Title: Sample Access Governance

TABLE OF CONTENT

Scope .................................................................................................................................................. 2
Introduction ......................................................................................................................................... 2
Section 1 PURPOSE ............................................................................................................................. 2
Section 2 DEFINITIONS ...................................................................................................................... 3
Section 3 ROLES OF IBBL .................................................................................................................. 4
  3.1. Physical Custodian ..................................................................................................................... 4
  3.2. Coordinator of sample access .................................................................................................. 4
  3.3. Partner ..................................................................................................................................... 5
  3.4. PI .............................................................................................................................................. 5
  3.5. Sponsor .................................................................................................................................... 5
Section 4 TYPES OF COLLECTION ................................................................................................... 5
  4.1. Research study derived collection ............................................................................................. 5
  4.2. Pure collection............................................................................................................................ 5
  4.3. Third party collection ................................................................................................................. 5
Section 5 POLICY ............................................................................................................................... 6
  5.1. Ethics Approval .......................................................................................................................... 6
  5.2. Primacy of Consent and Diagnosis ............................................................................................ 6
  5.3. Consent ................................................................................................................................... 6
  5.4. Beneficiaries .............................................................................................................................. 7
  5.5. Sample Access Procedure ........................................................................................................ 7
  5.6. IBBL Scientific Advisory Board (SAB) ..................................................................................... 7
  5.7. No Personally Identifying information (PII) ............................................................................ 7
  5.8. Cost Recovery without financial gain ......................................................................................... 8
  5.9. Data Protection ........................................................................................................................ 8
  5.10. Acknowledgements and (Co-)Authorship ............................................................................. 8
  5.11. Return of Results ..................................................................................................................... 9
  5.12. Intellectual Property ............................................................................................................... 9
  5.13. Logistics for sample collection .............................................................................................. 9
Related Documents & Exhibits ........................................................................................................... 10
References .......................................................................................................................................... 10
Document Information ...................................................................................................................... 11
Revision History ............................................................................................................................... 11
POLICY

Scope

This policy (the “Policy”) covers the management of the Chain of custody related to the collection, storage and use of Samples collected from donors whether healthy donors or patients.

This Policy covers the management of any collection for which IBBL has a role of custodian with respect to Samples. The role of custodian here can range from full legal custodianship and responsibility for all aspects of a collection, to the limited physical custodianship of Samples on behalf of a third party.

The scope in particular addresses ethical aspects, confidentiality of donors, compliance with data protection regulations [2 and 3], procedures for granting access to Samples and their future use, return of end research results, acknowledgements and financial considerations.

This Policy applies to all IBBL staff involved in the set up and management of human biological sample collections.

Introduction

IBBL is an autonomous Institute within the Luxembourg Institute of Health established in accordance with Article 35 of the law of 3 December 2014 on the organisation of public research centres [1]. Its mission is the creation, exploitation and autonomous management of a biobank respecting international ethical and safety rules and the confidentiality of donor information. IBBL supplies resources such as the annotated biological Samples, the technological platforms and the scientific expertise needed for the development of knowledge for the prevention, diagnosis and treatment of disease.

IBBL acts as a neutral and independent service provider to biomedical researchers. It does not itself undertake such research, but supports others specializing in this activity. IBBL undertakes research limited to Biospecimen Research.

IBBL’s ultimate aim is to facilitate the development of better health care, respecting all contributors to this endeavour in particular the donor.

Section 1  PURPOSE

Collection and storage of human biological material for use in research is indispensable for the development of knowledge for the prevention, diagnosis and treatment of disease. This Policy defines the position of IBBL concerning the collection, storage and use of Biological resources collected from donors.

This Policy is a set of principles which IBBL seeks to follow. The translation of these principles into procedures for staff to follow is Collection specific. For example, while the requirement for each Collection to have a committee deciding whether to accept or reject a request for samples from a researcher is a principle, the membership of this committee and its decision rules are defined in collection specific procedures, or in IBBL’s standard Sample Access Procedure.

IBBL seeks to follow these principles in all the Projects and for all the collections in which it has a role. However, the specific nature of a Project or Collection may require other measures to be agreed.

Donor’s rights are not modified by this Policy.

