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Biobanking: Safeguarding the Future of Research with Standardized Repositories and Advanced Tracking Systems

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Abstract

The demand for standardized methods in collecting, storing, and distributing high-quality biological and environmental specimens for research underscores the crucial role of repositories. These entities, responsible for receiving, processing, and disseminating biospecimens like urine, blood, tissues, cells, DNA, and RNA, serve as vital libraries supporting clinical and research activities. Biobanking, encompassing the collection, processing, and long-term storage of biological samples, emerges as a cornerstone in biological, biomedical, and industrial research and laboratory diagnostics. The increasing importance of biobanking is evident through numerous facilities' establishment worldwide, each characterized by unique preserving techniques and functional protocols. In India, several biorepositories contribute to national scientific programs, although comprehensive data remains limited. Efficient repository facilities necessitate Quality Assurance Programs, temperature control, air circulation, lighting, flooring, and security systems to ensure safe storage and operational effectiveness. Specific storage equipment like liquid nitrogen freezers and RFID technology aids in maintaining specimen integrity and accurate tracking from collection to shipment, enhancing biological material tracking and ensuring accurate specimen identification and retrieval.

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.

A **repository** is an entity that receives, stores, processes and disseminates specimens, as needed. It encompasses the physical location and the full range of activities associated with its operation. A repository should have sufficient professional staff and a commitment to maintain and preserve records for future reference and historical continuity (Bernstein and Dayal, 1994).

Biospecimens are biological materials such as urine, blood, tissues, cells, DNA, RNA, that are derived from humans, animals or plants. Biospecimens are being collected and stored for a long time to support clinical and research activities.

Biorepository/Biobanking is a facility that collects, processes and stores biospecimens. Biorepository is a facility that acts as a library for biosamples, allowing the samples to be available for use in future research. A biorepository will be involved in collecting, cataloguing and storing biosamples and will also be involved in managing access to and distributing biosamples to researchers (Karen, 2008).

Why Biobanking?

The majority of relevant studies on microbial pathogenesis, etiologies of infectious diseases, epidemiology and environmental microbiology are based on obtaining biological samples. Biobanking, intended as the process of collecting, processing and long-term storage of biological samples, represents an essential tool for biological, biomedical and industrial research and for laboratory diagnostics (Paolo, 2015).

The characteristics of an ideal specimen bank were described by Lee in 1990 as having a secure funding source, a cryogenic storage facility, developed criteria for selection of the best samples to be stored and at the same time each facility must develop ongoing research to optimize sample collection/processing and storage conditions (Lee *et.al.*, 1990).

Because biobanking has gained an emerging importance in diagnostics, research and epidemiology, many organizations have now their own biobanking facilities, characterized by different preserving techniques, their own functional protocols and ideally, their own bioinformatic procedures. For these reasons, although it requires huge investments in personnel, automation and storing facilities, biobanking is becoming a part of biomedical and environmental national scientific programs.

In the microbiological setting, the most important reasons for biobanking could be summarized as follows:

- Conducting epidemiological studies using stored samples allows for comparisons within the same epidemic episode, across different time points, or distant locations. This aids in understanding genetic characteristics, transmission modes, and supports the development of infection control plans, including vaccines.
- Advancing diagnostic procedures involves comparing samples over time, employing new analytical methods on stored samples, and enhancing sensitivity or specificity in infectious disease detection.
- Large-scale research studies, requiring diverse samples or multiple parameters, benefit from repositories with samples collected globally and analyzed in specialized laboratories.
- Establishing repositories of human or animal cell lines, microorganisms, and reference reagents supports diagnostic and research programs, ensuring quality control in laboratories.
- Creating collections of microorganisms contributes to characterizing global microbial diversity and evolution, providing valuable insights for research.

