CELL PRESERVATION TECHNOLOGY
Volume 6, Number 1, 2008
Mary Ann Liebert, Inc.
DOI: 10.1089/cpt.2008.9997

2008 Best Practices for Repositories

Collection, Storage, Retrieval and Distribution of Biological Materials for Research

International Society for Biological and Environmental Repositories

Second Edition

These Best Practices are reviewed periodically and revised to incorporate improved application and research findings that would affect repository work. The reader is advised to check the ISBER web site (www.isber.org) to ensure that the most recent version is available for use.

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2008 Best Practices for Respositories: Collection, Storage, Retrieval and Distribution of Biological Materials for Research

INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITORIES (ISBER)

INTRODUCTION

THE AVAILABILITY of high quality biological and environmental specimens for research purposes requires the development of standardized methods for collection, long-term storage, retrieval and distribution of specimens that will enable their future use. Sharing successful strategies for accomplishing this goal is one of the driving forces for the International Society for Biological and Environmental Repositories (ISBER). For more information about ISBER see www.isber.org.

ISBER's Best Practices for Repositories (Best Practices) reflect the collective experience of its members and provide repository professionals with a comprehensive tool to guide them in all their repository activities. The Practices presented here reflect input from individuals within and outside *ad hoc* committees. The ISBER Best Practices are reviewed bi-annually and are revised to reflect advances in research and technology.

Adherence to ISBER Best Practices is strictly on a voluntary basis. It is important to note that some aspects of specimen management are governed by national, regional and local regulations. The reader should refer directly to regulations for their national, regional and local requirements, as appropriate.

Throughout this document effective practices are presented for the management of specimen collections and repositories. In cases wherein a level of operation is indicated that is above the basic recommended practice or more specifically designates the most effective practice, a designation of "Best Practice" is indicated.

The focus of the second edition of the ISBER Best Practices has been expanded to include best practices for environmental specimen collections in addition to human specimen collections and to more effectively represent international best practices. ISBER has strived to include terminology appropriate to the various specimen types covered under these practices, but the reader should take steps to ensure the appropriateness of the recommendations to their particular repository type prior to the implementation of any new approaches.

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SECTION A: ORGANIZATIONAL REQUIREMENTS OF A REPOSITORY

A1.000 GENERAL

A repository is defined as an entity that receives, stores, processes and/or disseminates specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation. The mission of a repository should be clearly formulated and documented. It should be defined as to whether it is a freestanding entity, virtual, or part of an institution. A repository should have sufficient professional staff and a commitment to maintain and preserve records for future reference and historical continuity.

A2.000 SPECIMEN ACQUISITION, ACCESS AND CULLING

Policies should be established for the acquisition of new specimens, access to specimens for research purposes, for culling of collections when specimen resources have fulfilled their original purpose or are no longer suitable for their intended purpose, or if participants request the withdrawal of their specimens. These policies should be clearly described and openly available, as appropriate, to users and potential users of the specimen collections.

A3.000 STAFFING

A3.100 Director

A3.110 Responsibilities

The Director should be qualified by training and experience to fulfill the scope of activities conducted by the repository.

A3.111 General Operations

The Director should implement policies of the organization and should be responsible for all operations, including compliance with current national, state and local regulations. The Director is the person with overall responsibility for management of the repository. Depending upon organizational structure of the repository, the Director may have other responsibilities including: (i) ensuring that the repository operates within budget, (ii) ensuring that the repository has adequate funding for operations which may require the development of cost-recovery strategies to ensure the repository's short and long-term financial stability, (iii) ensuring that an adequate policy is in place for access to the specimens stored in the repository and that requests for specimens are met in a timely fashion, and (iv) serving as a liaison to key users.

A3.112 Personnel Supervision

The Director should construct and maintain an organizational chart that delineates the functional relationships within the repository. Candidates for the supervisory and technical staff should be approved by the Director. The Director should also approve and maintain job descriptions and document staff responsibilities. The Director should ensure that personnel responsible for performing repository activities are adequate in number and experience, and are assigned responsibilities commensurate with their capabilities.

The Director should also be responsible for developing and reviewing employee training programs, and should ensure that the repository is in alignment with all federal, state and local requirements.

A3.113 Quality Assurance Program/Quality Management System

The Director or other responsible party should ensure that a Quality Assurance (QA) Program (also termed a Quality Management System or QMS) is in place to make certain that the entire

operation conforms to the repository's standard operating procedures (SOPs), necessary audits, and government regulations. The Director should require regular, documented, internal reviews or audits to ensure compliance with the SOPs and regulations.

Best Practice: Where possible and appropriate, the QA/QMS program staff should report independently of the Director, such as to the director of a separate department or division. In some organizations the QA/AMS staff may report to the organizations' lead officer.

A3.200 Technical Staff

A3.210 Responsibilities

Staff should possess sufficient educational background, experience, and training to assure that assigned tasks are performed in accordance with the repository's established procedures.

Technical staff should be responsible for adherence to policies and procedures as established by the Director. Duties of each staff member should coincide with written job descriptions. Staff should demonstrate competency in operations for which they have received training and to which they are assigned. Authority and reporting relationships for each member of the staff should be clearly described.

A4.000 CONTRACTED LABORATORY SERVICES

Repositories that contract for laboratory services should retain records pertaining to the name and address of the contracted facility, the name and contact information for key personnel at the location where the services are being provided, documentation of the inclusive dates of the contract period and copies of the contract as well as any accompanying documentation. The scope of work for all contract services should be clearly articulated.

SECTION B: RECORDS MANAGEMENT

B1.000 GENERAL

Each repository should develop and maintain a records management system that permits detailed records to be made concurrently with the performance of each step in the collection, processing and distribution of specimens. Records maintained may include but are not limited to: training documents, protocols, standard operating procedures (SOPs), informed consent documentation, procurement documentation, processing records, testing, equipment maintenance, audit/review documents, specimen storage location information, sample distribution, and quality control activities. Records should be created and maintained in a manner that allows steps to be clearly traced and ensure sample chain of custody. Security systems should be adequate to ensure the confidentiality and security of all stored records. Access to records should also be on a "need to know" basis.

In some cases it may be necessary to either destroy or remove specimens at the request of study participants. Under these circumstances, records should be appropriately amended to indicate that the specimen is no longer part of the collection and the information management system should be adequately updated to reflect this event.

Best Practice: Paper files containing confidential patient, subject, or client information should be stored in locked, fire and water proof enclosures with controlled access.

B2.000 TEMPLATE FORMS AND SPREADSHEETS

A repository may develop a variety of forms to allow for effective record keeping. Uniform systems of documentation improve consistency in the tracking and monitoring of repository ac-

tivities. Examples of effective forms include those to monitor equipment operations and repair, incident reports, and activity check lists.

Best Practice: Forms should have a unique number and a distinct title, and include the date that the version of the form was created (*i.e.,* version tracking).

B3.000 RECORD CORRECTIONS AND/OR CHANGES

Corrections or changes in a hard copy record should be made in ink with a single line drawn through the altered text. Corrections should be initialed and dated by the individual making the correction or change. Changes in electronic records should be noted and tracked. Changes tracked should include the name of the individual making the change, the time and date at which the change was made and the reason for the change.

Best Practice: Dates should implement a format that is unambiguous such as ddmmyyyy, where d stands for day, m stands for month, and y stands for year.

B4.000 RECORD RETENTION

Unless otherwise specified by contract, corporate or government policy or other agreement, each repository should establish a period of time during which all records are retained. A policy should be in place for the destruction or return of records that no longer need to be retained. The length of time that records are maintained will depend on the nature of the record. For example, a repository may retire equipment maintenance and repair records following the retirement of the equipment. Records pertaining to a particular collection that is no longer active (*e.g.,* closed) or where the samples have been destroyed may also be retired, destroyed, or returned to the sponsor.

B5.000 ARCHIVAL SYSTEM

A repository may develop a system for archiving records that are not needed as a part of daily activities that the repository requires to be maintained as defined in Section B4.000. This system should be accessible for audits and inspection as defined in Section B7.000.

B6.000 SECURITY

Electronic records should be backed up daily on a network or remote server and periodically (*e.g.,* daily or weekly) on a CD, DVD or other appropriate media.

Best Practice: Arrangements should be established with an off site data security company that retrieves and stores all critical data at a remote location.

Best Practice: Computers operated by repository staff should be password protected and should make use of automatic timeout mechanisms that lock the computer (*e.g.,* screensaver).

Best Practice: Permission levels should be created for staff at different operational levels as well as for users who are not repository staff, where this access is allowed.

B7.000 AVAILABILITY FOR INSPECTION

Records should be readily accessible for inspection by authorized personnel from regulatory agencies (these may vary for each state or country, depending on the regulatory agencies with jurisdiction over those activities) and Quality Assurance (QA) personnel. Access to privacy records or confidential client information should be restricted to specified repository staff members that are permitted to allow access for inspectors from regulatory agencies and other appropriate auditing groups.

SECTION C: FACILITIES

C1.000 GENERAL

An efficient repository has many particular design elements to ensure the safe keeping of the material stored, support the equipment employed, and provide a safe and effective working environment for the repository staff. Knowledge of the types of material being stored, the required storage and handling conditions, the projected retention periods, projected growth of the specimen numbers, and the projected use of the materials is essential to good repository design. The design should include sufficient space to accommodate the material planned for initial as well as future storage and also provide for the safe movement of people, equipment and specimens, as needed or as required by law and/or other regulatory agencies.

C2.000 HEATING, VENTILATION AND AIR CONDITIONING

C2.100 Temperature

In most repositories it is critical to maintain ambient temperature within defined limits. Sufficient heating capacity should be provided to prevent the freezing of water in drain lines. Likewise, sufficient air conditioning should be provided to prevent excess load on the compressor systems of mechanical freezers and refrigerators that may result in excess wear and early failure.

Best Practice: For optimal life of the mechanical refrigeration equipment, repository ambient temperatures should be maintained between 15 °C and 22 °C (65 °F – 72 °F).

C2.200 Air Flow and Circulation

Sufficient air circulation should be provided to prevent excess moisture and condensation. Left unchecked, excess humidity can lead to fungal growth, which may affect specimen integrity and may 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 (see Section C2.100). Adequate ventilation and monitoring are also critical in repositories where liquid nitrogen and dry ice are used to ensure that sufficient oxygen levels are maintained (see Section D2.400). Similarly, when services are performed in which potentially harmful vapors are generated (*e.g.,* formaldehyde) the ventilation system should ensure that personnel are protected and that regional and national standards for the removal of specific harmful vapors are met.

Best Practice: It is recommended that applicable or appropriate oxygen monitoring devices and subsequent exhaust systems are designed or installed within areas where there is the potential for a low oxygen level to develop.

C3.000 LIGHTING

C3.100 General Lighting

Lighting in a repository should 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 specimen type, and the labeling/identification system employed.

Lighting may be both general and task, depending on the situation. General area lighting may be incandescent, fluorescent, metal halide, or other appropriate source. Some repositories may contain materials which are sensitive to light levels or to particular frequencies of light.

Best Practice: Where possible and appropriate, determine if specimens that are planned for storage have sensitivities to certain lighting conditions and plan storage conditions appropriately.

C3.200 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.

Best Practice: 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.

C3.300 Emergency Lighting

In case of power loss it is critical that emergency lighting be available to indicate exit routes from the repository and to provide an illuminated, safe environment to aid in monitoring equipment and responding to the needs of the emergency. Emergency lighting should 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. Repositories should also have portable lighting (*e.g.*, 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.

C4.000 FLOORING

Flooring surfaces used in repositories should be appropriate for the equipment and refrigerants used in daily repository activities. Flooring should be easy to clean and facilitate the movement of equipment when circumstances warrant. Special consideration should be given to the flooring in regions where liquid nitrogen is used, as vinyl tile will crack and cause a hazard if liquid nitrogen is spilled directly onto it.

C5.000 BACKUP POWER

Repositories that store specimens in constant temperature environments require a constant source of electrical power. Given that all commercial power will be interrupted at some time, a backup power system is required.

C5.100 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 is inserted between the source of power (typically commercial utility power) and the load it is protecting. When a power failure or abnormality occurs, the UPS will effectively switch from utility power to its own power source almost instantaneously.

Best Practice: Computer systems and electronic systems, such as environmental monitoring systems, safety systems (*e.g.*, oxygen sensors, ventilations systems, *etc.*) or controllers for liquid nitrogen freezers, should be protected by a UPS. UPSs used in repositories should be tested on an annual basis to ensure their proper backup capabilities.

C5.200 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. Typically they are fueled by diesel, natural gas or propane. Where it is available and appropriate, natural gas supplied by a pipeline may serve as an optimal source, since it can serve as an unlimited source of fuel provided supply lines are not interrupted.

Dual fuel generators that can run on more than one type of fuel (*e.g.,* natural gas and propane) provide a high level of flexibility for fuel supply sources. Quick disconnects are also available which allow portable generators to be brought in and connected in a matter of minutes.

Based on risk tolerance assessments and financial stewardship, it may be determined that a backup generator support only designated pieces of equipment deemed critical.

Best Practice: A generator should have a fuel supply to run continuously for a minimum of 48 hours and preferably a minimum of 72 hours, with an ability to re-fill fuel storage supplies.

Best Practice: Repositories should 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.

C5.210 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.

Best Practice: The power generator system should be tested weekly 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 (*e.g.,* every six months).

Best Practice: Repositories located in or associated with larger facilities (*e.g.,* hospitals or universities) that automatically initiate backup power upon power interruption, should link their freezers and other essential equipment into these emergency systems. The operational safety and testing should be performed by professional caretakers of the larger infrastructure.

C6.000 ACCESS

Repositories should be equipped with a system that adequately limits access to appropriate staff and protects against physical intrusion from unauthorized individuals. Doors should be locked. Keys should be controlled, with a record maintained of each person having access to the repository. Only persons assigned to repository operations should have access to the material stored within. Freezers or environmental storage equipment that store valuable or sensitive specimens should be individually locked.

Best Practice: Mechanical keys employed should be ones that cannot be readily duplicated.

Best Practice: Magnetic locks which control and record entry should be placed at entry points to the repository.

C6.100 Visitor Access Policy

Where feasible and appropriate, repositories should develop an access policy for individuals visiting the repository. 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 repository. 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.

Best Practice: Written or electronic records of repository visitors should be maintained and the records archived according to the repository's established archive practices.

C7.000 SECURITY SYSTEMS

Every repository should employ basic security systems to ensure protection of the specimens stored therein. The systems should be monitored and alarms responded to twenty four hours per day, seven days per week. A responsible individual should be available at all times to take the necessary action(s) to respond to an alarm in a time frame that prevents or minimizes loss or damage to the stored materials. Systems should initiate calls to other staff trained in emergency response from a list of phone numbers when the first individual fails to acknowledge the alarm.

