PROCEDURE

Metro South Health Research Biorepositories – Material Transfer Agreements, Packaging and Shipping

PR2017/107
Version No. 3.0

PURPOSE

Rights to a sample or biospecimen may vary as it passes from patient/participant to clinical caregivers, to a Metro South Health (MSH) research biorepository and finally to the researcher. This procedure describes the processes for researchers to formally receive samples contained within a MSH research biorepository via Material Transfer Agreements (MTAs). Additionally, the procedure ensures compliance with MSH packaging and shipping requirements.

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 and researchers in the formal MTA process and requirements for packing and shipping of samples from MSH research biorepositories. 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.

- Research biorepositories must seek to serve the interests of the community. In meeting this requirement, some biorepositories may make biospecimens available to a broad scientific community for use in high quality research.
- Research biorepositories must ensure the use of a MTA to transfer tissue and information to any outside organisation or individual. The use of a specific MTA for academic and commercial collaborators may be warranted.
- MSH research biorepositories are responsible for tissue and personal information in its custody, including information transferred to a third party for research purposes.

- The research biorepository must use contractual means to provide a comparable level of protection while the tissue and information is being used by the third party and the transport of biospecimens including packaging and shipping must conform to all governing regulations.
- MSH research biorepositories should only supply to users who have the appropriate facilities and meet the specific requirements for receipt as required by relevant national and international regulations and policies. An order should only be accepted when the required accompanying documentation is complete, signed and returned.
- MSH supports principles outlined within the Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials (Fourth Edition 2013) document which provides the requirements for the packaging and transportation of biospecimens from the point of first collection to the laboratory/research site where analytical testing is carried out. Several modes of transport may be required, each of which is covered in the National Pathology Accreditation Advisory Council document.
- All researchers accessing MSH biospecimens must be aware that samples have not been screened for potential pathogens and therefore may result in severe illness or even death if not handled properly. Following dispatch, the responsibility for the correct handling of the samples lies solely in the hands of the end user (the approved researcher) and is not the responsibility of the issuing research biorepository. Any illness resulting from the mishandling of these samples is not the responsibility or liability of the research biorepository, MSH, Queensland Health or any associated sponsors. Please see Emergency Preparedness and Work Health and Safety Procedure (PR2017/108) for more information.

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

- Government of Western Australia: Guidelines for Human biobanks, genetic research databases and associated data
- International Society for Biological and Environmental Repositories (ISBER): Best Practices: Recommendations for Repositories Fourth Edition
- International Air Transport Association (IATA) Dangerous Goods Regulations
- National Cancer Institute: Best Practices for Biospecimen Resources
- National Pathology Accreditation Advisory Council, Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials (Fourth Edition 2013)

- Organisation for Economic Co-operation and Development (OECD)
    - Best Practice Guidelines for Biological Resource Centres
    - Guidelines on Human Biobanks and Genetic Research Databases
- Queensland Biotechnology Code of Ethics
- The Royal College of Pathologists of Australasia: Biobanking Guideline 2014
- 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)
- Finance Management Practice Manual (FMPM)

RESPONSIBILITIES

Executive Management

Ensure collaborative, harmonised, clear and detailed publicly available policies, procedures and Standard Operating Procedures (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 clarification around formal MTA processes and requirements for packing and shipping of samples from MSH research biorepositories.

Custodian/Principal Investigator – responsible officer

Ensure the research biorepository's processes for formal MTAs and requirements for packing and shipping of samples from MSH research biorepositories, not only supports individual and institutional interests; but also ensures that high quality biospecimens will be available for future use.

Research biorepository manager

Write, revise and update organisational and administrative SOPs pertaining to formal MTA process and requirements for packing and shipping of samples from MSH research biorepositories.

