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Human Biological Material Collection, Storage and Use

POL020

Version 2.1

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1 PURPOSE

Collection and storage of human biological material (HBM) for use in research is indispensable for finding better treatments for patients. This policy defines the position of the EORTC concerning the collection, storage and use of HBM collected from participants enrolled in EORTC studies and projects. It outlines the minimal principles that shall apply to both EORTC and third parties.

This policy outlines key principles to be respected within the framework of EORTC studies and projects. This includes ethical aspects, guarantees to ensure confidentiality of participants, compliance with data protection regulations, logistical aspects of collection and storage of HBM, minimum quality criteria for HBM storage facilities, processes for further access to HBM and their future use, availability of end research results and publication rules etc... This policy applies to the specific portion(s) of HBM that is collected for, or made available to, EORTC within the framework of its studies or projects. The principles can also be implemented where applicable in intergroup studies and projects in which the EORTC participates but for which another organization is leading (e.g. another academic group or pharmaceutical company).

2 DEFINITIONS

The definitions below are specifically formulated for the purpose of this policy and are not intended to supersede any existing legal notion using the same or similar terms.

- **Human biological material (HBM):** Any type of tissue, body fluid or derivative, including (but not limited to) nucleic acids.

  In the framework of EORTC activities three categories of HBM will be distinguished:

  - Additional HBM collected within and under the scope of the EORTC study, expressly for the purposes of research (e.g. additional blood samples, second biopsy, etc.) and identified as such in the informed consent;
  - Pre-existing HBM without diagnostic value (e.g. any HBM collected and stored by, or being available to, the institution having recruited the patient concerned);
  - Pre-existing HBM with diagnostic value (e.g. a unique diagnostic biopsy).

- **Translational research (TR):** "Bench-to-bedside" translation of scientific discoveries arising from clinical, laboratory or population-based research into clinical applications to improve the prevention, diagnosis and/or treatment of a disease. In this policy, the definition is limited to research using HBM.
- **TR project leader:** The person who is coordinating or requesting access to HBM collected within the framework of an EORTC study for the purpose of carrying out a specific TR project. This person is scientifically responsible for this specific TR project, its coordination and for working in compliance with this policy and applicable legal requirements and ethical principles.
- **Custodian:** Usually the legal entity responsible for safeguarding HBM and oversight of its use. Formal responsibility for custodianship rests with organizations rather than individual persons. The EORTC is open for institutes to remain the custodian (if requested or required by regulation) and in this case the institution decides the final use of the HBM at all times. In those countries where the term custodianship is defined by law, the formal legal definitions would apply and these are not superseded by this policy.
- **Chain of custody:** The flow of HBM between the different parties involved in collecting, handling and using HBM (e.g. the hospital/site, service providers, storage facilities and sites performing TR). During the course of the clinical study different people and organizations will be responsible for the day-to-day

physical management of HBM. However, formal custodianship usually rests with organization(s) rather than individuals.

- **Coordinator of the chain of custody:** the entity (i.e., sponsor or its delegate) responsible for ensuring all organizations participating in chain of custody act in compliance with the project, applicable legislation and existing contractual agreements.
- **EORTC HBM collection:** the HBM collected within the framework of one or several EORTC studies or projects being appropriately approved and stored within storage facilities appropriately assessed and approved by EORTC (validated storage facility). EORTC collections may be established for defined or undefined TR purposes. Normally, only a portion of the HBM being collected by sites from patients participating in EORTC projects will be requested, e.g. one block out of several blocks prepared from a surgical specimen or freshly cut slides from an FFPE block. This policy does not preclude that HBM may be collected, stored and used by sites or any other party for other purposes outside the scope of EORTC studies (and this policy).
- **Validated storage facility:** an operational definition describing any infrastructure validated by the EORTC that is responsible for centralized storage of HBM (and eventually associated data) collected from multiple sites within the framework of a single or multiple studies or projects and this for short or long term storage. EORTC storage facilities are part of the chain of custody.
- **Validated research facility:** any infrastructure responsible for the analysis of HBM (and eventually associated data) within the framework of an EORTC study. Validated research facilities may also act as storage facility and this for short or long term storage. Research facilities are a part of the chain of custody.
- **Coded:** Refers to the result of the process of replacing personal identifiers linked to data or HBM by a code for confidentiality and privacy reasons (also known as "linked anonymized" or "pseudonymized"). To be distinguished from “anonymized” that refers to when the link between the data and HBM is irreversibly broken.
- **Primary use of HBM:** The use of HBM for research purposes that were specified at the time of HBM collection for which study participant informed consent has been obtained.
- **Secondary use of HBM:** The use of residual HBM for TR aims that were not mentioned at the time of HBM collection because they were as yet unknown.
- **Sponsor:** an individual, company, institution or organization which takes responsibility for the initiation, management of a clinical study and/or financing of a clinical study.