C7.100 Intrusion Detection Systems

When the facility is not occupied by authorized personnel, an alarm system should be in place to monitor unauthorized entry. Motion detectors, glass break and door entry sensors should be integral components of the system.

Best Practice: Repositories should establish an automated building access detection system that simultaneously governs facility access and records who enters and exits the facility. The system should accommodate changes to security codes and keys when individuals leave the organization.

C8.000 FIRE PREVENTION SYSTEMS

In many countries and municipalities a fire prevention system is required by building codes for newly constructed facilities. Compliance with codes is usually required if a facility is being converted or renovated.

C8.100 Sprinkler Systems

The most common type of fire suppression is a sprinkler system that sprays water upon activation. The standard system has water in the pipes at all times. Excess heat causes the system to activate, spraying water into the area.

When computer equipment and electrical systems are in place, a “pre-action” sprinkler system can be employed. In such a system, the sprinkler pipes are dry until a fire is detected. This type of system prevents water damage from accidental activation of the sprinkler system.

C8.200 Non-Water-Based Fire Retardants

Due to the nature of certain equipment and stored materials, water may be an unsuitable tool for fire suppression. In these instances, other chemicals may be employed. The chemicals used in these systems generally smother the fire by cutting off the supply of oxygen. While these systems can be very effective and may be critical for valuable collections adversely affected by exposure to water, they are costly and may present safety hazards. Personnel should be trained to evacuate the facility immediately upon activation to prevent asphyxiation.

C9.000 EMERGENCY PREPAREDNESS

C9.100 Emergency Response Planning

Emergencies can cover a wide range of natural and man-made disasters, all of which may have varying effects on the facility and on the ability of the repository to carry out its essential functions. The type and duration of disasters may depend on the geographic location at which the repository is located. Depending on the “value” and the ability to replace certain samples, some repositories may decide to divide collections and store them in different environmental storage containers or even at different geographic locations so that a disaster affecting one component of the collection would not eliminate the entire collection.

Repositories should have a written disaster recovery/incident response and business conti-

nuity plan for responding to a wide variety of emergency situations. This plan should be tested periodically (*i.e.*, at least annually) to ensure that all personnel are trained and that the plan meets the anticipated needs. Copies of these plans should be distributed to all applicable staff.

Best Practice: Emergency contact numbers should be posted in prominent locations in the repository and should be carried by staff members at all times who are "on call". The contact information should be reviewed on a regular basis to ensure that the information contained therein is current.

Best Practice: The Director or other designated staff member should communicate with local power providers before an emergency occurs to request that the repository be placed on a list of "high priority" users for power restoration following an emergency.

Best Practice: Key individuals should be identified who will serve as being "on call" or who will be able to respond to an emergency at the repository. Leave and vacation schedules should be monitored to ensure that coverage of essential responsibilities is in place should key individuals be unavailable.

Best Practice: Repositories should have a check list of activities for on call staff to follow during an emergency. On call staff should be familiar with the location and operation of certain key equipment and controls (*i.e.,* circuit boards) that may need to be checked during an emergency. Telephone numbers for professional assistance should be clearly posted in the repository and accompanying administrative areas (*e.g.,* engineering or facilities personnel, power companies, fuel supply companies and transportation services).

Best Practice: Call out features of security and environmental monitoring systems should be verified on a routine basis. Where possible, emergencies should be simulated to ensure proper follow-through for the established emergency plan.

SECTION D: STORAGE EQUIPMENT AND ENVIRONMENTS

D1.000 GENERAL

The variety of storage systems available for specimen collections continues to expand as technologies advance. Storage equipment selections should be based on the type of specimens to be stored, the anticipated length of time the specimens will be stored, and on the intended use for the specimens. Also important are the size and physical design of the repository and the number of specimens stored (as well as predictions for future growth in number of specimens stored). Some freezers and refrigerators now provide automated sample entry and retrieval components which may reduce long-term costs for the repository. Often these larger systems are accompanied by increased initial costs which may be more than smaller repositories are capable of supporting. Equipment selections should take into consideration staffing requirements, quality issues and equipment support and maintenance.

D2.000 LIQUID NITROGEN FREEZERS

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

D2.100 Vapor or Liquid Storage

In general, vapor phase storage is preferred over storage in the liquid phase of nitrogen because the vapor phase provides sufficiently low temperatures to maintain temperatures below

the T_g. Storage in the vapor phase also avoids 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. However, certain containers, like cryogenic straws, are hermetically sealed and specifically designed for the safe storage of specimens in the liquid phase of nitrogen.

D2.200 Storage Containers

Liquid nitrogen expands to 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 liquid nitrogen is trapped inside the container when it is removed from the freezer.

Best Practice: Any container used or stored within these ultra low temperatures should be rated for these temperatures.

D2.300 Liquid Nitrogen Supply

Where liquid nitrogen (LN_2) refrigeration is employed, an adequate supply of refrigerant should 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 a minimum supply of 20% of the bulk tank capacity, or greater than three days' working capacity. Bulk supplies should be checked for re-supply at least once a week.

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, a number of 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. This unlikely event, which is usually caused by an error during the filling of the bulk tank, can be mitigated by well-designed procedures and practices.

Best Practice: Daily liquid nitrogen usage should be recorded either by monitoring the display levels or by manual means. Excessive liquid nitrogen usage can indicate problems with the vacuum component of the freezer.

Best Practice: Self contained breathing apparatus (SCBAs or "air packs") should be available for use in the event of a "whiteout" condition. If a SCBA or other respiratory protection gear is used, compliance with regulatory standards may be required. (See Appendix A for helpful resources). Repository personnel should receive training on the effective use of this equipment.

D2.400 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 should always be employed when LN_2 freezers are used in a repository. 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 liquid nitrogen freezers operate because the sensors in installed units will degrade over time and sound false alarms.

D2.500 Protective Wear

In addition to the oxygen deficit risks described under Section D2.400, use of liquid nitrogen as a refrigerant poses special safety problems because of its low temperature and rate of ex-

pansion when placed at ambient conditions. Eye protection is mandatory every time liquid nitrogen is handled to protect against splashes that inevitably occur. Face and ear protection is recommended when handling vials removed from a liquid nitrogen freezer or when dispensing liquid nitrogen from low pressure lines. Heavy gloves (appropriate for LN_2 use) should be worn over protective latex or non-latex laboratory gloves to protect hands when handling samples stored within the liquid phase or when transferring LN_2 or other coolants to Dewar flasks. Normal laboratory personal protective equipment (*e.g.,* closed toed shoes, full cover of legs and feet and goggles) should be worn when handling coolants.

D3.000 MECHANICAL FREEZERS

Mechanical freezers are employed in a variety of storage temperature ranges, including −20, −40, −70 to −80 °C, and occasionally as low as −140 °C. Mechanical freezers come in a wide variety of sizes, configurations, and electric voltages.

Because mechanical freezers are devices attached to commercial power systems, a backup power plan and emergency response plans should be in place (see Section C5.000). 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 (thermal loading) the ambient conditions and the design and maintenance of the unit. It is the responsibility of the facility operator to establish and enforce the critical temperatures and response times to alarms.

Some mechanical freezers are equipped with emergency backup systems that automatically cool their contents with either liquid nitrogen 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 utilized and adequate supplies of refrigerant gas should be kept on hand at all times to operate the system.

D4.000 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. 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, vaccines for example, should be maintained precisely between 2 °C and 8 °C. The facility operator should ensure that high and low set points are monitored, and that alarm response time is adequate to prevent excessive temperature fluctuations.

D5.000 WALK-IN ENVIRONMENTAL STORAGE SYSTEMS

D5.100 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.

D5.200 Door Release

In most countries building codes require that walk-in units have internal safety releases to prevent a person from being trapped within a unit by the accidental closing of doors (*i.e.,* interior door release mechanism).

D5.300 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. Both types of units should have some type of mat or grate to prevent slipping.

D5.400 Dry Ice

Walk-in freezers should be kept free of dry ice (*i.e.,* the solid phase of CO_2). 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 carbon dioxide can displace oxygen, presenting an asphyxiation hazard. Where dry ice is employed there should 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 CO_2 monitors.

D5.500 Motion Detection Devices

Because of the special hazards involved in personnel working in a -20 °C 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.)

Best Practice: Engineering controls may be designed to support an audible alarm system coupled with a safety procedure to allow for the safest operating conditions.

D6.000 BACKUP STORAGE CAPACITY

Adequate backup capacity for low temperature units should be maintained in anticipation of possible equipment failure. In general, extra capacity equipment should be equal to the capacity of the largest single storage unit and should be maintained in reserve at operating temperature.

Best Practice: The total amount of backup storage required for large repositories should be determined empirically, but will typically be 1.5% to 3% of the total freezer capacity for liquid nitrogen storage and will be 10% for mechanical freezer storage.

Best Practice: Repositories should have a written procedure for transferring samples from a failed unit (one that has exceeded or is on the verge of exceeding its acceptable operating temperature range) and for the return of the samples to their original location once it is considered safe to do so. The procedure should include the freezer or refrigerator name or number as well as the location within the freezer where the samples have been placed.

D7.000 ENVIRONMENTAL MONITORING SYSTEMS

Acceptable temperature ranges should be determined for any specimen 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 that 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 should be used for evaluating the performance of all fixed temperature storage units. Storage units with defined environmental conditions should have temperature-monitoring devices that can be visually inspected on a regular basis (*e.g.,* a chart recorder or unit controller display).

In addition to regular temperature monitoring activities performed by repository staff, an automatic temperature monitoring system should be utilized 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 repository can be beneficial as well.

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

Depending on the size of the repository and number of staff available, more than one individual should carry a pager at all times, in case the first pager called is not functioning or the 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 minimizes the likelihood of damage to the stored material. Personnel with adequate training who can take corrective action should be on call 24 hours per day, seven days per week (see Section C9.000).

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 minimize 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.

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

Best Practice: Visual inspection of equipment temperatures should be performed at least once each working day and a record kept of the temperatures observed. Temperature records should 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.

Best Practice: Temperatures should 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.

Best Practice: In repositories where samples are stored in the vapor phase of liquid nitrogen, staff should regularly employ a technique whereby a physical measurement of the liquid nitrogen level is taken with a tool such as a dipstick to confirm the liquid nitrogen level. Alternatively, probes may be placed at various levels in the freezer to monitor liquid nitrogen levels (*e.g.*, temperatures below −196 °C indicate that the probe is submerged in liquid nitrogen and temperatures warmer than −196 °C indicate that the probes are in the vapor phase of the chamber. If tools are used to measure liquid levels it should be treated with ethanol, bleach or other disinfectants for the purpose of disinfecting the tool before it is used.

Best Practice: Alarms should be tested on a regular basis (*e.g.,* weekly or monthly) to ensure proper functioning and call-out to pagers and other notification devices used by staff that are on call.

Best Practice: In repositories 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.

D8.000 EQUIPMENT MAINTENANCE, REPAIR AND REPLACEMENT

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

D8.100 Calibration

A system for the calibration of all instruments should be in place. Any device that provides analog or digital measurements is considered an instrument and requires calibration. Calibration should be done annually or per manufacturer's recommendation. Calibration should be performed against standards established for the country in which the repository resides.

Best Practice: Calibration records should include the appropriate standard readings taken both before and after calibration.

Best Practice: A log of calibration records should 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 Standard Operating Procedure used to perform the calibration.

D8.200 Verification of Equipment Functionality

The proper performance of all equipment should be verified or qualified prior to use or following repairs that affect the instrument's measuring capabilities. Documentation of the testing should be maintained and made available for audits.

Certain federal regulations may require a more rigorous process employed to formally compare the performance of the equipment with manufacturer's specifications on a specified basis. The repository Director should ensure that all required regulatory practices are implemented.

D8.300 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 repository 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 should 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 specimens stored near the doors and walls of the unit.

Maintenance records should 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.

Best Practice: Well-qualified personnel with expertise in monitoring and repairing repository equipment (especially freezers and refrigerators) should be used for regular and emergency repairs. These trained technicians may be on the repository staff, may be on staff within the larger organization within the institution in which the repository resides, 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.

Best Practice: Repositories should maintain spare parts for critical equipment (*e.g.,* spare compressors for mechanical freezers or refrigerators), especially for aging equipment for which parts may not be readily available.

D8.400 Repair *vs.* Replacement

While most manufacturers of repository 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. Liquid nitrogen freezers may have lifetimes extending through 10 to 35 years.

Long-range plans should be made to address the possible repair and replacement of equipment essential to the functioning of the repository. 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.

Best Practice: Repositories should 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.

Best Practice: Resources for equipment repair and replacement should be identified when the repository is being established before an emergency is experienced. These resources should be reviewed on an annual basis.

SECTION E: QUALITY ASSURANCE AND QUALITY CONTROL

E1.000 GENERAL

It is critical that repositories be able to carefully track each of the specimens that is received, processed and disseminated from the facility. Accuracy and timeliness are critical to ensure their effective future use. Systems should be established to verify that all specimens are handled appropriately. Such systems involve the accurate descriptions of tasks performed (Standard Operating Procedures or SOPs) and may involve the verification activities by more than one repository technician or by a supervisor. When manual processes are followed, double and even triple checking of records may be required to ensure that appropriate steps have been followed.

E2.000 QUALITY ASSURANCE PROGRAM

Quality Assurance (QA) is an integrated system of management activities involving planning, implementation, documentation, assessment, and improvement to ensure that a process, or item, is of the type and quality needed for the project. Quality Control (QC) is the system of technical activities that measures the attributes and performance of a process, or item, against defined standards, to verify that the stated requirements are fully met.

Each repository should have a Quality Assurance Program/Quality Management System (QA/QMS) or adhere to the QA program of the organization with which the repository is associated. The program should describe the repository's commitment to its QA and QC programs and describe approaches for ensuring that the requirements of the QA and QC programs are met.

Should it not be possible to have a formal Quality Assurance Program with dedicated staff, a program should be in place to review procedures and records to assess the efficacy and quality of repository operations. This review should be conducted at least on an annual basis.

E2.100 QA/QMS Staff Responsibilities

Quality Assurance personnel should have responsibility for assuring compliance with all SOPs, policies and regulatory requirements. QA/QMS staff should have the responsibility and authority to inspect and approve specimen handling, processing and storage practices, as well as

discontinue processing and/or release of specimens when errors warrant. QA/QMS personnel should be responsible for managing audits.

