

Standard Operating Procedure

Biological specimens to be stored at the Biobank

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TABLE OF CONTENTS

1. ABBREVIATIONS	3
2. SCOPE	3
3. FIELD OF APPLICATION	3
4. RESPONSIBILITIES	3
5. PROCEDURE	4
5.1 Relevant information to be reported in the trial protocol/manual	5
5.2 Informed Consent	5
5.3 Biological specimen management	6
5.3.1 Set-up	6
5.3.2 Pseudonymization	6
5.3.3 Collection	6
5.3.4 Processing and Storage	7
5.3.5 Shipment to a central laboratory	7
5.4 Data Reporting	7
5.5 Archive	7
6. REFERENCES	8
7. TEMPLATES	8
8. VERSION HISTORY	8

1. ABBREVIATIONS

ASST-PG23:	Azienda Socio-Sanitaria Territoriale – Papa Giovanni XXIII
BBio:	Biobank
COC:	Clinical Operations Coordinator
CSC:	Clinical Study Coordinator
DM:	Data Manager
EC:	Ethics Committee
FROM:	Fondazione per la Ricerca Ospedale di Bergamo
GCP:	Good Clinical Practice
IC:	Informed Consent
ICH:	International Conference on Harmonization
PI:	Principal Investigator
PIS:	Patients Information Sheet
PM:	Project Manager
QAM:	Quality Assurance Manager
SD:	Scientific Director
SOP:	Standard Operating Procedure
TSC:	Technical Scientific Committee

2. SCOPE

The purpose of this SOP is to detail the mandatory information that have to be included in the protocol or in a trial manual, and in the related informed consent sheet regarding the management (i.e. collection, processing, storage and shipping, if any) of biological specimens (e.g. blood and its components, cells, tissue, liquids, nucleic acids).

3. FIELD OF APPLICATION

This SOP is applicable to clinical trials sponsored or supported by FROM and sponsored or conducted at ASST-PG23.

4. RESPONSIBILITIES

Principal Investigator (PI)

FROM trials

- Defines the scope of specimens use and endpoints of research to be included in the trial protocol and in the related Informed Consent.

- Identifies the most suitable laboratory, where the analysis can be performed and ensures that a contract ratifying terms of the collaboration is executed.
- Involves the Biobank at ASST-PG23 for the storage of biological specimens when required.
- Drafts IC (initial and amended) before submission to the Regulatory Authorities for approval.

All trials

- Provides all relevant information to patients about goal and procedures for the biological specimen collection and storage, collects the duly signed IC and documents it on the medical records.
- Delegates the management of biological specimens to personnel qualified for the assigned tasks and provides training in this respect.
- Collects the tissue specimens and those obtained by surgery that will be stored in Biobank for the time defined by the protocols.
- Maintains in a confidential way the Patient Identification List reporting the patient identification information and the trial patient code also used to identify the biological specimens.

Project Manager (PM) / Data Manager (DM)

FROM trials

- Ensures that appropriate instructions are provided in the protocol and amendments, ICF trial template and/or in a specific manual and submits them to the PI for review.
- Organizes and maintains connection among central laboratory and investigators of centers involved in a trial.

All trials

- Interfaces with the central laboratory responsible for the analysis on biological specimen.
- Archives the biological specimen documentation in the trial files.

Biobank Manager

- Verifies the specimen condition when delivered to the Biobank, the storage conditions at the Biobank and the delivery to the central laboratory, when applicable.

5. PROCEDURE

Analysis of biological specimens offers opportunities to investigate many questions and hypotheses that are related to diseases and treatment. The goals and procedures relevant to analysis of biological specimens should be detail in the trial protocol as well as the acquisition and storage of specimens and data entails additional processes and considerations relating to the informed consent of patients potentially eligible for a clinical trial.

The proper management of biological specimens for laboratory testing and analysis is essential to assure the quality and integrity of data collected in clinical trials.

5.1 Relevant information to be reported in the trial protocol/manual

The instruction for the management of biological specimens (collection, coding, shipment, storage and destruction) included in the protocol and/or in a trial specific manual and the following information should be detailed:

- rationale of research / scope of specimen use,
- objective / endpoints of the research,
- type and quantity of specimens required,
- timing of specimen collection(s) from patients, if applicable,
- level of anonymization of specimen and related data,
- organization of specimen collection, storage, shipment and analysis,
- final disposition of the specimens (once the analysis foreseen in the protocol is performed).

