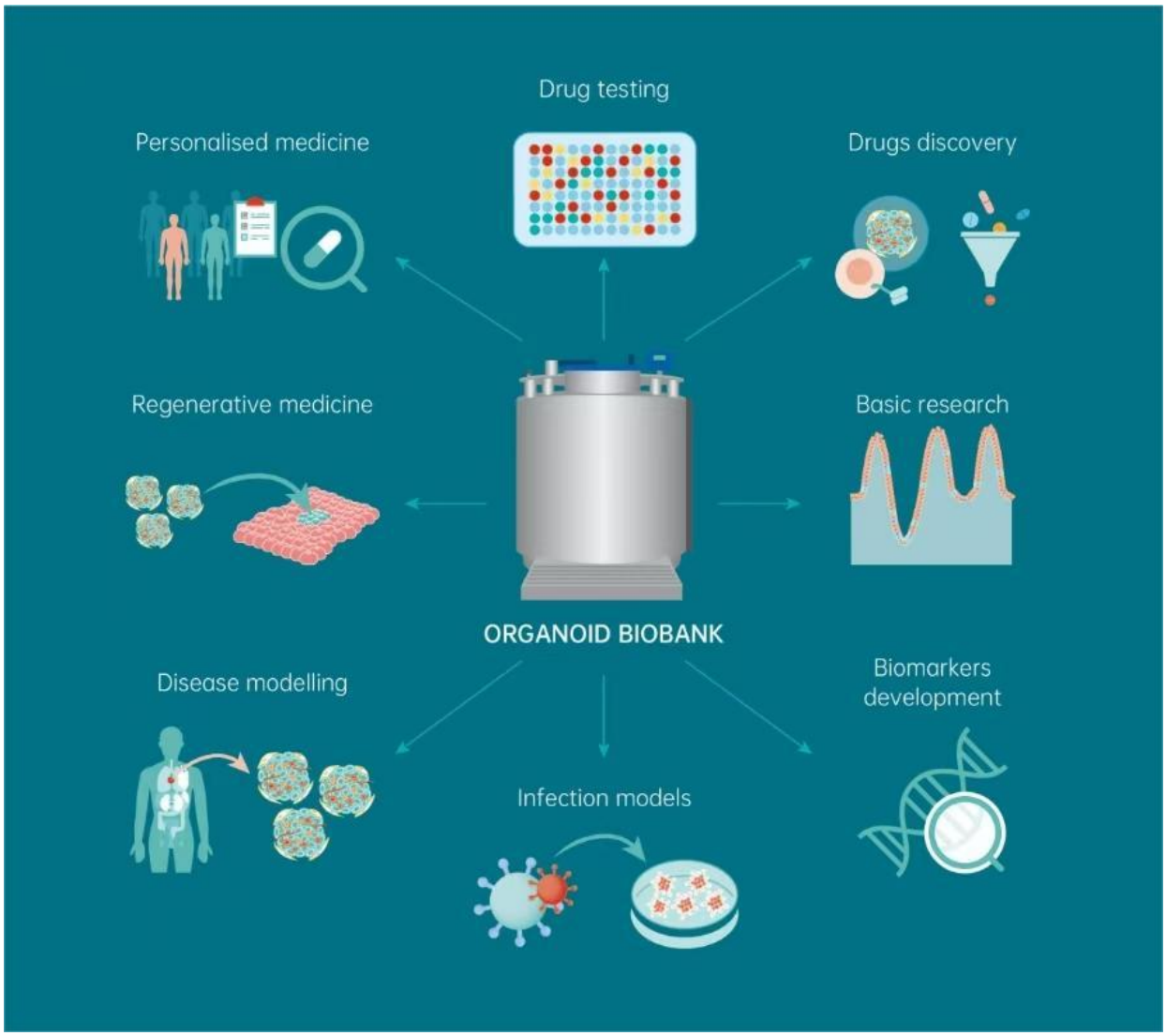
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Foreword

In the ever-evolving landscape of biomedical science, the role of “Organoid Biobanking” (OBing) has emerged as a critical component in advancing our understanding of human health and disease. The International Society of Organoid Research (ISoOR) acknowledges the necessity for a standardized approach to this field, which ensures the quality, reliability, and ethical use of organoids in research and clinical applications.

This foreword introduces the ISoOR-International Standard for Organoid Biobanking (hereinafter referred to as "ISoOR-ISOB"), a document that encapsulates the collective expertise and best practices of the international organoid research community. Developed through a collaborative and consultative process, this standard aims to provide a comprehensive framework for organizations and stakeholders engaged in OBing.

The standard outlines the essential principles and procedures that govern the establishment, management, and operation of Organoid Biobanks (OBs). It addresses key areas, including “ethical considerations”, donor consent, sample acquisition and processing, storage conditions, “data management”, and the sharing of OB resources.

The development of this standard has been informed by the wealth of knowledge and experience accumulated within the scientific community. It reflects a commitment to excellence and a dedication to advancing the field of organoid research in a responsible and impactful manner.

The ISoOR-ISOB is intended to serve as a guiding document for researchers, institutions, and organizations involved in OBing. It is our hope that the adoption of this standard will lead to a more unified and rigorous approach to organoid research, ultimately contributing to the betterment of human health.

As we move forward, the ISoOR-ISOB will be a living document, subject to periodic review and refinement to ensure its continued relevance and alignment with the latest scientific advancements.

We extend our heartfelt thanks to all those who have contributed to the development of this initiative.

This document employs the following verbal expressions:

— "shall" denotes a mandatory requirement;

— "should" conveys a recommended practice;

— "may" grants permission;

— "can" signifies either a possibility or an ability.

Additionally, terms with specific definitions will be italicized and placed in quotation marks (e.g., “term”) upon their first occurrence, with their definitions available in the glossary on page 43.

1 Scope:

The ISoOR-ISOB provides a framework for the establishment, management, and operation of OBing facilities. The standard covers all aspects of OBing, including ethical considerations, quality management, sample “traceability”, data security, and technical performance.

The standard is intended for organizations that handle the collection, storage, preservation, and distribution of “organoids” for various applications, including research, clinical, and therapeutic purposes. The standard is designed to ensure high-quality and competent practices in OBing on a global scale.

The standard is applicable for OBing facilities, regulatory authorities, accreditation bodies, and stakeholders within the organoid community.

2 Objectives:

2.1 Quality Assurance

To conduct OBing operations under a robust quality management system that adheres to international standards and is tailored to the specific needs of organoid technology.

2.2 “Ethical Compliance”

To establish guidelines that respect ethical considerations in OBing, emphasizing “informed consent”, confidentiality, and the responsible use of human biological materials.

2.3 Traceability and Provenance

To implement systems ensuring the traceability of organoids from collection to distribution, maintaining accurate records of their history and manipulation.

2.4 “Data Integrity and Security”

To protect the integrity and security of data associated with organoid samples, in compliance with international data protection regulations.

2.5 Standardize Applications

Standardize the applications of organoids in drug screening and personalized medicine to ensure safety and efficacy.

2.5 Standardization of Practices

To develop standardized operating procedures for “organoid culture”, preservation, and analysis that reflect the best practices in the field.

2.6 “Risk Management”

To adopt a proactive approach to risk management, identifying and mitigating risks to organoid quality and integrity.

2.7 Resource Management

To ensure OBing facilities have access to appropriate resources, including trained personnel, suitable facilities, and validated equipment.

2.8 Accessibility and “Equity”

To promote equitable access to OB resources, extending the benefits of organoid technology across various user groups and disciplines.

2.9 Continuous Improvement

To encourage the adoption of new technologies and methodologies that enhance the quality and efficiency of OBing.

2.10 International Collaboration

To support international collaboration in organoid research and OBing by providing a harmonized standard that facilitates global partnerships and data sharing.

3 Basic Criteria

3.1 Overview

The OB shall conduct specific risk assessments to address potential risks and opportunities. The overall requirements include:

- The OB should have an appropriate scale and a well-organized, comprehensive organizational structure.
- The OB shall employ a dedicated team of professional technical and management personnel.
- The OB shall operate with standardized procedures and a robust quality management system.
- The OB shall facilitate an adequate level of development and sharing of biological sample resources.
- The OB shall possess professional research and development capabilities for organoid samples.
- The OB shall provide a mature, comprehensive, and stable experimental technology service platform.

The specific process for the establishment of the OB should encompass: collection, procurement, acquisition, reception, marking, recording, cataloging, classification, inspection, preparation, processing, preservation, cell/tissue culture, storage, data management, disposal, packaging, protection, and transportation and distribution.

3.2 Equity

- The OB shall ensure equity by promoting equal access, fair treatment, and just distribution of benefits and resources for all stakeholders. This includes making the OB's services accessible to all potential users, regardless of background or affiliation, and continuously addressing risks to equity and integrity.
- The OB management shall be committed to maintaining and safeguarding the equity and integrity of the OB. This includes continuously assessing and identifying risks, both internal and external, that may compromise fairness and integrity.
- If any equity risks are identified, the OB shall take prompt measures to mitigate or minimize these risks and document the entire process.

3.3 OB Specimens Management and Ethical Compliance

- The OB shall understand the requirements for biomaterials and related data, ensuring repeatable research outcomes, and adhere to ethical principles.
- The responsibilities of the OB shall be clearly defined and readily available.
- Information related to the activities, processes, and procedures of the OB shall be documented in an understandable format.
- Documentation should include procedures related to the quality management system and relevant information from OB/dedicated area management.
- The OB shall adhere to international and national ethical principles related to biomaterials and associated data.
- The OB shall record the identity of personnel conducting activities.
- The OB shall specify the retention period for record information and related data for each type of biological material after its complete distribution, disposal, or destruction.

3.4 Traceability of Process Information

Ensuring complete and accurate traceability of all process-related information is essential to maintaining the integrity, “reproducibility”, and quality of OBs. This subsection outlines the minimum requirements for documenting and tracking the process steps involved in organoid handling, storage, and distribution.

3.4.1 Scope of Traceability

All critical process steps within OBing shall be tracked in a detailed and transparent manner. This includes, but is not limited to:

- Collection of biological materials (e.g., tissue samples, cells).
- Organoid preparation and culture methods.

- Use of reagents, scaffolds, and matrices (with batch numbers and expiry dates).
- "Cryopreservation" procedures and thawing processes.
- Quality control checks and associated results.
- Distribution and shipment of organoids to third-party users.

The traceability system shall allow the reconstruction of the entire process flow for any organoid or batch in the OB.

3.4.2 Documentation and Recording Systems

To support traceability, both paper-based and electronic documentation systems are acceptable, provided they meet the following criteria:

- Unique Identification Codes: Each organoid sample, batch, and associated processes shall be assigned a unique identifier (e.g., barcode or alphanumeric code) that is linked to its complete history.
- Timely Updates: All records shall be updated immediately following any process step to avoid data discrepancies.
- "Audit Trails": Any changes to records, including updates or corrections, shall be traceable with a timestamp, the identity of the person making the change, and the reason for the amendment.

3.4.3 Compliance Verification

The traceability system shall undergo periodic internal audits to ensure accuracy and completeness. Records shall be kept in accordance with regulatory requirements and best practices for data integrity, allowing for easy retrieval and review by authorized personnel or external auditors.

3.4.4 Digital Systems for Process Traceability

Where digital or automated systems are used for OBing processes, they shall be qualified or validated, as appropriate for their intended use, in accordance with 5.3.6.5, to demonstrate reliability and compliance with applicable data security requirements. The digital system shall:

- Allow secure access only to authorized personnel.
- Provide robust backup and recovery mechanisms.
- Ensure all process-related data are stored in a way that preserves their integrity over time (e.g., protection against data loss or corruption).