E2.200 Standard Operating Procedures Manual

E2.210 Purpose and Design

Each repository should develop policies and procedures in a standardized written format that should be incorporated into a Standard Operating Procedures (SOP) manual. The SOPs contained therein should state policies and define and describe in detail, all procedures. These SOPs should be utilized to ensure that all samples are appropriately collected and stored so that they may be effectively disseminated for subsequent uses.

Current trends in networking between biobanks allow research investigators to take advantage of larger specimen collections that they might not otherwise have access to. Where possible, it is advantageous for biobanks to share their quality practices to ensure commonalities for specimen integrity and associated data.

E2.220 Essential Components for Standard Operating Procedures

SOPs serve as the description of how tasks pertaining to repository operations should be handled by staff assigned to those specific responsibilities. SOPs allow for uniformity and reproducibility in specimen handling. SOPs should be written by an individual or group of individuals with experience in successfully performing the processes described. Draft SOPs should be reviewed before they are finalized. Essential features of an SOP are included in the following list of components:

- Title – Each SOP should be given a unique name which captures the essence of the practice described.
- Number – Each SOP should be given a unique number that can be used for easy reference. The numbering system should include the revision number for the practice so that the most recent version can be easily identified.
- Date – The date the procedure was first introduced as well as the date of the most recent version. The date format should be based on the ddmmyyyy system where d represents day, m represents month and y represents year.
- Department/Division/Staff Covered – The individuals to whom the SOP will apply.
- Protective Wear – Protective equipment that should be worn by staff when performing the procedure described.
- Equipment – A list of the equipment needed to perform the procedure. Equipment description may include but is not limited to the name, model, date of purchase, serial number, inventory tracking number, and manufacturer.
- Supplies – All materials and supplies should be recorded. The SOP may ask for a record of the lots and expiration dates for the materials and supplies utilized.
- Step-by-Step Guidance – The procedure should be written in specific detail to ensure that the procedure can be repeated in a reproducible fashion to include the order of steps that should be followed, the times allowed for each step (as needed) and the temperatures at which the steps are performed.

E2.230 Critical Topics for Standard Operating Procedures Manuals

The Standard Operating Procedure (SOP) manual should specifically include, but should not be limited to procedures regarding the following:

- Specimen handling.
- Laboratory procedures for tests performed in-house and any specimen aliquoting or other specimen processing.

- Where appropriate, human subjects protection documentation, including informed consent, privacy and confidentiality protections, and other legal, ethical and cultural issues.
- Where appropriate, access and sharing of specimens and associated data.
- Shipping and receiving of specimens.
- Records management practices. These should include policies regarding the shredding of confidential documentation at the appropriate time.
- Quality assurance (QA) and quality control (QC) for instruments, reagents, labels, and processes employed in sample collection, processing and retrieval.
- Equipment qualification, maintenance, repair and calibration.
- Safety programs including reporting of staff ergonomics, near miss incidents, injuries and exposure to potential bloodborne pathogens.
- Investigation, documentation and reporting of incidents and near miss incidents, errors, complaints and adverse outcomes.
- Disposal of medical and other hazardous waste.
- Training programs.

E2.240 Implementation

Either the repository Director and/or the individual responsible for the QA Program should review and approve all SOPs and associated process validation studies prior to implementation. Upon implementation, all SOPs should be followed as written.

E2.250 Modifications

Each repository should have document control policies in place that govern retention and modifications or revisions to SOPs. Prior to implementation, each modification should be approved by the Director and other appropriate individuals. Implementation dates should be recorded for all procedures.

A system should be in place to ensure that only current versions of documents are available for use and that previous revisions are removed when new revisions are issued.

E2.260 Review of Standard Operating Procedures

SOPs should be reviewed regularly to be sure that the current method for performing the procedure is described. SOPs should be examined at least every two years. A system should be in place to document the revision number and date of release of the revised document.

E2.270 Staff Access and Review

Current copies of the SOP manual should be stored in designated locations and available to the staff at all times. New and revised policies and procedures should be reviewed by the staff prior to implementation.

Best Practice: A system should be in place to document staff review of the most recent versions of an SOP.

Best Practice: Training associated with SOPs should be maintained in a training record (see Section G2.700).

E3.000 QUALITY STANDARDS

A variety of systems have been devised to allow for confidence and reproducibility in repository practices. Each system described in this section has been developed to ensure that good practices are in place; complete with careful documentation and traceability. While each of the standards described below are resources for repositories, there are costs involved in the attainment of each standard and all the standards may not be appropriate for every repository.

E3.100 Current Good Practices

Current Good Practices (cGP) are regulatory guidelines that should be interpreted by the repository to fit its particular circumstances. cGP may be preclinical (Good Laboratory Practice, or GLP), clinical (Good Clinical Practice or GCP) or manufacture (Good Manufacture Practice, or GMP). cGP may be more relevant to large corporate repositories, but academic and other small repositories may wish to aim toward cGP guidelines to instill confidence in the implementation of its SOPs. Generally, these standards are interpreted as follows:

- The facility is in a secure, locked area with limited access.
- Personnel should be trained in all procedures and successful completion of such training is documented with evidence of updates, if required, on a periodic basis.
- The facility is subject to internal QA audits and/or site visits by external clients and agencies as appropriate. The agencies that would audit vary by local, state, national or international regulations.
- Policies and procedures are documented in SOPs that are approved by appropriate personnel and are changed or updated only under strict document control rules.
- Records are maintained with respect to the purchase of new equipment, maintenance and repair activities, as well as equipment disposal. Examples of information tracked may include but are not limited to the name and model number for the equipment, manufacturer name and contact information, serial number, date of acquisition, maintenance and repair, *etc.*
- Records should also be maintained for critical materials and reagents used by the repository. Examples of information tracked may include, but not be limited to, the item name, company from which the item was purchased, date of purchase, expiration date and all related MSDS.
- Deviation reports are produced for all events that fall outside SOPs.

E3.200 INTERNATIONAL ORGANIZATION FOR STANDARDIZATION

ISO9001 was created through the International Organization for Standardization (ISO). ISO is a worldwide federation of national standards bodies with headquarters in Geneva, Switzerland. The organization was founded in 1946 to develop a common set of standards for manufacturing, trade and communications organizations.

E3.210 ISO9001:2000 Requirements of Quality Management Systems

ISO9001:2000 is a system standard, not a product standard. Its primary purpose is to provide organizations with useful internationally recognized models for operating a quality management system. ISO9001:2000 specified requirements for a quality management system where an organization needs to demonstrate its ability to consistently provide products that meet customers' and applicable regulatory requirements. It aims to enhance customer satisfaction through the effective application of the system. ISO9001:2000 is the benchmark of all standards. It is a level of quality standardization that some repositories are working to implement. ISO is similar to cGMP but is more recognizable in international settings.

E3.220 ISO/IEC 17025 Quality Systems for Testing and Calibration Laboratories

ISO/IEC 17025 provides general requirements for producers of reference materials including tests and/or calibrations, and sampling. ISO/IEC 17025 covers the use of standard methods, non-standard methods, and laboratory-developed methods. ISO/IEC 17025 incorporates key requirements of ISO9001:2000.

E3.230 ISO Guide 34:2000 General Requirements for the Competence of Reference Material Producers

The ISO Guide 34:2000 provides the general requirements that a reference material producer should demonstrate if they are to be recognized as competent to carry out the production of reference materials. ISO guide 34 references ISO/IEC 17025 as a normative document.

E4.000 AUDITS

Repositories should be subjected to regular audits. Audits cover the implementation of all SOPs that govern the repository. Audits may be done on a quarterly, semi-annual or annual basis. A designated individual familiar with the specific work being reviewed but not directly involved in that work should be responsible for each audit. For this function the individual should be someone who is not directly supervised by the Director (*e.g.*, they should report to a separate department or division responsible for quality assurance).

E5.000 QUALITY CONTROL CONSIDERATIONS FOR TISSUE BIOSPECIMENS

Quality control examination of tissues designated for research should be appropriate for the research protocol. Quality control of tissue ranges from microscopic examination of an aliquot representative of a specific tissue by a pathologist or cell biologist, or an equivalently trained individual, to molecular quality control in which nucleic acids and proteins are characterized. The highest quality control measures ("platinum" level) involve enriching the diseased population of tissue through macro-dissection of frozen sections and potentially performing molecular analyses as well. Platinum-based approaches are, however, cost prohibitive and potentially exhaust specimen availability. A cost effective approach for tissue resources requires simple methods of quality control that can be expanded per investigator request.

Best Practice: For pathology research, if tissue is prospectively removed from a patient with a particular diagnosis, verification of disease state criteria meeting the research request should be affirmed. The percent of specimen that is diseased should be documented along with the percent necrosis/fibrosis and percent of mucin formation present in the tissue.

Best Practice: For each tissue specimen collected, an aliquot, representative of that tissue specimen, should be microscopically examined by a trained pathologist or other trained professional experienced with the organism from which the tissue originated.

Best Practice: In situations where the tissue obtained is too small to obtain an adequate aliquot for QC, the QC examination should be made on the diagnostic specimen from whence the research tissue was obtained, as close as possible to the area where the tissue supplied for research was procured.

Best Practice: Selected methods for preserving tissues should be investigated in advance of collection to be sure that any preservatives, dehydration or other protective treatments used do not have a deleterious effect on future analyses.

Best Practice: Depending upon the molecular analyses that will be performed by the end-user, it may be advisable to extract and analyze matching molecular entities (*e.g.*, DNA, RNA or proteins) as a part of the tissue quality control testing.

SECTION F: SAFETY

F1.000 GENERAL

Issues related to safe operation of a repository are complex and depend on the particular activities of the repository. Regulations governing safety may be covered by national, regional or

local statutes. Each repository should determine which areas of safety affect it and develop an appropriate safety program to protect its employees.

Safety plans are used to prevent or to minimize injuries to employees. In order to develop an effective safety plan, the likelihood and source of specific injuries for each employee should be identified. These will depend upon the procedures and activities that employees perform as well as rooms in which the employees are likely to spend time. Each person and their supervisor should work together to identify potential sources of injury and how the likelihood of injury can be minimized via changes in procedures or engineering changes including the use of safety equipment or the improvement of ventilation within a specific area.

F2.000 NATIONAL, REGIONAL AND LOCAL REGULATIONS

In developing an effective approach to ensuring safety in a repository there are many extensive national, regional and local regulations that should be met in order to protect the health and safety of employees. Along with these regulations, most regulatory authorities provide guidance concerning how to meet these regulations. Some web-based aids to understanding national regulations concerning safety are listed in Appendix A.

F3.000 SAFETY INFRASTRUCTURE

The Director or other designated individual (this may even be the CEO in some organizations) has primary responsibility for the safe operation of all components of the repository. While the individual with this responsibility may be primarily responsible, the responsibility for safe operation lies with each employee.

The institution in which a repository resides usually establishes a Safety Committee that is responsible for the overall safety plan of the institution and for periodic monitoring and updating of the plan. The Safety Committee usually appoints a Safety Officer to administer the program.

The Safety Officer establishes a safety training program and monitors and maintains compliance with the program, evaluates incidents and injuries, and recommends changes to the Safety Committee, as needed. The Safety Officer works closely with area supervisors to ensure adherence to all safety regulations.

F4.000 TRAINING

Certain risks may be present when repository, laboratory or field staff come in contact with patients during the consenting process (*e.g.,* HIV or tuberculosis) or non-human species during the specimen collection process (*e.g.,* zoonotic pathogens that are transmissible from animals to humans). Individuals performing these tasks should be trained in the possible hazards, and should take appropriate precautionary measures. For example, staff members working with human patients are encouraged to be vaccinated against hepatitis. See Section G for a full discussion of training issues.

F5.000 PERSONAL PROTECTIVE WEAR

All persons, including visitors, should wear appropriate clothing (lab coats, long pants, and covered shoes; not shorts, skirts, or open-toed shoes) as well as eye protection. Appropriate gloves are recommended in handling any specimens, chemicals or hot or cold equipment and supplies. Gloves should be chemically resistant to the particular material handled.

F6.000 SAFETY TOPICS

F6.100 Biological Safety

All human specimens and to a lesser extent animal specimens, whether fixed, paraffin-embedded, fresh frozen or freeze-dried should be considered as potential biohazards. As the ex-

tent of alteration of tissue increases (*e.g.,* fresh to frozen to fixed to paraffin-embedded) the risk from various infective agents usually is reduced. However, certain agents such as prions [*e.g.,* the causative agent for Creutzfeldt-Jakob disease ("mad cow disease"), scrapie, deer/elk wasting disease, or other transmissible spongiform encephalopathies (TSEs)] may still be infective even when tissues are fixed and processed to paraffin blocks. Consequently, all human and animal specimens independent of their state should be treated with universal precautions, *i.e.,* should be handled as if infected with agents that may be pathogenic to humans. Individuals should receive training so that they can recognize symptoms that accompany the exposure to certain harmful compounds and diseases to which staff are exposed.

Applicable regulations covering occupational exposure to bloodborne pathogens should be determined. Any organization that deals with human and some non-human specimens may need to meet the requirements of these regulations.

F6.200 Chemical Safety

Many countries have developed regulations that govern activities relating to chemical safety that may affect repositories (see Appendix A). These laws may mandate that employers develop a written chemical hygiene plan. The chemical hygiene plan should be capable of protecting employees from hazardous chemicals in the laboratory and capable of keeping chemical exposures below the action level or in its absence the Permissible Exposure Limit (PEL).

After handling hazardous materials, hands and other possible exposed areas of skin should be washed.

All chemicals used in repositories should have material safety data sheets (MSDS) available for reference for employees who potentially will come into contact with these chemicals and auditors who will look for these documents. MSDS are available from manufacturers and should be provided either in hard-copy or from a provided URL for downloading.

F6.210 Chemical Hygiene

Chemical hygiene plans should include the following:

- Approaches to prevent, contain, and clean up chemical spills. The plan should include a description of how waste and other chemically contaminated materials resulting from the clean-up are to be disposed.
- Approaches to the safe and lawful disposal of all repository materials no longer deemed necessary.
- Approaches to ventilation failure, evacuation, medical care, reporting of chemical exposure incidents and chemical safety drills.
- A description of the allowable areas for eating, drinking, storing food and beverages, drinking, smoking, gum chewing and the application of cosmetics. None of these should be permitted in areas where specimens are processed, stored or handled.
- Guidance on allowable pipetting methods (*e.g.,* mouth pipetting and mouth suctioning for starting a siphon should be prohibited).
- Guidance on the appropriate use of all chemicals used in fixation of tissues.
- Requirements for the use of biological safety hoods to minimize exposure to vapors from hazardous chemicals (*e.g.,* formaldehyde or xylene).