3 POLICY

Clinical and translational researches are fundamental for improving therapies for cancer patients such as for the development of individualized therapeutic approaches. HBM collection in clinical studies is a fundamental part of clinical research activities that are driven by molecular data. Access to HBM, in sufficient quality and quantity and linked to high quality clinical data is essential to accelerate clinical and translational research. HBM collected in the context of clinical studies with quality long term follow up data are therefore a key resource for research. By including HBM collections in clinical studies, it is possible to add value and increase the amount of information collected from each individual patient's participation to further research efforts towards better patient care.

Hence, translational research and the creation of quality assured centralized HBM collections associated with clinical studies are important and should be considered in every EORTC study or project.

All collections of HBM that are within the framework of EORTC studies and projects should comply with all applicable ethical and legal requirements and quality assurance requirements.

All HBM collections should be stored in a validated storage facility complying with the criteria delineated in this policy.

Any use of HBM should comply with all other applicable EORTC policies.

3.1 Sponsorship, HBM and coordination of the chain of custody

EORTC often acts as the sponsor of studies, but on occasion the EORTC may also act as the sponsor's delegate. In such cases, the EORTC is responsible for ensuring that these studies are successfully completed, performed in compliance with applicable legislation and in accordance with specific conditions eventually set-up by Competent Authorities and /or Ethics Committees and within the scope of the patient's consent. For all studies that include the collection and/or storage and/or use of HBM, these responsibilities apply to the way HBM is collected, stored and used, independently of other responsibilities which may exist locally (e.g. at the institution level that are not related to any specific EORTC study).

Therefore, to clarify roles and responsibilities, researchers and their host institutions must reach agreement with the study sponsor on arrangements for the HBM (which can be included in the general agreement around a study).

In the case of intergroup studies or sponsorship by another (non-EORTC) organization, the scope of the EORTC's responsibility regarding the HBM will be discussed before the project commences.

Due to the nature of international project collaborations frequently involving centralized biomarker analysis, there is a need to temporarily centralize and store HBM for variable lengths of time. Transfer of HBM to different research facilities is therefore needed but must also be accompanied with timely return of HBM (when required) to the originating institute, e.g. blocks are sent for tissue microarray construction and the residual block can be returned afterwards.

The EORTC may be the sponsor of trials and not be the custodian of the HBM. As the sponsor (or sponsor's delegate) of studies and other TR projects the EORTC has a responsibility and duty to manage the practicalities and to ensure the chain of custody of the HBM. This ensures that all organizations involved in the chain of custody act in compliance with the project, prevailing applicable legislation and existing contractual agreements. The EORTC therefore acts as the coordinator of the chain of custody.

3.2 Ethical aspects

3.2.1 Core principles

As the primary care of the patient is of paramount importance, the core principles of the EORTC POL002 on the protection of human subjects participating in clinical and translational research are applicable.

3.2.2 Consent

- HBM can only be collected, stored and used with the appropriate consent of the study participant and/or Ethics Committee, as applicable. This is mandatory to comply with high ethical standards.