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 - MTA Template

Attachment 3 - Sample Dispatch Coversheet Template

Attachment 4 - Transport of Samples Template

Attachment 5 - MTAs, Packaging and Shipping Checklist

DEFINITIONS

See the MSH Research Biorepositories Glossary

PROCEDURE - MATERIAL TRANSFER AGREEMENTS, PACKAGING AND SHIPPING

STEP 1: MTAs

Where access to the samples and data collected from patients/participants is allowed, a MTA or other appropriate agreement must be developed. Please see Access and Applications for Samples Procedure (PR2017/106) for further information about the application process.

The MSH Research Governance Office may facilitate access to samples through the provision of support for establishing formalised MTAs. Please see Attachment 2 - Material Transfer Agreement Template for more information. Please see MSH Research Management - Research Governance (Site Specific Assessment) Procedure (PR2017/116) for more information.

STEP 2: Data Access Agreements

The terms of access to associated data for researchers may be set out in a Data Access Agreement Please note within MSH the Data Access Agreements and MTAs are classified as the same as both can be classified as material.

STEP 3: Classification of samples

The shipper should first determine how to classify the biospecimens that are to be transported. There are many questions to consider when choosing the mode of transport for biospecimens, including:

- Should the biospecimens be kept cold or frozen?
- Are the biospecimens being sent within Australia and to whom?
    - Operating theatre to research biorepository?
    - Research biorepository to research laboratory?
    - Research biorepository to research biorepository?
    - Within hospital (ie from ward to research biorepository)?
    - Externally from one part of a hospital campus to another?
- Are the biospecimens being sent overseas?
- What packaging is required to send these biospecimens safely?
- What paperwork or documentation is needed?
- Are there additional hazards such as chemicals (flammable, acid or other substance), dry ice, liquid nitrogen etc?

STEP 4: Packaging

Research biorepository personnel must ensure packing is compliant with regulations and appropriate for the sample being shipped. The packaging required for biospecimens depends on the mode of transport that is to be used, and therefore can vary.

STEP 5: Transport

The '*Matrix for determining mode of general packaging requirements for biological material by various modes of transport'* contained within the Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials (Fourth Edition 2013) must be adhered to when determining the most suitable method for packaging and transporting a biospecimen according to the mode of transport that is necessary.

STEP 6: Shipping

Dispatch from the research biorepository

Upon planned shipment of a package, documentation of the transfer in the form of a MTA and requisition from the resource inventory is needed. Research biorepository personnel must ensure shipping is compliant with regulations and appropriate for the sample being transferred and/or released.

With particular biospecimens with a high risk rating the sample must have a written and signed document proving the user has the appropriate authorisation to import and handle such biospecimens

Dispatch to the research biorepository

Biospecimens must be dispatched, where practical, as soon as possible once necessary licences and/or documentation are provided. Please see Attachment 3 - Sample Dispatch Coversheet Template and Attachment 4 - Transport of Samples Template for more information.

STEP 7: Invoicing

If a cost recovery charge applies, the invoice must be progressed in accordance with MSH financial policies and procedures — Finance Management Practice Manual (FMPM).

STEP 9: Self-audit, review and compliance

Utilise Attachment 5 - Material Transfer Agreements, Packaging and Shipping Checklist to aid in self-auditing, review and compliance.

PROCEDURE DETAILS

Procedure Number
PR2017/107

Procedure Name
MSH Research Biorepositories – MTAs, Packaging and Shipping Procedure

Policy Reference
PL2017/53
MSH Research Biorepositories Policy

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05 July 2024 (within the next 3 years)

ATTACHMENT 1 - Application

1.0 MTA

A MTA is a contract that governs the transfer of tangible research materials between two organisations, a provider and a recipient, when the recipient intends to use it for his or her own research purposes. It ensures that Custodianship of samples is clearly and formally passed onto the new recipients of the samples and sets out the conditions under which a recipient is granted access to data or samples.

The MTA defines the rights of the provider and the recipient with respect to the materials, data associated with the materials and any derivatives. Biospecimens such as reagents, cell lines, plasmids and vectors, are the most frequently transferred materials, but MTAs may also be used for other types of materials, such as chemical compounds and even some types of software.