F6.300 Electrical Safety

Electrical injuries can be avoided by ensuring that all equipment is properly grounded. Equipment should be tested for grounding when first purchased and yearly thereafter. Similarly, all electrical base plugs should be in good condition (grounding should be checked/verified) and electrical work should be done with great care ensuring that personnel in the affected work area are protected by removal of fuses and with written warnings at the fuse box. Also, care should

be taken with electrical appliances/equipment around water sources, especially sinks and bathrooms/showers.

Best Practice: Surge protectors are recommended for stand-alone freezers if this is not part of the building electrical infrastructure.

F6.400 Fire Safety

The local fire department can inspect a repository to evaluate fire safety prevention plans. Prior to such inspections and at least yearly, fire drills should be conducted, fire suppression equipment and safety showers should be tested, and emergency pathways should be posted at all room exits. Emergency exits should never be blocked, obstructed or locked and hallways should not be obstructed or cluttered. Flammable agents should be stored appropriately, including storage of large amounts of flammable agents in fire cabinets if more than several quarts are present in one area. Refrigerators/freezers can be purchased that are noncombustible, specifically for use in research laboratories. Smoking, if permitted at all, should be limited to designated external areas. Furniture, rugs, and equipment should be constructed of non-flammable material. Regulations for types of doors to serve as fire barriers should be followed as should fire requirements for construction of buildings that house specific activities (*e.g.,* laboratories). Fire safety will be governed by national, regional and local requirements. (See Internet sites in Appendix A.)

F6.500 Physical Safety

The physical safety of employees should be considered in all repositories and for all employees. Physical safety ranges from preventing falls to ensuring employees are not physically injured by other means. Ensuring physical safety involves careful maintenance of the physical plant and facilities. Tears in rugs, broken steps and water, soap, paraffin and other slippery substances on floors, power cords, and inappropriate use of ladders or chairs as ladders, may all lead to unnecessary falls. Similarly, unsecured gas cylinders, unbalanced file cabinets, and inadequately secured shelves all can lead to injuries via falling or moving agents or structures.

Also included in causes of physical injuries are repetitive-motion injuries and back injuries resulting from inappropriate lifting and movement. Repository staff members may be required to stand on step stools and lift heavy racks vertically out of the freezer in order to access specimens. Back injuries can be avoided by installing an automatic pulley mechanism to aid in the removal of the racks from the freezers. By analyzing an employee's work environment and improving the proper placement of objects and/or provision of the proper tools, the potential for injury will be greatly reduced. When ergonomics is applied correctly in the work environment, visual and musculoskeletal discomfort and fatigue are reduced significantly. Where feasible, repositories may consider automated specimen input and retrieval systems to reduce physical strain on technical staff.

Physical injuries that are difficult to avoid include minor cuts (*e.g.,* paper), bumps and strains due to inattentive actions. However, such minor injuries should not be compounded by exposure to biohazards. The overall safety program should address other hazards that can be prevented or ameliorated by wearing proper protective equipment and clothing such as the use of gloves to avoid thermal burns from both heat and cold (*e.g.,* dry ice or liquid nitrogen). Check the occupational safety laws of your region (see Appendix A.)

F6.600 Radiological Safety

Few repositories will store or use radioactive material. For those repositories that do use radioactive material, a radiological safety plan is needed. Specific training is required for personnel who use or come into contact with radioactive material as well as in the use of specific radiation monitoring equipment. Work with radioactive materials in many countries requires a

license from a federal regulatory committee. Repository staff should refer to the appropriate guidelines for the country or region in which the repository is located.

SECTION G: TRAINING

G1.000 GENERAL

All repository staff should be adequately trained to perform the tasks required by their particular position description. Proper training is important to promote quality in specimen handling, good ethical practices and compliance with appropriate policies and regulations related to repository operation. In some areas of safety, adequate training may be mandated by federal law and severe penalties may be imposed on the repository and repository personnel if training is not provided as required.

Support for training is essential for adequate implementation of certain tasks, and in some cases might require additional resources or time off from regular responsibilities to ensure that the training required is achieved in the most effective manner possible.

G2.000 TRAINING INFRASTRUCTURE

G2.100 Training Program

Every individual who enters the repository for the purpose of performing work should be trained in the particular functions or tasks which they are asked to complete. Training should be task and location specific and be designed for the particular position required to carry out the work. Training should involve instruction in the use of any equipment used and involve appropriate quality control and quality assurance practices.

Training for some functions may be provided by departments outside of the repository (*e.g.,* maintenance staff) but repository staff should make sure that all individuals who enter the repository follow required safety and other precautions in performing their particular tasks. Training should be in a language with which the employee is conversant and the level of training should be appropriate to the employee's level of comprehension.

Repository staff should be asked to review any written procedures for which they are responsible prior to the commencement of their "hands-on" training. A written record indicating that the employee has read and can perform the pertinent procedures should be kept in the employee's training file (see Section G2.700). This record should include the title of the procedure (or SOP number), the employee's initials, and the date upon which the training was completed, the name of the trainer and the trainer's initials. It is preferable that a short test be administered to personnel concerning the material that is presented for the employee's review.

Best Practice: To ensure quality in the performance of repository activities employee performance should be routinely monitored to identify needs for additional training between regular training intervals. Staff should be informed when first hired that regular checking of work does not necessarily suggest doubt in the employee's performance, but rather may be a part of regular practices for ensuring quality and is applicable to repository staff working at all levels in the facility

G2.200 Individual Responsible for Training

Each repository should have an Individual Responsible for Training (IRT) who will maintain the SOP manual and will coordinate with the supervisor responsible for that particular procedure when any revisions are needed either due to the expiration of the SOP or for technical reasons.

The IRT will closely coordinate issues related to training in safety with the organization's

Safety Officer and with other individuals responsible for specific areas of repository procedures (*e.g.,* shipping and handling).

The IRT is responsible for monitoring training and its appropriate documentation of all employees. The IRT will maintain records of employees who need to be trained in each required area and the time of their periodic updates of training. The IRT will inform the employees of potential times of training and will monitor whether the training is completed according to the required timeframe.

The IRT will closely coordinate documentation of training and education activities with personnel who maintain employee records, as needed.

G2.300 Trainers

The trainer is one who regularly performs the procedures in question, has completed the training program previously and is skilled in explaining the elements of the task. The trainer is responsible for assuring that the trainee understands each procedure and task. For special areas of training (*e.g.,* human subjects protection, privacy, safety), personnel with special expertise may provide the training. Experts via audio-visual methods including web-based technologies may also provide training. This approach may permit employees to complete special areas of training at their own pace when time can be scheduled based on the employee's daily activities.

During the training period, the trainer will demonstrate, explain and review the standards to be followed in conducting the procedure(s). The trainer should provide appropriate feedback, as necessary, on the trainee's performance of the procedure. The trainer should supervise the trainee in all tasks contained in the procedure(s) until the training phase has been completed. Upon successful completion of the training phase and after the appropriate documentation has been completed, the trainer should ask the trainee if they are comfortable conducting the procedure(s) without supervision or if they feel that additional training is needed.

Best Practice: Even after the training has been completed, the trainer should be available to answer questions when the task is being performed by the trainee for the first few times.

G2.400 Frequency of Training

Training and repeat training should be conducted in accordance with applicable regulations and also in accordance with the needs of the particular tasks and positions held by repository staff. In many countries, regulations require training before the employee begins working and yearly thereafter (*e.g.,* biohazard, chemical hazard and IT training). Training for regular repository tasks should be implemented before staff is permitted to perform those particular tasks and repeat training should be performed according to a defined schedule described by SOPs. Modifications to SOPs may require additional training. Supplemental training may also be required following the evaluation of particular incidents in order to prevent their recurrence.

G2.500 Cross-Training

Repositories may find it advantageous to implement a system of cross-training. Cross-training is the practice in which the staff is trained in a variety of procedures and individuals are able to perform each of these at any time requested. Cross-training alleviates staff burn-out, reduces staff turnover and allows for coverage of key activities in case staffing levels change either on a temporary or a permanent basis. Also, since some tasks require repetitive motion, cross-training may minimize physical strain among those performing those particular responsibilities.

G2.600 Training Documentation

Once the training is complete, a written record of the completed training should be made that includes the trainee's signature as well as the trainer's signature and the date that training was successfully completed. Electronic signatures should be used for documentation of any electronic training that is received.

G2.700 Training Records

A training file should be maintained for each repository staff member and should include, but may not be limited to the following:

- Position description that includes the job title and responsibilities, as well as the educational experience required to perform the specified task.
- Resume.
- Example of the employee's signature and initials. This is important to be able to identify the individual who may have performed certain tasks required by SOPs pertaining to certain repository activities, or to identify an individual who may have signed for the receipt or shipment of specimens (or supplies or equipment) to or from the repository.
- Copies of any certificates documenting that the employee has had specialized training. This should include training in shipping, safety, and applicable regulations such as those required in the country in which the repository is located (see Appendix A).
- Documentation that an employee has read and understands all SOPs pertinent to the employee's responsibilities.

The training file should be kept in the repository and be available for Quality Assurance or client review. The training file should be archived according to the repository's SOPs after the employee is separated from the organization. If an employee moves from the repository to another department within the organization, the employee's training file should be transferred to the new department.

SECTION H: BIOLOGICAL MATERIAL TRACKING

H1.000 GENERAL

In order to make certain that specimens can be tracked accurately from the site at which they are collected through their arrival and subsequent shipment from a repository, effective tracking systems should be in place. Critical components of these systems include the use of unique specimen identifiers, appropriate specimen labels, inventory systems for specimen tracking, and other features that are described in detail below.

H2.000 LABELS

Each specimen container should receive a computer-printed label that tightly adheres under all projected storage conditions. Information encoded on labels should be resistant to all common laboratory solvents. Labels should include readable indications as to what is stored in the container (see Sections H2.200 and H2.300). Flexibility should be allowed in the location of the label to allow for label legibility on a wide variety of containers.

Material used in composition of containers for environmental specimens may pose special problems for label adherence and therefore, in some cases, the label should be able to adhere to itself.

Best Practice: The adherence of labels to containers as well as the use of particular types of ink should be tested under the anticipated storage and processing conditions before they are put into regular use.

Best Practice: For biological specimens, it is important for the label to create a link between the sample ID and the voucher or e-voucher. This link is established when the tissue sample and the voucher are sampled (*e.g.,* in the field) using numbers provided by the biobank or biological resource center (BRC) for both.

H2.100 Barcoding

Whenever possible, labels should be printed with a linear (one-dimensional or 1D) barcode that uniquely identifies the specimen. Under some circumstances, two-dimensional (2D) barcodes may be utilized. 2D barcodes have the advantage that scanning error rates may be lower and more information can be included on the label and may be optimal for use on smaller vials. Cost considerations may influence the systems selected for creating and reading barcodes.

H2.200 Labels for Human Specimens

Human specimens should be labeled in such a way that protects privacy and confidentiality and is in compliance with applicable laws and institutional policies. The unique identifier for each specimen should be printed on the label in both barcode format and human readable form. Specimens should be labeled with a unique code not derived from information about the subject or related to its storage location in the repository. No other study or personal health information should be encoded in the specimen ID. In addition, the specimen ID should not be tied to the storage location.

H2.300 Labels for Non-human Biological Specimens

A unique identifier should be included on the label for non-human specimens. This identifier may be a field identification number assigned during collection of the sample or another standardized numbering system used by the repository and its users. Labels should provide a link to information on the taxon (usually the species name), collection details (*e.g.,* geographical locations, geo-referencing, date, collector) and the sample type and original volume.

H3.000 INVENTORY SYSTEMS

A computer-based inventory system should be in place that tracks the location and status of every specimen in the repository. The system should also track significant events such as sample thaws, loss, destruction, processing of any kind, as well as specimen distribution. (See Section H3.200 for additional elements to be tracked.) The system should assign a unique ID to each specimen in the database and where appropriate, there should be a unique link to the voucher. This ID should be printed on the specimen label, where possible. If the ID assigned by the repository is not printed on the specimen label, both the database ID and the current label ID should be unique and linked in a database. Other IDs that may be tracked include parent specimen ID, source specimen ID, subject ID, study or protocol ID, collection kit ID, *etc.* These IDs will provide internal and external links to other data about the specimen.

The inventory system should include a full audit trail of changes made to the database. This should include, but not be limited to, the original data; the changed data; who made the changes; when, how, and if possible, why the changes were made. This audit trail should be automatically recorded and available for read-only access.

The inventory system should have the ability to generate configurable reports and data files in order to provide the most complete information on the history of the specimen.

Access to the computerized inventory system should be tightly controlled. Security roles with defined privilege levels should be assigned to repository staff and other users of the system. For example, some individuals may be able to view specimen availability whereas others can enter or modify specimen descriptions and make requests to have specimens shipped from the repository.

Best Practice: Inventory management systems should have the ability to link or communicate with other established databases if additional data are needed.

Best Practice: Where possible and appropriate, data should be electronically convertible into formats that can easily be shared among collaborating institutions.

H3.100 Specimen Location

Each freezer, refrigerator or room temperature storage cabinet should have a unique identifier. A convention should be established for numbering shelves, racks, boxes, as well as each location within the container. Each location combination *(e.g.* freezer, rack, box, row, and column) should uniquely identify a location in the repository. The inventory system should also be able to report on available storage space and assign and reserve space for incoming specimens.

Best Practice: A random check to be sure that the correct specimens are in the location specified by the inventory system (database) should be conducted on a small percent of samples on an annual basis.

H3.200 Additional Specimen Descriptors

The inventory system should track sample identifiers such as material type, vial type (*e.g.,* vial, tube, ampoule, straw, bag, *etc.*), volume, date of collection, voucher, and date of receipt or processing, processing method, storage temperature, preservatives and any other characteristics needed for the collection. Information should be included on the history of sample processing and movement, including the location of shipments to and from external sites. Finally, any information about the sample being compromised in any way (*e.g.,* temperature excursion, freeze/thaws, *etc.*) should be recorded and available to the user to aid in selecting specimens for testing.

