WP2 – Data collection, integration and sharing

RD biobanking manual for ERN-wide biobanking projects (outline of v.1)

1. Introduction

The term biobank has evolved from a more general concept to others more specific and limited. Currently, there are different definitions apart from biobank as for example sample collections or biorepositories.
Besides definitions, the main goal of creating a structure as a biobank, is to provide and preserve a repository of biospecimens and which objective may be related to clinical purpose as diagnosis or scientific research. It is mandatory that samples being always linked with associated data.

1.1. Recommendations for proper project design and systematic collection

1.1.1. Distinctive features of a given biobank

1.1.2. Types of biobanks and infrastructures

According to the Organization for Economic Cooperation and Development (OECD) in **a first level of classification** there are two types of biobanks:

- *Disease-oriented biobanks* where it contains clinical data and tissue samples

- *Population-based biobanks* where the focus is on the study and development of complex and common diseases.

A **second level of classification** is based on to the type of research supported:

-Population study biobank
-Basic research biobank
-Translational study biobank
-Clinical trial biobank
-Pathology archive biobank

1.2. Definitions and characteristics.

1.2.1. Types of sample collection and infrastructures

Biorepository

According to the National Institutes of Health (NIH), "biorepositories are 'libraries' where biospecimens are stored and made available for clinical or research purposes." A biospecimen is defined as any biological material, such as tissue, blood, plasma, or urine, and is often accompanied by medical and demographic information. In biorepositories, specimens are derived from variety of sources including human, animal or plant life.

Biobank

A biobank is a type of biorepository containing biological samples used for human research. It is a non-profit organization regulated by national and international laws. It can be part of institution public or private. It guarantees and manages a systematic collection of biological samples and related associated data, with their consequent long-term storage and distribution for diagnosis and research purposes and promotes the achievement of the objectives of

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precision medicine. A biobank therefore performs a function of: public service, third party and guarantee of the biobank process towards all the actors involved (citizens, patients, clinicians, researchers and reference authorities).

Collection of samples

A collection is a group of biological samples, generally pathology-oriented (disease-oriented collections), according to specific projects and / or clinical protocols. Generally, specific informed consent is collected for a specific research activity.

Biological Resource Center (BRC)

The Center for Biological Resources is an organization that provides conservation services for living cells, tissues, the genomes of organisms or parts of them and information relating to the inheritance and the functions of biological systems. The BRC coordinates and manages the biobanking activities of the institution and guarantees interoperability criteria of the individual biobanks and participating collections. The BRC defines the procedures for the collection, treatment and storage of human biological materials homogeneous and functional, and standardizes both the methods of collecting and storing molecular, physiological and structural information, and the related bioinformatics.

Research Infrastructure

Structure whose main purpose is to promote cooperation on a pan-European scale in order to offer the scientific community efficient access to advanced methods and technologies, in an ethical and sustainable way.

European reference networks (ERNs)

ERNs are virtual networks involving healthcare providers across Europe. They aim to facilitate discussion on complex or rare diseases and conditions that require highly specialised treatment, and concentrated knowledge and resources.

1.2.2. General overview of the types of biospecimens to collect.

DNAs/RNAs, serum/plasma, whole blood samples, peripheral blood lymphocytes, muscle and nerve tissues, tissues derived from fetal loss and cell lines (amniocytes, trophoblast cells, fibroblast, myoblasts, lymphoblasts…)

1.2.3. General overview of the data:

Data associated with biological samples

Information relating to the participant (personal, genealogical, clinical, genomic data, etc.) and to the sample (characteristics, date of collection, etc.). For quality research, samples have value only when linked to data.

1.3. Types of stakeholders

- Patients / Patients Organizations
- Researchers and clinicians
- Citizens
- Companies
- Institutions

2. Regulatory requirements and best practice standards

2.1. Legal framework

The samples will be processed for the storage as long as the sample was obtained after a written informed consent signed by the patients, parents or legal guardian. ICH guidelines.