Types of Biorepositories

- **Tissue type:** Blood, serum, tissue, DNA, RNA, microorganisms etc.
- **Purpose or intended use:** Research, forensics, therapeutics, diagnostics etc.
- **Ownership:** Academic or research institutions, Hospital based and Pharmaceutical industries (Annaratone *et.al.*, 2021)

Current Biobanks/Biorepositories in India:

- The exact data on biorepositories in India is inadequate

Some of the biorepositories in India are:

- **NCVTC- National Centre for Veterinary type cultures – Hisar**
- MTCC-Microbial type cell cultures - Chandigarh
- ICAR-National Bureau of Animal Genetic Resources, Haryana
- ICAR-National Bureau of Plant Genetic Resources, Pusa
- ICAR-National Bureau of Fish Genetic Resources, Lucknow
- ICAR-National Bureau of Agriculturally Important Microorganisms, Uttar Pradesh
- ICAR-National Bureau of Agricultural Insect Resources, Bengaluru

- National Centre for Cell Science, Pune
- National Cancer Tissue Biobank, IIT Madras
- Advanced Centre for Treatment, Research and Education in Cancer, Mumbai
- CSIR- Institute of Microbial Technology
- National Institute of Mental Health and Neurosciences, Bengaluru
- National JALMA Institute for Leprosy and Other Mycobacterial Diseases
- NCTB, Chennai, Tamil Nadu
- NLDB , New Delhi
- RGCIRC Biorepository , New Delhi
- NIMHANS, Bangalore , Karnataka **(Biobank India foundation-BBIF)**

Basic Facilities for a Repository

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 (Hallmans and Vaught, 2011).

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. (John,1982).

1. **Temperature:** Maintaining ambient temperature within specific boundaries is crucial in most repositories. Sufficient heating capacity is necessary to avoid water freezing in drain lines, while adequate air conditioning is essential to prevent excessive strain on mechanical freezer and refrigerator compressors, which can lead to premature wear and failure. To prolong the lifespan of mechanical refrigeration equipment, it's recommended to maintain repository ambient temperatures between 15 °C and 22 °C (65 °F – 72 °F) (Hallmans and Vaught, 2011).
2. **Air Flow and Circulation:** Ensure proper air circulation to prevent excess moisture, as unchecked humidity can lead to fungal growth, impacting specimen integrity and posing health risks for staff. Provide adequate space for air circulation, especially in areas with freezers and refrigerators, to prevent excessive heat accumulation that may adversely affect compressor function. Critical ventilation and monitoring are necessary in repositories using liquid nitrogen and dry ice to maintain sufficient oxygen levels. It is advisable to install oxygen monitoring devices and exhaust systems in areas where a low oxygen level may develop (Hallmans and Vaught, 2011).
3. **Lighting**

General Lighting: Ensure sufficient lighting for a safe working environment and accurate storage and retrieval of materials. Lighting levels depend on spatial conditions, activity type, volume, specimen characteristics, and the labelling system (Karen, 2008).

Task Lighting: Use task lighting when necessary for tightly packed materials, label reading, or areas with impaired overhead lighting. Caution is advised to prevent adverse effects on sample integrity or storage conditions, such as thawing due to heat from incandescent lighting (Hallmans and Vaught, 2011).

Emergency Lighting: Critical during power loss, emergency lighting is essential for indicating exit routes, providing a safe environment, and aiding equipment monitoring and emergency response. Ensure battery backup and connection to generators, consider small night lights for low-level illumination, and keep portable lighting (e.g., flashlights) available for focused use during emergencies. Regular testing and annual battery checks are recommended as part of safety and maintenance procedures (John, 1982).

