. Consult the manufacturer for recommended requirements.

Both fixed and mobile/personal monitors may be appropriate depending on the size of the facility. Even when installed units indicate an alarm condition, it may be useful to employ a personal monitor to enter the room carefully to validate the alarm condition if the area is not visible from the outside. Mobile oxygen monitors may be the best to use in a secure area where LN_2 freezers operate because the sensors in installed units will degrade over time and sound false alarms.

2.6 Mechanical freezers

Mechanical freezers are employed in a variety of storage temperature ranges, including -20°C, -40°C, -70°C to -80°C, and -140°C, and come in a wide variety of sizes, configurations, and electric voltages. Because these are devices attached to commercial power systems, a backup power plan and emergency response plans must be in place. Freezers must be equipped with alarms set at about 20°C warmer than the nominal operating temperature of the unit.

The length of time that results in the significant warming of the stored material will vary by the properties of the stored material, the temperature of the material stored in the freezer, the ambient conditions and the design and maintenance of the unit. It is the responsibility of the research biorepository manager to establish and enforce the critical temperatures and response times to alarms.

Adequate back-up capacity at standby is needed. Some mechanical freezers are equipped with emergency backup systems that automatically cool their contents with either LN_2 or liquid carbon dioxide (CO_2) in the event of an extended power loss. Any freezer implementing this type of emergency backup cooling system should be specifically designed to accommodate whatever coolants are utilised and adequate supplies of refrigerant gas should be kept on hand at all times to operate the system. Safety precautions with the backup system (O_2 or CO_2 monitoring systems) should be taken into consideration in the event of an emergency situation.

Independent of backup cooling solutions, efforts must be made to ensure that freezers (as well as refrigerators) are positioned in research biorepository locations to allow for adequate air flow. Insufficient distance between units or between units and walls may lead to overheating of compressors that may shorten compressor life. In addition, inadequate air circulation may lead to the growth of mould and other harmful microbial contamination situations.

2.7 Refrigerators

Refrigerators are commonly employed where the longevity of the material being stored is enhanced by storage below ambient temperature. This is the preferred storage medium when the material should be kept cool, but does not require freezing. Refrigerators may also be used for storage of media and additives. It is important to ensure that the temperature is maintained within the specified operating range, not just below a maximum temperature. Some high value materials should be maintained precisely between 2°C and 8°C. The research biorepository manager must ensure that temperatures are monitored.

2.8 Ambient temperature storage

Recent developments have allowed for the identification of biological storage matrices that allow for long-term maintenance of certain biological components at room temperature. These matrices have been used for the storage of RNA and DNA and soon are expected to be available for other biological materials. They may be helpful when mechanical or cryogenic equipment is not available or may serve as an alternative method for back-up storage for some material types. Prior to implementation, all matrices must be evaluated by the research biorepository manager to be sure that they are appropriate for downstream applications. Storage cabinets for ambient-temperature storage of biospecimens can be equipped with passive or active humidity controls to maintain biospecimens preserved at ambient temperature. These storage cabinets can be fully integrated with automation and robotic controls as well as tracking and sample management software.

2.9 Dry ice

Dry ice or solid-phase carbon dioxide is frequently used as a refrigerant for shipping and emergency backup for mechanical freezers. Handling precautions must be employed when handling this material, which exists at a nominal -70°C. As dry ice sublimates, the CO2 level in the surroundings can increase. In confined areas the carbon dioxide can displace oxygen, presenting an asphyxiation hazard.

2.10 Walk-in environmental storage systems

2.10.1 Compressors

For the storage of valuable materials, walk-in refrigerators and freezers should be equipped with dual compressors that operate under an electrical alternating control system.

2.10.2 Door release

Metro South Health requires that walk-in units have internal safety releases to prevent a person from being trapped within a unit by the accidental closing of doors (eg interior door release mechanism).

2.10.4 Floor covering

Refrigerators can generate slipping and falling hazards if water condenses on the floor. Freezers can occasionally create ice on the floor, or water if the unit is defrosting.

Some type of mat or grate must be placed in front of these types of units to prevent slipping. A warning sign must be posted at the entrance of walk-in cold storage areas advising that the area may be slippery.

2.10.5 Dry ice

Walk-in freezers must be kept free of dry ice (ie the solid phase of CO2). Carbon dioxide can rapidly build-up, displace the oxygen in the room, and cause personnel working in the units to lose consciousness. In confined areas the CO2 can displace oxygen, presenting an asphyxiation hazard. Where dry ice is employed there must be adequate ventilation to ensure that sufficient air or oxygen levels exist. In these circumstances, it is recommended that walk-in freezers have both oxygen and CO2 monitors.