3.4.5 Traceability in Collaborative Projects

When OBing activities involve collaborations between multiple institutions or international parties, it is imperative that the traceability systems employed by all involved parties are interoperable. A standardized framework for data sharing, material transfer, and process recording shall be established at the outset of the project to ensure traceability is maintained across institutions. This shall include the implementation of a "Material Transfer Agreement" (MTA) governing the exchange of organoid materials, which specifies traceability requirements and the responsibilities of each party.

3.4.6 Incident Management and Non-Compliance Reporting

If any deviation from the standard process occurs, the event shall be documented, including the nature of the incident, the corrective actions taken, and any potential impact on organoid quality or consistency. Non-compliance with traceability requirements shall be addressed promptly, and documented actions shall be taken to prevent recurrence.

3.5 Legal and Ethical Requirements

3.5.1 "Legal Ownership" of Organoids and Data

- The legal ownership of organoids and associated data may vary based on local, national, or international laws. OBs shall clarify ownership through formal agreements and ensure that the terms of ownership are clearly defined for both biological samples (organoids) and any derived data.
- Ownership agreements shall be reviewed periodically to remain compliant with evolving legal frameworks.

3.5.2 “Data Protection and Privacy”

- OBs shall implement appropriate safeguards to protect the privacy and confidentiality of personal and sensitive data associated with organoid samples, in accordance with data protection laws.
- Any identifiable data linked to organoid samples shall be processed and stored in a manner that complies with applicable data privacy laws and the principles of confidentiality, integrity, and availability.

3.5.3 “Access to Organoids and Data”

- OBs shall clearly define and document “access agreements” that specify who can access organoid samples and related data, under what conditions, and for what purposes.
- Access agreements should be in place to ensure that any sharing of organoid materials complies with the informed consent process and ethical standards.
- A MTA shall be established prior to any transfer of organoid materials to external parties. The MTA shall outline the terms of access, traceability requirements, and the obligations of the receiving party regarding the use, storage, and further distribution of the materials.

3.6 Compliance with “Intellectual Property (IP) Rights”

3.6.1 Intellectual Property Considerations

- OBs shall clarify the ownership and rights to any IP generated from research using organoid samples.
- Agreements should outline the terms of IP ownership, whether it is held by the OB, the researcher, or external stakeholders.
- OBs shall respect and adhere to intellectual property laws when commercializing organoid-based research or products.

3.7 Legislative and Policy Awareness

3.7.1 Monitoring and Implementation of Legislative Changes

- OBs shall have mechanisms in place to regularly monitor changes in legislation and research policies that may impact the collection, storage, or use of organoid samples.
- It is the responsibility of the OB to adapt its procedures and practices in response to new legislative or regulatory developments, ensuring continued compliance with all applicable laws.

4 Structural Requisites

4.1 Organizational Structure

The organizational structure of the OB should be designed to clearly define roles, responsibilities, and lines of authority among management, scientific, and technical staff. This structure is crucial for maintaining operational efficiency and ensuring compliance with legal and ethical standards. The roles and responsibilities shall be clearly documented, with an emphasis on accountability and oversight to support the ethical and legal use of human biological materials. Management should ensure that the structure is adaptable to changes in regulatory requirements and emerging best practices, aligning with general requirements set forth in OBing and quality management standards.

4.2 Facilities and Infrastructure

The OB shall provide specialized facilities that support all aspects of OBing, including but not limited to culture, processing, storage, and administrative functions. The infrastructure should meet the statutory and regulatory requirements of the operating jurisdiction, ensuring that it supports both quality and risk management objectives. OBs should be equipped with appropriate safety features and designed to maintain environmental conditions that preserve the integrity of organoids. The facility's layout shall support the workflow and minimize cross-contamination risks, reflecting the guidelines for best practices in OBing.

4.3 Equipment and Materials

The OB shall be equipped with the necessary instruments, equipment, and materials essential for organoid culture, cryopreservation, and analysis. This includes standard cell culture equipment, cryogenic storage systems, and other critical apparatus. All equipment shall be regularly calibrated, validated, and maintained to ensure accuracy and reliability. The selection and procurement of materials should be based on documented protocols to ensure consistency and quality in the OBing process, reflecting the requirements for quality control and the handling of biological specimens.

4.4 Information Management System

An effective Information Management System (IMS) is vital for the comprehensive management of records, tracking samples, and ensuring the traceability of organoids throughout the OBing process. The IMS should be architected to uphold data integrity, security, and confidentiality, in alignment with relevant regulatory frameworks for data protection and OBing standards. Key features should include robust backup and recovery solutions to ensure that records are securely stored and easily retrievable. Additionally, the IMS shall facilitate compliance with legal and ethical standards, providing comprehensive audit trails and documentation control to support operational transparency.

4.5 “Quality Management System” (QMS)

The OB shall implement a comprehensive QMS that establishes the structural requisites necessary for effective quality oversight. This includes a quality policy, quality objectives, and defined management responsibilities. The QMS should encompass all operational aspects of OBing, from procurement to distribution, and outline processes for continuous improvement and internal audits. This framework ensures that all operations are conducted under controlled conditions, with ongoing monitoring to maintain high standards of quality and consistency.

4.6 Personnel Competence

All personnel involved in OBing shall have the necessary education, training, skills, and experience to perform their tasks competently. The OB should implement a training program that ensures all staff are regularly assessed and receive ongoing education to stay current with advancements in the field. Competence should be maintained through continuous professional development, and training records shall be meticulously maintained.

4.7 Safety and Environmental Conditions

The OB shall maintain a safe working environment and establish environmental conditions that ensure the integrity and stability of organoids during culture, storage, and processing. Safety protocols should include biohazard

containment, emergency response plans, and regular safety audits. Environmental monitoring systems should be implemented to continually assess and maintain optimal conditions, with provisions for immediate corrective actions if needed.

4.8 Ethical Considerations

Ethical guidelines shall be established and strictly followed, addressing key issues such as informed consent, confidentiality, and the responsible use of organoids and associated data. These guidelines should ensure that all practices respect the rights and dignity of donors and align with broader ethical standards in research.

4.9 “Regulatory Compliance”

The OB shall ensure full compliance with all relevant international, national, and regional regulations governing research, biobanking, and the use of human biological materials. This includes adhering to specific legal requirements within the jurisdiction, as well as any applicable international agreements or guidelines. Regulatory compliance should be integrated into all aspects of the OB's operations, with regular reviews and updates to reflect changes in the legal and regulatory landscape.

4.10 External Services and Supply Chain

The OB shall establish robust procedures for the evaluation, selection, monitoring, and re-evaluation of external suppliers and service providers. These procedures should ensure that all external resources, including supplies and services, meet the required standards for quality and suitability in OBing operations. The supply chain should be managed to minimize risks and ensure the consistent quality of inputs, reflecting best practices in supply chain management and quality control.

5 Resource Criteria

5.1 Overview

The OB shall ensure sufficient staffing, materials, equipment, and infrastructure to support its operations. Maintaining strategic normative documents and advanced information systems is essential for the smooth and efficient functioning of all production processes. Additionally, the OB shall secure a continuous stream of funding to support its activities, including the regular updates needed for resources within the OB. This financial stability is crucial for maintaining high standards and meeting the dynamic needs for OBing.

5.2 Human Resources

- Personnel shall adhere to established norms and processes, with regular competency assessments and training. The OB should provide detailed job descriptions, clearly defining roles and responsibilities according to its standards. Regular reviews of personnel abilities and qualifications should be conducted, with comprehensive records maintained, including names, signatures, identification codes, and employment dates.
- The health and safety of all personnel shall be ensured through adherence to safety regulations and protocols, with comprehensive records of all processes maintained to prevent workplace hazards. This includes conducting risk assessments for all biological and chemical materials, processes, and equipment, and providing the necessary safety training to mitigate potential risks.
- All personnel, including internal staff and external collaborators, shall maintain impartiality and confidentiality, particularly regarding access to biological database data.

5.2.2 Competence and Skill Evaluation

- All personnel shall pass competency assessments before independently performing designated activities. If a personnel's abilities do not meet the required standards, corrective measures should be taken, including professional skills training when necessary.
- The OB should conduct regular competency assessments of relevant personnel annually, based on task requirements and the unique characteristics of different positions. This ensures continuous improvement and adaptation to evolving standards.
- For personnel involved in high-complexity testing, more periodically competency reviews should be conducted in their first year of work. Their capabilities should be evaluated whenever new processes and requirements are introduced.
- Personnel competency assessment files shall be meticulously recorded and maintained as evidence of professional abilities and education/training. These records serve as proof of the OB's commitment to maintaining high standards.

5.2.3 Training

The OB shall establish, implement, and maintain policies, processes, and procedures to ensure that personnel are trained, competent, and comply with quality, safety, and ethical standards. The training program shall cover the following:

5.2.3.1 Preliminary job training

The OB shall provide induction training to all new personnel. This shall introduce OB policies, protocols, and laboratory procedures, emphasizing good practices in laboratories.

5.2.3.2 Quality system training

The OB shall conduct training on QMS to maintain and continuously improve performance across all OBing activities.

5.2.3.3 Job-specific training

The OB shall ensure personnel receive training specific to their assigned tasks, including updates as responsibilities evolve.

5.2.3.4 Continuing education

The OB should facilitate continuing education programs to ensure personnel, particularly technicians performing key tasks, maintain competence and meet OB certification requirements.

5.2.3.5 "Good Laboratory Practice" (GLP) training

The OB shall train personnel in GLP principles, including aseptic techniques, equipment handling, laboratory hygiene, and waste management.

5.2.3.6 Biosafety training

The OB shall ensure personnel receive biosafety training appropriate to the risk level of OB operations, covering biological material handling and emergency procedures.

5.2.3.7 Traceability procedures training

The OB shall train personnel in traceability requirements, emphasizing accurate record-keeping, sample labeling, and chain-of-custody maintenance throughout the organoid lifecycle.

5.2.3.8 Ethical and legal compliance training

The OB shall ensure that personnel are trained in ethical requirements, including informed consent, data protection, and MTAs.

5.2.3.9 "Standard Operating Procedures" (SOPs) training

The OB shall ensure that personnel are trained to follow relevant SOPs for organoid collection, culture, storage, transportation, and data management.

The OB shall maintain records of all training provided and assess personnel competency at regular intervals to confirm compliance with applicable standards and procedures.

5.3 Equipment

5.3.1 Acquisition and Installation Process

The OB shall establish policies for equipment acquisition, operation, maintenance, calibration, and traceability. Equipment specifications and selection criteria should be defined before purchase. All critical equipment shall be qualified for its intended use, with repairs and upgrades evaluated and requalified as appropriate.

- Equipment shall be installed according to the manufacturer's specifications to ensure proper functioning and compliance with industry standards.

5.3.2 Verification and Operation of Technical Resources

- The functionality of equipment shall be verified before use against applicable manufacturer specifications and requirements for its intended use. Information and data management systems and their components shall be qualified or validated, as appropriate for their intended use, in accordance with 5.3.6.5. AI systems shall additionally meet the validation requirements of 5.3.7.4.
- The OB shall demonstrate that equipment performs as expected for its intended use, meeting or exceeding the manufacturer's specifications. This includes regular testing and validation.
- Equipment shall be used in accordance with the manufacturer's written instructions, with processes for scheduled monitoring and maintenance in place to ensure continued compliance and performance.

5.3.3 Calibration and Accuracy of Tools and Devices

- The OB shall identify equipment that requires maintenance in a calibrated state. Measurements and accuracy requirements shall be determined, with a detailed calibration process defined, including equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and limitations.
- Equipment used for inspection, measuring, and testing shall be calibrated before initial use, after repair, and at prescribed intervals. Equipment shall be safeguarded from adjustments that may invalidate calibration settings, ensuring accurate and reliable results.