2.1.1. Traceability requirements

A material transfer agreement (MTA) should accompany each sample and should include a sample data (code, type, data of collection). Traceability of the samples is kept by separate clinical and paraclinical patient's data recordings. See chapter 5.

2.1.2. Handling human tissues and cells: technical requirements

Codification and processing.
Stabilization/preservation
Type of long-term preservation
Storage temperature
Shipping temperature from patient/source to preservation or research use

2.1.3. Handling human tissues and cells:

Relative to sample donation, procurement, testing, processing, preservation, storage and distribution.

3. Guidelines, recommendations and ethical standards

3.1. Biobanking. ISBER best practices: recommendations for repositories.

ISBER Best Practices covers: planning biobank setup and facilities; biobank storage and sample processing equipment; biobank quality management and quality control; biobank staff safety and training; and inventory management from sample collection right through processing, storage, packing and shipping.

3.2. Data sharing. BBMRI.ERIC policy for access to and sharing of Biological samples and data.

https://www.bbmri-eric.eu/wp-content/uploads/AoM_10_8_Access-Policy_FINAL_EU.pdf

4. General information and main orientation of International standards for QA recommendations

4.1. ISO 20387:2018 Biotechnology. General requirements for biobanking.

The aim is to:

(1) improve access to qualified biological resources and data
(2) ensure an appropriate quality of sample to fit an intended use
(3) harmonize and standardize procedures to enable exchange of biological material and related data among Biobanks and researchers
(4) increase stakeholder confidence and assurance
(5) foster the reproducibility of biomedical research thus reducing costs.
ISO 21899:2020 General requirements for the validation and verification of processing methods for biological materials in biobanks.

This ISO specifies the validation and verification requirements applicable to a biobank to be able to demonstrate that it operates its processing of biological materials with validated and/or verified methods that are fit for purpose.

https://www.iso.org/obp/ui/#iso:std:iso:21899:ed-1:v1:en

4.2. ISO 9001:2015 Quality management systems.

International standards for biobanking. Georges Dagher. Cell Prolif. 2022;55: e13282.

5. Ethical, legal and societal issues and their particularities for Rare Disease research

Biobanks have to protect the patient/donors' confidentiality according to national and international regulations. In addition, it is essential the sample traceability in order to accurately associated it with the patient/family/donor in the case of use of scientific results. The candidate biobanks should adhere to Ethical, Legal and Societal issues (ELSI) principles.

5.1 Informed Consent: It should contain all aspects related to the handling of the samples and data including:

-Sample usage.
-Results.
-Confidentiality.
-Service guarantee.
-Consent withdrawal.

5.2 Data and Material agreement forms (MTA/DTA)

It minimally should include donor'/patient's generalities (name, date of birth, address, ethnic origin, gender), phenotype (affected/not affected), essential anamnestic data (presence of consanguinity and/or familiarity, tissue and/or organ anomalies, laboratory test anomalies, etc.), diagnosis data (modality, center performing diagnosis) plus sample data (code, type, data of collection).

6. Recommendations for governance

An evaluation and adherence to a minimum entry condition should be ensure to take part in a biobanking network.

Some of these criteria are:

-Presence and availability of collections of biological samples (based on disease or population).
-A quality-control system for the management of the biobank based on standard operating procedures (SOPs) regulating sample and data acquisition and sample processing, storage and distribution.
-Adhesion to ELSI tools and ECD TASK Force on Biological Resource Centers.
-Compliance with national and European laws and regulations.

6.1. General structure.

Charter containing objectives and organizational structure: assembly, committees, Access Committee, advisory board and forums.

The general structure comprises several committees or boards:

-Network board, which is the decision-making committee.
-Scientific and legal advisory board, which is a consultative committee.
-Access Committee for the evaluation of the requests for samples and data.
Besides, depending on how large the biobank was it could exist a stakeholder forum, management committee…

6.2. Patients 'associations.

Active involvement of patient representatives and patient organizations in the drafting of policies and procedures for the improvement of the biobank structure and they could be an active part of advisory activities.