Other types of agreements without the title of MTA may be used, but generally would serve the same purpose and have the same components as a MTA.

There are legal requirements to be aware of when transferring samples and data internationally. The MSH Research Governance Office can facilitate access to samples through the provision of support for establishing formalised MTAs. Please see MSH Research Management - Research Governance (Site Specific Assessment) Procedure (PR2017/116) for more information.

1.1 MTA for biospecimens

A MTA must be executed to document the obligations and responsibilities of parties involved in the transfer of materials from a research biorepository prior to shipment. The agreement must be initiated as soon as possible, as additional time may be required for legal or regulatory approval prior to transfer. A MTA (or other document) for transfer of biospecimens to a recipient should address:

- Purpose of the transfer.
- Clarification about Custodianship of the samples.
- Tissue being supplied ‘as is’ with no representations or warranties unless otherwise specified by the MTA.
- Potential for tissue to have unknown characteristics or carry infectious agents.
- Restrictions on the use of the biospecimens (eg biospecimens may not be banked, sold or redistributed to third parties) if any.
- Instructions about return, retention or disposal of unused tissue if applicable.
- Specific conditions for publication of research results if any. Requirement to publish research findings and/or to disseminate them more generally, and to acknowledge the resource in publications.
- Specific conditions for provision and sharing data if any. Arrangements concerning requirement to return research findings to the resource owner to enrich the resource.
- Requirement to act in accordance with patients/participants’ consent, and any procedures in the event of withdrawal of consent.
- Requirement to act in accordance with relevant legal and regulatory requirements, and obtain ethical approval (where applicable).

- Specific conditions for managing intellectual property rights if any (eg whether or not intellectual property rights are asserted by the provider over existing or future intellectual property, or any licenses sought by them to future intellectual property rights).
- The credentials of the end user.
- Fees (or royalties) payable.
- Specific conditions about compensation for material transfer if relevant.
- List of samples (identification codes) released to researcher.
- Tissue cannot be provided by a third party without written consent and the development of a new MTA.
- Requirements for maintaining Privacy and Confidentiality principles (that must be adhered to).
- Restrictions on re-identification (where de-identified biospecimens are provided).
- Requirements for appropriate biosafety training if any.
- Limits on (prohibition of or additional safeguards required for) the transfer of data or samples to third parties, including cross-border:
    - disclaimers of responsibility for data/sample quality
    - return or destruction of residual samples and data at the end of a project
    - termination (eg for default).
- Any other factors that may govern the transfer.

The research biorepository should provide the quantity of materials and data consistent with that required for the research to be carried out. The research biorepository should request information from the researcher on whether the quantities provided were sufficient and that there was no excess materials or data.

1.2 Data Transfer Agreement

MSH research biorepositories may also execute an agreement with recipients, prior to data transfer, who receive biospecimen-associated data from the research biorepository. This agreement may constitute a stand-alone Data Transfer Agreement, or the necessary terms may be included in the MTA.

Depending on the nature of the resource, the data/sample provider and the end user, access agreements (including Data Transfer Agreements and MTAs) may address some or all of the following:

- Description of the data to be distributed. What is to be provided, specification of data and samples, format and timing of release.
- Purpose for which the data will be used. What the data and samples provided can be used for (this is often limited to a specific project), and what they can’t be used for (this may be everything other than the specified project, or something more specific for example, data linkage).
- Whether redistribution or forwarding of the data to others is permitted and under what circumstances.
- Protection of data against unauthorised access.
- Protection of participant privacy and anonymity upon transfer (prohibiting attempts to learn a subject's identity and publishing identifying information or re-contact participants).

- Requirements for human subjects/ethics committee or applicable animal use approval or other approvals concerning data use.
- Ownership, access and control of transferred data.
- Disposition of data (destruction) upon research completion or agreement termination.
- Terms of agreement, indemnification, payment of fees and rights and title to the research performed.