2.10.6 Motion detection devices

Because of the special hazards involved in personnel working in a -20°C or colder walk-in environment, it is desirable that some form of monitoring system be employed. This is especially applicable if only one person is working in the freezers. Systems which detect and alarm when motion does not occur are readily available (such systems are commonly employed by firefighters and other emergency personnel.)

For a -20°C or colder walk-in environment engineering controls may be designed to support an audible alarm system coupled with a safety procedure to allow for the safest operating conditions.

2.10.7 Contamination issues

Contamination by fungus can frequently develop in cold rooms. This is facilitated by storage of non-biospecimen materials in containers such as cardboard boxes. It is, therefore, important to periodically survey the cold area to eliminate factors (eg damp, unclean areas, cardboard boxes) that can facilitate fungal growth. Similarly, it is not appropriate to use cold rooms to store hazardous or flammable material, or food. Periodic monitoring of cold rooms should be encouraged to visually monitor for fungal contamination and for items that may be inappropriately stored.

2.11 Purchasing and procurement from vendors

Familiarity with purchasing as well as the overall procurement process can help support best practices; decrease errors in purchasing and product selection; streamline workflow; decrease lags in ordering/purchasing; and increase awareness of institutional documentation requirements, purchasing limitations, and rules. When possible, evaluating multiple vendors for equivalency will reduce the impact to business continuity, for example, if a vendor needs to be replaced or augmented. Please see Procurement Policy (PL2015/44) for more information.

3.0 Equipment maintenance, repair and replacement

A system for preventative maintenance and repair of storage equipment, supporting systems and facilities must be in place. System maintenance must be performed at regular, established intervals per

manufacturer's recommendation. Equipment exposed to infectious (or potentially infectious) materials must be properly disinfected. The choice of disinfectant to be used depends on the particular situation.

Some disinfectants have a wide spectrum (kill many different types of microorganisms), while others kill a smaller range of disease-causing organisms but are preferred for other properties (they may be non-corrosive, non-toxic, or inexpensive). For example, bleach should not be used on stainless steel as it can result in pitting of the metal and damage to the equipment.

3.1 Calibration

A system for the calibration of all instruments must be in place. Any device that provides analogue or digital measurements is considered an instrument and requires calibration. Calibration must be done annually or per manufacturer's recommendation. Calibration must be performed against Australian standards. Calibration records must include the appropriate standard readings taken both before and after calibration. A log of calibration records must be kept that includes the date of the calibration, the name of the individual performing the calibration, the name of the device used against which the instrument is calibrated, and a reference to the SOP used to perform the calibration. Please see Attachment 2 for more information on Maintenance and Calibration Requirements for Equipment Commonly Used in Research Biorepositories.

3.2 Verification of equipment functionality

The proper performance of all equipment must be verified or qualified prior to use or following repairs that affect the instrument's measuring capabilities. Documentation of the testing must be maintained and made available for audits. The Custodian must ensure that all required regulatory practices are implemented.

3.3 Equipment preventative maintenance and repair

Essentially all equipment comprised of multiple components wears out with time and exposure to various environmental conditions. The duration of the lifetime for equipment used in the research biorepository may be significantly extended by performing routine assessments and modifications to the equipment according to the manufacturer's specifications. For mechanical freezers this may include a periodic changing out of fluids, cleaning of filters, calibration of probes, or manually removing ice from the tops and sides of the interior chamber of the freezer. Routine maintenance recommendations must be determined before a piece of equipment is put into service. Frost-free freezers should be avoided, since the daily heating cycle built into the doors of these models will gradually cause deterioration/desiccation of biospecimens stored near the doors and walls of the unit.

Maintenance records must provide a description of the cause of the equipment failure (where possible), the date on which the incident occurred and was observed (these dates may be different), the corrective action that was taken, tests that were performed to verify proper functioning of the equipment, and the results compared to available standards and manufacturer recommendations.

Well-qualified personnel with expertise in monitoring and repairing research biorepository equipment (especially freezers and refrigerators) must be used for regular and emergency repairs. These trained technicians may be on the research biorepository staff, may be on staff within the larger organisation within the institution in which the research biorepository resides (eg Translational Research Institute), may be available through a 'fee for service' arrangement with a commercial entity with this expertise, or repair services may be obtained from a similar entity on a retainer basis.

Research biorepositories should maintain spare parts for critical equipment, especially for aging equipment for which parts may not be readily available.Equipment management SOPs including use, control of performance, maintenance and calibration should be laid out in a predefined schedule. Instructions for these activities must be laid out in the manufacturer's handbooks/manuals or in research biorepository SOPs.

3.4 Repair vs replacement

While most manufacturers of research biorepository equipment offer projections for the expected lifetime of that equipment, actual lifetimes vary depending on a variety of factors including preventative maintenance, availability of replacement parts, environmental conditions in the area in which the equipment is located etc. For example, manufacturers of mechanical freezers offer projections of lifetimes that range from 8-12 years, but actual lifetimes might run for a period of 5 to 15+ years. LN_2 freezers may have lifetimes extending through 10 to 35 years.