6.3. Procedures for internal auditing.

BBMRI offers internal auditing throughout Self-Assessment Surveys (SAS), which help to determine relevant requirements for your work processes in biobanking.

https://www.bbmri-eric.eu/services/quality-management/

6.4. Governance examples:

- Biobanking and Bimolecular resources Research Infrastructure (BBMRI)
  https://www.bbmri-eric.eu/governance-structure/

- Telethon Network of Genetic Biobanks (TNGB)
  Filocamo et al.: Telethon Network of GeneticBiobanks: a key service for diagnosis and research on rare diseases.Orphanet Journal of Rare Diseases 2013 8:129

7. Dedicated and qualified staff.

7.1 Definition of the organization chart and job descriptions
7.2 Competence and competence assessment
7.3 Training plan

8. Sustainability

8.1. Financial dimension (continuity)
- 8.1.1. Institutional commitment and support
- 8.1.2. Cost-recovery system
- 8.1.3. Project participation
- 8.1.4. Support from private funds

8.2. Operational dimension (efficiency)
- 8.2.1. Quality System efficiency and user satisfaction monitoring
- 8.2.2. Scientific impact: publications acknowledging the biobank service
- 8.2.3. Biobank marker paper (e.g. CoBRA guidelines/ Open Journal of Bioresources)- Ref Bravo & Napolitani

8.3. Social dimension (acceptance)
- 8.3.1. Biobank promotion among stakeholders (trust, awareness, education, etc…)

8.4. Business plan-long term sustainability
-Cost recovery related to access to samples
-Commercialization of research results or derived products.
-Funding from private for-profit entities (biotech companies or pharmaceutical companies)
-Funding through governmental institutions.
-Personalized medicine.

9. General overview of European infrastructures in relation to bio banking activities for RD

9.1. RD-connect: integrated global infrastructure for Rare Disease Research – Ref. Thompson2014
9.2. Biobanking and Biomolecular Resources Research Infrastructure (BBMRI).

9.3. Euro Biobank (EBB) – Ref. Mora 2015

9.4. Cataloguing initiatives of sample collections for rare diseases

BBMI-ERIC catalogue

EuroBioBank catalogue

Orphanet catalogue

9.5. Example of National infrastructures

9.5.1.1. Telethon Network of genetic Biobanks (TNGB) – Ref. Filocamo 2013

9.5.1.2. Spanish NATIONAL Rare Disease Biobank (RDR-BioNER) and National RD Registry. http://bioner.isciii.es/home/

9.5.1.3. Others

10. International initiatives International Rare Diseases Research Consortium (IRDiRC)

https://irdirc.org/activities/task-forces/

*'The IRDiRC **Task Forces** are created to tackle specific topics within rare diseases research proposed by the Constituent and/or Scientific Committees and selected as prioritized actions by the Consortium Assembly and the Operating Committee.*

11. Relevant references (preliminary)

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- Filocamo M., et al Biobanking for Genetic Diseases, In Encyclopedia of Life Sciences (eLS), Chichester, John Wiley & Sons Ltd, 2017
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- Bravo E, 2015 doi: 10.1186/s12916-015-0266-y.
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12. Appendixes (preliminary)

- BBMRI.it Matrix/ Prototype for a Material Transfer Agreement (https://repository.bbmri.it/s/BwKjDLom4x4TbbS)
- BBMRI.it Matrix for a Informed consent (https://repository.bbmri.it/s/stC8Lc4kPDn2qQt)
- TNGB Informed consent (from BBMRI.it Informed Consent matrix) – designed on Italian law
- Example of data transfer agreement
- https://www.bbmri-eric.eu/elsi-topic/international-data-sharing-mta-dta/
- Biobanco Nacional de Enfermedades Raras, BioNER. http://bioner.isciii.es/home/