H3.300 Additional Information for Human Specimens

In addition to the information regarding specimen location, information relating to the following data may be maintained for a biospecimen resource, depending upon the nature, purpose and type of the resource (if relevant, available, or not stored in another interoperable information management system):

- Subject information: Age of subject at the time of collection, sex, occupation, race/ethnicity.
- Diagnosis: Site, histology, stage at diagnosis, date of diagnosis.
- Diagnostic procedures: Procedure, date of procedure.
- Type of treatment (*e.g.,* chemotherapy, radiation, hormonal, immunotherapy) prior to specimen donation.
- Surgical procedure information: Surgery, primary site, metastatic site, stage of disease at time of surgery, diagnosis code (ICDO), diagnosis text.
- Medical history: Drug name, dose/frequency, date started.
- Family history: Relationship, diagnosis, age at diagnosis.
- Smoking history: Smoke type, smoke years, date quit.
- Vitals: Height (cm), weight (kg), alcohol history, recreational drug history, special diet, date of last menstrual period, date last follow-up, disease status at follow-up, cause of death.
- Clinical laboratory values (*e.g.,* calcium, hemoglobin, *etc*.).
- Availability of other biological specimens (*e.g.,* normal *vs.* diseased tissue, other tissues, blood, buffy coat, and plasma, paraffin-embedded tissue, H&E slide, formalin fixed tissue, DNA, RNA, urine, feces, saliva, ascites fluid, and synovial fluid) from the same donor.

An inventory system may also be designed so that digitally-scanned documents are available such as surgical pathology reports, H&E slides of tissues collected, clinical lab reports, patient consent forms and material transfer agreements (MTAs, see Section H4.000).

Best Practice: The information stored will vary according to the purpose, nature, and intended uses for the biospecimen collection. Since a repository may track samples of many different studies, consideration should be given to what the inventory database can contain and what should be stored in an external database and linked to the inventory.

H3.400 Additional Information for Non-Human Specimens

Many items listed in H3.300 can also be applied to the information tracked for non-human biological samples, specifically animal samples, as well as additional information not included above. The following information is important when collecting for environmental or other types of specimen banks:

- Collection information: Species of specimen (or other taxonomic rank if this is not possible), sex (if applicable), age, size and mass of individual sampled, assessment of health, assessment of population size (if applicable), and notation describing typical or unique traits of the specimen compared to the overall population (if applicable). Photographs of the individual and site.
- Collection and processing location (if different, list both): latitude and longitude, altitude; soil type (if applicable); climatic or weather conditions; ocean/bay/sea, city/island, indoors or outdoors, under clean-air conditions.
- Date and time the tissue was removed from organism or site location, processed and frozen for storage. Temporary preservation procedures.
- Type of instrument used to collect and sub-sample (if necessary) the sample (stainless steel blade, titanium knife).
- Type of container used to store the sample (Teflon®, polypropylene, glass, stainless steel).

H3.500 Validation

Validation of computer systems and software may be required by federal regulation and sometimes by clients. All inventory systems, whether or not they have been validated, should be subject to regular Quality Assurance audits.

H4.000 MATERIAL TRANSFER AGREEMENTS

A Material Transfer Agreement (MTA) is an agreement that governs the transfer of tangible research materials (and associated clinical data, as relevant) between two organizations, when the recipient intends to use it for his or her own research purposes. An MTA defines the rights and obligations of the provider and the recipient with respect to the materials. The MTA may also address future distribution of modifications and derivatives made by the recipient, and it may document the process for determining each party's interest in the modifications or derivatives. Biological materials, such as reagents, cell lines and nucleic acids, 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 and data. Terms of confidentiality may be added to an MTA to address confidential information or data transferred to the recipient along with the material. Both the sender and the recipient (and their respective institutions) should agree to the terms of the MTA prior to the shipment.

Other types of agreements or contracts may be implemented when biospecimens are transferred, without the title of "MTA". Even if they are called something other than an MTA, all documents of this type should contain specific information on how the material that is to be transferred may be used and may include such issues as intellectual property and publication rights. A variety of models for these agreements are available on the internet.

Best Practice: Prior to initiating a shipment of specimens to an outside entity, an MTA or similar agreements should be executed to document the transfer of materials. The MTA or similar agreement should be initiated as soon as possible, as there may be additional time required for legal or regulatory approval before the transfer can be initiated.

H5.000 SHIPPING LOG

Each repository should maintain a shipment log to record the receipt and dissemination of shipments sent from the repository. The log may be computerized or it may be kept in a log-

book (or notebook). If computerized, it should be included in the functionality of the inventory management system described above. Each shipment entry should be given a unique shipment number. The log should track the following elements:

- Shipment/Invoice Number.
- Recipient/Source.
- Date received or shipped.
- Courier name and ID# for tracking package.
- Sample description.
- Number of samples received or sent.
- Study name if available.
- Study number if available.
- Shipping conditions (*e.g.,* dry ice, room temperature, *etc.*)
- Key investigator name(s).
- Signature of individual receiving the specimen.
- Any discrepancies between the shipping manifest and the actual shipment.
- Any indication that a specimen has been compromised.

SECTION I: PACKAGING AND SHIPPING

I1.000 GENERAL

Packaging and shipping should conform to all governing regulations. Air shipments should conform to International Air Transport Association (IATA) standards. Ground shipments should conform to applicable federal standards. All personnel involved in shipping biological materials should be trained properly for both air and ground shipments. As regulations change, training may need to be updated.

I2.000 TRANSPORT SPECIFICATIONS

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

I2.100 Regulatory Requirements

The shipper should first determine how to classify the specimens that are to be transported. Specimens routinely shipped from repositories may be considered dangerous goods such as infectious substances, diagnostic specimens, biological products, genetically modified organisms and microorganisms or toxic substances. The preservatives that have been applied to the specimens may be considered toxic, flammable liquids, non-flammable gases, or corrosives, all of which are dangerous goods. In order to properly classify the specimens to be included in a shipment, one should consult their federal transport regulations as well as those from International Civil Aviation Organization (ICAO) and IATA.

Many countries require that personnel involved in the transport of dangerous goods receive training in this area before they begin their shipping responsibilities.

I2.200 Temperature Requirements

Specimens may be exposed to temperature fluctuations during transit. The following are typical temperature conditions required for transport of specimens and the insulation/refrigerant helpful to maintain that temperature:

- Ambient (20 °C to 30 °C) - insulated packaging to protect from extreme heat/cold ambient conditions.
- Refrigerated (2 °C to 8 °C) - wet ice, or gel packs designed for refrigerated temperatures, conditioned at −15 °C 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, dry ice blocks, or dry ice sheets. Note that dry ice (solid CO_2) employed for frozen shipments is considered a hazardous material and appropriate labeling 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.

Best Practice: Shipments of material that are subject to cold chain management should be shipped with sufficient refrigerant to maintain temperature throughout the shipping cycle, with allowance for at least a 24-hour delay in arrival time.

I2.300 Humidity Requirements

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

I2.400 Light Sensitivity Requirements

Light sensitive material should be sent in packaging that does not allow penetration of light such as amber vials or amber coated bags.

I2.500 Arrival Time Requirements

Time sensitive specimens 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 it does not arrive on the day it is scheduled for delivery. Shipments should also be scheduled so that they do not arrive on a holiday in the recipient location.

I2.600 Specimen Quantities

The quantity of specimens to be transported will affect the type of packaging and amount of refrigerant required to maintain appropriate temperatures for all specimens in the shipment. The container size should be appropriate for the amount of refrigerant needed and for the number of specimens that will be included in the container. Avoid sending an excessive amount of specimens in a single container.

I2.700 Other Packaging Considerations

- Specimens should be positioned between the refrigerants used, rather than to be placed on top of or underneath the refrigerant.
- Empty spaces in the container present after the specimens and the refrigerant have been loaded should be filled with wadded paper to prevent movement of the specimens during shipment.
- Remove or mark through any labels remaining on the exterior of the shipping container from a previous shipment.
- Airbills should not be reused.

I3.000 VERIFICATION OF SHIPPING CONDITIONS

I3.100 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.

I3.200 Verification of Packaging

Packaging should be tested prior to use with specimens. Tests should include measuring all parameters that could influence specimen integrity (*i.e.*, temperature, humidity, light sensitivity, structural quality, and spill containment).

Shipments of specimens 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.

I3.300 Test Shipments

In some situations, especially relating to extremely valuable samples, repositories 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 to identify any potential obstacles for the successful shipment. When test shipments (as well as subsequent specimen 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.

I3.400 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 specimens or have specific requirements concerning the import/export of such specimens. 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 (CITES) 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 for delivery for the customs information that needs to be displayed.

Best Practice: Identify all requirements for shipping to a designated country prior to the initiation of the shipment.

Best Practice: Due to possible delays in completing Customs requirements, temperature sensitive material may be consigned with a courier capable of replenishing refrigerant in the event of a delay. As much as three additional days' worth of refrigerant may be recommended for shipments in cases where Customs clearance may be difficult.

Best Practice: International shipments should include a letter on institution letter head (as appropriate) documenting the contents and handling requirements. Copies of all import permits and sanitary certificates should be included, as needed.

I4.000 TRACKING SHIPMENTS DURING TRANSPORT

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

I4.100 Notification of Shipment

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.

I4.200 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.

I4.300 Confirmation of Receipt

Confirmation of receipt and the condition upon arrival should be obtained for every shipment coming to or leaving a repository. A form that collects this information should be sent with the shipment. Information as to how the condition report should be returned to the shipper should be clearly indicated.

SECTION J: SPECIMEN COLLECTION, PROCESSING AND RETRIEVAL

J1.000 GENERAL

Although specimen processing practices vary according to the specific type of specimen being studied, collection and retrieval practices have many elements in common. Specimen availability and the intended analytic objectives need to be considered prior to initiation of collection. Many specimen collection protocols have special requirements for preservation of macromolecules and/or analytes of interest. In addition to specimen type, things to consider when planning to collect specimens include: the collection method, the collection tubes or containers needed, the population that will provide the specimen, personnel required to collect the specimen (and training in the collection process), the distance from the collection point to the processing lab and to the storage facility (if this is a different location), stabilizing or preservation techniques for maintaining/preservation of macromolecules required for the specific analyses, and specimen labeling and tracking strategies.

J2.000 PILOT STUDIES AND PROOF OF PERFORMANCE STUDIES

Whenever a new protocol, piece of equipment, laboratory test or testing service is used for the collection and processing of specimens, repositories may wish to implement small-scale pilot studies for the validation of the equipment or services employed. Pilot or feasibility studies can be helpful in the early identification of problems in the collection, handling and processing of specimens before a larger study is undertaken. These pilot studies may also help in determining the new processes and training needs required before the implementation of a new protocol.

J3.000 TIMING OF SPECIMEN COLLECTION

The relative importance of the period of time between receipt and processing of a specimen varies with the research application. Molecules degrade at different rates and degradation can begin under a variety of circumstances. For specimens from vertebrate animals, molecular degradation may begin when the vascular supply to an organ is affected during surgery or when the tissue is removed and placed in a cold container. The speed at which the degradation occurs will depend upon the temperature and hydration level at which the specimen is maintained, the organ from which the tissue will be obtained, and the stability of the molecules that will be studied.[1] In general, specimens should be processed as rapidly as possible and it is important to doc-

[1]Jewell S.C., Srinivasan M., McCart L.M., Williams N., Grizzle W.E., LiVolsi V., MacLennan G., Sedmak D.D. (2002). Am. J. Clin. Pathol. 118: 733–741.

ument the collection, processing, and storage times. By documenting this information and making it available to end-users, it will enable an end-user to make sensible assumptions and conclusions about the experimental outcome.

J4.000 TEMPERATURE

The temperatures at which specimens are collected and subsequently processed and stored should be carefully considered depending on the type of specimen and intended analyses. A warm storage environment, even for a short period of time may lead to macromolecular degradation. It may be necessary to maintain a cold chain from the point of collection through processing and storage.

J4.100 Freeze/Thaw Cycles

Freeze/thaw cycles can be deleterious to the macromolecules intended for analysis. Therefore, it is important to select aliquot sizes that are appropriate for the intended uses for the specimens in order to minimize the number of times a sample is thawed and frozen before it is used.

J5.000 STERILITY

Consideration should be made regarding the requirement for the sterility of the instruments, surfaces and equipment used in specimen processing and handling. RNA is particularly sensitive to RNAses that may be present on tools and surfaces that have not been sterilized.

J6.000 SPECIMEN STABILITY

In addition to the issues discussed above, specimen stability may also be affected by other parameters such as the use of anticoagulants and stabilizing agents (*e.g.*, EDTA and ascorbate). For some applications, rapid dehydration is an effective method to stabilize molecules. Dehydration methods may be more practical in field settings where access to refrigerants or chemical fixatives are dangerous or cumbersome.

J7.000 COLLECTION AND STORAGE CONTAINERS

Collection and storage containers vary according to specimen types being collected and the analytical goals of the study and the same containers used for specimen collection may not be suitable for specimen storage. In some cases contaminants associated with the container (*e.g.*, persistent organic pollutants or heavy and trace metals) may interfere with subsequent analysis. This issue is especially true for specimens stored for environmental analysis.

J8.000 COLLECTION PROCEDURES

A variety of protocols exist for the collection of different specimen types. The protocol chosen should be suited to the particular needs of the study. Special considerations for specimen collection procedures are presented below.[2,3]

Staff should wear personal protective equipment, as appropriate, when working with specimens (see Section F5.000). At a minimum, lab coats and disposable gloves should be worn when handling specimens. In addition, when working with liquid nitrogen, it is mandatory to wear freezer gloves, as well as either a face shield or goggles.

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[2]Holland, N.T., Smith M.T., Eskenazi B., Bastaki M. (2003). Mutat. Res.543(3):217–34.

[3]Landi, M.T. and Caporaso N. (1997). IARC Scientific Publication 142:223–236; International Agency for Research on Cancer, Lyon

J8.100 Specimens Obtained from Human Subjects

Depending on the needs of the investigator for whom the samples are collected, or the protocol of the study for which the material is collected, tissues can be collected from several sources (*e.g.,* surgery or autopsy).

Best Practice: Collection of specimens for research should under no circumstances interfere with appropriate patient diagnosis or care.

Best Practice: A pathologist should review all potentially diagnostic tissue specimens to determine what material can be made available for research. Blood, and other body fluids, as well as some other solid tissues not required for diagnosis or prognosis can be collected in accordance with approved protocols and may not require pathologic review.

J8.110 Surgical Samples

Remnant samples may be collected from diagnostic procedures or, with proper IRB/ethics committee approval and appropriate informed consent, specimens may be resected specifically for research. In case subsequent pathology is involved in the diagnostic process, a pathologist should examine the specimen to identify tissue that can be made available for research without compromising diagnostic integrity.

Specimens should remain fresh, not fixed, and placed in a sterile container on wet ice for transport from surgery to pathology or to the repository. The optimal procedure would be to handle all specimens in a sterile manner; however, that is not always practical, as few surgical pathology gross rooms have a sterile hood. In addition, many research protocols do not require that their tissue specimens be procured following sterile procedure. If a sterile hood is not available, the repository staff can set up a "clean" area on a sterile surface. Specimens should not be resected on a dry towel, or other absorbent material, as this procedure rapidly desiccates the specimen and may compromise its usefulness. The prosector should be provided with sterile gloves and sterile instruments for resection of the tissue. Fresh blades and instruments should be used with each new specimen as well as in different areas of the same specimen.