This Policy is a “policy” within IBBL’s Quality Management System, which covers all aspects of IBBL’s biobanking operations and processes, including other policies, general management, operations, infrastructure, and quality management.
Section 2  DEFINITIONS

The definitions below are for the purpose of this Policy only and in the context of the scope. They are not intended to supersede any existing legal notion using the same or similar terms.

“Anonymized” means (when referring to Biological resources) that no information, linked directly or indirectly to the Biological resource, would allow them to be traced back to the identity of the donor. In this case the link between the Personally Identifiable Information (PII) and the Biological resource is irreversibly broken.

“Biological resource” means a Sample or Biospecimen.

“Biomedical Research” means research with the aim of elucidating disease states or leading to improved health care for the benefit of the patients.

“Biospecimen” means a quantity of any type of human tissue or body fluid as collected and before any processing, and its associated data.

“Biospecimen research” means research into the behavior of Biological resources under different conditions of collection, processing and storage, with respect to a given intended use.

“Chain of custody” means the flow of Biological resources between the different parties involved in collecting, handling and using them (e.g. the hospital/site, service providers and storage facilities). During the course of a Project different people and organizations may be responsible for the day-to-day physical handling of Biological resources, but overall responsibility for the Chain of custody remains with the Custodian.

“Collection” means a set of Biological resources and can be a pure collection, a research study derived collection or a third party collection:

“Pure collection” means a Collection established for future, but yet unknown, research, in which IBBL has a role of Partner, PI or Sponsor.

“Research Study Derived Collection” means a Collection established as part of a biomedical research project, in which IBBL has a role of Partner, PI or Sponsor.

“Third party collection” means any collection, which is under the control of a third party and over which IBBL has no rights or responsibilities beyond the provision of services such as physical custodianship or coordination of sample access.

“Custodianship” means the caretaking responsibility for Biological resources that starts at the planning of a Project which will give rise to the constitution of a Collection, and continues inter alia through authorizations, consent, collection, processing, analysis and storage, to distribution.

“Legal Custodian” or “Custodian” means the entity responsible for the Custodianship of Biological resources.

“Partner” means any entity contributing to the Project and which also is party to an agreement with the Sponsor.

“Primary use” means the use of Samples for the research purposes that were specified at the time of collection and for which donor informed consent was initially obtained.

“Principal Investigator”/ “Investigator” (PI) means the person responsible for the conduct of the Project at a site. If a team of individuals at a site conducts a Project, the Investigator is the responsible leader of the team and may be called the Principal Investigator. The Custodian may delegate responsibilities to the Investigator.

“Project” means a research project or clinical trial whether observational, non interventional or interventional, which gives rise to a Collection.

“Pseudonymisation” means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organizational measures to ensure that the personal data are not attributed to an identified or identifiable natural person.
“Sample” means a quantity of any type of human tissue, body fluid or derivative thereof and its associated data.

“Secondary use” means the use of Samples other than for use for the initial Project. Secondary use is covered either by appropriate informed consent/ethics approval or by an ethics waiver.

“Sponsor” means an individual, company, institution, or organization, which takes responsibility for the initiation, management, and/or financing of a Project. In the context of this Policy the Sponsor is always a legal entity.

Section 3  ROLES OF IBBL

IBBL’s activities cover a variety of roles. These are agreed with the Sponsor and Partners, or the clients to whom IBBL provides services. In any given Project, IBBL may have more than one role. These roles may be described in the collaboration or service agreement.

IBBL can have the following roles:

3.1. Physical Custodian

On behalf of the Custodian, IBBL may act as a sub-contractor and ensure the physical security of the Biological resources by measures including:

- ensuring integrity of Biological Resources,
- controlling physical access to premises,
- controlling access to information systems,
- maintaining and taking instructions from a limited list of persons authorized by such organization to give instructions,
- maintaining an appropriate Quality System Management,
- ensuring the competence of its staff

In this role, IBBL has no responsibility for or influence over decisions related to requests for access to Samples from researchers.

3.2. Coordinator of sample access

IBBL may implement the Sample access procedures, established by the Custodian.