1.3 Confidentiality

Transfer, access and use of samples and data must be consistent with the terms of participation and respect the privacy of the patient/participant, confidentiality of the samples and data, and ensure good safety and laboratory methods.

The Custodian must ensure the transfer of samples and data is only authorised when there are adequate standards in place regarding the privacy of the participant, confidentiality of the samples and data, and good safety and laboratory methods, and in accordance with applicable law and regulations.

1.4 Access regulations

International researchers who request and have been approved access to samples or data held by the research biorepository must have a collaboration agreement with the Custodian.

1.5 Incorporation of results

Where results of research using the samples are incorporated into the research biorepository, the Custodian must ensure consideration is given to how access to such results for further research should be managed, particularly if the results can be linked to other information about the patient/participant.

1.6 Data Access Agreements

The research biorepository may implement a localised Data Access Agreement in addition to a formal Material and Data Transfer Agreement. Localised Data Access Agreements may include:

- What is to be provided (specification of data and materials, format and timing of release).
- What the data and materials provided can be used for (this is often limited to a specific research project), and what they can't be used for (this may be everything other than the specified research project, or something more specific, for example, data linkage).
- The credentials of the end user and fees (or royalties) payable.
- Arrangements concerning intellectual property rights (eg whether or not intellectual property rights are asserted by the provider over existing or future intellectual property, or any licences sought by them to future intellectual property rights).
- Requirement to return research findings to the resource owner to enrich the resource.
- Requirement to publish research findings and/or to disseminate them more generally, and to acknowledge the resource in publications.
- Requirement to act in accordance with patients/participants' consent, and any procedures in the event of withdrawal of consent.
- Requirement to act in accordance with relevant legal and regulatory requirements and obtain ethical approval (where applicable).
- Requirement to preserve confidentiality and/or maintain anonymisation (and not attempt to re-identify or re-contact patients/participants).

- Limits on (prohibition of or additional safeguards required for) transfer of data or materials to third parties, including cross-border.
- Limits on (prohibition of) certain uses of materials or data.
- Disclaimers of responsibility for data/sample quality.
- Return or disposal of residual samples at the end of a research project.
- Termination (eg for default).

1.7 Custodianship

Where biospecimens are physically released to third parties by the research biorepository, consideration should be given to the implications for the Custodianship of any data derived from the analysis of such material that relates directly to patients/participants (eg genotype data derived from DNA), particularly where such data can be linked to significant amounts of phenotypic data about the same patients/participant.

Such issues should be addressed in the MTA which governs the release of biospecimens and data from the research biorepository to the researchers. The research biorepository should ensure that its governance mechanism is able to deal with problematic situations pertaining to data derived from the analysis of biospecimens and other information. Please see MSH Research Management - Research Governance (Site Specific Assessment) Procedure (PR2017/116) for more information.

1.8 Handling complaints and anomalies

The research biorepository must record all user queries or complaints and acknowledge as soon as possible (preferably on the same day) by fax, email or telephone. The research biorepository must investigate the complaints as soon as received and implement the necessary corrective actions. All complaints should be included in a regular trend analysis. Records of responses/solutions should be stored.

2.0 Packaging

The research biorepository must pack and send its biospecimens according to current, International Air Transport Association (IATA) and Australian Design Rules (ADR) regulations. It should also meet additional requirements imposed by other regulations such as quarantine, biosafety and/or biosecurity regulations.

The basic triple packaging system applies to all substances. It consists of three layers as follows:

- Primary receptacle: a primary watertight, leak-proof receptacle containing the biospecimen, packaged with enough absorbent material to absorb all fluids in case of breakage.
- Secondary packaging: a second, durable watertight, leak-proof packaging to enclose and protect the primary receptacle. Several primary receptacles may be placed in one secondary packaging but sufficient additional absorbent material should be used to absorb all fluid in case of breakage.
- Outer packaging: an outer, shipping packaging of suitable, cushioning material, protecting its contents from outside influences while in transit.