- Briefly, for HBM collection specified in the clinical study protocol, the EORTC foresees a Patient Information Sheet and Informed Consent (PIS/IC) document with appropriate Ethics Committee approval, that will allow the study participant to give or refuse consent for the storage and use of HBM in research defined within the clinical study protocol and also to give or refuse consent for storage of HBM for future research as yet undefined.
- The EORTC will ensure that the PIS/IC complies with applicable legal and ethical requirements by use of a standard PIS/IC template and checklist of principles relating to HBM that are based on current recommendations and guidance (see references).
- In the case of future research studies (i.e., as yet undefined projects), the protocol and PIS/IC will define the general scope of research as precisely as possible. For example, future use of HBM will be limited to: research aimed at studying biological characteristics of the tumor (e.g. biomarkers), refining patient diagnoses and tailoring patient treatment options, amending patient follow-up protocols or identifying any element likely to further our understanding of cancer, the tumor's behavior and the mechanism(s) of action and effects of the treatments administered, etc.
- Study participants will be informed at the time of giving consent that their HBM may be used by third parties (academic partners, research laboratories etc.) for the purposes of scientific collaborations within the same scope as above. Study participants will also be informed when the results of the research performed on HBM might contribute to the development of commercial products and services.
- At the time of use, the need for a patient's re-consent or information or any other form of communication with the patient will be assessed in view of each specific project, applicable legislation and will be put in place in accordance with the Ethics Committee's opinion.
- Patient's rights are not modified by this policy.

3.2.3 Ethics Committee approval

Any collection of HBM is subject to approval by Ethics Committee. HBM may be collected, stored and used for a purpose other than that for which it was collected. For the use of HBM in TR where no specific consent for a TR project had been obtained (e.g. in older studies), Ethics Committees (and/or other regulatory bodies as applicable) will be approached for review and approval prior to starting the project (on the basis of the declaration of Helsinki 2013, art 32 and any other applicable laws). EORTC Headquarters should be contacted for recommendations on the prevailing applicable legislation. Whether or not the participant needs to be re-contacted in order to be informed or to obtain his or her consent for use of his or her coded HBM will be determined individually for each study in compliance with all applicable legislation and as approved by the competent Ethical Committee.

3.2.4 Withdrawal of consent

If the participant wishes to withdraw his or her consent, he or she is free to do so at any time (see EORTC POL002). In such an event, the investigator should notify EORTC Headquarters. The consequences of this withdrawal (for example, no further use of HBM and/or destruction, return or anonymization of HBM to the institution origin) will be made clear to the participant.

3.2.5 Access to pre-existing HBM with diagnostic value for patient care

Pre-existing diagnostic material can be temporarily (for the duration of the study) stored in a centralized storage, and shall be returned to the institute of origin unless otherwise agreed in advance and specified in the protocol. Timelines and practicalities will be clearly described in the agreements with institutions. Similarly,

should the HBM be needed at any time for the purpose of confirmation of patient diagnosis or choice of treatment plan, pertinent HBM (if not yet used) will be returned to the institution.

3.2.6 No financial gain

HBM will not be sold. Research participants will not be offered financial or material inducement to provide HBM, but reasonable expenses may be reimbursed, e.g. travel expenses.

3.3 Confidentiality and data protection

The confidentiality and data protection principles of EORTC POL002 also apply, mutatis mutandis, to HBM: in order to keep a participant's identity confidential, all HBM must be coded and must comply with all applicable legislation.

3.4 Logistics for HBM collection

The key principles are as follows:

- HBM should be traceable to the patient it originates from and its actual location should be tracked all along the chain of custody;
- Study specific guidelines for HBM collection will be described prospectively;
- EORTC Translational Research Division (TRD) members can be consulted to discuss HBM guideline requirements to optimize quality in collaboration with the key persons of the study (e.g. Study Coordinators, pathologists, TR project leader from the Group);
- In the case of the involvement of a service provider, a service agreement will be written. The Groups are responsible to notify EORTC Headquarters of any subcontracting of service providers;
- Reimbursement of pathologist(s) or clinical site staff for their efforts in retrieving/collecting HBM will be clarified at an early stage in the setting up of the HBM collection logistics.

3.5 Criteria for validated storage facilities

For quality assurance purposes and to facilitate HBM traceability and logistics, storage facilities should be validated by the EORTC.