Unless a researcher specifies otherwise, tissue provided to the repository may be placed directly in appropriately labeled sterile containers of saline or media for transport to the repository for processing. If the tissue is to be frozen immediately, it is not necessary to place it in saline, which may cause ice crystals to form on the outside of the specimen when freezing. It is important to educate/train all personnel who will be handling the specimen on the specific handling requirements unique to each protocol.

Samples requiring snap-freezing (cooling at sufficiently high rates to limit damage to cell structure from intracellular ice formation or prevent compositional changes in labile molecules.) can be cooled in a Dewar of liquid nitrogen or on dry ice at the time of collection. Where specimen morphology needs to be conserved, snap-freezing should be done in pre-cooled iso-pentane (at a maximum of -80 °C) or sub-cooled in liquid nitrogen. Data should be maintained and tracked on the time that elapsed between collection and processing/storage. A date and time stamp can be utilized for maintaining these records efficiently. This information can then be transferred into a database.

If a frozen section is cut for diagnostic reasons, then the repository staff should make every effort to obtain an extra slide for quality control (QC). If sufficient amounts of tissue are available following a diagnosis, the repository staff should save some of the tissue as snap-frozen and a representative section for making a paraffin block that will become the property of the repository. An H&E slide may then be cut from each paraffin block which will serve as the QC for that specimen. If insufficient amounts of tissue are provided by the pathologist to allow for making a paraffin block, then the repository staff should request an H&E slide to be made from the pathology department's diagnostic paraffin block to serve as the QC material for the repository.

All samples should be labeled appropriately (Section H.200) and all relevant accompanying data should be documented (Section I4.000).

Best Practice: Pre-label specimen collection containers with barcode/patient ID before surgery to ensure accurate labeling and specimen tracking.

Best Practice: All personnel who will be handling the specimen (surgeons, nurses, and pathologists) should be trained on the specific handling requirements of each protocol.

J8.120 Autopsy/Necropsy

Remnant samples may be collected from autopsy/necropsy procedures consistent with relevant regulations, as appropriate. Requests should specify a maximum time interval post mortem prior to processing. Autopsy/necropsy procedures may yield "normal" tissues or large quantities of a specimen that would not otherwise be available from surgical procedures (*e.g.* heart or brain). Specimens that are not removed as part of the routine autopsy procedure (*i.e.,* leg, arm, hand, foot, or face tissue) are not usually available as their procurement may result in disfigurement of the body.

Tissue specimens collected at autopsy should be appropriately labeled as to the organ site, tissue type, and time of resection, and then placed immediately into a container of saline on wet ice for transport to the tissue repository for processing. These organs could be dissected into smaller sections for processing and storage. Detailed information should be obtained about the decedent such as disease condition, age, sex, cause of death, time and date of death, and time of organ procurement. Information about the procured organ should include the condition (normal or diseased).

J8.130 Transplant

Occasionally, organs that are inappropriate for transplant may be offered or made available to a repository for research purposes. It is not unusual for the organ to have been out of the body for many hours beyond the normal time frame identified for procurement of samples. However, because transplant tissue is usually placed in a preservative to keep it viable for transplant, most researchers will still accept transplant tissue as it is likely to be of superior quality to either surgical or autopsy specimens. Transplant organs may also be dissected into smaller sections for processing and storage. Information about the donor from whom the organ was procured should be obtained from the transplant center.

J8.200 Solid Tissues

Tissues may be collected prospectively, as a part of a population-based study, or for general purposes for future research activities. The collection of samples for research should never compromise the diagnostic and prognostic integrity of a specimen. This is especially important when human solid tissue specimens are collected during surgery and where pathology is involved in the subsequent diagnostic process. This is because attributes of the sample (*e.g.* the margin of the tumor or the number of tumor positive lymph nodes) may have a direct impact on the care that a patient subsequently receives (*e.g.,* chemotherapeutic treatment *vs.* radiation therapy *vs.* no treatment).

The appropriate handling of tissues procured for research purposes is facilitated if a practicing pathologist supervises the actual procurement of the tissue; this is especially important to prevent the compromise of diagnostic specimens. Information from the pathologist on the purity of the biopsy or surgical material (% normal, % tumor, and % necrosis and/or fibrosis) should be recorded for future use so that the end user will be able to determine the usefulness of the tissue. Where possible, multiple sections or samples should be created to allow for greater use of the specimens.

J8.300 Blood Samples

One of the primary decisions in storing blood samples is whether to collect anticoagulated (plasma/buffy coat/RBC) whole blood or coagulated (serum/clot) blood. When serum is collected without anticoagulant, the blood clot obtained after processing can be used as a source

of DNA for genotyping and other DNA related studies.[4] When multiple blood collection devices/containers are involved there is a prescribed priority order of draw (see Appendix A for internet resources.) It is also important to determine which anticoagulants are acceptable for a particular downstream procedure. For example, some immunoassay procedures disallow the use of EDTA as an anticoagulant for plasma collection.

Blood samples may be collected in different manners depending upon the amount of blood needed for a study and the distance between the sample source, processing location, and the repository. For example, blood samples may be collected at a location that is far away from the research site, in either small quantities as dried blood spots on treated or untreated cards or collected in large quantities in tubes that provide 2-5 days stability at room temperature.

J8.400 Urine Samples

Urine samples should be maintained on ice or refrigerated for the duration of the collection. Plastic or glass containers should be clean and dry, and have a 50 mL to 3 L capacity, a wide mouth, and a leak-proof cap. Depending upon the analyte to be measured, a preservative may be needed. The type of preservative may differ according to test methodologies, time delay and transport conditions. EDTA and sodium metabisulfite are examples of preservatives commonly used in urine collections.

J8.410 First Morning Urine Samples

Before going to sleep, the patient/donor voids a urine specimen. Immediately on rising, the patient or donor collects the "first morning" urine specimen. First morning specimens are best for detecting substances in a more concentrated solution (*e.g.,* white and red blood cells or urinary hormones).

J8.420 Random Urine Samples

A random urine sample is good for routine screening and cytology studies.

J8.430 Fractional Urine Samples

Fractional urine samples are used to compare the concentration of an analyte in urine with its concentration in blood. First morning urine, which contains solutes and metabolites from the evening meal, is discarded and a second urine sample following a period of fasting is collected.

J8.440 Timed Urine Sample

Timed urine collections allow for comparisons of patterns of excretion of certain biomolecules. Typical collection times are 12 and 24-hour. For the 24-hour collection on day one, the subject empties his/her bladder and for the next 24 hours all subsequent urine is collected.

J8.500 Nail and Hair Clippings

Nail and hair clippings are used for trace metal analysis to provide a longer-term measure of exposure. These samples are simple to collect, store and ship. They can also be used as a source of DNA.

J8.600 Saliva and Buccal Cell Samples

Collection devices for these specimens include non-covered cotton roll, polypropylene-covered polyether roll and paraffin wax chewing stimulation. Some researchers may request patients to provide saliva samples directly into a container. The container opening should be adequately large to facilitate this collection.

Buccal cell specimens may be useful as a source of DNA. A variety of collection techniques and containers have been developed specially for these collections. See references for several of these in Appendix A.

[4]Somiari SB, Somiari RI, Hooke J, Garguilo G, Mittal V, Hu H, Bronfman L, Bombatch J, Deyarmin B, Heckman C, Russell S, et al., (2004). *TIBETS*,1:131–143.

J8.700 Breast Milk Samples

Breast milk collection can be initiated when breast-feeding starts. It can be collected by manual expression or vacuum pump and should be collected in autoclaved or specially cleaned bottles.

J9.000 RETRIEVAL OF SPECIMENS FROM STORAGE

Retrieval of specimens for shipment or analysis requires strict adherence to protocols for proper specimen inventory and tracking, as well as adherence to established safety standards in working with freezers and other storage equipment.

J9.100 Locating Specimens in Storage

The location of specimens to be retrieved should first be verified in the appropriate specimen inventory system (Section H3.000). A specimen requisition is generated according to procedures applicable to the institution's tissue requesting, tracking and inventory protocols. The requisition is checked for accuracy before transmission to the repository, according to established SOPs (see Section E2.220) and QC standards (see Section E3.000).

J9.200 Specimen Retrieval

Specimens should be located and pulled from storage as documented on specimen requisition forms. If specimens are frozen, speed is necessary during the retrieval process. Such speed may require that at least two individuals carry out the retrieval process. If possible, specimens being retrieved should be maintained at the storage temperature throughout the process (*e.g.,* specimens stored at -80 °C should be kept on dry ice during the retrieval process).

Once retrieved, staff should confirm that all requisitioned specimens have been accounted for. Quality control checks should be performed to confirm that all specimens listed on the requisition were retrieved. Confirmation of this information at least a second time by a separate person is recommended.

If specimens appear to be missing, protocols should be followed in order to locate the missing specimens. Inventory systems should be updated to indicate that samples are in fact missing or that they were improperly located when placed in the inventory.

J9.300 Thawing and Aliquoting Frozen Specimens

J9.310 Thawing Specimens

Specimens in plastic cryovials should be thawed at room temperature for a brief period of time or at refrigerated temperature (4-8 °C) overnight. Specimens in glass vials should preferably be thawed overnight in a refrigerator to prevent the glass from cracking. Specimens in resin straws can be thawed directly at room temperature or in a 37 °C water bath.

J9.320 Aliquoting Thawed Specimens

Large-volume liquid samples (*e.g.,* sera, plasma, urine) may need to be divided into smaller aliquots for distribution to multiple end-users. The proper pipette and tip to use is determined by the required volumes and eventual analysis. If analyzing for persistent organic pollutants, using a plastic pipette and tip may contaminate the sample further. A different pipette tip should be used for each specimen.

Best Practice: Specimen containers should be opened and the specimens aliquoted in a biological safety hood. Sterile vials and pipettes should be used to avoid contaminating samples.

J9.330 Freezing and Defrosting Viable Cells

The rate and method of freezing and thawing specimens can have serious effects on the via-

bility of cells. The following points should be taken into consideration when freezing and thawing specimens for which cellular viability is important. Exact freezing and thawing protocols should be developed to ensure that the method used supports the known or anticipated use for the specimens.

The rate of cooling controls the size and location of ice crystals, which may affect cell recovery. A uniform cooling rate of –1 °C per minute from ambient temperature is effective for a wide variety of cells. The steady decline of temperature can be achieved by the use of commercially available devices that control the rate of freezing. Once cooled to a predetermined temperature (usually between −25 and −30 °C), the sample is then transferred to a liquid nitrogen freezer for long-term storage. This is called a 2-step cooling procedure, and is distinguished from snap-freezing procedures described previously.

The temperature at which frozen preparations are stored affects the length of time after which cells can be recovered in the viable state (generally, the lower the storage temperature, the longer the viable storage period). In addition to storage temperature, handling during removal from storage will affect the viability of cells and may result in degradation of cellular components. Every time a vial is exposed to a warmer environment -even briefly-, it experiences a change in temperature.

Although slow cooling is generally best to ensure cell viability, the opposite process is required when thawing from the frozen state. Agitation of the vial/ampoule/straw in a 37 °C water bath for a brief period of time is preferable, but this process may be detrimental to certain cell types if the time required is too lengthy.

It is often useful to determine the number of recovered cells. There are several methods, usually by a dye exclusion (*e.g.,* trypan blue), to accurately estimate the number of viable cells in a non-motile population.

J10.000 RECEIVING SPECIMENS

All specimens received by the end-user should be confirmed and a record of the receipt should be maintained by the repository (Section I4.000). SOPs should be in place for receiving specimens into the repository. Documentation should include the date and time the specimens were received, the tracking number assigned by the courier service, inspection of package and container for visible signs of damage, confirmation of the condition of the coolant used during specimen transport, confirmation that specimens received match those listed on the manifest, and documentation of all problems or discrepancies.

Best Practice: Any problems encountered with a shipment should be communicated to the sender to aid in the prevention of similar problems in the future.

SECTION K: LEGAL AND ETHICAL ISSUES FOR HUMAN SPECIMENS

K1.000 GENERAL

The collection, storage, distribution and use of human biological materials in research raise many legal and ethical issues. On an international level, the collection and use of these materials is currently regulated by an amalgam of differing and occasionally conflicting laws and policies. Thus, repositories should proceed carefully, not only in their daily work, but also with respect to international exchange of samples and associated data.

It is important to understand key terminology related to the legal and ethical issues for human specimens. Terms that describe whether and how specimens are linked to subject identity are often used in different ways and with different meanings in different contexts. Therefore, it is critical to pay careful attention to how the terms used are defined. Definitions of key terms have been included in the Glossary found in Appendix B.

Key discussions of ethics in human subjects' research are found in a number of documents, including the Declaration of Helsinki adopted by the World Medical Association in 1964 and revised several times subsequently, most recently in 2000. These issues are also discussed in the Belmont Report published by the U.S. Department of Health and Human Services in April 1979 and include several fundamental key concepts:

- Freely-given informed patient consent is necessary before research on humans may be conducted.
- Research should be well designed, conducted by persons with appropriate expertise and lead to meaningful conclusions.
- Every effort should be taken to reduce the risks to patients and ensure that the risks do not exceed the benefit of the expected findings.
- Studies in animals should provide reason to believe that the study of humans is needed and is the only way to get the necessary information.

The collection, storage, and use of human specimens and associated data should be done in a way that respects the individual and maintains privacy and confidentiality. In addition to following appropriate protections for privacy and confidentiality, repositories should be cognizant of and adhere to relevant national human subjects regulations, privacy regulations and other relevant national, state and local laws. For example, some regions prohibit the use of fetal tissues, embryos, or embryonic stem cells in biomedical research. Regulations that govern the import and/or export of human specimens should also be observed. These may include regulations in some countries addressing the ethical issues related to import and/or export of specimens, as well as shipping regulations.

A thorough analysis of the applicable regulations in different countries is outside of the scope of this document. References and links to applicable regulations and guidelines are included in Appendix A.

K2.000 COMMON PRINCIPLES

K2.100 Institutional Review Board/Ethics Review Committee

An Institutional Review Board (IRB) (or ethics review committee) is any board, committee, or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of the research and conduct periodic review of such research. As a component of an IRB/Ethics review, a repository's processes and procedures for collection, storage, distribution, and use of human specimens for research should be evaluated to ensure that these procedures are appropriate to protect human subjects.