Use appropriate insulation (eg for 8°C to -20°C use gel packs, for -80°C use dry ice and if samples need to be kept at -150°C) transport them in a dry shipper containing liquid nitrogen (LN_2). Ensure enough refrigerant is included to allow for a 24-hour delay in shipping.

When shipping biospecimens overseas, the sender must be aware of the requirements and regulations in the destination country prior to the initiation of the shipment, and ensure that the consignment adheres to these regulations.

All outer packages must bear a United Nations packaging specification marking according to the category in which the biospecimens fall. For category A, the packaging instruction Pi602 applies. For category B, the relevant packing instruction is Pi650. Detailed instructions are described in the IATA Dangerous Goods Regulations, 2007 (International Air Transport Association, 2007).

The triple packaging system also applies to exempt human biospecimens such as Guthrie cards (that should be transported in watertight plastic bags) or histopathological slides (that need to be cushioned to prevent breakage). In all cases, desiccants should be used for samples sensitive to humidity:

- Biospecimens should be positioned between the refrigerants used rather than being placed on top of or underneath the refrigerant.
- After the biospecimens and the refrigerant have been placed into the container, empty space should be filled with Styrofoam or wadded paper to prevent movement of the biospecimens during shipment.
- Remove or mark through any labels remaining on the exterior of the shipping container from a previous shipment.
- Air-bills should not be reused.

2.1 Review of packaging test report

The shipper is responsible for choosing appropriate packaging for the shipped material. The shipper should review all test reports for the packaging to ensure that the packaging regulations are met.

Packaging that has undergone stringency testing should be used in the same configuration under which it was tested. Tests may include measuring all parameters that could influence biospecimen integrity (ie temperature, humidity, light sensitivity, structural quality and spill containment).

2.2 Information provided with the supplied biospecimens

The research biorepository must provide at least the following information to the user:

- Biospecimen identified, accession number and batch number.
- A Minimum Data Set according to the type of resource (see Acquisition, Attainment and Recruitment Procedure (PR2017/102) for more information).
- An estimate of shelf-life, storage conditions, storage instructions, and if appropriate, conditions of growth.
- Instructions for opening ampoules or vials (when appropriate and in all cases where materials are being provided to new users).
- The conditions needed to maintain the biospecimen/s (temperature, medium and culture conditions etc) as well as transport conditions.
- A safety data sheet including the containment level required for handling the biospecimen, disposal measures and measure to take in case of spillage. Human cells, tissues should always be treated a hazardous unless they are tested for infection diseases or treated with an appropriate inactivation measure (eg fixation with formaldehyde). The safety data sheet must be mandatory for any dangerous material and must be included in the package, together with instructions for handling.

Please see Emergency Preparedness and Work Health and Safety Procedure (PR2017/108) for more information.

- A MTA: an essential requirement to protect the intellectual property rights and mandatory where they are required by law. They are used to relay the depositor's and/or country of origin requirements on use of biospecimen.
- Fax-back sheet to acknowledge receipt of materials may be desirable.

3.0 Transport

Biospecimens and associated materials must be transported and packaged in a suitable manner to:

- protect the safety of everyone required to handle the biospecimens and package
- ensure that the material is maintained under suitable conditions.

The key steps to correctly package and transport biospecimens and associated materials are presented within National Pathology Accreditation Advisory Council, Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials (Fourth Edition 2013). To find the information required to package a biospecimen correctly, Custodians must follow relevant steps pertaining to:

- Use the hazard classification guide and flowchart to determine whether the biospecimen is Category A, Category B, Exempt/Category C or another hazard class.
- Use the matrix in Section 3 for the appropriate mode of transport for the biospecimen.
- Refer to Section 4 for materials that are not covered by this document.

These requirements are intended to serve as minimum standards in the accreditation process and have been developed with reference to current and proposed Australian regulations.