3.5.1 Criteria for validation of storage facility

To be validated storage facilities are subject to fulfilling the following criteria:

- Have an assigned administrator responsible for the facility and a designated contact person to facilitate communications and keep an up-to-date organizational chart detailing all roles and responsibilities and the persons in charge;
- Keep an inventory of HBM and status of the collection, including location of HBM or other relevant information such as collection and processing procedures. Reports must be provided by the EORTC storage facilities upon request;
- Only be in institutes where the EORTC has a contractual commitment to ensure continuity in the event of change in personnel;
- Comply with any international, national or other applicable legislation.

3.5.2 Quality management of HBM

In validated storage facilities, the quality management system of HBM must cover all the following key processes: staff training, infrastructure, equipment maintenance and repair, safety and contingency plans, assessment of HBM quality, processing, storage management and distribution, document and record management, personal data protection measures and compliance with ethical and legal regulations. Some of these processes may be installed nationally to ensure compliance with local legislation. The EORTC will not duplicate existing procedures, but evaluate and recognize their equivalence to the requirements put in place by the EORTC.

Specialists in the TRD, e.g. PathoBiology Group members, may, if needed, facilitate quality management set-up by contributing their expertise.

3.5.3 Assessment of storage facilities

A storage facility that will centralized HBM in the context of an EORTC study will be assessed as follows:

- The storage facility will complete and return a self-assessment questionnaire on which expert recommendations will be given from specialized EORTC officers including members of the EORTC PathoBiology Group (PBG);
- A report will be issued and serve as basis for discussion with the storage facility on any corrective action needed;
- Formal EORTC approval will only be given after evaluation by the EORTC officers from PBG and operational check by EORTC HQ of the written and supportive documentation of the response to the deficiency;
- The EORTC Board may, on an as-needed basis, mediate any discussion between the EORTC Headquarters, the PBG and Representative(s) of the storage facility;
- EORTC storage facilities (procedures, infrastructures and resources) are further subject to audit by the EORTC.

3.6 How to access HBM

- The EORTC will ensure that access to and uses of HBM and data are in line with those described in the research protocols, consistent with the participant's informed consent, applicable laws and respect the privacy of the participant and confidentiality of the HBM and data;

To facilitate access to HBM, EORTC Groups will put in place:

- An appropriate study steering committee (SC) that will review proposals to access HBM, prior to the commencement of any HBM use;
- The SC would be typically composed of: Study Coordinator(s), Group Chair, Chair of TR or pathology subcommittees (if applicable), manager of the EORTC storage facility, e.g. pathologist or designee (as applicable), EORTC Clinical Research Physician and Statistician(s) of the relevant study(ies);
- The SC can be extended in function of the situation for the specific TR project under review. In the absence of a SC (e.g. older clinical studies) responsibilities of the SC are transferred to the Group Board or appropriate Group committee;

- The role of the SC is to define access procedures for project prioritization (see section 3.6.2);

  Project prioritization by the SC should:

  - be strongly based on clinical and scientific merit;
  - consider the contribution of the different investigators in the trial and TR project;
  - take into consideration whether or not the applicant is an EORTC member (whilst maintaining the principle of access to the wider scientific community and commitments owed to study participants and Ethics Committees);
  - respect the principle of access to HBM for the wider scientific community;
  - respect commitments owed to study participants and Ethics Committees;
  - respect protection of participant confidentiality.

- When TR projects of similar scientific and ethical value are proposed, projects presented by sites hosting the EORTC storage or research facility and sites having directly contributed to the collections will be prioritized to those presented by other/external parties.

3.6.1 Primary use of HBM

- The description of the HBM collection (e.g. type, quantities, time points), the scope (optional, mandatory or future TR) and purpose of the collection will be described in the full protocol of the clinical study approved by the Protocol Review Committee (PRC);
- The EORTC Translational Research Advisory Committee (TRAC) and TRD can comment on the relevance and feasibility of the HBM collection within each study protocol (see EORTC POL014);
- TR projects that are described in the clinical study protocol will undergo review by TRAC as part of the PRC linked protocol review procedure.