5.3.4 Equipment Inspection, Maintenance, and Servicing

- A defined process shall be in place for handling equipment found to be out of calibration or specification. This includes assessing the validity of previous inspection and test results and determining the conformance of provided OB services to required specifications.
- Cleaning and sanitization methods and intervals shall be defined for each piece of equipment. Suitable environmental conditions shall be ensured for calibrations, inspections, measurements, and tests.
- Equipment shall be monitored to ensure defined parameters are maintained, with maintenance and repairs performed by qualified individuals according to the manufacturer's instructions.

5.3.5 Monitoring of Equipment

The OB shall maintain records of equipment use to ensure unique identification and traceability. This includes linking specific equipment to all associated OB activities, ensuring comprehensive documentation and accountability.

5.3.6 Data Management and Information Management Systems

5.3.6.1 General

- The OB shall establish, document, implement and maintain one or more information and data management systems appropriate to the nature, scale, sensitivity and intended use of the biological material and associated data.
- The implementation of these requirements may be integrated into existing organizational processes and responsibilities, provided that their effectiveness can be demonstrated and documented.
- The systems shall support data quality, integrity, traceability, metadata completeness, interoperability, controlled access and sharing, privacy, security and availability throughout the data lifecycle. Requirements for data integrity and security, documentation and record keeping, and lifecycle traceability specified in 7.9, 7.14 and 7.15 shall apply.

5.3.6.2 Governance and risk management

- The OB shall define accountability, authority and competence for the governance, operation, review and improvement of its information and data management systems. Documented policies and procedures shall be maintained to identify, assess, control and review risks to data and associated biological material.
- Controls shall be proportionate to risk and shall address, as applicable, loss, corruption, unauthorized access or alteration, inappropriate use or sharing, data leakage, breach of privacy, loss of traceability and unavailability of critical information. Residual risks and exceptions shall be reviewed and accepted by authorized personnel.

5.3.6.3 Data quality, metadata and provenance

- The OB shall define and maintain data and metadata sufficient to identify biological material and associated data, interpret their meaning, assess fitness for intended purpose, and support traceability and reproducibility. Links among source material, organoids and derivatives, processing history, quality-control results and associated datasets shall be maintained throughout their lifecycle. For organoid-related biological material, metadata shall include, as applicable to the intended use, relevant biological and culture variables such as organoid type and source, culture conditions, dissociation method, passage number, extracellular-matrix material and lot, and other variables that may materially affect organoid characteristics, quality or reproducibility.
- The OB shall establish appropriate controls to preserve the completeness, accuracy, consistency, traceability, accessibility for authorized users, and availability of critical data. Critical data shall be identified and documented based on the potential impact of their loss, inaccuracy, alteration or unavailability on organoid quality, traceability, donor rights or suitability for intended use. Their integrity shall be verified at defined stages and following events that could affect their integrity.
- Data quality requirements and acceptance criteria shall be defined for critical data. Data that do not meet specified requirements shall be identified and controlled to prevent unintended use or distribution. Such controls may include documented correction, restriction of access or use, or other authorized measures, as appropriate. The creation, revision, correction, transfer, import, export, migration and deletion of critical data shall be controlled and traceable. Changes and corrections shall not obscure the original record. Records of changes shall identify the person or system making the change, the date and time of the change, and the reason for any amendment or correction.

- Acceptance criteria shall distinguish data-quality deficiencies from expected biological heterogeneity or phenotypic variation. Organoids or associated data that differ from reference morphological or phenotypic characteristics shall not be excluded solely on that basis unless predefined and scientifically justified quality criteria indicate that they are unsuitable for the intended use.
- Data sets used for AI development, validation, testing, evaluation or operation shall be identified and controlled to prevent inappropriate overlap or transfer of information that could compromise the validity of performance assessments, and to preserve provenance and applicable use restrictions. AI outputs that inform quality, access, distribution, safety, research or reporting decisions shall be managed as critical data where applicable and shall remain traceable to the applicable data, AI system and version.

5.3.6.4 Interoperability, access and sharing

- The OB shall use documented data structures, identifiers, terminology and exchange arrangements that preserve the meaning, quality, provenance and applicable restrictions of data. Recognized community practices shall be used where suitable to support interoperability and long-term accessibility.
- Human-related data shall be classified according to sensitivity and identifiability. Data shall be considered potentially identifiable where their combination with other reasonably available information could permit re-identification. Pseudonymized or de-identified data shall be protected according to documented residual re-identification risk and shall not be treated as non-sensitive solely because direct identifiers have been removed.
- Before human-related data are made available for use or sharing, the OB shall determine and document the controls necessary for the authorized purpose, including, as applicable, data minimization, pseudonymization, de-identification, aggregation, access restriction and conditions for re-identification. Re-identification keys or equivalent linking information shall be separately protected and accessible only to authorized personnel.
- Access to and sharing of data shall be authorized and controlled in accordance with applicable consent, ethical, legal, privacy and contractual requirements. Access to human-related data shall be limited to the minimum data necessary for an authorized purpose, granted to authorized personnel and periodically reviewed at intervals determined by the OB based on the sensitivity of the data, associated risks, applicable legal and regulatory requirements, and the nature of the authorized use. The OB shall retain sufficient records of access, disclosure, transfer and distribution and shall provide recipients with applicable restrictions, responsibilities and subsequent material changes affecting permitted use.
- Where data are shared with external organizations, the OB shall establish documented data-sharing arrangements defining the permitted purposes and uses, the responsibilities of the providing and receiving parties, applicable safeguards, and conditions for further sharing, retention and disposal, as appropriate to the nature and sensitivity of the data and applicable requirements.

5.3.6.5 System control, continuity and lifecycle management

- Information and data management systems and their components, including hardware, software, databases and supporting infrastructure, shall be qualified or validated as appropriate for their intended use before implementation. Documented configuration and version information, including authorization for modifications, shall be maintained. Internally developed software shall be subject to documented lifecycle requirements appropriate to its intended use.
- Information and data management systems shall remain controlled throughout operation, modification, migration and retirement. Changes that may affect data quality, integrity, traceability, availability, privacy or security shall be authorized, assessed and documented. The impact of such changes on previously recorded, processed or shared data shall be assessed where applicable.
- The OB shall establish documented arrangements for backup, recovery, retention, archiving and authorized disposal. Backup and recovery arrangements shall protect the confidentiality and integrity of data. The ability to restore essential data and perform critical activities shall be verified at planned intervals.
- The OB shall maintain documented and verified contingency arrangements to ensure the continuity of critical activities and access to essential data in the event of electronic-data unavailability. These arrangements may include alternative electronic systems or controlled manual procedures, as appropriate to the nature and risks of the activities. Their readiness and reliability shall be verified at planned intervals, including the accessibility, currency, integrity and security of essential data. Records generated through manual contingency procedures

shall remain traceable and shall comply with the applicable documentation and record-keeping requirements of this standard.

- The effectiveness of the systems and controls shall be monitored and periodically reviewed, and identified failures or nonconformities shall be addressed through corrective action and continual improvement.

5.3.7 Appropriate and Responsible Use of Artificial Intelligence Systems

5.3.7.1 General

- The OB shall use an AI system only for a defined, justified and approved purpose. The extent of governance, evaluation and oversight shall be proportionate to the intended use, operational context and potential impact of the system.
- AI development and use relying on data controlled under 5.3.6 shall meet the requirements specified in that section. The requirements for traceability in 3.4 and for legal and ethical handling of organoids and associated data in 3.5 shall apply to AI-assisted activities.
- This section shall apply to AI systems developed by the OB, acquired from or operated by third parties, embedded in other systems, or otherwise used in OB activities. The OB shall ensure that the use of AI complies with applicable legal, regulatory, ethical, consent, privacy, security and contractual requirements.

5.3.7.2 Governance and accountability

- The OB shall establish accountability structures for the governance of AI risks. Policies, processes, procedures and practices shall be in place to support the mapping, measurement and management of such risks throughout the AI system lifecycle.
- The OB shall maintain an up-to-date inventory of AI systems used in OB activities. The inventory shall identify, as applicable, the system, version or provider, intended purpose, accountable owner, authorized users, risk classification and current authorization status. Where relevant information about a third-party AI system is unavailable, the OB shall document the information gaps, assess their impact on validation, traceability and risk, and implement appropriate controls before authorizing use.
- Each AI system shall have a defined accountable owner, authorized users and appropriate human oversight. Responsibilities for approval, operation, evaluation, monitoring, change and incident response shall be assigned to competent personnel. Third-party systems and services shall remain subject to the OB's governance and risk-management requirements.
- AI governance shall be integrated into the IMS and QMS established under 4.4, 4.5 and 7.2. AI inventories, approvals, risk assessments, validation evidence, monitoring records, change records and incident records shall be controlled as documented information in accordance with 6.3 and 7.14. Relevant AI governance activities and results shall be included in internal audits and management review under 7.11 and 7.12.
- At planned intervals, the OB shall review emerging AI technologies, cybersecurity threats, scientific evidence, applicable standards and regulation, and material provider changes, and shall document whether its controls remain adequate.

5.3.7.3 Risk assessment and authorization

- Before development, acquisition or use, the OB shall document the intended purpose, users, operating context, expected benefit, relevant limitations and reasonably foreseeable misuse or failure of the AI system. The documented context shall include the categories, sensitivity and identifiability of data used by the system and the applicable consent, use and sharing restrictions. Risks shall be assessed against defined acceptance criteria, and a documented decision shall determine whether development, deployment or continued use may proceed. The rationale for determining risk classification, acceptance criteria and the adequacy of selected controls shall be documented and available for review.
- The assessment shall consider, as applicable, scientific validity, reliability, safety, security, data leakage, breach of privacy or re-identification, harmful bias or discrimination, legal and ethical obligations, human consequences and operational continuity. AI shall not be used outside its approved purpose or conditions unless the change has been assessed and authorized.
- Identifiable, potentially identifiable or sensitive data shall not be submitted to an external AI system or service unless the OB has documented authorization and an assessment demonstrating that the intended processing complies with applicable consent, legal, privacy, security and contractual requirements. The assessment shall

define the data categories, permitted processing, provider responsibilities, access restrictions and safeguards applicable to the use.

- Where an AI system or service is provided, hosted, operated or supported by an external party, the evaluation, selection, monitoring and re-evaluation requirements of 4.10 and 5.5 shall apply.