In particular, IBBL is responsible for implementing the procedures for responding to requests for Samples, by verifying the availability of suitable Samples, seeking decisions from the persons authorized to approve such requests and organizing the retrieval and distribution of Samples.

In this role, IBBL has no responsibility for or influence over decisions related to requests for access to Samples from researchers.

3.3. Partner

IBBL may act as a Partner with others in a Project. The relations between the Partners, their rights and obligations, are established in an agreement.

According to the terms of this agreement, IBBL may have a voice in Sample access decisions.
3.4. PI

In agreement with Good Clinical Practices (GCP) [3-7], IBBL may act as the Principal Investigator in two types of research projects, typically Biospecimen Research related and in Pure collection Projects. According to the terms of this agreement, IBBL may have a voice in Sample access decisions.

3.5. Sponsor

IBBL may act as Sponsor to the Project.

It is the Sponsor’s responsibility to ensure all relevant approvals and authorizations are obtained and notifications submitted.

Except in exceptional circumstances the Sponsor is the Custodian.

According to the terms of this agreement, if IBBL has the role of Sponsor, IBBL may have a voice in Sample access decisions.

Section 4 TYPES OF COLLECTION

4.1. Research study derived collection

The Primary use of a Research study derived collection is to provide Biological resources for that specific research project.

The secondary use of such a Collection is to provide Biological resources for other research projects for which they are suitable, subject to the consent covering such broader use. Secondary use may be limited to the same clinical/disease domain as the primary research project.

Ethics committee approval is required for the specific research study, with secondary use included in the consent.

4.2. Pure collection

For Pure collections, the Ethics Committee approval is for the collection, processing, storage and analysis of Biological resources, not for any particular research study. Downstream research using the Biological resources is the subject of separate approvals. Consent is typically broad.

4.3. Third party collection

The services provided by IBBL to a third party are described in a service agreement between the parties. The agreement includes a provision that it is the responsibility of the third party to ensure samples have been collected in accordance of applicable laws and are covered by appropriate Informed Consent.
Section 5  POLICY

5.1. Ethics Approval

Any Research study derived collection or Pure collection is submitted to the competent Ethics Committee for approval. Any intended Secondary use of the Samples forms part of the submission.

5.2. Primacy of Consent and Diagnosis

The will and benefit of the donor take precedence over other considerations.

The will of the donor is expressed through the informed consent. IBBL will not store Sample unless such storage is covered by the consent or by an explicit waiver of consent from a competent Ethics Committee. IBBL will make no use of Samples unless such use is covered by the consent, or by an explicit waiver of consent from a competent Ethics Committee.

The only exception is when there is a need to protect IBBL staff from potential injury. In such emergency cases, Samples may be tested without consent.

Where the Sample is derived from the same surgical piece or Biospecimen which is also used for diagnostic purposes, the needs of diagnosis prevail and only “left over” quantities will be stored and used for research purposes. Any requests for research samples needed for the purpose of confirmation of patient diagnosis or choice of treatment plan will be handled promptly and the pertinent samples (if not yet used) distributed to the relevant health care professionals.

5.3. Consent

Use of Samples is conditional on receiving consent from the donor. When IBBL is the Sponsor IBBL submits the Informed Consent Form (ICF), including the choices offered to the donor, and the Subject Information Sheet (SIS) to competent Ethics Committees for approval.

Given the complexities of biological systems and the interactions of co-morbidities, it is not possible to predict the research purposes for which Samples will be suitable in the future for the benefit of patients.

Therefore, while respecting applicable regulations on the use of personal data and the need to provide consent choice to the donor, IBBL in general seeks approval for broad consent in the Projects for which it is Sponsor, from the competent Ethics Committees.

Broad consent in this context means consent not limited to the use of the Samples for a specified Biomedical Research project, but consent limited to Biomedical Research in general. IBBL respects the provisions of the General Data Protection Regulation (GDPR) (EU) 2016/679 [8] and gives donors the choice to give their consent (i) only to certain areas of scientific research, such as Biomedical research, or (ii) to parts of research projects, to the extent allowed by the intended purpose.