3.6.2 Secondary use of HBM

HBM may be used for purposes other than that for which it was originally collected, subject to conditions of specific agreements with its custodian(s), that it is covered by appropriate informed consent/ethics approval commensurate with the ethical principles of this policy and it being in compliance with applicable legislation. Interested parties (EORTC and non-EORTC) may apply for the use of HBM in TR projects that were not originally specified in the study protocol. For requests for access to HBM from outside the EORTC network, the EORTC is open for discussion on collaborations for the use of HBM and these will be discussed on a case by case basis. However, as a general principle, the HBM should remain within the EORTC network.

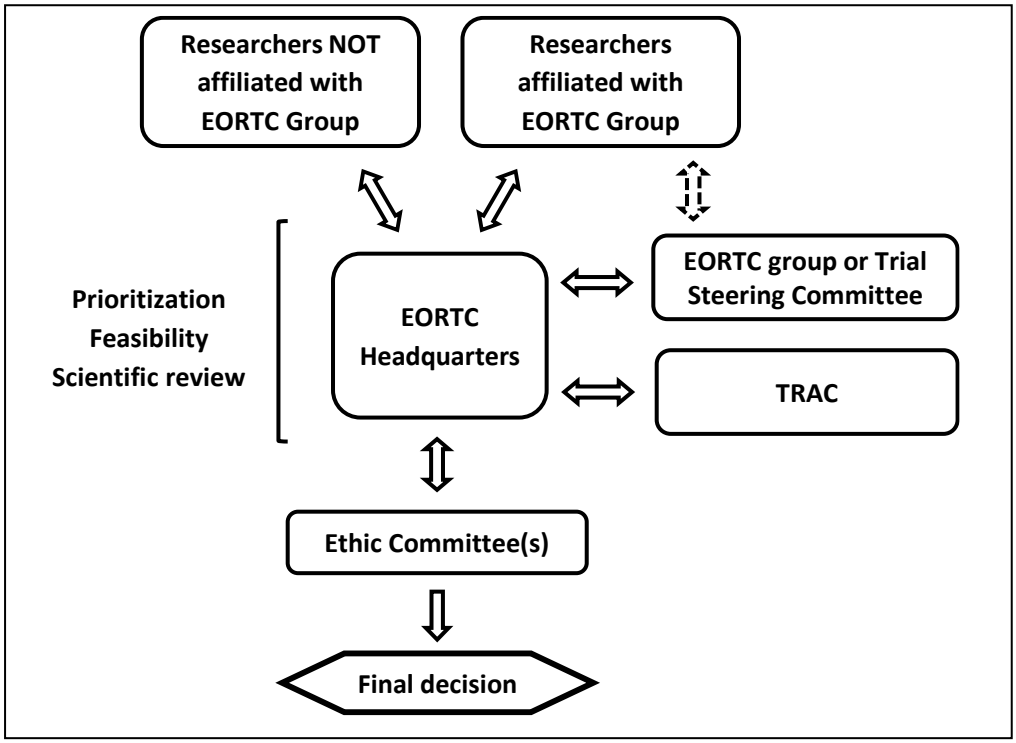
In the case where secondary use of HBM is requested, the institution from which the HBM originated will be informed if sufficient HBM is left to conduct the research.

In the case of secondary use of HBM, (i.e. for new TR projects that are not specified in the clinical study protocol) interested parties may apply for the use of HBM and will follow the next steps (see also Figure 1):

- Before submission to EORTC Headquarters, the TR projects should be discussed within the appropriate Disease Oriented Groups (DOG) and prioritized by the appropriate SC (to define the priority order of projects to use the HBM);
- A short description of the new TR project(s) will be written and submitted to EORTC Headquarters;