5.3.7.4 Validation, monitoring and lifecycle control

- An AI system shall be tested, evaluated, verified and validated before use to provide objective evidence that it is suitable for its intended purpose. The methods, acceptance criteria and degree of independent review shall be proportionate to risk. Validation may incorporate documented evidence provided by developers, suppliers or independent evaluations, supplemented by verification under the OB's intended operating conditions, where appropriate to the associated risks. The OB shall remain responsible for demonstrating the suitability of the AI system for its approved intended use. Limitations, uncertainty and conditions affecting performance shall be documented and communicated to relevant users. Validation evidence shall be retained as evidence of conformity in accordance with 7.8.
- Where AI systems are used to evaluate organoids or associated biological data, validation shall consider, as applicable, the variability of organoid types, biological sources, culture conditions, passage numbers and other relevant factors that may affect system performance. Validation shall adequately represent the conditions and relevant biological variability within the approved intended use. Limitations and conditions not covered by validation shall be documented and addressed through appropriate risk controls.
- For each AI system, the OB shall define performance and risk measures, monitoring methods, review intervals and action thresholds appropriate to its intended purpose and risk classification. Monitoring methods and frequencies shall reflect the frequency of use, availability of reference outcomes, potential consequences of performance deterioration and associated risks. Performance and risk shall be monitored during use. Monitoring shall include changes in data characteristics, quality, completeness, distribution, source population, operating context or output patterns that could indicate data drift or deterioration in model performance. Where AI performance may be influenced by biological variability, monitoring shall also consider relevant changes in the biological characteristics of organoid cultures, including passage-associated changes, differentiation state, contamination status, culture conditions, and batch-dependent effects of extracellular-matrix or other critical culture materials. Where suitable reference outcomes are available, performance shall be assessed against the approved acceptance criteria. Where suitable reference outcomes are unavailable or delayed, the OB shall establish alternative risk-based monitoring arrangements, which may include surrogate performance indicators, periodic expert review, enhanced human oversight or restrictions on AI-assisted activities, as appropriate to the intended use and associated risks. The limitations of such monitoring arrangements shall be considered when determining whether continued use of the AI system remains acceptable.
- An exceedance of an action threshold or other material deterioration in performance or risk shall be investigated and shall result in appropriate corrective action, including restriction, suspension, revalidation, update or retirement of the AI system. Investigations of AI performance deterioration shall consider relevant data-related, biological, technical and operational factors when determining appropriate corrective actions. Material changes in the system, data, operating context, provider or intended purpose shall be assessed and shall trigger revalidation before continued use where the previous validation evidence no longer applies. Any update intended to address data drift or performance deterioration shall be assessed, authorized and validated before use. Material failures, deteriorations or nonconformities shall be managed in accordance with 7.10.
- The OB shall maintain a documented process for reporting, investigating and managing AI incidents and near misses, including unsafe outputs, privacy leakage, harmful bias and security compromise. The process shall provide for containment, corrective action, recovery or reversion, controlled suspension or retirement, and documented lessons learned.
- Records necessary to reconstruct an AI-assisted activity, including the relevant data, AI system and version, validation status, output and relevant change history, shall be maintained in accordance with 3.4, 7.9, 7.14 and 7.15. For consequential activities involving adaptive or generative AI, records shall include, as applicable, the inputs, instructions, configuration, retrieved sources, output and model version. Where required information cannot be obtained from an external AI provider, the OB shall document the limitation, assess its impact on traceability and accountability, and determine whether the available evidence and additional controls are sufficient for the intended use.

5.3.7.5 Human oversight, transparency and guardrails

- The role and authority of human decision-makers shall be defined. Relevant personnel shall be able to recognize limitations, review and challenge outputs, intervene or override the system, and escalate cases that are uncertain, anomalous or outside the approved scope.
- Controls shall prevent unauthorized or inappropriate AI use and shall reduce the risk of unreliable output, data leakage, breach of privacy, re-identification, harmful bias and discrimination. Decisions arising from consequential AI-assisted activities shall not be fully automated unless such automation has been specifically justified, validated and authorized. Documentation shall be sufficient to support accountability, traceability, review and corrective action while protecting confidential and personal information.
- Where AI supports access, distribution, result selection, review, release or reporting, the applicable requirements of 6.16 and 6.17 shall be met. AI-assisted outputs shall not replace authorization by competent personnel where such authorization is required by this standard or applicable legal and regulatory requirements.

5.3.7.6 Competence and awareness

- Personnel who develop, acquire, operate, oversee, evaluate or approve AI systems shall be trained and competent for their assigned responsibilities. For AI systems used to evaluate organoids or organoid-associated biological data, the personnel responsible for development, validation and evaluation shall collectively possess, or have documented access to, appropriate competence in organoid biology, culture processes, relevant quality attributes and sources of biological variability. Training and awareness activities shall address, as applicable, data protection, authorized data use, system limitations, performance monitoring, data drift, model performance deterioration, human review, override, escalation and incident reporting.
- The OB shall maintain records of relevant training and competence assessment and shall review competence when the assigned role, AI system, operating context or applicable requirements change. The competence and training record requirements of 4.6, 5.2 and 6.4 shall apply to personnel assigned AI-related responsibilities.

5.4 Infrastructure and Ambient Parameters

Infrastructure and the ambient conditions required for the execution of OBing activities shall be identified, controlled, and maintained to meet specified quality control standards. This includes preventing cross-contamination and ensuring suitable conditions for organoid storage.

- Procedures shall ensure that biological materials and related data are aligned with their intended use, biosafety, and biosecurity standards.
- Facilities housing incompatible activities shall be effectively isolated from each other to prevent cross-contamination.
- Environmental conditions shall be suitable for organoid storage, ensuring they do not adversely impact the suitability for intended use.
- Environmental conditions shall be measured, monitored, controlled, and recorded as required to maintain the quality of biological materials and related data, and to ensure the health and safety of personnel.

5.5 Third-Party Operations

- The OB shall evaluate and monitor external suppliers to ensure they meet OB requirements. Documented information and necessary actions from evaluations shall be retained, and external processes shall be communicated to providers, recipients, and users.
- Performance evaluation, selection, monitoring, and re-evaluation standards for external suppliers shall be determined based on their ability to meet the OB's requirements.
- The owner of intellectual property rights arising from the collaboration with external suppliers should be clearly defined in advance.

5.6 Laboratory Supplies, Chemicals, and other Consumables

5.6.1 Overview

The OB shall manage the selection, procurement, storage, and use of reagents and consumables to ensure quality and consistency. These protocols are essential for maintaining the integrity and reliability of biological samples and experimental results.

5.6.2 Receipt and Storage

Upon receipt, all reagents and consumables shall be inspected for damage, correct labeling, and compliance with order specifications. Storage conditions should be defined and strictly adhered to, including temperature, humidity, and light exposure requirements, as specified by the manufacturer. Appropriate storage logs shall be maintained.

5.6.3 Acceptance Testing

New batches of critical reagents and consumables should undergo acceptance testing to verify their performance and suitability for intended use. This testing shall be documented and include criteria for acceptance or rejection. Records of these tests shall be maintained and reviewed periodically.

5.6.4 Inventory Management

An inventory management system should be in place to track the availability and usage of all reagents and consumables. This system shall include details such as batch numbers, expiration dates, storage locations, and quantities. Regular audits of inventory should be conducted to ensure no expired or low-quality items are used in the OB.

5.6.5 Instructions for Use

All personnel shall have access to and follow detailed instructions for the proper use of reagents and consumables. These instructions should be based on manufacturer recommendations and validated internal protocols to ensure consistency and accuracy in experimental procedures.

5.6.6 Adverse Incident Reporting

A system for reporting, investigating, and resolving adverse incidents involving reagents and consumables shall be established. This system should include a process for identifying the root cause of the issue, implementing corrective actions, and preventing recurrence. Records of all adverse incidents and resolutions shall be maintained.

5.6.7 Records

Detailed records of all reagents and consumables shall be kept, including purchase orders, certificates of analysis, receipt dates, storage conditions, and usage logs. These records ensure traceability, facilitating quality control and regulatory compliance.

5.6.8 Standardization of Reagents for Organoid Development, transportation and Storage

5.6.8.1 General Requirements for Reagents

The reagents used throughout the lifecycle of organoids, including development, storage, and transportation, shall be standardized to ensure consistency, reliability, and compatibility with organoid-specific requirements. Reagents shall be formulated and selected to replicate the biochemical, nutritional, and environmental conditions necessary for cellular behavior, tissue organization, and functionality. This includes but is not limited to reagents for culture media, cryopreservation, and “extracellular matrix (ECM)” preparation.

5.6.8.2 Biochemical Composition and Optimization

All reagents shall avoid components that are not representative of physiological conditions, and the composition shall be optimized to match the specific biochemical environment of the organ being modeled. Nutrient concentrations, growth factors, and other critical additives shall reflect the metabolic and functional requirements of the organoid, ensuring physiological relevance.

5.6.8.3 Heterogeneity and Functional Support

Reagents shall support the cellular heterogeneity and physiological complexity of organoid models, ensuring that the natural diversity of cell types and tissue structures is maintained. This includes providing necessary signaling molecules, ECM components, and other factors critical to replicating the in vivo environment. The reagents shall contribute to preserving the functional traits of the native organ, ensuring the organoid's relevance for research and clinical applications.

5.6.9 "Biochemical Consistency"

Consistency in biochemical composition shall be maintained across all batches of reagents and materials used in organoid generation, culture, storage, and transportation. This includes ECM materials, culture media, supplements, additives, cryoprotectants, and other critical reagents. Uniformity in these components is essential for ensuring reproducibility, reliability, and quality in organoid-based research and applications.

Any changes in formulation, material sourcing, or manufacturing processes for these reagents shall be thoroughly documented, validated, and communicated to end-users. Validation processes shall confirm that such changes do not negatively affect organoid quality, consistency, or performance.

Batch-to-batch consistency for all reagents shall be monitored through robust quality control measures. Deviations from established standards shall trigger corrective actions to maintain the integrity of the OBing process and research outcomes.

5.6.10 ECMs

ECMs, in the context of organoid culture, refer to the supportive scaffolding materials either natural or synthetic that provide structural and biochemical support for the growth, maintenance, and functionality of organoids.

5.6.10.1 Material Selection

Biocompatible materials that closely mimic the native components of the ECM should be selected to effectively support organoid growth, development, and function.

5.6.10.2 Composition and Batch Consistency

For organoids developed in ECM mimetics, such as scaffolds and hydrogels, consistency is essential to ensure reproducibility and standardization within OBing. The formulation of these materials shall be clearly defined and controlled to support reliable outcomes in research and other applications.

5.6.10.2.1 Avoidance of Undefined Matrices

The use of undefined matrices, such as those derived from animal sources that may introduce variability, shall be minimized. Preference shall be given to chemically defined or synthetic matrices, where the composition is tightly controlled.

5.6.10.2.2 Use of Animal-Derived Products

In some instances, animal-derived materials may be the only viable option for certain organoid models. In these cases, variability inherent in these materials shall be carefully managed.

5.6.10.2.3 Quality Control and Mitigation of Variability

Where animal-derived products are used, stringent quality control measures shall ensure consistency between batches. These measures include:

- Comprehensive batch testing to verify and document biochemical consistency.
- Establishing minimum purity and composition standards.
- Ongoing performance evaluations, such as organoid growth rates, differentiation potential, and functional properties.

If significant variability is detected, alternative materials or refined quality control protocols shall be implemented to mitigate risks.

5.6.10.2.4 Balancing Quality and Reproducibility

When reproducibility is paramount, chemically defined or synthetic alternatives shall be prioritized. However, the controlled use of animal-derived products is acceptable, provided the potential for variability is minimized through rigorous quality control protocols.

5.6.10.3 "Biocompatibility"

All ECMs shall undergo rigorous biocompatibility testing to ensure they are non-toxic, non-immunogenic, and suitable for long-term organoid culture.

5.6.10.4 Mechanical and Physical Properties

The mechanical properties of ECMs, including strength, elasticity, and porosity, should be tunable to replicate the physiological environment of the specific organ being modeled. These properties shall be optimized for the intended organoid system.

5.6.10.5 Decellularized Tissue ECM

Hydrogels derived from decellularized tissues shall be processed in a manner that preserves essential biochemical signals for organoid growth, while maintaining batch-to-batch consistency to ensure reliable performance.

5.6.10.6 Stiffness and Elasticity of ECMs

The mechanical properties of ECMs such as the stiffness and elasticity should be monitored and consistent to mimic the physiological environment of the specific organ being modeled. This standardization will be achieved through the use of defined hydrogel systems with tunable mechanical properties.

5.6.10.7 Mechanical Pressure Exerted by ECMs

Due to the significant effect that ECM-induced mechanical pressure can have on organoids, it is essential to standardize the properties of the ECMs to ensure consistent mechanical conditions. Variations in mechanical pressure may lead to changes in organoid morphology and function, compromising the reproducibility and reliability of organoid models. Therefore, maintaining consistent ECM properties is critical to avoid undesired variations in organoid culture and ensure reliable outcomes in research and clinical applications.