The donor may withdraw consent at any time following a process given in the ICF/SIS. This process may vary from one project to another, but in all cases ensures that IBBL is never in contact with the donor and never receives information that would allow IBBL to identify the donor. At the time of withdrawal IBBL provides choice to the donor as to how the withdrawal will be implemented, for example the choice between destruction and anonymization of Biological resources.

As examples of choice, (i) the donor would have the choice to give broad consent separately from consent to participation in the primary study; (ii) the donor would have a choice related to the handling of incidental findings.

IBBL ensures that the ICF and SIS comply with applicable legal and ethical requirements by use of standard templates and its process of regulatory watch.
For example, study donors are informed at the time of giving consent that their Samples may be used by third parties (academic partners, research laboratories etc.) for biomedical research with the purpose of contributing to improved health care, and that these parties may not be within the European Union.

5.4. Beneficiaries

Samples will be distributed to beneficiaries according to the applicable Sample access procedure. In case of the need to prioritize, the following considerations will be taken into account:

- clinical and scientific excellence;
- the contribution of the requestor to constituting the Collection;
- the contribution of the study to Luxembourg Biomedical Research

5.5. Sample Access Procedure

The detailed access procedure is determined at the level of the Collection. The Partners agree and document the decision process to approve requests for Biological resources. The procedure states whether decisions are taken unanimously or by majority and how the decision-making body is constituted.

Sample access procedures for Research study derived collections recognize the priority of the research study itself for access to Samples, over the use of those Samples for other research.

With respect to the Sample access procedure, IBBL may act as coordinator of Sample access or as a member of the decision making body, or both.

IBBL maintains a default Sample access procedure (WI PM-016 Sample Access Procedure) in case there is no Collection specific procedure defined.

5.6. IBBL Scientific Advisory Board (SAB)

IBBL has an independent Scientific Advisory Board (SAB) which reviews yearly IBBL’s activities and strategic decisions from a scientific point of view and the Sample and Data Distribution decisions.

The SAB reports to the IBBL (LIH) Board of Directors and makes recommendations.

THE SAB reports any recommendation regarding the Sample and Data Distribution decisions to the IBBL (LIH) Board of Directors.

5.7. No Personally Identifying Information (PII)

IBBL does not receive PII in the course of its biobanking activities. IBBL’s agreements with its partners stipulate that all Samples and Data will be transferred to IBBL pseudonymised or anonymized.

In the case that by error IBBL is sent PII, the information will be returned to sender or destroyed, and no copy retained.

While covered by the confidentiality obligations of medical staff towards personal data, IBBL’s pathology staff may however handle PII where required for the fulfillment of IBBL’s obligations, subject to this information remaining under the control of such staff and not being recorded in or connected to the database used for the Collection.
5.8. Cost Recovery without financial gain

Research donors are not offered financial or material incentives to provide Samples. Reasonable expenses, such as travel expenses, may be reimbursed.

IBBL distributes Biological resources to the scientific community (public and private) without deriving any profit from this activity.

In line with (i) the Performance contract between IBBL and IBBL’s funding Ministry, the Luxembourg Ministry of Higher Education and Research (MESR), and (ii) IBBL’s mission to support biomedical research, IBBL may seek a contribution towards its costs from those receiving Biological resources and who are therefore benefitting from the activities of the biobank.

In line with European recommendation, a cost recovery contribution may be sought when those Samples have undergone costly processing or analysis, or when the collection process has generated external costs (such as for shipment or external nurses or hospital operations) [9, 10].

IBBL is a not-for-profit organization and does not derive any profit from these contributions, only a partial recovery of the costs of its biobanking activities (costs of collection, transport, processing, storage, tracking in database, retrieval, documentation, quality control).

Furthermore, where IBBL is part of a project consortium and receives funds from that consortium to perform biobanking services, IBBL will not in addition seek any financial contribution from that consortium for access to the corresponding Samples.

IBBL applies preferential conditions for cost recovery to Luxembourg institutions and researchers.

5.9. Data Protection

The protection of information concerning donors is of primary importance to IBBL. IBBL puts in place formal procedures to ensure compliance with applicable national and European laws and regulations following IBBL’s Data Protection Policy (ref POL IT-001).

IBBL also makes notifications and requests for authorization to competent authorities where relevant.