4.0 Shipping

Air shipments must conform to IATA standards. Ground shipments must conform to applicable national/federal standards. All personnel involved in shipping biospecimens should be trained properly for both air and ground shipments. If biospecimens cannot be delivered within the specified delivery time, the research biorepository should contact the user with an estimated supply date.

The research biorepository may recommend, where possible, other national or international research biorepositories to supply biospecimens not held in their collection. Personnel should be trained to ship samples appropriately. Periodic retraining according to governing regulations should be conducted and documented.

4.1 Risks

Biospecimens are considered as "dangerous goods", that is, "articles or substances which are capable of posing a risk to health, safety, property of the environment". MSH research biorepositories must train their personnel in matters regarding universal precautions (ie to handle all biospecimens as though they are potentially hazardous).

Research biorepository staff that may become exposed to biospecimens must be vaccinated against possible risks. These staff members should also be regularly checked for their level of immunity.

This same level of safety must be extended to clients who receive biospecimens from research biorepositories. Namely, clients must be advised of the potential hazards associated with all biospecimens, and sign-off on their agreement to handle all biospecimens with the necessary safety methods. In this agreement, the client also agrees that the research biorepository will not be liable for any health risk or damage that may result from unsafe handling of the biospecimens.

4.2 Transport specifications

The first step in the preparation of a shipment for transport is the determination of the specifications for the biospecimens. The shipper must determine what regulatory requirements are to be met as well as the physical requirements necessary to ensure proper shipping conditions.

When seeking to regulate sample temperature during shipping, the shipping time, distance, climate, season, method of transportation, regulations, as well as the type of samples and their intended use, should be considered. To maintain proper temperature during shipping, appropriate insulation, gel packs, dry ice or liquid nitrogen (dry shipper) should be used and these materials should be qualified for their intended use.

To maintain refrigerated temperatures (2C to 8C), gel packs conditioned at -15C or phase-change material rated for refrigerated transport may be used. To maintain frozen temperatures, gel packs conditioned at or below -20C should be used. For frozen temperatures at -70C, dry ice pellets or sheets should be used; dry ice is considered a hazardous substance for shipping purposes.

For maintaining temperatures at or below -150° C, a liquid nitrogen dry shipper should be used. Insulated packaging may be used to protect biospecimens from extremely hot or cold ambient conditions. Whenever intending to maintain samples below ambient temperature, enough refrigerant should be included to allow for at least a 24 hour delay in transport. Temperature-sensitive material should be handled by a courier with resources to replenish the refrigerant in case of a shipping delay. A simple colorimetric or other constant temperature-measuring device should be included with biospecimens shipments to indicate the minimum and/or maximum temperature within the shipping container.

4.3 Regulatory requirements

Biospecimens routinely shipped from research biorepositories such as infectious substances, diagnostic biospecimens, biological products, genetically modified organisms and microorganisms or toxic substances may be considered dangerous goods. Also, the preservatives that have been applied to the biospecimens may be considered toxic, flammable liquids, non-flammable gases, or corrosives, all of which are dangerous goods.

In order to properly classify the biospecimens to be included in a shipment, one should consult their federal transport regulations as well as those from their International Civil Aviation Organisation (ICAO) and IATA. The shipping and dispatch of biospecimens is subject to international regulations. The ICAO rules apply on all international flights. For national flights (ie flights within one country, national civil aviation authorities) apply national legislation. This is normally based on the ICAO provisions, but may incorporate variations. State and operator variations are published in the ICAO.

4.4 Technical instructions and in the IATA dangerous goods

Each person involved in the transport of biospecimens classified as dangerous goods by IATA, must follow and validate a training session. It concerns persons involved in the preparation of documentation but also persons involved in packaging biospecimens.

When preparing to transport biospecimens, it is important to consider shipping time, distance, climate, season, method of transport and regulations as well as the type and number of biospecimens to be sent and their intended use. Some general guidelines and regulations are included below.