5.6.10.8 Reference-Stock ECMs for Functional Testing

Reference-stock ECMs and any other critical reagents, such as culture media, shall be maintained to ensure the reproducibility of functional tests. These materials shall be stored under conditions that preserve their properties and used for comparison against the original source in functional assays. Documentation of batch numbers, storage conditions, and expiration dates shall be required to ensure traceability and consistency.

5.6.10.9 Risk Assessment

A thorough risk assessment should be conducted for all ECMs to identify potential hazards. Appropriate risk management strategies shall be implemented to mitigate any identified risks.

6 Operational Criteria

6.1 Overview

These criteria apply to all stages of OBing, from the procurement of biological samples to the storage, processing, and distribution of organoids.

6.2 Quality Management

A comprehensive QMS shall be implemented to govern all operational aspects of the OB, ensuring consistency, traceability, and continuous improvement.

6.3 “Documentation and Record Keeping”

All procedures, processes, and transactions shall be thoroughly documented, with records maintained in a secure, accessible, and organized manner.

6.4 Staff Training and Competence

Personnel involved in OBing shall undergo regular training to ensure they are competent in their respective roles and are kept abreast of current best practices and advancements in the field.

6.4.1 Training Programs

All personnel involved in OBing operations shall participate in structured training programs that cover the theoretical and practical aspects of their roles. These programs should be designed to address the specific needs of organoid culture, handling, storage, and data management.

6.4.2 Initial Training

New staff members shall receive comprehensive initial training that includes:

- An overview of organoid biology and its relevance to OBing.
- Detailed procedures for organoid culture, maintenance, and manipulation.
- Safety protocols, including biosafety and biosecurity measures.
- Introduction to QMS and SOPs.

6.4.3 Ongoing Professional Development

Regular staff shall be kept up to date in the following essentials:

- The latest advancements in organoid technology and biobanking.
- Changes in regulatory requirements and ethical guidelines.
- New SOPs and best practices in OBing.

6.4.4 Refresher Courses

Regular refresher courses should be mandatory to reinforce knowledge and skills, ensuring that all staff members maintain a high level of competence in their roles.

6.4.5 Specialized Training

Staff may require specialized training in areas such as:

- Advanced techniques for organoid culture and differentiation.
- Cryopreservation and thawing methods.
- Use of specialized equipment and software for organoid analysis and data management.

6.4.6 Assessment and Certification

Training programs should include a formal assessment process to evaluate staff competence. Certified professionals should be recognized for their expertise in OBing.

6.4.7 Cross-Training

Cross-training initiatives should be encouraged to enhance versatility and ensure that staff members are familiar with multiple aspects of OBing operations.

6.4.8 Mentorship and Supervision

Experienced staff should act as mentors to guide and supervise less experienced colleagues, facilitating knowledge transfer and skill development.

6.4.9 Continuous Learning Culture

OBs should foster a culture of continuous learning within the OB, encouraging staff to actively seek out new information and learning opportunities.

6.4.10 Access to Resources

OBs should ensure that staff have access to resources such as scientific literature, training manuals, and online courses to support their learning and development.

6.4.11 Training Records

OBs shall maintain detailed records of all training activities, including attendance, assessments, and certification, to document staff competence and professional development.

6.5 Sample Handling

SOPs shall detail the procedures for collecting organoid samples, including the type of collection tools, techniques, and environmental conditions to preserve sample viability.

6.5.1 Sample Collection

6.5.1.1 Collection Tools

SOPs shall specify the tools and containers used to collect organoid samples, ensuring they are sterile and appropriate for preserving sample viability.

6.5.1.2 Conditions

SOPs shall define the environmental conditions under which samples should be collected (e.g., temperature, humidity) to avoid degradation.

6.5.1.3Documentation

SOPS shall include detailed procedures for recording sample metadata, such as source, collection time, and any relevant conditions.

6.5.2 Sample Processing

6.5.2.1 Initial Processing

SOPs shall outline the steps for processing organoid samples immediately after collection to preserve their quality.

6.5.2.2 Handling Procedures

SOPs shall define protocols for handling organoids to prevent contamination or damage, including aseptic techniques and appropriate tools.

6.5.2.3 Processing Conditions

SOPs shall specify temperature and time conditions for processing, such as centrifugation, washing, or any other preparatory steps required.

6.5.2.4 Sample Preservation

SOPs shall provide procedures for preserving organoid samples, including the use of cryoprotectants if freezing, or media if maintaining in culture.

6.5.3 "Organoid Quality Characterization"

6.5.3.1 Defining Quality Metrics

Organoid quality is defined by how closely organoids replicate the patient's original tissue. This includes molecular, morphological, and functional similarities to the source tissue.

6.5.3.2 "Molecular Characterization"

Organoids shall undergo gene/protein expression analysis to assess their molecular profile, with gene expression patterns compared to those of real tissue to ensure fidelity.

6.5.3.3 Genetic Stability

The genetic stability of organoids shall be assessed by evaluating whether their genetic information remains consistent after multiple passages or amplifications. This assessment shall include genome integrity analysis, karyotyping, and screening for potential mutations or chromosomal abnormalities to ensure long-term reliability and reproducibility of the organoid models.

6.5.3.4 "Functional Validation"

Organoid function shall be assessed to determine whether molecular and physiological characteristics are retained over time.

6.5.3.5 Morphological Assessment

Organoid morphology shall be measured, and its relationship to organ function should be assessed to ensure that the structural features align with expected physiological properties.

6.5.4 Quality Control (QC)

Comprehensive QC measures shall be implemented to ensure that all procedures, from collection to storage and characterization of organoids, are conducted correctly and consistently. The objective of QC is to maintain the integrity, viability, and reproducibility of organoids throughout their life cycle within the biobank.

6.5.4.1 Key elements of QC

- "Sample Integrity and Viability Testing": Protocols shall be established to test the viability and functionality of organoids post-preservation (e.g., freezing and thawing) as well as after prolonged storage. The biological and functional properties of the organoids shall be maintained throughout their storage period.
- Supervision and calibration of instruments: All equipment used for collection, processing, and storage (e.g., freezers, incubators, liquid nitrogen tanks) shall be regularly calibrated and maintained to ensure optimal operating conditions. Equipment checks shall be performed according to a predefined schedule to guarantee sample quality.

6.5.4.2 Audits and Reviews

Regular audits of SOPs and OB practices shall be conducted to ensure compliance with established standards and to identify areas for improvement.

- Internal Audits: Scheduled internal audits shall be carried out to verify adherence to SOPs and quality requirements. These audits shall review documentation, equipment maintenance logs, sample handling procedures, and storage conditions.
- Third-party Audits: Periodic external audits by independent entities should be conducted to ensure the objectivity and robustness of the QMS.
- Continuous Improvement: Findings from audits shall be used to inform continuous improvement efforts in OB operations, including enhancements to processes, equipment, and staff training. Action plans to address deficiencies shall be developed and implemented.

6.5.4.3 Corrective Actions

A systematic approach shall be established for addressing any issues identified during the processing, characterization, or storage of organoids. Corrective actions should be focused on both rectifying the issue and preventing future occurrences.

- Root Cause Analysis: Non-conformance events shall be followed by a root cause analysis to identify the source of the problem, whether related to SOP deviations, equipment failures, or human error.
- Preventive Actions: Appropriate preventive actions shall be developed and implemented to ensure that the identified issue does not recur. This may involve updating SOPs, enhancing staff training, or upgrading equipment.
- Issue Documentation and Reporting: Detailed records of issues encountered, as well as corrective and preventive actions taken, shall be maintained. The effectiveness of these actions should be reviewed during subsequent audits to ensure long-term compliance and improvement.
- Competency Checks: OB personnel shall receive regular training on corrective action procedures, and competency assessments shall be conducted to ensure that staff can effectively apply the necessary QC measures.

6.5.5 Alignment with Relevant Standards

Ensure that SOPs for sample collection, processing, and characterization align with the ISoOR-ISOB standard and other internationally recognized best practices in sample processing, storage, and auditing procedures.

6.6 “Metrics”

6.6.1 Overview

Metrics refer to the quantitative measures used to assess the quality, functionality, and performance of organoids. These may include size, morphology, viability, growth rate, cumulative growth, “genetic stability”, nutrient and oxygen distribution, and the presence of necrotic regions.

6.6.2 Selection of Metrics

The facility shall identify and select appropriate metrics based on the specific requirements of OBing.

6.6.3 Standardization of Measurement Methods and Audit

6.6.3.1 Overview

Given the challenges associated with measuring organoids, it is crucial to standardize measurement techniques to yield a more accurate representation of organoid size, cellular composition and cumulative growth.

6.6.3.2 Inclusion of Metrics

Metrics should account for not only live cells but also dead cells and those that have contributed to the cumulative growth. This approach addresses the specific characteristics of organoid diversity.

6.6.3.3 Measurement Techniques

6.6.3.3.1 Morphological Evaluation

Morphological evaluation involves quantifying organoid size, shape, and structure using imaging techniques such as microscopy. Image analysis methods shall be employed for detailed assessment of organoid architecture, ensuring accurate representation of tissue morphology.

6.6.3.3.2 Functional Measurement

Functional measurement includes evaluating the organoid's ability to replicate tissue-specific functions, such as secretion, response to stimuli, or drug metabolism. Assays and functional imaging techniques shall be utilized to assess the organoid's physiological activities, ensuring it mimics the function of the original tissue.

6.6.3.3.3 “Molecular Resemblance”

Molecular resemblance shall be quantified through techniques such as gene expression analysis, protein profiling, and DNA sequencing. These methods shall be employed to compare the molecular signature of the organoid with that of the native tissue, confirming the organoid's molecular fidelity.

6.6.3.4 Additional Metrics

Facilities should implement metrics evaluating nutrient and oxygen distribution, overall structural integrity, and the presence of any necrotic regions.

6.6.3.5 Validation of Data

6.6.3.5.1 Impact of Device Type on Quantification

The OB shall ensure that the type of device used for organoid quantification does not compromise the accuracy or reproducibility of results. Devices shall be calibrated and validated according to established protocols to ensure the precision and reliability of the data for downstream applications. The OB shall ensure that measurements used for inter-sample or longitudinal comparisons are obtained using the same device to minimize device-specific variability and ensure that observed differences reflect biological rather than measurement-related factors.

6.6.3.5.2 Recommended Techniques and Equipment

The following factors should be considered in selecting the appropriate devices and techniques for quantifying organoids:

- Calibration and Validation: Devices shall be calibrated regularly using reference standards to ensure accurate measurements.
- Performance and Sensitivity: Equipment should meet the required sensitivity thresholds for organoid detection and quantification.
- Reproducibility: The quantification method shall be validated for reproducibility across different devices, operators, and conditions.
- Technological Advancements: This standard shall allow for the integration of new, validated technologies that improve quantification accuracy, provided they maintain consistency with established protocols.

6.6.3.6 Regular Audit and Review

The use of metrics and the results derived from them shall be subject to regular audit and review as part of the QMS.

6.6.4 Metrics for Quality Control and Assurance

The OB shall establish criteria for the acceptance or rejection of organoids based on these metrics.

6.6.5 Data Recording and Analysis

All metric data shall be accurately recorded and systematically analyzed. The facility should maintain records that are clear, indelible, and traceable.

6.6.6 Continuous Improvement

The facility shall use metric data to identify areas for improvement and implement necessary changes to enhance the quality of OBing.

6.7 Storage Conditions

Organoids shall be stored under conditions that ensure their viability and stability, with regular monitoring and documentation of storage parameters.

6.7.1 Monitoring

Storage conditions shall be meticulously controlled and continuously monitored to ensure the integrity of the organoids.

6.7.2 Temperature Control

Organoids should be stored at optimal temperatures that support their growth and metabolic activity. For most organoids, this involves cryopreservation at ultra-low temperatures (typically -150°C to -196°C in liquid nitrogen tanks) or refrigeration at 2-8°C for short-term storage.