4. **Flooring**: Choose flooring surfaces in repositories that suit the equipment and refrigerants used daily, ensuring easy cleaning and facilitating equipment movement when necessary. Pay special attention to areas using liquid nitrogen, as direct spills onto vinyl tile may lead to cracking and create hazards (Umeki, 2007).
5. **Uninterruptible Power Supply:** An uninterruptible power supply (UPS), also known as a battery backup, ensures a continuous flow of electric power to connected equipment during utility power outages. Positioned between the power source (typically commercial utility power) and the protected load, a UPS swiftly switches to its own power source in case of power failure or abnormalities. It safeguards computer systems, electronic devices like environmental monitors and safety systems (e.g., oxygen sensors, ventilation systems), and controllers for liquid nitrogen freezers. Regular annual testing is recommended to verify the UPS's reliable backup capabilities (Hallmans and Vaught, 2011).
6. **Access**: Ensure repositories have a system effectively restricting access to authorized staff and preventing physical intrusion by unauthorized individuals. Maintain locked doors, control keys with a recorded list of individuals granted access, and limit repository material access to personnel assigned to repository operations. Individually lock freezers or environmental storage equipment containing valuable or sensitive specimens. Utilize non-duplicatable mechanical keys and install magnetic locks at entry points to control and record access (John, 1982).
7. **Security Systems**: Each repository must implement fundamental security systems to safeguard stored specimens. These systems should undergo continuous monitoring, with alarms addressed 24/7. A responsible individual should be on standby at all times to promptly respond to alarms, preventing or minimizing potential loss or damage to stored materials. If the initial responder fails to acknowledge the alarm, the system should automatically initiate calls to other staff members trained in emergency response from a predefined list of phone numbers (Karen, 2008).
8. **Intrusion Detection Systems**: In the absence of authorized personnel, repositories should deploy alarm systems to detect unauthorized entry, utilizing motion detectors, glass break sensors, and door entry sensors. Additionally, repositories should implement an automated building access detection system to oversee facility access and log entry and exit records. This system should be adaptable to changes in security codes and keys when personnel leave the organization (Umeki, 2007).
9. **Storage Equipment and Environments:** 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.

Liquid nitrogen freezers: Cryogenic storage with liquid nitrogen is effective for long-term storage, slowing chemical and physical reactions that cause specimen deterioration. On-site liquid nitrogen minimizes reliance on power-dependent mechanical freezers (Wang et.al., 2018).

Vapor or Liquid Storage: Vapor phase storage is preferred over liquid phase storage due to lower temperatures and safety advantages. Careful selection of vials is crucial, as not all are penetrable by liquid nitrogen. Cryogenic straws offer hermetic sealing for safe liquid nitrogen storage (Wang et.al., 2018).

Oxygen Sensors: In areas using LN2 freezers, the displacement of oxygen poses a risk, with sensor use recommended. Mobile oxygen monitors are suitable in LN2 freezer-operated secure spaces to avoid false alarms caused by sensor degradation in installed units (Ramamoorthy et.al., 2003).

Mechanical freezers: Employed in various temperature ranges, mechanical freezers operate from -20, -40, -70 to -80 °C and occasionally as low as -140 °C. They come in diverse sizes, configurations, and voltages.

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 extent 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 (Abramova *et.al*., 2023)

Biological Material Tracking

To ensure accurate tracking of specimens from collection sites through repository arrival and subsequent shipment, effective tracking systems are essential. Key components include unique specimen identifiers, durable labels resistant to laboratory solvents, readable container indications, and additional features detailed below:

Labels:

- Each specimen container requires a computer-printed label that adheres securely under anticipated storage conditions.Labels should resist common laboratory solvents and include readable indications of the container's contents.
- For containers with materials posing label adherence challenges, self-adhesive labels may be necessary (Meijering et.al., 2009).

Barcoding:

- Labels should ideally feature linear (one-dimensional) barcodes that uniquely identify each specimen.In certain situations, two-dimensional barcodes may be employed, offering lower scanning error rates and the ability to include more information, particularly for smaller vials.
- Selection of barcode systems may be influenced by cost considerations (Hanner and Gregory, 2007).

Radiofrequency Identification (RFID):

- RFID is a method using magnetic induction for remote data storage and retrieval between reader and tags. Comprising a reader, a writer for input/output, an antenna for data communication, and a tag or transponder for data storage, RFID offers an alternative to barcodes. Tags, serving as substitutes for barcodes, store specimen and patient information and come in various shapes and sizes, such as sticker or insertion types.
- The tag, equipped with a coiled antenna connected to an electro-chip, holds specimen information, while the reader with an antenna access and interprets the labelled tag data (Shim et.al., 2011).

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