4.5 Temperature requirements

Biospecimens may be exposed to temperature fluctuations during transit. Shipments of biospecimens with high value or those with critical temperature requirements should include a temperature-recording device that can verify the temperature of the material being shipped throughout the transport cycle. The following are typical temperature conditions required for transport of biospecimens and the insulation/refrigerant helpful to maintain that temperature:

- Ambient (20 to 30˚C) — insulated packaging to protect from extreme heat or cold ambient conditions.
- Refrigerated (2 to 8˚C) — wet ice or gel packs (conditioned at -15˚C designed for refrigerated temperatures or phase change material rated for refrigerated transport).
- Frozen (-20˚C) — gel packs designed for frozen temperatures, conditioned at or below -20˚C.
- Frozen (-70˚C) — dry ice pellets, blocks or sheets. Note that dry ice (solid CO_2) employed for frozen shipments is considered a hazardous material and appropriate labelling should be included.
- Frozen (at or below -150˚C) — liquid nitrogen dry shipper. Dry nitrogen shippers are insulated containers that contain refrigerated liquid nitrogen that is fully absorbed in a porous material and is therefore considered a non-dangerous product and is not subject to IATA regulations as a dangerous good.

Shipments of cold or frozen material must be shipped with sufficient and appropriate refrigerant to maintain temperature throughout the shipping cycle with allowance for at least a 24-hour delay in arrival time.

Paraffin blocks and slides may be shipped at room temperature in an insulated package via overnight carrier. The use of insulated packages is considered important to minimise the effect of temperature fluctuations and to protect the blocks from temperatures higher than 27˚C.

There is convincing research that tissues stored in FFPE blocks may rapidly lose antigen expression for certain immunomarkers even when maintained in hospital storage areas at ‘room temperature’, which may fluctuate widely in non-temperature controlled areas.

Flat biospecimens, such as dried blood samples on absorbent pads or cards, may be enclosed in watertight plastic bags and shipped in a sturdy outer package or commercial envelope.

Samples on glass or plastic slides should be cushioned and shipped inside a sturdy (not flexible) outer package. Inclusion of a simple maximum temperature indicator in each package and documentation of the maximum temperature upon receipt are recommended.

The number of biospecimens per package also affects whether the appropriate temperature can be maintained for all biospecimens in the shipment. A test shipment (eg frozen water samples) should be made before shipping extremely valuable samples to check the adequacy of coolants and any potential obstacles to a successful shipment. In addition, conditions throughout a critical shipment should be monitored by enclosing a device that records temperature during transport.

4.6 Humidity requirements

Biospecimens sensitive to humid conditions may need to be shipped in sealed bags with desiccant to prevent exposure to moisture during transit.

4.7 Arrival time requirements

Time sensitive biospecimens such as fresh whole blood should be consigned to couriers with a proven reputation of successful on-time delivery. Time required for shipment processing should be considered as well. Shipments should be initiated when there are at least two working days left in the week, in case they do not arrive on the day scheduled for delivery. Shipments should also be scheduled so that they do not arrive at the recipient location on a holiday.

4.8 Biospecimen quantities

The quantity of biospecimens to be transported will affect the type of packaging and amount of refrigerant required to maintain appropriate temperatures for all biospecimens in the shipment. The container size should be appropriate for the amount of refrigerant needed and for the number of biospecimens that will be included in the container. Shipments involving a large number of biospecimens should be divided into multiple, smaller shipments.

4.9 Test shipments

In some situations, especially relating to extremely valuable samples, research biorepositories may choose to first send a test shipment that approximates the characteristics of the actual shipment. This may inform the shipper as to the adequacy of packing coolants and also serve to identify any potential obstacles for the successful shipment. When test shipments (as well as subsequent biospecimen shipments) are performed it may be helpful to use a temperature-recording device or an irreversible temperature indicator during the shipment to ensure that temperature requirements have not been exceeded.