6.7.3 Humidity and Gas Composition

In addition to temperature, the storage environment's humidity and gas composition shall be regulated, particularly for organoids requiring specific atmospheric conditions to maintain their phenotype.

6.7.5 Freezing Process

The freezing process for organoids, including their ECM and cellular components, shall follow standardized protocols to preserve their viability, structure, and molecular integrity. Specific procedures shall be established for the following:

- Cryopreservation of Single Cells: Single cells should be isolated and cryopreserved in a manner that prevents cell disruption and maintains cellular integrity. The cryoprotectants used should be validated for compatibility with the cell type to prevent ice crystal formation, cellular damage and differentiation.
- Cryopreservation of Organoid Fragments or Clusters: When organoids are stored as fragments or clusters, specific protocols shall be developed to maintain their structural integrity, cellular composition, and potential for reaggregation upon thawing. Cryoprotectants and freezing conditions shall be optimized to prevent damage and ensure viability.
- Cryopreservation of Entire Organoids: For entire organoids (e.g., Living Skin Equivalents - LSE), protocols shall ensure that the three-dimensional structure and function of the organoids are preserved during the freezing process. This includes using appropriate cryoprotectants and controlled-rate freezing techniques to minimize damage.

6.7.6 “Freezing Rate”

6.7.6.1 Controlled Freezing Conditions

Organoids should be frozen under controlled conditions that maintain cell viability. This involves a gradual temperature reduction to prevent ice crystal formation that may damage the organoid structure. Different freezing procedures should be discussed according to the type of organoids.

6.7.6.2 Freezing Protocol Documentation

Detailed protocols for freezing organoids, including the rate of temperature decrease and the method of freezing (e.g., using a controlled-rate freezer or a cryopreservation container with isopropanol), should be documented and followed.

6.7.7 Thawing Process

6.7.7.1 Controlled Thawing Conditions

Organoids, whether in the form of single cells, organoid fragments/clusters, or entire organoids, shall be thawed under controlled conditions to preserve their viability, cellular integrity, and functionality. The thawing process shall be rapid and conducted in a manner that minimizes osmotic shock, prevents ice crystal formation, and maintains structural integrity.

The frozen material shall be quickly transferred into a water bath at a temperature between 37°C and 42°C, followed by immediate transfer into pre-warmed culture medium to restore osmotic balance and promote cellular recovery.

The thawing process shall include the following:

- The material shall be thawed gradually in a controlled environment to minimize osmotic stress, thermal shock, and cellular damage.
- Thawing rates shall be controlled to prevent aggregation, structural collapse, or loss of cellular function.
- Specific thawing solutions shall be used to facilitate the recovery of cellular function and maintain the structural integrity of the material.

The thawing process shall be optimized to ensure the highest recovery rates, prevent damage, and maintain the functional potential of the cells or organoid material, regardless of its form.

6.7.7.4 Thawing Protocol Documentation

A detailed protocol for the thawing process should be documented, including specific instructions on how to handle the vial during thawing, the temperature and duration of the water bath, and any post-thaw treatments required to recover and culture the organoids. The documentation should also include guidelines on the acceptable thawing duration to prevent loss of cell viability.

6.7.7.5 Post-Thaw Culture and Recovery

Following the thawing process, organoids should be cultured under optimized conditions to promote recovery and growth. This includes using pre-warmed culture media and appropriate supplements that support cell viability.

Monitoring of the organoids during the recovery phase should be part of the standard protocol, ensuring that they meet predefined criteria for viability, morphology, and function.

6.7.7.6 Post-Thaw Viability Assessment

As part of the quality control process, a post-thaw viability assessment should be conducted. This assessment should evaluate the organoids for key viability markers, such as metabolic activity, structural integrity, and gene/protein expression, to ensure they meet the established quality standards. The results of the post-thaw viability assessment should be documented and reviewed as part of the overall biobanking QMS.

6.7.7.7 Documentation and Record Keeping

Accurate records of the thawing process, including any deviations from the standard protocol, should be maintained. This documentation should be integrated into the OB's IMS to ensure traceability and to support compliance with regulatory and quality requirements.

6.7.7.8 Alarm Systems Surveliance

Real-time monitoring systems should be in place to continuously track storage conditions, with automated alarms to alert personnel of any deviations from the set parameters.

6.7.7.9 Data Recording and Traceability

All storage parameters, including temperature, humidity, and gas composition, shall be recorded and documented for traceability and quality assurance purposes.

6.7.7.10 Periodic Quality Assessments

Regular quality assessments shall be conducted to evaluate the effectiveness of storage conditions in maintaining organoid viability and functionality.

6.7.7.11 Incorporation of Contamination Management Procedures

OBs shall incorporate protocols for detecting microbial contamination, including bacteria, fungi, mycoplasma, and endotoxins, immediately after the thawing process. These procedures may involve commercially available kits or other appropriate techniques, including but not limited to Culture-Based Methods, Molecular Techniques, Polymerase Chain Reaction (PCR), Real-Time PCR, Multiplex PCR, Enzyme-Linked Immunosorbent Assay (ELISA), Fluorescent In Situ Hybridization (FISH), ATP Bioluminescence, and Mass Spectrometry. Regular sterility checks post-thawing shall be implemented to ensure the integrity of organoid cultures and prevent contamination.

6.7.8 Storage Capacity and Organization

The OB's storage capacity should be planned to accommodate the current and projected future needs, with an organized system for efficient sample retrieval and inventory management.

6.7.9 Disposal and Decommissioning

Guidelines for the ethical and secure disposal of organoids that are no longer needed or that do not meet quality standards shall be established.

6.7.10 Storage and Handling Training

All personnel involved in the storage and handling of organoids shall be trained on the importance of storage conditions and the procedures for maintaining them.

6.8 Staining Procedures

6.8.1 Standardization of Staining Protocols

All staining procedures for organoid samples shall follow standardized protocols to ensure consistent, reproducible, and high-quality results. These protocols should be clearly defined and validated for various types of staining techniques used in organoid characterization, including but not limited to histological, immunohistochemical, and fluorescent staining.

6.8.2 Selection of Staining Agents

The selection of staining agents (e.g., dyes, antibodies, fluorescent markers) shall be based on their ability to effectively and specifically bind to the target structures within the organoid. All reagents shall be:

- Validated for Specificity and Sensitivity: Staining agents shall be proven to provide clear and reliable differentiation of organoid components without cross-reactivity.
- Compatible with the Organismal Model: Staining reagents should be compatible with the species and specific characteristics of the organoids being studied.

6.8.3 Consistency Across Batches

Staining protocols shall also be consistent across all batches of organoids to ensure comparability of data. Deviations in staining results due to variations in reagent lot numbers, processing conditions, or operator technique should be minimized. Any changes in reagents, equipment, or procedures shall be documented and validated.

6.9 "Passaging" of Organoids

6.9.1 Impact on Molecular Characteristics

The OB shall evaluate and document the impact of passaging on the molecular and functional properties of organoids. Passaging, which involves transferring organoids to new culture conditions for continued growth, may result in the loss of certain molecular characteristics inherent to the original organoid. The OB shall ensure that the potential effects of passaging on the reproducibility and consistency of research or clinical applications are assessed and accounted for. The OB shall implement measures to mitigate any adverse impact on organoid integrity during passaging to maintain the fidelity of the model for its intended applications.

6.9.2 Determination of Passage Limits

The OB shall define the maximum number of passages for each type of organoid before molecular characteristics are compromised, considering specific culturing methods and reagents. These limits shall be based on empirical data, and OBs shall establish and implement guidelines to ensure organoids are passaged within the optimal range, preserving their properties for reliable downstream applications.

6.9.3 Documentation and Monitoring

OBs shall maintain records of the passage number for each organoid culture, including the specific methods and reagents used. These records will help ensure traceability and allow for the evaluation of the effect of passaging on the organoid's integrity. Monitoring should be performed at regular intervals to identify any signs of molecular drift or loss of function, ensuring the quality of the organoid bank remains high.

6.9.4 Standardization of Passaging Procedures

Standardized passaging protocols should be implemented and followed to minimize variation in organoid quality across different batches. These protocols should include recommendations on culture conditions, passaging techniques, and methods for assessing the molecular and functional status of organoids after each passage. Regular reviews of these protocols should be conducted to ensure continued efficacy in preserving organoid characteristics.

6.10 Molecular Profiling

6.10.1 Purpose and Scope

Molecular profiling is essential for characterizing the genetic and molecular properties of organoids. This process ensures that organoids are suitable for research applications, including disease modeling, personalized medicine, quality control, and functional validation.

6.10.2 Donor and Tissue Characterization

The OB shall implement molecular profiling to document the genetic characteristics of donor tissue, including identifying specific genetic mutations or polymorphisms that influence organoid behavior. This ensures accurate capture and maintenance of these characteristics.

6.10.3 Disease Modeling and Personalized Medicine

For organoids derived from diseased tissues, molecular profiling shall confirm the presence of disease-specific genetic alterations. The OB shall ensure that these profiles align with known disease pathology and correlate with clinical data, facilitating their use in personalized medicine. This correlation shall be documented, enabling alignment of organoid characteristics with specific patient outcomes and treatment responses.

6.10.4 Quality Control and Functional Validation

Molecular profiling shall be utilized as a fundamental quality control measure to ensure the genetic and phenotypic consistency of organoids over time. Additionally, molecular profiling shall validate the functional similarity of organoids to their source tissue through rigorous comparative analysis. Any identified deviations from expected characteristics shall be thoroughly documented, and appropriate corrective actions shall be implemented in accordance with established SOPs.

6.10.5 Cryopreservation Impact Assessment

The OB shall assess the impact of cryopreservation and thawing on organoid biology through molecular profiling, ensuring that these processes do not adversely affect viability or genetic integrity.

Note: For additional information related to cryopreservation, refer to the 6.7 Storage Conditions, 6.7.6 Freezing Rate and 6.7.7 Thawing Process subsections.

6.10.6 Genome Editing Verification

For organoids subjected to genome editing, molecular profiling shall confirm the successful introduction of genetic modifications. The OB shall document these changes and their implications for the organoid's function and relevance to research objectives.

6.10.7 Inter- and Intra-Tumor Heterogeneity

For cancer organoids, molecular profiling shall capture and document genetic diversity within and between tumors. This analysis shall detail how this heterogeneity may affect tumor behavior and treatment responses.

6.11 Mimicry of Organ Fidelity and Functions

The OB shall establish procedures to ensure that organoids replicate the structure and functions of specific organs for use in research, drug testing, and therapeutic applications. These procedures shall include rigorous methods for assessing and validating the organ-like characteristics of organoids to ensure their suitability and reliability for downstream purposes.

6.11.1 Structural and Functional Fidelity

Organoids shall be evaluated for their ability to closely mimic the key structural and functional properties of the corresponding organ. This includes, but is not limited to:

- Cellular Composition: Verification that the organoid contains the appropriate cell types, distributed in a manner reflective of the natural organ.
- Architectural Organization: Assessment of tissue organization, including the spatial arrangement of cells, tissue layers, and any microenvironmental structures that are relevant to the target organ.
- Functional Outputs: Monitoring of key physiological functions, such as secretion of specific hormones, production of metabolites, or response to stimuli, to confirm that the organoid behaves similarly to the organ it represents.

6.11.2 Advanced Validation Techniques

Given the complexity of organoids and their intended applications, standard validation methods may not be sufficient. The following advanced techniques should be considered:

- Molecular Characterization: Proteomics, and metabolomics can be employed to ensure that the organoid's molecular profile matches that of the native organ.
- Functional Assays: Specialized assays should be developed to measure the functional performance of organoids, such as electrical activity in neuronal organoids or filtration capacity in kidney organoids.

- Comparative Analysis: Organoids should be compared to in vivo organs or ex vivo tissue samples to verify the accuracy of their physiological and functional mimicry.

