

Protection of Human Subjects Participating in Clinical and Translational Research

**POL002
Version 2.3**

**ALWAYS REFER TO THE INTRANET
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1 PURPOSE

This policy provides guidance on how to ensure protection of the rights, safety and well-being of trial subjects pertaining to all EORTC activities within the European (EU) regulatory framework. Adequate information of each patient and efficient monitoring of drug/treatment safety through pharmacovigilance is a particular focus of this policy. Moreover, it complements Policies 020 and 021 and ensures a homogeneous conduct of studies involving personal data and/or human biological material.

2 DEFINITIONS

- ◆ **Declaration of Helsinki:** a statement of the World Medical Association that spells out the ethical principles for medical research involving human subjects, including research on identifiable human material and data.
- ◆ **International Conference on Harmonization – Good Clinical Practice (ICH-GCP):** an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.
- ◆ **European Directives/Regulations:** EU Directives/Regulations are legislative acts which set minimum requirements that Member States of the European Union are obliged to reflect in national laws, regulations and administrative provisions.
- ◆ **EORTC Headquarters (HQ):** the central trial management unit of the EORTC. It provides scientific, logistic and administrative support for the conduct of EORTC trials.
- ◆ **EORTC Independent Data Monitoring Committee (IDMC):** 1) Committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.
(2) An independent committee of clinicians and statisticians whose task is to review the status of a clinical trial and make recommendations to the clinical research group concerning the trial's continuation, modification and/or publication.
- ◆ **Human Biological Materials (HBM):** Any type of tissue or body fluid or derivative, including but not limited to nucleic acids, taken from participants in clinical studies. This includes residual HBM left after laboratory testing.

3 POLICY

Research conducted under the auspices of EORTC is performed in compliance with the principles laid down in the Declaration of Helsinki (and its amended versions), unless other version applies by virtue of any national law. The EORTC policy on collection, storage and use of the HBM is also applicable to clinical studies involving research on HBM.

In addition to the Declaration of Helsinki, EORTC adheres to the principles expressed in ICH-GCP (International Conference on Harmonization - Good Clinical Practice, E6(R2)).

Requirements of the EU Data Protection Regulation (EU 2016/679, GDPR) and applicable national requirements, limitations and derogations must be complied with in the scope of all EORTC activities.

Moreover, the CPMP/ICH/135/95 note from the European Medicines Agency (EMA), Directives 2001/20/EC and 2005/28/EC, laying down principles, detailed guidelines for good clinical practice, and Clinical Trials Regulation (EU No 536/2014), as it becomes applicable.

Any other applicable national requirements are also binding to EORTC and EORTC investigators. This pertains in particular to any national laws, regulations, and administrative provisions reflecting the EU Directives that govern or are applicable to research involving human subjects.

4 PROTOCOL APPROVAL

Protocols for clinical trials and other clinical studies such as translational research studies using HBM under the auspices of EORTC state that research is conducted in compliance all applicable EU and national laws.

EORTC protocols provide treating physicians/investigators and their staff with information to ensure that studies are performed at the highest possible standard, with particular attention to the patients' rights and their protection. Study protocols including consent documents must be approved in advance by the EORTC Protocol Review Committee, as per POL016 "Protocol Development Process, Selection and Approval Procedures for EORTC Studies".

Study protocols, including clinical studies involving collection and use of the HBM, are approved by competent authorities (as applicable), leading and/or local ethics committee(s), and any other regulatory bodies (as specified by national regulations). A proof of protocol approval by the applicable regulatory bodies must be provided to the EORTC HQ prior to the site authorization.

5 CONFIDENTIALITY AND DATA PROTECTION

EORTC ensures that all safeguards are in place to minimize any eventual risk of potential data breaches and the GDPR requirements are implemented, as per data protection policy (POL021).

Besides, EORTC regularly monitors all its data processing of activities to ensure compliance with the privacy by design principle.

6 ADEQUATE INFORMATION TO PATIENTS

6.1 Research participant information and consent

In compliance with principles of ICH-GCP, participants in EORTC studies and prospective research projects are adequately informed prior to their inclusion. In particular, all patients are informed about the voluntary nature of their participation, confidentiality, and protection of personal data, potential risks and benefits of participation, insurance coverage and the possibility of withdrawal at any time. The principle of patient autonomy is clearly enforced.

Freely given informed consent for participation to a study or project is obtained from and documented in writing, signed and dated personally by each patient (or by an individual or juridical, or other body authorized under applicable law to consent on behalf of a prospective subject). This consent must be obtained prior to the inclusion in a study or project. At registration / randomization, EORTC HQ documents the date of the actual patient's consent, which must not be posterior to the date of entry to the trial. The correctness of this date is one of the priority checks during the on-site

monitoring. Where patients are given a choice during the information and consent process, EORTC records choices made in order to ensure they are respected.