IBBL may take on different roles with respect to data protection and the information related to a Collection, depending on the Project.

Project specific documentation describes the respective roles of the Partners in a Project, in particular determining who is the data controller or co-controllers, the processor(s), the supplier(s) and the recipient(s).

5.10. Acknowledgements and (Co-)Authorship

IBBL seeks to ensure that contributions to scientific publications, papers and articles are acknowledged in accordance with accepted international standards.

IBBL expects to be acknowledged when IBBL contributes to the:

- collection of Biospecimens, processing (by standard IBBL Standard Operating Procedures (“SOPs”)) of Biological resources, and supply of Samples except substantially modified derivatives
- collection of Biospecimens, processing (by project specific, but not validated, SOPs) of Biological resources, and supply of Samples except substantially modified derivatives

IBBL expects to have the co-authorship of the publication, paper or article when IBBL contributes to the:

- collection of Biological resources, processing (by project specific and validated SOPs) of Biological resources, and supply of Samples except substantially modified derivatives
- analyses of Biological resources
• collection of Biological resources, processing and supply of substantially modified derivatives.

Material Transfer Agreements for Samples distributed by the biobank include a section specifying acknowledgements and potential (co) authorships.

5.11. Return of Results

IBBL may request a return of results from researchers where such return would increase the value of the remaining Biological resources in the biobank. This is not however a condition of distribution. Particular value is placed on results from accredited laboratories.

5.12. Intellectual Property

In general, IBBL does not seek intellectual property rights from those to whom it distributes Biological resources for the simple act of providing these Biological resources. Only where there is significant intellectual contribution to a product or service of the third party, will IBBL seek such rights.

5.13. Logistics for sample collection

Traceability of the location of Biological resources, of the “parent-child” relations between Biospecimens and derivatives and of the Chain of custody is ensured for the entire cycle from collection through to distribution for research use.

Agreements are established for all services provided by service providers.

Material Transfer Agreements are signed between IBBL and institutions to whom Samples are distributed.
References


[2] Luxembourg’s modified law of 2 August 2002 on the Protection of Persons with regard to the Processing of Personal Data


[4] Integrated Addendum to ICH E6 (R1): Guideline For Good Clinical Practice E6(R2) 11JUNE2015


[9] Recommendation CM/Rec (2016)6 on research on biological materials of human origin was adopted by the Committee of Ministers of the Council of Europe on May 11, 2016

[10]Explanatory Memorandum to Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin drawn up under the responsibility of the Secretary General of the Council of Europe. During the 1256th meeting – 11 May 2016, the Deputies took note of the abridged report of the 8th meeting of the DH BIO, as it appears in document CM(2016)14
Document Information

<table>
<thead>
<tr>
<th>Document Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Document Code &amp; Version:</td>
<td>POL PM-002.03</td>
</tr>
<tr>
<td>Application Date:</td>
<td>17/04/2018</td>
</tr>
<tr>
<td>Replaces:</td>
<td>POL PM-002.02</td>
</tr>
</tbody>
</table>

Authorship & Approval

<table>
<thead>
<tr>
<th>Names</th>
<th>Functions</th>
<th>Approval Date(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominic ALLEN</td>
<td>Chief Operating Officer</td>
<td>06/04/2018</td>
</tr>
<tr>
<td>Christelle BAHLAWANE, Fay BETSOUL, Catherine LARUE, Marc VANDELAER</td>
<td>Project Manager, Chief Scientific Officer, Chief Executive Officer, Chief Information Officer</td>
<td>09/04/2018, 09/04/2018, 13/04/2018, 09/04/2018</td>
</tr>
<tr>
<td>Sabine LEHMANN</td>
<td>Quality Manager</td>
<td>16/04/2018</td>
</tr>
</tbody>
</table>

Changes Compared to Previous Version

Revised to make it more general.

Revision History

<table>
<thead>
<tr>
<th>Version</th>
<th>Effective Date</th>
<th>Author</th>
<th>Summary of changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>.01</td>
<td>20/FEB/2014</td>
<td>Dominic ALLEN</td>
<td>New document</td>
</tr>
</tbody>
</table>

*** End of document ***