6.11.3 Fidelity Assessment

To maintain high standards of organoid fidelity, ongoing monitoring should be conducted throughout the culturing process. This includes regular assessment of structural and functional characteristics, as well as adaptations to protocols if deviations from organ-like behavior are detected. Any significant variations in organoid behavior should be documented, and corrective actions should be implemented to restore fidelity.

6.11.4 Documentation and Reporting

All procedures, assessments, and validation results shall be thoroughly documented to ensure reproducibility and transparency. Data related to organoid fidelity should be stored and accessible to relevant stakeholders for future reference, including researchers, OB staff, and regulatory authorities.

6.12 Emergency Protocols

Emergency protocols shall be developed to address equipment failure or power outages, ensuring the rapid response and minimal impact on stored organoids.

6.12.1 Equipment Failure Response

Emergency protocols shall include detailed procedures for addressing equipment failure, such as the malfunction of cryogenic storage units or temperature monitoring systems. Immediate actions should involve transferring organoids to backup storage units that have been pre-validated to maintain the required storage conditions. All personnel shall be trained to recognize and respond to equipment alarms, ensuring that organoids are not exposed to temperature fluctuations that may compromise their viability.

6.12.2 Power Outage Contingency Plans

A robust contingency plan shall be in place to manage power outages. This plan should include the availability of backup power sources, such as generators or uninterruptible power supplies (UPS), which are capable of maintaining critical storage conditions until normal power is restored. The protocol should also include clear instructions on how to monitor storage conditions during a power outage, and the procedure for prioritizing organoid transfers if extended outages occur.

6.12.3 Emergency Training and Drills

Regular training sessions and emergency drills should be conducted to ensure all personnel are prepared to execute the emergency protocols effectively. This training should cover the identification of potential risks, immediate response actions, and the use of backup systems. Personnel shall be familiar with the location and operation of emergency equipment, as well as the communication plan for notifying key stakeholders during an emergency.

6.12.4 Emergency Communication Plan

An emergency communication plan shall be established, outlining the steps for notifying key personnel, stakeholders, and emergency services in the event of a crisis. This plan should include up-to-date contact information for all relevant parties and clearly define the roles and responsibilities of each team member during an emergency.

6.12.5 Documentation and Review

All emergency responses and actions taken during equipment failure or power outages shall be documented in detail. This documentation should be reviewed regularly as part of the OB's QMS to identify any areas for improvement in the emergency protocols. Regular reviews and updates to the emergency protocols ensure they remain effective and aligned with the latest best practices and technological advancements.

6.12.6 Risk Mitigation and Preventive Measures

As part of the emergency protocols, preventive measures should be implemented to minimize the risk of equipment failure or power outages. This includes regular maintenance and testing of storage units, backup systems, and alarms, as well as conducting risk assessments to identify potential vulnerabilities in the OB's infrastructure. These measures help to ensure the continuous protection of stored organoids, even in unforeseen circumstances.

6.13 Data Management

Robust data management practices shall be employed to handle sensitive information related to donors, samples, and research data, ensuring data security and confidentiality.

6.14 Risk Management

A proactive risk management approach shall be adopted to identify, assess, and mitigate potential risks associated with OBing operations.

6.15 Ethical Considerations

Ethical principles shall guide all aspects of OBing, with particular attention to informed consent, privacy, and the responsible use of biological materials.

6.16 Distribution and Access

Clear policies and procedures shall govern the distribution and access to organoids, ensuring equitable and transparent allocation for research purposes.

6.16.1 Policy Development

A clear and comprehensive policy framework shall be established to govern the distribution and access to organoids. This framework shall ensure that the allocation of organoids is transparent, equitable, and aligns with the ethical principles and objectives of the OB. The policy should address criteria for eligibility, priority, and access, taking into account the scientific merit, potential impact, and ethical considerations of proposed research.

6.16.2 Request and Approval Process

A standardized process for requesting access to organoids shall be implemented. This process should include the submission of a detailed research proposal, an ethical review, and a feasibility assessment. An independent review board or committee, comprising scientific, ethical, and legal experts, shall evaluate each request to ensure compliance with the OB's policies and international standards.

6.16.3 Transparency and Accountability

The OB shall maintain transparency in its distribution and access practices by documenting and publicly disclosing the criteria used for decision-making. Records of all requests, approvals, and distributions shall be maintained, with regular audits conducted to ensure accountability and adherence to established policies.

6.16.4 MTAs

Before the distribution of organoids, MTAs shall be executed between the OB and the recipient institution. These agreements shall clearly define the terms of use, including intellectual property rights, confidentiality, and reporting obligations. MTAs shall also stipulate that organoids are to be used exclusively for the approved purposes and that any deviations require prior approval from the OB.

6.16.5 Ethical Considerations

The distribution and access policy shall incorporate ethical considerations, ensuring that the use of organoids aligns with the consent provided by donors and respects the cultural and societal values of the communities involved.

6.16.6 Transparency Tracking

The OB shall regularly monitor the distribution and access processes to ensure they remain fair, transparent, and aligned with the OB's mission. Periodic reviews shall be conducted to update policies and procedures in response to evolving scientific, ethical, and legal standards.

6.17 Reporting of Organoid Culture Results

6.17.1 General Reporting Requirements

Organoid culture results shall be reported in an accurate, clear, and unambiguous manner. The reporting should follow specific instructions outlined in the organoid culture procedure, ensuring all relevant data are complete and comprehensible.

6.17.2 Examination and Review of Results

All examination results shall be documented with precision and reviewed by authorized personnel before release. This review should include an evaluation against internal quality control measures and relevant clinical information to ensure reliability. Clear authorization protocols shall ensure that only competent personnel release results.

6.17.3 Notification and Documentation Procedures

- In cases of delayed or critical results, the OB shall have procedures in place to notify affected users promptly, considering the impact on research or clinical outcomes.
- All notifications, especially those related to critical decision limits, shall be thoroughly documented, including the date, time, responsible parties, and any actions taken.

6.17.4 Special Considerations for Reporting:

- With user agreement, simplified or preliminary reports may be provided, but it shall be clear that the initial findings are preliminary.
- Oral communications of results shall be documented and verified for accuracy.

6.17.5 Automated Reporting Systems

If automated systems are used for result selection, review, release, and reporting, the OB shall establish procedures to ensure their accuracy and reliability. Criteria for automated processes shall be validated, approved, and regularly reviewed.

6.17.6 Content of Organoid Culture Reports

Each report should include comprehensive information such as unique identifiers, sample collection dates, examination details, results with units and reference intervals, and any additional relevant information like collection time or contributions from referral laboratories.

6.17.7 Amendments to Reported Results

Any amendments to results shall follow a clear and documented procedure that ensures transparency and accuracy. Users shall be notified of any changes, with the reason for the amendment recorded.

6.18 Audit and Compliance

Regular audits shall be conducted to assess compliance with operational criteria and identify areas for improvement.

6.19 Continuous Improvement

The OB shall be committed to a culture of continuous improvement, leveraging feedback, audit findings, and research advancements to enhance operational efficiency and quality.

7 “Quality Assurance” (QA)

7.1 Overview

The QA framework is integral to ensuring that all operations within the OB adhere to the highest standards of quality, reliability, and ethical conduct. The framework is designed to maintain the integrity of processes and outcomes, ensuring consistent delivery of high-quality OBing services.

7.2 QMS

A comprehensive QMS shall be established and maintained in accordance with the ISoOR-ISOB document and other relevant international standards. This QMS shall focus on QA, serving as the foundation for continuous improvement and risk management within the OB.

The QMS will encompass the following requirements:

- Continuous Improvement: Systems and processes that foster a culture of ongoing enhancement based on data and feedback.
- Risk Management: Proactive identification and mitigation of risks to ensure QA throughout operations.

Additionally, the QMS shall ensure that QA practices are embedded in all processes and that performance metrics are utilized to drive quality improvements and accountability. Emphasis will be placed on integrating these practices to uphold excellence and reliability in outcomes.

7.3 Quality Policy

A formally documented Quality Policy shall be established, articulating the OB's commitment to maintaining excellence in quality, adhering to ethical standards, and complying with applicable regulatory requirements. The Quality Policy shall be communicated to all stakeholders and reviewed periodically for relevance and effectiveness.

7.4 Quality Objectives

Quality Objectives shall be defined in alignment with the OB's overall mission and goals. These objectives shall be Specific, Measurable, Achievable, Relevant, and Time-bound (SMART) to provide clear guidance and a basis for performance evaluation across all biobanking activities.

7.5 Quality Planning

Comprehensive Quality Plans shall be developed and implemented for all critical stages of the OBing process, including procurement, processing, storage, and distribution of organoids. These plans shall detail the steps necessary to achieve the defined Quality Objectives and mitigate potential risks.

7.6 Responsibilities and Resources

The OB shall ensure the clear assignment of responsibilities and the provision of adequate resources, including trained personnel, facilities, equipment, and materials, to support the effective implementation of the QMS and achieve the Quality Objectives.

7.7 Process Control

All processes within the OB shall be controlled and, where necessary, validated to ensure they consistently produce organoids that meet established quality criteria.

7.8 Evidence of Conformity

Appropriate monitoring and measurement procedures shall be established to provide evidence of conformity to quality requirements and support continuous improvement.

7.8.1 Establishing Measurement Criteria

Measurement criteria shall be established to reflect the quality standards required for OBing, encompassing all critical aspects of the process.

7.8.2 Calibration and Maintenance

A strict schedule for the calibration and maintenance of all “monitoring and measurement devices” shall be implemented to ensure accuracy and reliability.

7.8.3 Data Collection and Analysis

Standardized procedures for data collection and analysis shall be created to ensure consistency, transparency, and the identification of trends or anomalies.

7.8.4 Corrective and Preventive Actions

Data from monitoring activities shall be used to identify the need for corrective and preventive actions, ensuring ongoing process improvement.

7.9 Data Integrity and Security

The OB shall maintain the integrity and security of all data through documented and controlled processes and information and data management systems that are qualified or validated, as appropriate for their intended use, in accordance with 5.3.6.5. These controls shall ensure the accuracy, confidentiality and availability of data.

7.10 “Nonconformity” and Corrective Action

A procedure for the identification, investigation, and correction of nonconformities shall be established, along with preventive measures to avoid recurrence.

7.11 Internal Audits

Regular internal audits shall be conducted to verify compliance with the QMS and identify opportunities for improvement.

7.12 Management Review

Top management shall periodically review the QMS to ensure its continued suitability, adequacy, and effectiveness in achieving the OB's Quality Objectives.

7.13 Continuous Improvement

The OB shall be committed to continuous improvement, utilizing quality data and feedback to enhance processes and outcomes.

7.14 Documentation and Record Keeping

Documentation and record-keeping practices shall be established to provide a reliable account of all activities, ensuring transparency, traceability, and compliance with regulatory standards.

7.14.1 Documentation Control

A system for controlling all documentation shall be established to ensure that documents are current, accessible, and protected from unauthorized changes.

7.14.2 Record Maintenance

Records shall be maintained in a clear, complete, and indelible manner, stored to prevent loss or deterioration.

7.14.3 Confidentiality and Security

Documentation and records shall be protected with security measures to prevent unauthorized access or tampering.

7.15 Lifecycle Documentation Tracking and Conditions Management

7.15.1 General Requirements

All organoid samples shall be thoroughly documented and traceable throughout their lifecycle. A robust system shall ensure data reliability and reproducibility to meet the needs of clinical and research applications.

7.15.2 “Barcoding Systems” for Organoid Sample Identification

7.15.2.1 Essentials

A standardized barcoding system shall be used to ensure accurate identification and tracking of organoid samples. The system shall:

- Comply with any applicable national, regional, or local regulations and standards governing OBing practices.
- Assign each organoid sample a unique, permanent identifier to eliminate duplication and reduce errors.
- Be compatible with automated biobanking technologies and laboratory information management systems (LIMS).