K2.200 Informed Consent

Informed consent for the collection, retention and use of specimens is a process that offers subjects information sufficient to allow them to make an informed choice about whether to provide specimens and data to the repository and agree, where applicable, to future research use. Consent should only be obtained under circumstances that provide the prospective subject or the subject's representative sufficient opportunity to consider whether or not to participate and minimizes the possibility of coercion or undue influence. The information that is given to the subject or the representative should be understandable to the subject or his/her representative.

Consent may be obtained for a specific research project, such that the details of the project can be specifically outlined; alternatively consent may be obtained for unspecified future research, in which case general information about the possible future research uses is provided, in accordance with applicable national or local regulations and policies. Mechanisms should be in place to assure that future research uses of identifiable specimens are consistent with the original con-

sent (*e.g.,* through an IRB, ethics committee review or other mechanisms consistent with applicable regulations and guidelines).

Subjects should have the right to withdraw consent and to have their unused specimens and data removed from the repository unless the specimens and data are anonymous and cannot be linked by the repository to subject identities. The conditions under which a subject may make this request as well as the logistics for how a subject initiates this request should be specifically outlined in the informed consent document and process.

Best Practice: Subject consent should be obtained unless waived by an authorized institutional review board (or ethics committee) constituted in accordance with applicable law or regulation.

K2.300 Protection from Research Risks

Care should be taken to minimize the risks to subjects, and ensure that risks do not outweigh the benefits of the expected findings from studies using the specimens. This includes minimizing physical risks and psychosocial risks associated with the collection of specimens and/or data and ensuring that the collection of specimens and data does not affect patient care.

The repository should follow well-documented procedures to protect the privacy and confidentiality of the subjects from whom the specimens and/or data are obtained. These may include completely anonymizing specimens and data, where appropriate or assigning a unique code and or removing all identifying information from the specimens and data, storing specimens and data securely, restricting access to specimens and/or data, and providing firewalls between the subject identity and the recipient investigator. Such firewalls prevent inappropriate data from passing in either direction through the firewall (*e.g.*, patient identifying information to the researcher or specific research results that have not been validated to the patient/subject). In addition, identifying information should be removed before allowing the recipient investigator to have access to specimens and/or data.

Best Practice: The collection of specimens and data for research should not adversely affect patient care.

Best Practice: Every effort should be made to protect the privacy and confidentiality of data associated with the specimens.

K2.400 Consideration of Perspectives of Communities, Populations, Ethnic and Social Groups

In some cases there may be risks to social groups or communities due to the release of aggregate research findings even when no individually identifiable information has been revealed. In addition, some populations or groups have specific beliefs about the disposition and use of their specimens, which should be respected.

Benefit-sharing is another important consideration, particularly when dealing with specimens or data from developing countries. Sharing the "benefits" from specimen research is important to ensure that providers of resources are treated in a fair and equitable way. The concept of benefit-sharing grew out of discussions about developing countries profiting from plant and animal materials collected in third world countries without benefit to those who provided the raw material. An international protocol, the convention on biodiversity (http://www.cbd.int/convention/convention.shtml) was signed by 150 countries. How the concept applies to specimen research is not always clear, but certainly involves avoiding exploitation (*e.g.*, in developing countries). There are numerous ways that "benefits" can be shared. These include sharing of technology or sharing benefits of research with the study population or providing security backup of stored specimens in an established repository with quality practices in place. Some countries (*e.g.,* India) only allow specimens for research performed elsewhere to leave the coun-

try if a collaborating investigator from the country accompanies them and participates in the research. This practice promotes technology transfer and capacity building.

Best Practice: The repository procedures for collection, storage, distribution, use and disposal of specimens should respect the perspectives and traditions of subjects from whom the specimens were obtained and minimize the risks to communities, populations, and groups.

Best Practice: Repositories that import specimens and data from other countries should respect the autonomy of the providing country and ensure that fair and equitable benefits are made available to the providing country.

K2.500 Sharing and Distribution of Specimens

Specimen resources should provide responsible custodianship of the specimens and data that they collect, maintain and share. Mechanisms should be in place to maintain the quality of specimens and data, protect subject privacy and confidentiality, and to make sure that specimens are shared in a manner that is consistent with any consent obtained for the specimens.

Repositories should have well-established policies for sharing and distributing specimens and clear and transparent procedures for determining what constitutes appropriate research uses of the specimens and/or data. Requests to use samples should undergo some level of scientific review. The rigor of the review should be based on the value of the specimens and data that are to be made available and may range from simple review by an approving official at the repository to full scale peer review by scientists outside the repository. As a general rule, the greater the amount of data annotating a specimen and the extent to which additional processing or preanalysis of the specimen has been provided, the more rigorous the review and the higher the standards for access should be set.

Requests for access may be based on considerations such as the scientific merit and potential impact of the proposed research, whether the research use is appropriate to the nature and purpose of the repository, adequacy of the research design and funding, public health benefits and risks of the proposed research, legal and ethical considerations, and the qualifications of the research team and research environment.

Wherever possible, specimens and/or data should be distributed with identifying information removed. All access policies should be in compliance with existing human subjects, privacy regulations and all other applicable laws and policies. When investigators are required to obtain IRB or ethics committee review and approval for the research use of specimens and/or data, documentation of such approval should be obtained prior to providing specimens/data.

Best Practice: Use of specimens and associated data should be consistent with informed consent and authorization.

Best Practice: Specimens and/or data should only be made available for ethical and scientifically appropriate research that is expected to contribute to scientific discovery.

Best Practice: Custodians for specimen collections should have a well-documented and clearly defined process for sharing specimens and data, prioritizing requests for access to specimens and data with limited availability and a mechanism for evaluating competing requests for scarce resources. Requests should be reviewed by in a timely manner by qualified individuals.

K2.600 Termination of Specimen Resources

Specimen resources should develop plans at the time of their establishment for the disposition of specimens and/or data should the resource be terminated for any reason. The disposition, including any transfer of specimens and/or data to third parties, should be consistent with the informed consent under which specimens and/or data were obtained.

APPENDIX A: INTERNET RESOURCES

These internet references are made available for information only. ISBER does not warrant any of the information contained therein.

Subject	Website	Organization	Topics
Best Practices for Biological Resource Centers	http://www.oecd.org/dataoecd/7/13/38777417.pdf	Organisation for Economic Co-Operation and Development	Consensus Best Practices for Biological Resource Centers in OECD Countries
Bioethics	http://bioethics-international.org/iab-2.0/index.php?show=objectives	International Organisation of Bioethics	The IAB facilitates the exchange of information between those working in bioethics in different parts of the world
Bioethics Advisory Committee	http://www.bioethics-singapore.org/	Bioethics Advisory Committee, Singapore	Resources for the ethical, legal and social issues arising from biomedical sciences research in Singapore
Biorepository Protocols	http://www.abrn.net/protocols.htm	Australasian Biospecimen Network	Protocols and best practices for collecting and processing human biospecimens
Biosafety	http://governance.iarc.fr/ENG/Docs/safetymanual.pdf	The Division of Biosafety and Biotechnology (SBB), Scientific Institute of Public Health in Belgium.	Biosafety risk assessment tools and Biosafety manuals, laws and regulations, guidelines on containment facilities, equipment and practices, shipping and transport
Biosafety	http://www.ebsaweb.eu/Resources.html	European Biosafety Association	Conferences and other resources on European biosafety issues
Biosafety	http://www.ebsaweb.eu/ebsa_media/Downloads/Biosafety7-view_image-1-called_by-ebsa.pdf	World Health Organisation	Laboratory biosafety manual covering equipment and facility design and techniques
Biosafety	http://www.cjd.ed.ac.uk	UK Surveillance Unit for Creutzfeldt-Jakob Disease	Surveillance data on Creutzfeldt-Jakob Disease; technical information; links
Blood Collection Protocols	http://www.csmc.edu/5455.html	Cedars-Sinai Medical Center	Blood collection guidelines
Convention on Biological Diversity	http://www.cbd.int.	United Nations Environmental Programme	Sustainable development and Intellectual Property Rights
Convention on International Trade in Endangered Species of Wild Fauna and Flora	http://www.cites.org	IUCN (The World Conservation Union)	Trade in Endangered Species of Wild Fauna and Flora

Case Studies of Human Tissue Repositories	http://www.rand.org/pubs/monographs/2004/RAND_MG120.pdf	Rand Corporation and the National Cancer Institute	Best Practices for repositories based on information collected from a defined number of U.S.-based repositories
Chemical and Laboratory Resources	http://www.neis.com/environmental_resources.html	Chemindustry.com	A wide variety on resources to include laboratory equipment and supplies for over a hundred countries world-wide. Once you reach the site, click on the tab for "lab supplies".
Chemical Safety	http://www.cdc.gov/niosh/database.html	National Institute for Occupational Safety and Health (NIOSH), U.S.	Databases and information resource links and publications in the United States
Chemical Safety	http://www.ilo.org/public/english/protection/safework/cis/products/icsc/dtasht/index.htm	International Occupational Safety and Health Information Center	Chemical database; International Chemical Safety Cards (ICSC)
Chemical Safety	http://www.cdc.gov/niosh/chem-inx.html	Master Index of Occupational Health Guidelines for Chemical Hazards (NIOSH), U.S	U.S. National guidelines for chemical hazards of specific chemicals
Chemical Safety	http://www.who.int/ifcs/en/	Intergovernmental Forum for Global Chemical Safety	Policy guidance on chemical safety
Chemicals Management	http://www.environment.gov.au/settlements/chemicals/index.html	The Australian Government Department of the Environment and Water Resources	Chemicals management strategies to protect human health and the environment
Electrical Safety	http://www.ehs.uconn.edu/Word%20Docs/Electrical%20Safety%20in%20the %20Lab.pdf	University of Connecticut Environmental Health and Safety	Electrical safety in the laboratory
Environmental Health	http://www.environment.gov.au/approvals/index.html	The Australian Government Department of the Environment and Water Resources	Approvals, permits and licensing
Environmental Specimen Bank Design	http://www.ehponline.org/members/1995/Suppl-3/wise-full.html	U.S. National Institute of Standards and Technology	This paper was presented at the Conference on Human Tissue Monitoring and Specimen Banking: Opportunities for Exposure Assessment, Risk Assessment, and Epidemiologic Research held 30 March-1 April 1993 in Research Triangle Park, North Carolina.
Ethics Committee	http://www.hugo-international.org/committee_ethics.htm	Human Genome Organisation	This organization promotes discussion and understanding of social, legal and ethical issues as they relate to the conduct of, and the use of knowledge derived from, human genome research.
Ethics Guides	http://www.moh.govt.nz/moh.govt.nz/moh.nsf/indexmh/guidelines-use-human-tissue	New Zealand Ministry of Health	Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes

(*continued*)

APPENDIX A: INTERNET RESOURCES (*Continued*)

These internet references are made available for information only. ISBER does not warrant any of the information contained therein.

Subject	Website	Organization	Topics
Exposure Prevention	http://www.healthsystem.	Exposure Prevention Information	Provides standardized methods for recording and
Program Information	virginia.edu/internet/epinet/subpage2.cfm	Network; University of Virginia, International Health Care Worker Safety Center	tracking percutaneous injuries and blood and body fluid contacts
General Safety	http://www.osha.gov/comp-links.html	Occupational Safety and Health Administration, Department of Labor, USA	Current U.S regulations and regulations under development; technical, prevention and training information; links
General Safety	http://www.lbl.gov/ehs/pub3000	Lawrence Berkeley National Laboratory; University of California, California, U.S.	U.S.-based health and safety manual
Human Subjects	https://wcd.coe.int/ViewDoc.jsp?id=977859	Council of Europe; Committee of Ministers	Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
Human Subjects	http://www.hhs.gov/ohrp/international/HSPCompilation.pdf	Office of Human Research Protections; U.S. Department of Health and Human Services	Human subjects research legislation, regulations, or guidelines for 79 countries, two confederations and two organizations
Human Subjects	http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm	Office of Human Research Protections, U.S. Department of Health and Human Services	U.S. Federal Human Subjects Regulations
Human Subjects	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm	Food and Drug Administration, U.S. Department of Health and Human Services	U.S.-based human subjects regulations: 21 CFR parts 50, 56, 812
Human Subjects	http://www.hhs.gov/ohrp/policy/index.html	Office of Human Research Protections, U.S. Department of Health and Human Services	Policy documents from the Office of Human Research Protections, U.S.
Human Subjects	http://www.hhs.gov/ohrp/international/	U.S. Office of Human Research Protections, U.S. Department of Health and Human Services	International Compilation of Human Subjects Research Protections
Laboratory Standards Development	http://www.nccls.org	Clinical and Laboratory Standards Institute	U.S. based general and technical Information for the development of laboratory standards

National Cancer Institute Best Practices for Biospecimen Resources	http://biospecimens.cancer.gov/NCI_Best_Practices_060507.pdf	National Cancer Institute; National Institutes of Health; U.S. Department of Health and Human Services	Best Practices for biospecimen handling, processing, storage and retrieval for specimens collected through NCI-sponsored research
Natural History Museum Benefit Sharing Practices	http://www.canmexworkshop.com/documents/papers/III.5d.2.pdf	Int ernational Expert Workshop on Access to Genetic Resources and Benefit Sharing	Concepts in Benefit Sharing for Museum Collections
Occupational Health and Safety	http://governance.iarc.fr/ENG/Docs/safetymanual.pdf	International Agency for Research on Cancer	Health and safety manual
Occupational Health and Safety	http://www.ccohs.ca/	Canadian Centre for Occupational Health and Safety	Information on biological hazards, chemical and materials, health and safety programs
Packing and Shipping	http://www.iata.org/index.htm	International Air Transport Association (IATA)	Standards for shipping human specimens by air
Packing and Shipping	http://www.icao.int/	International Civil Aviation Organization (ICAO)	International Transport Regulations
Packing and Shipping	http://hazmat.dot.gov/hazhome.htm	U.S. Department of Transportation (DOT)	U.S.-based standards for shipping human specimens by ground
Plant Collection Protocols	http://www.uaf.edu/museum/herb/howtocoll.html	University of Alaska, U.S.	Guidance on collecting plant specimens
Privacy	http://www.hhs.gov/ocr/hipaa/	U.S. Department of Health and Human Services	Health Insurance Portability and Accountability Act of 1996 (HIPAA)
Privacy	http://privacyruleandresearch.nih.gov/	National Institutes of Health, U.S. Department of Health and Human Services	HIPAA Privacy Rule and research
Privacy	http://www.usdoj.gov/oip/04_7_1.html	U.S. Department of Justice	Privacy Act of 1974, 5 U.S.C. § 552a
Radiological Safety	http://www.jmu.edu/safetyplan/radiology/advisorycommittee.shtml	James Madison University	Example of U.S. radiation protection program
Resources for Pathology Laboratories	http://www.cap.org/apps/cap.portal?_nfpb=true&_pageLabel=reference	College of American Pathologists	General and Technical Information for lab management for U.S.-based laboratories

(*continued*)

APPENDIX A: INTERNET RESOURCES (*Continued*)

These internet references are made available for information only. ISBER does not warrant any of the information contained therein.