Long-range plans must be made to address the possible repair and replacement of equipment essential to the functioning of the research biorepository. When multiple repairs are required, the additional cost of making those repairs may lead to a decision to have the unit replaced. Since replacement of freezers and refrigerators can be expensive, it is best to anticipate these costs and have some financial reserves available to address this when decisions to replace equipment are made. Service records must be maintained and copies of key documents must be held in the research biorepository Equipment Maintenance and Calibration Log books in the care of the person responsible for quality management.

Metro South Health research biorepositories must plan for the orderly replacement of equipment. If multiple pieces of the same equipment need replacement at one time, it might be best to use interim equipment or backup equipment while introducing the new equipment in over time. This allows for a gradual introduction of new equipment so that likely repair and replacement schedules are likely to be staggered.

Resources for equipment repair and replacement should be identified when the research biorepository is being established before an emergency is experienced. These resources should be reviewed on an annual basis. See Establishment of a Research Biorepository Procedure (PR2017/100) for more information.

Before new equipment is purchased in Metro South Health, the Custodian must contact the Metro South Health Research Biorepository Strategic Oversight Committee to ascertain if alternative storage arrangements can be accommodated within pre-existing equipment and facilities. If new equipment is required an evaluation must be performed to identify the most energy-efficient equipment that effectively addresses the needs for that equipment. Attention should be given to the expected life of the equipment (eg mean time between failures).

3.5 Maintenance and inspection

Cleaning of laboratory benching and equipment must be performed by authorised and trained personnel using appropriate personal protection equipment and following documented SOPs. A contamination monitoring program must be in place to include environmental monitoring of laboratory air and surfaces. If a major contamination problem arises in the research biorepository the research biorepository manager is responsible for implementing a cleaning program and an investigation of the source of contamination. Details of decontamination processes must be located in a SOP. Quality audit and quality review should also be carried out. Please see Quality Management System (Assurance and Control) Procedure (PR2017/110) for more information.

4.0 Security

4.1 Access

Metro South Health research biorepositories must be equipped with a system that adequately limits access to appropriate staff and protects against physical intrusion from unauthorised individuals. Doors must be locked. Keys should be controlled, with a record maintained of each person having access to the research biorepository and/or freezer location. Some research biorepositories may employ magnetic locks which control and record entry. Only persons assigned to research biorepository operations should have access to the material stored within. Freezers or environmental storage equipment that store valuable or sensitive biospecimens should be individually locked. Mechanical keys employed in a research biorepository should be ones that cannot be readily duplicated. Research biorepositories must also give consideration to general security areas, restricted security areas and high security areas depending on their biosecurity risk assessment.

4.2 Visitor access SOP

An access SOP must be developed for individuals visiting the research biorepository. Where feasible and appropriate, sign-in sheets or log books should be used to record the name, affiliation of the visitor, purpose of the visit, as well as track the time at which the visitor(s) enters and leaves the research biorepository. Badges can be made available for the visitors that clearly indicate to staff that they have been formally received and their presence documented. Visitors should be accompanied by staff at all times during their visit. When written or electronic records of research biorepository visitors are maintained, the records should be maintained and archived according to the research biorepository's established archive practices.

4.3 Security systems

Storage facilities and instruments must be monitored and supported by appropriate alarm systems. Every Metro South Health research biorepository must employ basic security systems to ensure protection of the biospecimens stored therein. The systems must be monitored and alarms responded to twenty-four (24) hours per day, seven (7) days per week.

Response systems must be in place to ensure that a responsible individual can take the necessary action to respond to an alarm in a timeframe that prevents or minimises loss or damage to the collection materials. Systems should allow for calls to other key staff from a list of staff phone numbers if the first individual fails to acknowledge the alarm.

Adequate backup capacity for low-temperature units must be maintained. The total amount of backup storage required for large research biorepositories must be determined empirically, but will typically be 5%– 10% of the total freezer capacity. Please see Emergency Preparedness and Work Health and Safety Procedure (PR2017/108) for more information.

4.4 Intrusion detection systems

When either the research biorepository or the building in which it resides is not occupied by authorised personnel, a system must be in place to detect unauthorised entry. Motion detectors, glass break and door entry sensors should be integral components of the system. As appropriate, the system should accommodate changes to security codes and keys when individuals leave the organisation.

4.5 Biosecurity

The term ‘biosecurity’ refers to precautions that should be taken to prevent the use of pathogens or toxins for bioterrorism and biological warfare. Securing pathogens and toxins at research and diagnostic laboratories cannot prevent bioterrorism but can make it more difficult for potential terrorists to divert material from a legitimate facility so as to build a biological weapon.