5.2 Informed Consent

The biological specimens have to be managed according to ethical considerations, in respect of the privacy of the subject. Patients have to be informed and should give their consent about the sampling, storage and research aim for collecting such biological material.

The informed consent must be obtained from the trial participants before any specimen collection.

The process for informing patients is described in the **SOP Informed Consent and GP Letter (CLI02/2)**.

When the clinical trial requires mandatory participation in an ancillary trial, it would be reasonable to merge IC for biological specimens with the clinical one. When participation in the research is optional, a separate IC should be issued.

The following information should be included in the IC for biological specimens with research aim:

- research scope for collecting the biological material,
- if the specimen is already available or has to be taken/collected from the patient,
- how the biological specimens will be collected and stored (location and storage period),
- specimen anonymization and maintenance of subject privacy and confidentiality ,
- management of the data collected,
- information about the possibility that specimens are sent to countries with different level of data protection, if applicable,
- patient's right to revoke consent to the sampling at any time,
- patient's right to request the destruction of his/her material (if not completely anonymized),
- patient's right to access his/her own data/results (if not completely anonymized),
- patient's right to be informed about possible future analyses not foreseeable at the time of the current consent (if applicable),

- sponsor's right to maintain data already collected in order to avoid alteration of the trial results,
- direct access of trial sponsor or Health Authority representatives to the patient data/results,
- publication policies and dissemination of results.

5.3 Biological specimen management

5.3.1 Set-up

The PM/DM should ensure that the following information are available when a clinical trial includes research on biological specimens:

- Biobank contact information,
- Biobank materials to be used,
- requirements for specimen collection, labelling, processing and storage at Biobank,
- packaging and shipping specifications as defined by Biobank Manager Director and Project Manager or by the trial sponsor,
- final disposition of the specimens after the analysis completion as defined by Biobank Manager Director and Project Manager.

All required materials should be available prior to trial activation.

Biobank Manager for the storage and the laboratories responsible for analysis of specimens must provide adequate quality documentation (e.g. about personnel, equipment and procedures) to ensure compliance with ethical, legal, and local regulations for the handling of biological specimens (*PSpBBio01PG8MQ7 "Accettazione e conservazione di materiale biologico e dati associati presso la Biobanca"*).

5.3.2 Pseudonymization

The biological specimens collected from patients must be pseudonymized when delivered to an external laboratory in order to protect the patient privacy.

Clinical trial sample are usually coded with a unique patient number assigned to the patient for the clinical trial. As the specimens and associated data are directly traceable back to the subject, it is possible to undertake actions such as specimen withdrawal or the return of individual results in accordance with the subject request using a single coding key. The clinical investigators are responsible for maintaining the decoding key.

Biological specimens do not carry any personal identifiers if delivered outside ASST-PG23.

5.3.3 Collection

Before the specimen collection, the following activities should be performed by the PM/DM:

- prepare materials for specimen collection according to the protocol/specific manual ,
- fill in the form " Modulo accettazione campione per Studi e Sperimentazioni cliniche" (Mod01PspBBio08) issued by the Biobank to guarantee the specimen traceability.

Specimens must be collected according to the protocol /trial manual instructions.

The person delegated for this task (i.e. trial nurse) collects the biological specimens at scheduled visit/time according to the protocol.

A second person should verify that specimens are duly collected and labelled. A code will be assigned to each sample as appropriate according to the information provided in the protocol or specific manual of the trial.

5.3.4 Processing and Storage

The specimens are processed at the Biobank according to the protocol and/or specific manual (e.g. centrifuge speed, duration, temperature requirements) and the procedure PSpBBio01PG8MQ7 "Accettazione e conservazione di materiali biologico e dati associati presso la Biobanca".

Once in Biobank the biological specimens are tracked by *Freezerworks* software (PSpBBio06 "Gestione del software Freezerworks").

Each freezer and its compartments are identified with a code; the specimen are stored in suitable boxes arranged in racks or drawer identified with a code.