4.10 International shipments

Special permits or other requirements may be unique to certain countries and regions. Some countries have regulations related to ethical issues which prohibit the import/export of certain types of human biospecimens or have specific requirements concerning the import/export of such biospecimens. If collecting non-human biological samples that are endangered or protected, special permits such as the 'Convention on International Trade in Endangered Species of Wild Fauna and Flora' permit, as well as additional paperwork may be required. Most international shipments also require a customs clearance note to be clearly displayed on the outside of the package. Check with the country of delivery for the customs information that needs to be displayed. Identify all requirements for shipping to a designated country prior to the initiation of the shipment. Use of a customs broker can be helpful or even critical. Certain couriers can provide this service which can be essential for transport to/from a foreign country. Due to possible delays in completing customs requirements, temperature sensitive material should be consigned with a courier capable of replenishing refrigerant in the event of a delay. As a precaution, three additional days' worth of refrigerant is recommended for shipments in cases where customs clearance may be difficult. International shipments should include a letter on institutional letterhead (as appropriate) documenting the contents and handling requirements. Copies of all import permits and sanitary certificates should be included, as needed.

4.11 Tracking shipments during transport

Both the shipper and recipient should track all packages while in transit.

4.12 Notification of shipment

Biospecimens must be shipped from an attended shipping facility or picked up for shipping by an appropriately authorised person. The research biorepository should notify the recipient before shipping to confirm that someone will be present to accept the package and properly store the samples. The shipper should notify the recipient that a shipment is scheduled to arrive on a specific date.

The recipient should confirm that they are able to receive the package and that they have the proper facilities for storage before the shipper releases the shipment. The shipper should provide a 24-hour emergency contact for all packages transporting dangerous goods.

4.13 Shipping manifest

The shipper should send a shipping manifest (preferably electronic) to the recipient prior to the release of the shipment. A paper copy should also be included with the shipment itself.

Shipments from and to the research biorepository must be tracked in a written or computerised shipping log, which should include shipment/invoice number, recipient (or source), date shipped (or received), courier name and package tracking number, sample description, number of samples shipped (or received), condition on arrival, study name and number (if available), key investigator's name, and signature of biospecimen recipient.

Standardised paperwork should accompany shipments. Personnel should electronically send a shipping manifest, a list of sample identification numbers, and descriptions of samples to the biospecimen recipient and should include a hard copy of the manifest inside the shipment. Identifying data should be available for the use of shipping or customs agents. Some shipping agents require an itemised list of contents between the inner and outer packaging of diagnostic biospecimens.

Upon receipt, personnel should verify biospecimen labels and any other documents or data shipped with the biospecimen against the packing list for consistency and correctness. A questionnaire requesting feedback about the quality of samples received may be enclosed in each shipment for quality management purposes. In general, the concept and process for chain of custody should be applied when shipping biospecimens.

4.14 Confirmation of receipt

Confirmation of receipt and the condition upon arrival should be documented for every delivery or shipment of biospecimens. A form that records this information should be sent with the shipment/delivery. Information as to how the condition report should be returned to the shipper should be clearly indicated.

4.15 Traceability of biospecimens supplied

The research biorepository must keep records of all requests, including those requests refused for any reason, showing the biospecimen, method and date of shipment, and name and address of the person who sent the package. Where recorded delivery, courier or similar shipping mechanisms are used records of shipment receipt should be maintained.

5.0 Invoicing

If a cost recovery charge applies, the invoice must be progressed in accordance with MSH financial policies and procedures — Finance Management Practice Manual (FMPM). Invoices are normally dispatched at the same time as the material unless otherwise instructed or where pro forma invoices have been paid in advance.

5.1 Refunds

Despite rigorous quality control and SOPs being followed, it may be possible that the biospecimen provided may not have the property stipulated on the order or that is reasonably expected of it on receipt. If the user is not deemed at fault it is normal policy to provide the user with a replacement free of charge where this is possible. If refunds are considered appropriate they should be given.