The scope of laboratory biosecurity is broadened by addressing the safekeeping of all valuable biological materials, including not only pathogens and toxins, but also scientifically, historically and economically important biological materials such as collections and reference strains, pathogens and toxins, vaccines and other pharmaceutical products, food products, Genetically Modified Organisms (GMOs), non-pathogenic microorganisms, extra-terrestrial samples, cellular components and genetic elements.

Laboratory biosecurity measures should be based on a comprehensive programme of accountability for valuable biological material that includes: regularly updated inventories with storage locations, identification and selection of personnel with access, plan of use of valuable biological material, clearance and approval processes, documentation of internal and external transfers within and between facilities and on any inactivation and/or disposal of the material.

Likewise, institutional laboratory biosecurity SOPs must include how to handle breaches in laboratory biosecurity, including: incident notification, reporting protocols, investigation reports, recommendations and remedies. Adoption of these security requirements is important for research biorepositories maintaining pathogenic or toxic biospecimens.

4.6 Biosecurity risk assessment

Research biorepositories must ensure a detailed inventory of the different biospecimens they hold is available. A risk assessment of the biospecimens must be conducted for the purpose of assigning such materials to biosecurity risk level, which may be assigned as high, moderate, low or negligible. The level of biosecurity risk of biospecimen should be determined according to the best available information on its potential for malicious misuse (including economic consequences) as well as virulence. Risk assessments should address potential of biospecimens, should they be obtained and misused by unauthorised persons, to cause harm to the health of humans, crops, livestock or infrastructure.

The provision of biosecurity should be regarded as a benefit to society at large. The burden of risk analysis should thus be shared collectively by Metro South Health research biorepositories and the broader scientific community. Research biorepositories should engage and work together to develop expert networks that can contribute to the provision of risk analysis.

Research biorepositories should share their experience with other research biorepositories as results of qualitative risk assessment and the reasons for assigning the biosecurity risk level of a particular biological material, and make all such documentation available to competent national authorities.

Research biorepositories should determine a biospecimens biosecurity level as a function of its potential for malicious misuse and virulence. Establishing the biosecurity risk level of a particular material is instrumental to applying Biosecurity Risk Management Practices. Research biorepositories should assess potential for malicious misuse based on the following key factors:

- Availability: The number of facilities that stock biospecimen and their geographical location.
- Amplification: The ease with which the biospecimen can be replicated, for example whether it can be grown into culture and its growth rate.

- Skills and knowledge: the ubiquity or rarity of the skills and knowledge necessary to amplify and/or genetically modify the biospecimen.
- Dispersal: The ease and effectiveness with which the biospecimen can be dispersed, such as by air, water, food or by other means into the environment. This might include (but not limited to) a biospecimens aerosolisation and inhalation characteristics.
- Environment viability: The hardiness of the biospecimen across a range of temperatures, humidity levels and light exposures.
- Countermeasures: the existence and each of access to prophylaxis, post-exposure treatments and detection and decontamination measures.
- Economic consequence: The extent to which the biospecimen may be used to bring about harmful economic consequences for humans, crops, livestock or infrastructure.

Research biorepositories must assess virulence based on the following key factors:

- Infective dose: The smallest quantity of the biospecimen necessary to cause infection.
- Pathogenicity: The disease-causing ability of the biospecimen.
- Lethality: The ability of the biospecimen to cause death to the host.
- Transmissibility: The ease with which the biospecimen can spread either by vector to host, or host to host.

It is important to remember that in some cases, one risk factor may be so significant that it may determine the overall risk rating for a particular biospecimen. Thus, the research biorepository should carry out risk assessments in such a manner that risk factors are weighed.

Metro South Health research biorepositories, with the broader scientific community, should take steps, as a priority, to develop common methodologies for risk assessment and should seek to develop quantitative and qualitative tools and assessments that assist in completing appropriate and comparable risk assessment. In developing common tools and methodologies research biorepositories should be sure to draw upon appropriate existing, including international, tools and methodologies.

Research biorepositories must make biosecurity risk assessments part of the acquisition process of new biospecimen. When being transferred between research biorepositories a summary of a biological material's risk assessment should be made available.

Research biorepositories should re-asses the biosecurity risk level of materials for which there is new information about their virulence or potential malicious misuse. Custodians must refer to the Metro South Health risk management policies and frameworks when undertaking biosecurity risk assessments.

All Metro South Health research biorepositories should establish, or have access to a Committee which discusses laboratory work health and safety, general biosafety and biosecurity issues.

Research biorepositories should also establish a timetable for internal audits to check for the level of compliance with the risk management practices. These evaluations must conform to the rolling audit and review program as described in Quality Management System (Assurance and Control) Procedure (PR2017/110).