7.15.2.2 Specifications

Barcoding protocols shall include the following specifications:

- Use of durable barcode labels that can withstand cryogenic temperatures and routine handling.
- Adoption of high-capacity formats, such as 2D barcodes or QR codes, to ensure comprehensive data encoding.
- Implementation of QA measures to validate barcode readability and longevity.

7.15.3 Comprehensive Record-Keeping

7.15.3.1 Details

At every stage of the organoid sample lifecycle, detailed records shall be maintained, including:

- Metadata on the organoid's origin, such as donor information (adhering to ethical guidelines) and cell line characterization.
- Documentation of critical processing steps, such as derivation, passaging, cryopreservation, and thawing.
- Time-stamped records of environmental conditions and any deviations.

7.15.3.2 Platforms

Record-keeping systems may be paper-based, electronic, or a combination of both, provided that they are controlled, secure, traceable and appropriate for their intended use, in accordance with 3.4.2, 5.3.6 and 7.14. Where electronic platforms are used, they shall be capable of:

- Supporting long-term storage and efficient retrieval of records for analysis and audits.
- Enabling data sharing in compliance with regulatory and ethical frameworks.

7.15.4 Standardized Guidelines for Barcoding in OBing

7.15.4.1 Guidelines

Barcoding processes shall adhere to standardized guidelines that:

- Protect sample confidentiality and data integrity.
- Align with national, regional, or local regulations, if applicable.
- Ensure compatibility with cryopreservation protocols to maintain barcode functionality under ultra-low temperatures.

7.15.4.2 Training

Comprehensive training programs shall be established to educate personnel on barcoding standards, ensuring adherence to these practices across all operational levels.

7.16 Ethical Considerations

Ethical considerations shall be integrated into the QA system, ensuring respect for donor rights, informed consent, and responsible use of organoids in research.

7.17 Regulatory Compliance

Compliance with all relevant regulatory requirements and guidelines shall be ensured throughout all aspects of OBing operations.

Annexes: Standard Operational Procedures (SOPs)

Annex A: Development of NUT Carcinoma Organoids (The full document is available for separate download from the ISoOR-ISOB repository at www.isoor.org).

List of Abbreviations:

AI: Artificial Intelligence

ELISA: Enzyme-Linked Immunosorbent Assay

FISH: Fluorescent In Situ Hybridization

GLP: Good Laboratory Practice

IMS: Information Management System

IP: Intellectual Property

ISoOR: International Society of Organoid Research

ISoOR-ISOB: ISoOR-International Standard for Organoid Biobanking

MTA: Material Transfer Agreement

PCR: Polymerase Chain Reaction

QA: Quality Assurance

QMS: Quality Management System

SMART: Specific, Measurable, Achievable, Relevant, and Time-bound

Glossary of Terms:

- **Access Agreements:** Formal documents that define who is allowed to access organoid samples and related data, under specific conditions and purposes. These agreements are critical for ensuring that ethical standards and informed consent are met.
- **Adaptive AI System:** An AI system designed to modify its behavior or performance after deployment through learning or other adaptation mechanisms. Routine software updates, configuration changes or maintenance activities do not, by themselves, constitute adaptive learning.
- **AI Incident:** An event involving an AI system that results in an actual adverse impact on safety, privacy, security, data integrity, conformity or other relevant interests.
- **AI Near Miss:** An event involving an AI system that could reasonably have resulted in such an adverse impact but did not, because it was detected, prevented or otherwise did not progress to an adverse outcome.
- **Artificial Intelligence (AI) System:** A machine-based system that, for explicit or implicit objectives, infers from inputs how to generate outputs such as predictions, classifications, recommendations, decisions or content. AI systems may vary in their levels of autonomy and adaptiveness and may be developed internally, acquired from or operated by third parties, or embedded in other systems used by an OB.
- **Audit Trails:** Records that document the history of changes made to data or documents. These include timestamps, the identity of the person who made the change, and the reasons for those changes, essential for maintaining data integrity and regulatory compliance.
- **Barcoding System:** A method for labeling and tracking organoid samples using unique identifiers (e.g., barcodes or alphanumeric codes), ensuring proper documentation and traceability throughout the biobanking process.
- **Biochemical Consistency:** The uniformity in the composition of reagents, culture media, and other materials used in organoid culture. Ensuring consistency is vital for maintaining reproducibility and reliable outcomes in research.
- **Biocompatibility:** The ability of materials, such as extracellular matrix (ECM) components, to be used in contact with biological systems without causing harmful effects such as toxicity or immune rejection.
- **Biological Drift:** A change over time in the biological characteristics of an organoid culture or associated biological material that may result from passage, culture conditions, differentiation, selection, material variability or other biological or technical factors and that may affect quality, reproducibility or AI-system performance.
- **Biological Heterogeneity:** Variation in biological, morphological, molecular or functional characteristics among organoids or organoid populations arising from intrinsic biological differences or relevant culture and experimental conditions.
- **Consequential AI-Assisted Activity:** An AI-assisted activity that may materially affect quality, access, distribution, safety, donor rights, research conclusions or reporting.
- **Contamination:** The unintended presence of biological, chemical or other extraneous material in an organoid culture or associated biological material that may affect quality, biological characteristics, reproducibility or AI-system performance.
- **Cryopreservation:** A technique for preserving organoids and cells at ultra-low temperatures (typically between -150°C to -196°C), enabling long-term storage while maintaining viability and functionality.
- **Data Drift:** A material change in the characteristics, quality, distribution, source population or context of data used by an AI system that may affect performance or risk.
- **Data Integrity and Security:** Protecting data related to organoids and donors, ensuring it is accurate, confidential, and accessible, in compliance with international data protection regulations.
- **Data Management:** The practice of handling and storing sensitive information associated with donors, organoid samples, and research data, ensuring its security, confidentiality, and proper organization.
- **Data Protection and Privacy:** Measures and protocols designed to safeguard the privacy and confidentiality of personal and sensitive data associated with organoid samples, in alignment with data protection laws.
- **Equity:** The principle of ensuring fair and equal access to resources, opportunities, and benefits for all stakeholders in organoid biobanking activities.

- **Ethical Compliance:** Adhering to established ethical standards and regulatory requirements, particularly concerning informed consent, donor confidentiality, and responsible use of biological materials.
- **Extracellular Matrix (ECM):** A complex network of proteins and molecules that provide structural and biochemical support to organoids, facilitating their growth and maintenance in culture.
- **Freezing Rate:** The controlled rate at which organoids are cooled during cryopreservation to prevent ice crystals from damaging cellular structures, thereby preserving the sample's viability.
- **Functional Validation:** The process of assessing organoids to confirm that their molecular and physiological features remain consistent over time, ensuring that they replicate the function of the original tissue.
- **Generative AI System:** An AI system that produces new content in response to inputs or instructions.
- **Genetic Stability:** The maintenance of consistent genetic characteristics within organoids over time, ensuring that they remain representative of the original tissue.
- **Good Laboratory Practice (GLP):** Refers to a set of principles intended to ensure the quality, integrity, and reliability of non-clinical laboratory studies, particularly those related to the safety evaluation of chemicals and pharmaceuticals. GLP standards govern the organization, processes, and conditions under which laboratory studies are planned, performed, monitored, recorded, and reported.
- **Informed Consent:** The procedure by which participants or donors provide explicit permission for the use of their biological materials, with a clear understanding of the risks, benefits, and purpose of the research.
- **Intellectual Property (IP) Rights:** Legal protections for innovations and discoveries resulting from organoid research, including patents, copyrights, and trademarks, which define the ownership of these discoveries.
- **Legal Ownership:** The legal rights and responsibilities regarding organoids and their associated data, established through formal agreements and compliant with applicable laws.
- **Material Change:** A change to an AI system, data, intended purpose, provider or operating context that may affect validity, performance, risk or conformity.
- **Material Transfer Agreement (MTA):** Legal agreements that define the terms of use and sharing of organoids, addressing intellectual property, confidentiality, and reporting requirements.
- **Metrics:** Quantitative measures used to assess the quality, functionality, and performance of organoids, including parameters such as viability, growth rate, morphology, and genetic stability.
- **Molecular Characterization:** The analysis of gene expression, protein profiles, and other molecular features of organoids to verify their similarity to native tissue and ensure their functional relevance.
- **Molecular Resemblance:** The extent to which organoids replicate the molecular profile of the original tissue, which is assessed through techniques like gene expression analysis and DNA sequencing.
- **Monitoring and Measurement Devices:** Tools and equipment used to monitor and record important parameters such as temperature, humidity, and gas composition during the storage and handling of organoid samples.
- **Nonconformity:** The failure of a process or product to meet the required quality or regulatory standards, often necessitating corrective action.
- **Organoid:** A three-dimensional cellular structure derived from stem cells or tissues that replicates the anatomical, functional, and molecular properties of specific organs or tissues.
- **Organoid Biobanking:** The practice of collecting, storing, and managing organoids for research, clinical, and therapeutic purposes, ensuring their viability, integrity, and traceability.
- **Organoid Culture:** The process of cultivating organoids in vitro, using specific media and environmental conditions to support their growth and maintain their functional capabilities.
- **Organoid Quality Characterization:** The evaluation of organoids based on their molecular, morphological, and functional characteristics to ensure they closely resemble the original tissue.
- **Passaging:** The process of transferring organoids to new culture conditions to support continued growth. This step helps maintain quality and uniformity of the organoids over time.
- **Quality Assurance (QA):** The activities designed to ensure that all aspects of organoid biobanking meet defined quality standards, ensuring reliability, consistency, and ethical compliance.

- **Quality Management System (QMS):** A framework for managing quality within organoid biobanking, including policies, procedures, and responsibilities for maintaining high standards.
- **Regulatory Compliance:** Adherence to the laws, regulations, and guidelines that govern organoid biobanking practices, ensuring that all activities are conducted legally and ethically.
- **Reproducibility:** The ability to consistently achieve the same results across multiple iterations of the same process, ensuring reliability and standardization in organoid biobanking.
- **Risk Management:** The identification, assessment, and mitigation of potential risks in organoid biobanking activities, aimed at minimizing negative impacts and ensuring continuity.
- **Sample Integrity and Viability Testing:** Protocols and procedures for testing organoid samples after freezing, thawing, or prolonged storage to assess their biological and functional properties.
- **Standard Operating Procedures (SOPs):** Detailed guidelines that specify how tasks should be performed to ensure consistency and quality across all organoid biobanking activities.
- **Traceability:** The ability to document and track the history, application, and location of organoids and associated data from their collection through to their final disposition.

Source References:

1.ISO 20387:2018 - Biotechnology — Biobanking — General requirements for biobanking.

2.ISO/TR 22758:2020 - Biotechnology — Biobanking — Implementation guide for ISO 20387.

3.ISO 15189:2022 - Medical laboratories — Requirements for quality and competence.

4.ISBER BEST PRACTICES: RECOMMENDATIONS FOR REPOSITORIES FIFTH EDITION - International Society for Biological and Environmental Repositories.

5.IARC TECHNICAL PUBLICATION NO. 44 - Common minimum technical standards and protocols for biobanks dedicated to cancer research.

6.ISO/IEC 17025:2017 - General requirements for the competence of testing and calibration laboratories.

7.aaBB Standards for Cellular Therapy Services - 11th Edition of Standards for Cellular Therapy Services.

8.ISO 9001:2015 - Quality management systems — Requirements.

9.NIST AI 600-1 - Artificial Intelligence Risk Management Framework: Generative Artificial Intelligence Profile.

10.ISO13485-Third edition 2016-03-01- Medical devices — Quality management systems — Requirements for regulatory purposes.