Biobank staff will identify the specimen location in *Freezerworks*. The *Freezerworks* Software Report is downloaded upon PM/DM request and filed at the Biobank in the trial specific folder.

Refrigerator and freezer temperatures are monitored according to the hospital procedures (PSp04DML "Gestione degli allarmi SPYLOG"). Any deviations outside ranges have to be immediately communicated to the PM/DM or Principal Investigator for the appropriate actions.

5.3.5 Shipment to a central laboratory

The clinical team organizes the specimen delivery to the central laboratory responsible for the analysis according to the following steps:

- contact the courier contracted in advance and schedule the date and time for specimens shipping,
- remind the courier the shipping type,
- collect shipping materials as specified by the protocol (example: dry ice) and prepares the specimens for the delivery,
- draft a specimen delivery letter (example provide : **Biological Specimen Delivery Letter (T.CLI09.01/1)**) to be delivered with the specimens.

Copies of the delivery letter and the confirmation of specimen receipt at the central laboratory are archived at the central laboratory in a trial specific folder and copies are remitted to the PM/DM for archiving in the TMF (where applicable).

5.4 Data Reporting

The results and the analysis of biological ancillary research are included and discussed in a report issued by the central laboratory. The laboratory results should be evaluated and discussed in relation to the clinical data and reported in the Clinical Study Report.

5.5 Archive

All documents supporting the biological specimen management and analysis should be archived in a specific section of the Trial Master File/Investigator Study File according to the **SOP Trial Files (CLI06/2)**.

The sites involved in the trial have to retain documents supporting the biological specimen management in the Investigator Study File as well as the ICs signed by patients.

The central laboratory has to maintain all documents supporting the biological specimen receipt, storage, analysis and disposal.

6. REFERENCES

- Guideline for good clinical practice E6(R2) (CPMP/ICH/135/95).
- Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples - 28 February 2012 (EMA/INS/GCP/532137/2010).
- General Data Protection Regulation (GDPR) n. 2016/679.
- Decreto Legislativo 10 agosto 2018, n. 101 Disposizioni per l'adeguamento della normativa nazionale alle disposizioni del regolamento (UE) 2016/679 del Parlamento europeo e del Consiglio, del 27 aprile 2016, relativo alla protezione delle persone fisiche con riguardo al trattamento dei dati personali, nonché alla libera circolazione di tali dati e che abroga la direttiva 95/46/CE (regolamento generale sulla protezione dei dati).
- Provvedimento recante le prescrizioni relative al trattamento di categorie particolari di dati, ai sensi dell'art. 21, comma 1 del d.lgs. 10 agosto 2018, n. 101 (Garante per la protezione dei dati personali, Registro dei provvedimenti n. 146 del 5 giugno 2019).
- Decreto Legislativo 30 giugno 2003 n. 196: Codice in materia di protezione dei dati personali.
- Linee guida per i trattamenti di dati personali nell'ambito delle sperimentazioni cliniche di medicinali - 24 luglio 2008.
- Garante per la protezione dei dati personali - Autorizzazione generale al trattamento dei dati personali effettuato per scopi di ricerca scientifica - 11 dicembre 2014.
- Garante per la protezione dei dati personali - Autorizzazione n. 8/2014 - Autorizzazione generale al trattamento dei dati genetici - 11 dicembre 2014.
- PSpBBio01PG8MQ7 "Accettazione e conservazione di materiale biologico e dati associati presso la Biobanca".
- OSp04DML "Gestione degli allarmi SPYLOG".
- PSpBBio06 "Gestione del software Freezerworks".

7. TEMPLATES

T.CLI09.01/1 Biological Specimen Delivery Letter (example).

8. VERSION HISTORY

Version	Date	Reason for revision
1	30 Sept 2016	Starting document.

SOP CLI09/2
Biological specimens to be
stored at the Biobank

Version	Date	Reason for revision
2	28 Feb 2020	<ul style="list-style-type: none"> • New SOP title to better identify the content of the SOP. • Biobank included as facility for the storage of biological specimens. • Removal of the module T.CLI09.01 Biological Specimen Form and T.CLI09.02 Biological Specimen Register, replaced by the Biobank modules and electronic system <i>Freezerworks</i>. • Rewording of some SOP sections.