Subject	Website	Organization	Topics
Tissue Procurement Protocols	http://www.tubafrost.org	European Human Frozen Tumour Tissue Bank (TuBaFrost) project	Collection and storage of human tissues
Tissue Procurement Protocols	http://www.bd.com/vacutainer/pdfs/plus_plastic_tubes_wallchart_orderofdraw_VS5729.pdf	Becton-Dickenson	Wall chart on blood tube order for blood collection
Transnational Shipment of Chemicals	http://www.basel.int/	The Basel Convention.	Transnational boundary movements of hazardous wastes and their disposal
Transport of Infectious Substances	http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_9Final.pdf	World Health Organization	Recommendations developed by the United Nations Economic and Social Council's Committee of Experts on the transport of dangerous goods
Transportation Safety	http://www.cta-otc.gc.ca/legislation/index_e.html	Canadian Transportation Agency	Transportation related legislation and other related matters can be found here, along with details of the Statutes and Regulations enforced by the Canadian Transportation Agency.

APPENDIX B: GLOSSARY

Unless otherwise defined in another context in these Practices, important terms are defined below.

ADVERSE OUTCOME – An undesirable effect or untoward complication consequent to or reasonably related to specimen integrity.

AEROSOL –A suspension of tiny particles or droplets in the air, such as dusts, mists, or fumes. These particles may be inhaled or absorbed by the skin, and can sometimes cause adverse heath effects for workers.

ALIQUOT – A process wherein a specimen is divided into separate parts which are typically stored in separate containers as individual samples. The term aliquot may also be used as a noun to denote a single sample.

ANALYTE –A substance or chemical constituent that is determined in an analytical procedure.

ANNOTATION – Additional information associated with a particular point in a document or other piece of information.

ANONYMOUS – Identifiable personal information was not collected for the specimens and associated data or, if collected, was not maintained and cannot be retrieved, such that there is no way to trace the identity of the subject from whom the specimens were obtained.

ASEPTIC PROCESSING – Processing of specimens using methods to restrict or minimize the potential contamination with microorganisms from the environment, processing personnel and equipment.

AUDIT – A documented review of procedures, records, personnel functions, equipment materials, facilities, and/or vendors in order to evaluate adherence to written SOPs or government laws and regulations.

AUTOPSY – Postmortem examination of the organs and tissues of a body to determine cause of death or pathological conditions.

BANKING – The process of storing material or specimens for future use (see also BIOBANKING).

BATCH – A specific quantity of specimens that is intended to have a uniform character and quality, within specific limits, and is produced or processed according to a single processing protocol during the same processing cycle. (see LOT).

BIOBANK – See REPOSITORY.

BIOHAZARD – An organism, or substance derived from an organism, that poses a threat to (primarily) human health. This can include medical waste, samples of a microorganism, virus or toxin (from a biological source) that can impact human health. It can also include substances harmful to animals.

BIOLOGICAL SAFETY HOOD – Cabinet designed to provide microbe-free work free work environment which enables workers to perform work on samples in an isolated area.

BIOREPOSITORY – See REPOSITORY.

BIOSPECIMEN RESOURCE – A collection of biological specimens that is acquired for a defined purpose. Management responsibility of the biospecimen resource is led by the custodian for the collection. Biospecimen resources may be stored in a repository or laboratory, depending on the numbers of specimens contained therein.

CLEAN ROOM – A room in which the concentration of airborne particles is monitored and controlled to defined specification limits.

COLD CHAIN – A temperature-controlled supply chain.

COLLECTION – May refer to the practice or technique of collecting a specimen (See RETRIEVAL) or to a specific sample or group of samples that has been isolated for future research purposes.

CONSIGNEE – Any individual, agency, institution, or organization that receives specimens and assumes responsibility for storage, dispensing, and tracking the disposition of specimens.

CONTAINER – Enclosure for one unit or more units of specimen(s).

CONTROLLED AREAS – Restricted work areas of low microbial and particulate content in which non-sterile materials are prepared.

CRITICAL AREAS – Restricted work areas where containers and closures are exposed to the environment.

CROSS-CONTAMINATION – The transfer of any part of one specimen to another specimen (*e.g.,* microorganisms, blood, DNA, RNA, protein).

CRYOPROTECTANT – An additive that serves to minimize osmotic imbalances that occur with the progression of freezing fronts through a substance, and is intended to limit the amount of cell damage due to cell shrinkage and intracellular ice formation.

CULLING – Reviewing and eliminating specimens in a collection or an entire collection either by destruction or transfer to a new custodian.

CUSTODIAN – The individual responsible for the management of a biospecimen resource. The custodian works with other key stakeholders in the management of the resource including the tracking of all relevant documentation for the resource and for ensuring that policies regarding access to the resource are in place and implemented according to appropriate guidelines.

DATABASE – A structured collection of records or data that is stored in a computer system so that a computer program or person using a query language can consult it to answer queries.

DEHYDRATION – Removal of water from a tissue.
DESICCATION – Excessive loss of moisture; the process of drying up.
DEVIATION – An intentional or unintentional event that is a departure from a procedure or a normal practice.
DEWAR – A specialized container to hold liquefied gases. A Dewar may also be referred to as a Dewar flask or Dewar vessel.
DISINFECTANT – An agent that reduces the number of viable microorganisms.
DISINFECTION – A process that reduces the number of viable cellular microorganisms, but does not necessarily destroy all microbial forms, such as spores and viruses.
DISPOSITION – Final destination of specimens.
DISTRIBUTION – A process that includes receipt of request for specimens, selection of appropriate specimens, and final inspection, in conjunction with subsequent shipment and delivery of specimens to another repository, specimen collection center, or laboratory.
DONOR – See SUBJECT.
DRY ICE – Solid phase carbon dioxide (CO_2). CO_2 solidifies at -78.5 °C.
END-USER – A health care practitioner, scientist, or laboratory staff member who performs an appropriate procedure, test or archival function.
ENVIRONMENTAL MONITORING SYSTEM – An automated, centralized monitoring system that monitors environmental conditions and alarms in conjunction with remote access, security features and electronic data storage.
EQUIPMENT QUALIFICATION STUDIES – Protocols designed to adequately evaluate, prior to use, whether equipment will perform to expectations, and normally function within tolerance limits [*e.g.,* Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ)].
ERGONOMICS – The science that explores human abilities and limitations, and applies that knowledge to improve a person's interactions with their environment, tools, products, and practice.
ERROR – A deviation from an SOP during specimen retrieval, processing, testing, quarantining, labeling, storage or distribution that might adversely affect the specimen.
E-VOUCHER – Electronic, preferably geo-referenced, documentation of the individual from which a sample is isolated. Typically this is done where it is not possible to make a true voucher (*e.g.,* a preserved specimen) such as when the specimen is rare or too large to collect.
FREEZE-DRIED – Dehydrated for storage by conversion of the water content of a frozen specimen to a gaseous state under vacuum. Also called lyophilized.
GEO-REFERENCING – The geographical coordinates of the collection site.
HONEST BROKER – A neutral intermediary between the individual whose tissue and data are being studied and the researcher. The honest broker collects and collates pertinent information regarding the tissue source, replaces identifiers with a code, and releases only coded information to the researcher.[5]
IDENTIFIER/IDENTIFYING INFORMATION – Information (*e.g.,* name, social security number, medical record or pathology accession number, *etc.*) that would enable the identification of the subject. For some specimens this information might include the taxon name and collection number.
INCIDENT – Any unplanned occurrence that deviates from Standard Operating Procedures (SOPs) or applicable government laws and regulations during specimen retrieval, processing, labeling, storage or distribution that may affect subsequent use of those specimens.
INFORMED CONSENT – A decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence, inducement, or intimidation.[6]
IN-PROCESS CONTROLS – Any tests, samples, evaluations, monitoring, or measurements performed during processing or preservation that are designed to evaluate those procedures or the specimens subjected to processing or preservation for conformance to specifications in SOPs.
IN-PROCESS MATERIAL – Any material that is used in the processing of specimens, including but not limited to, incoming specimens, water, alcohol, acid, containers and closures.
INSTITUTIONAL REVIEW BOARD (IRB) – Any board, committee, or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of the research and conduct periodic review of such research.
LABEL – Any written, printed or graphic material on or affixed to a specimen container or package.
LIQUID NITROGEN – Coolant used to cool and store samples. Nitrogen becomes liquid at −196 °C. Samples stored in the vapor phase of liquid nitrogen are −190 °C and warmer, depending on the distance from the liquid phase.
LIQUID NITROGEN DRY SHIPPER – A container used for sending samples in the vapor phase of liquid nitrogen.
LOT – A quantity of reagents, supplies or containers that is processed or manufactured at one time and identified by a unique identification number (see BATCH).

[5]Eiseman E, Bloom G, Brower J, et al. Santa Monica, CA: RAND Corporation, 2003
[6]CIOMS. International Ethical Guidelines for Biomedical Research Involving Human Subjects

LYOPHILIZED – Dehydrated for storage by conversion of the water content of a frozen specimen to a gaseous state under vacuum. Also called freeze-dried.

MATERIAL TRANSFER AGREEMENT – An agreement that governs the transfer of tangible research materials and data between two organizations, when the recipient intends to use it for his or her own research purposes. It defines the rights and obligations of the provider and the recipient with respect to the use of the materials.

NECROPSY – See AUTOPSY.

PACKING SLIP – Written material accompanying a specimen bearing further information about the specimen, directions for use, and any applicable warnings.

POLICIES AND PROCEDURES MANUAL – See STANDARD OPERATING PROCEDURES (SOP) MANUAL.

POOLING – Intentional mixing of specimens from two or more sources into a single container.

PRESERVATION – Use of chemical agents, alterations in environmental conditions or other means during processing and storage to prevent or retard biological or physical deterioration of a specimen.

PROCEDURE – A series of steps designed to result in a specific outcome when followed in order.

PROCESS CONTROLS – A system of checks and balances incorporated into standard operating procedures involving critical operations to prevent errors.

PROCESS VALIDATION STUDIES – The process of demonstrating that a specific procedure will consistently produce expected results within predetermined specifications.

PROCESSING – Any procedure employed after specimen collection but prior to its distribution, including preparation, testing, and releasing the specimen to inventory and labeling.

PROCUREMENT – See RETRIEVAL.

QUALITY – Conformance of a specimen or process with pre-established specifications or standards.

QUALITY ASSURANCE (QA) – An integrated system of management activities involving planning, implementation, documentation, assessment, and improvement to ensure that a process or item is of the type and quality needed for the project. Same as Quality Management System (QMS).

QUALITY CONTROL (QC) – Specific tests defined by the QA or QMS Program to be performed to monitor procurement, processing, preservation and storage; specimen quality; and test accuracy. These may include but are not limited to: performance evaluations, testing, and controls used to determine accuracy and reliability of the repository's equipment and operational procedures as well as monitoring of the supplies, reagents, equipment and facilities.

QUALITY MANAGEMENT SYSTEM (QMS) – Same as Quality Assurance (QA).

REMOVAL – See RETRIEVAL.

REPOSITORY – An entity that receives, stores, processes and/or disseminates specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation. It may also be referred to as a BIOREPOSITORY or BIOBANK.

RETRIEVAL – The removal, acquisition, recovery, harvesting, or collection of specimens.

SAFETY – Processes, procedures and technologies to ensure freedom from danger or harm.

SAMPLE – A single unit containing material derived from one specimen.

SHIPPING MANIFEST – A written description of the contents of the shipped package.

SPECIMEN – A specific tissue, blood sample, etc. taken from a single subject or donor at a specific time. For some biological collections "specimen" may have the same meaning as "individual."

STANDARD OPERATING PROCEDURES (SOP) MANUAL – A group of standard operating procedures (SOPs) detailing specific policies of a repository and the procedures required to be used by the staff/personnel.

STERILITY – Absence of detectable, viable, contaminating microorganisms.

STERILIZATION – A physical or chemical process validated to destroy, inactivate, or reduce microorganisms to a sterility assurance level of 10^{-6}.

STORAGE – Maintenance of specimens under specified conditions for future use.

SUBJECT – Living or deceased individual who is the source of the specimen in accordance with established medical criteria, procedures and privacy regulations. In some countries the term DONOR or "individual" may be used in the same context as subject, especially as the context relates to human specimens.

TAXON – Any recognized category in the taxonomic hierarchy. For many purposes, the category "species" is the most important.

Tg – The glass transition temperature marks the temperature at which a fluid becomes so viscous it appears solid. The extreme viscosity reduces diffusion and molecular restructuring, slowing reactions that might otherwise cause samples to deteriorate. The T*g* for pure water is −132 °C.

TOLERANCE LIMITS – Limits that define a range of acceptable values that are established for each testing procedure which, when exceeded, require the implementation of corrective actions designed to produce results within the acceptable range in future tests.

TRACEABILITY – The ability to locate a specimen during any step of its donation, collection, processing, testing, storage and disposition.

VOUCHER – A physical specimen or part thereof (*e.g.,* pressed plant, pinned insect or bird skin, etc.) that establishes a link between the specimen from which it was procured and an actual biological specimen. Animal vouchers are usually in museums; plant vouchers are in herbaria.

APPENDIX C: ABBREVIATIONS

Below is a list of abbreviations that are used throughout this document:

1D – One dimensional
2D – Two dimensional
BRC – Biospecimen Resource Center
cGCP – Good Clinical Practices
cGLP – Good Laboratory Practices
cGMP – Current Good Manufacturing Practices
cGP – Current Good Practices
CO_2 – Carbon dioxide
DNA – Deoxyribonucleic Acid
EDTA – Ethylenediaminetetraacetic Acid
ESB – Environmental specimen bank
H&E – Hematoxylin-Eosin
IATA – International Air Transport Association
ICAO – International Civil Aviation Organization
ID – Identification Reference
IRB – Institutional Review Board
IRT – Individual Responsible for Training
ISO – International Organization for Standardization
LN_2 – Liquid Nitrogen
MSDS – Material Safety Data Sheet
PEL – Permissible Exposure Limit
PHI – Protected Health Information
QA – Quality Assurance
QC – Quality Control
QMS – Quality Management System
RBC – Red Blood Cell
RNA – Ribonucleic Acid
SCBA – Self Contained Breathing Apparatus
SOP – Standard Operating Procedures
T_g – Glass Transition Temperature