- An EORTC Headquarters feasibility check, including recommendations for regulatory and ethical matters, and checks on other restrictions on the use of the HBM, will take place. If in the event HBM collections are still retained at individual clinical sites, the TR project leader and the involved EORTC Group are responsible for collecting and providing information on availability of HBM for the feasibility assessment, and EORTC Headquarters is responsible for informing the custodians of the HBM (individual institutions) as agreed in existing agreements;
- Prioritized TR projects will be reviewed by TRAC (EORTC POL014);
- TRAC approved TR projects will be submitted for notification or approval to Ethics Committees (and/or other regulatory bodies if applicable);
- Once approval by the SC, EORTC Headquarters feasibility assessment and TRAC review is complete and when all applicable competent Ethics Committees approvals are in place and ethical principles are met, the TR project can be activated and laboratory analysis of the HBM can commence;
- The EORTC Board will, on an as-needed basis, mediate any discussion between the opinion of the TRAC, EORTC Headquarters feasibility assessment, the SC and the TR project leader(s);
- The minimum amount/volume of HBM required for the aims of the TR project will be released.

Figure 1. Access to HBM for secondary use.



3.6.3 Intergroup studies: Access to HBM collected by a non-EORTC group

- For intergroup studies, use of HBM in TR projects may be performed outside the EORTC network. The same principles of access to HBM, project review, approval and oversight apply.
- If an EORTC investigator wishes to collaborate with a non-EORTC group for the purposes of using HBM collected by a non-EORTC group, the non-EORTC group shall be contacted and permission granted for use of the HBM by the identified representative.

3.6.4 How to access clinical data

- The clinical data of the study associated with the HBM will be collected by, and a complete copy held at, EORTC Headquarters according to EORTC policy. Data accuracy is ensured through the various EORTC working procedures that address data handling (see EORTC POL002).
- In the case where clinical data need to be released for use in TR projects e.g. for ancillary studies from non-EORTC parties, this will be done on a project by project basis and in accordance with the EORTC POL008. If the TR project involves secondary use of HBM, the project leader should first submit the project through the process described in section 3.6 of this policy prior to requesting clinical data. Clinical data will be released once TRAC approval is obtained.

3.7 Distribution of research (end) results and publication

- On completion of a TR project, a summary shall be submitted to the Ethics Committee or Competent Authority, the SC and EORTC Headquarters.
- The results of TR projects shall be made available (e.g. in journals) within a reasonable time frame in accordance with EORTC POL009 and POL008 applicable to TR projects (ancillary studies).

3.8 Intellectual property rights

Intellectual property rights may differ between projects and will be clearly specified in written agreements between the EORTC and institutions. These will comply with existing trial arrangements or other agreements already in place.

3.9 Finances

Travelling expenses of EORTC members or external experts acting as voluntary consultants for the EORTC (e.g. for auditing of HBM storage facility infrastructures) will be refunded according to EORTC policy.

Describe briefly the objective of the POL.

Additional sections might be added as necessary.

4 ASSOCIATED DOCUMENTS

Document title	Reference (file name or path)
Protection of human subjects participating in medical research	EORTC POL002
Release of data from EORTC studies for use in External Research Projects	EORTC POL008

Document title	Reference (file name or path)
Disclosure of Results and Publication Policy	EORTC POL009
Translational Research Advisory Committee (TRAC)	EORTC POL014

5 REFERENCES

- Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on human rights and biomedicine, Oviedo, 4.IV.1997.
- Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin – (CoE Rec(2006)4).
- Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Strasbourg, 25.I.2005.
- OECD Guidelines on Human Biobanks and Genetic Research Databases (2009).
- EU Clinical Trials Directive 2001/20/EC.

6 DOCUMENT HISTORY

Version number	Brief description of change	Author	Effective date
1.00	Initial version	Jacqueline Hall and the EORTC PathoBiology Group	31 Jan 2011
2.00	Custodianship remains with institution. Custodianship differentiates from geographical storage. EORTC is responsible to ensure the integrity of the chain of custody. Definition of Biological material includes 3 types: additional material (collected for research purposes), pre-existing material of diagnostic value and pre-existing material not of diagnostic value.	Jacqueline Hall and the EORTC PathoBiology Group	29 Mar 2012
2.1	EORTC storage facilities updated to validated storage facilities. Assessment process of validated storage facilities update. Administrative changes.	Emilie Varin	05 Jun 2015
2.1	No change	Marie Morfouace	22 May 2018