There may be exceptional circumstances where the nature of disease is such that it is not possible to obtain an appropriate consent prior to the entry in the research project. In this case, participant inclusion without consent (eventually yet) will only be permitted if approved by the competent Ethical Committee and if allowed by applicable legislation in this specific situation.

Further use of research participants' data and/or HBM will be performed either after obtaining a new participant's consent or based on another legal basis in compliance with the GDPR, and any applicable Ethical review(s) and national laws.

6.2 Patient Information Sheet and informed Consent Form (PIS/IC)

EORTC has developed informed consent templates in English which are regularly reviewed to ensure that EORTC patient-facing documents comply with existing and legally binding requirements.

The PIS/IC master version for a particular trial in English is developed from the above-mentioned templates and provides necessary information to be communicated to the patients. The master version of the PIS/IC in English is considered as an integral part of any protocol and/or project (as applicable).

A copy of a translated and version-controlled PIS/IC in the local language is adequately reviewed by relevant experts, including, when relevant, the national coordinator in each participating country and (when possible) by patient representatives. In countries where EORTC has a liaison office, these activities may be performed and/or coordinated by the EORTC liaison office.

Any written, visual representation, or otherwise any form of information provided to the patients within the framework of EORTC studies and projects must be approved by the competent Ethics Committee(s) and (if applicable) by the Competent Authorities as per applicable legislation.

EORTC, as sponsor, actively participates in all steps of the above reviews. When acting on behalf of a third-party sponsor, EORTC may be involved in the review of PIS/IC, where delegated.

7 PHARMACOVIGILANCE: DRUG/TREATMENT SAFETY

Protection of human subjects can be ensured by an adequate monitoring of drug/treatment safety.

The Pharmacovigilance Department at the EORTC HQ is in charge of recording all Serious Adverse Events occurring in EORTC trials and taking care of all regulatory requirements.

In addition, all safety aspects of each on-going EORTC trial are reviewed by a medical review team of the trial.

If specified by the study protocol (mainly for large phase III trials) or in case suspicious safety issues emerge, the support of the EORTC Independent Data Monitoring Committee (IDMC) can be requested. Please refer to the EORTC policy on Independent Data Monitoring Committee and Interim Analyses (POL004).

Given the above-mentioned safeguard procedures and structures, any exposure of patients to an unacceptable level of risk will be detected early on, so that appropriate action, including early termination of a trial, can be taken without undue delay.

EORTC ensures that Ethics Committees are kept informed on the trial progress with an emphasis on the safety information via yearly reports. All comments and questions concerning Ethics Committees (if any) are appropriately replied and addressed.

8 PRINCIPLES APPLYING TO TRANSLATIONAL RESEARCH

8.1 Translational research specified in the study protocol

Study protocols or research projects may foresee that the patient authorizes storage of and access to his/her HBM for a defined research project specified in the protocol. HBM of a concerned patient is to be identified using a code (in accordance with privacy and confidentiality principles).

Research projects may be mandatory (e.g. integrated into the clinical study), optional, or they can constitute a stand-alone prospective research project. EORTC needs to clearly specify the type of a proposed research and provide a justification for mandatory research. Specific wording should be foreseen in the EORTC PIS/IC templates.

In compliance with applicable legislations, all research projects are covered by the appropriate approval of the competent ethics committee.

8.2 Storage of HBM for further, not yet defined, research

It is possible that HBM is stored for a further research, which cannot be described at the time of the initial collection. If this is the case, the general scope of such research should be described in the protocol. Specific mandatory wording should be foreseen in the EORTC PIS/IC templates.

EORTC mandates that all further research projects are conducted in compliance with the declaration of Helsinki, following recognized ethical standards, and applicable legislation. Whether or not the patient can be contacted to obtain his/her consent for a specific research project will be determined on a case-by-case basis. EORTC takes into account the scope of the new research project (specifically in the view of the scope of initial consent), the feasibility and means of information/consent at the time of research (given some patients may not be alive anymore), as well as the applicable legislation and opinion of the relevant Ethics Committee(s).

EORTC policy on Collection, Storage and Use of Human Biological Material (POL020) further describes modalities related to the processing of HBM.

8.3 Withdrawal of consent for use of HBM in research

If the patient wishes to withdraw or alter his/her consent for the use of the HBM in research, he/she is free to do so at any time. In such an event the investigator should notify the EORTC HQ. Further use of the HBM in research is halted. However, parts of the project prior to the date of withdrawal will be completed, and data and information already generated by the time of withdrawal will continue to be used (except for further research). Leftover of HBM is either returned to the originating clinical site, fully anonymized or destroyed.

9 FEEDBACK OF INDIVIDUAL RESULTS TO PARTICIPANTS

Where relevant, principle investigator of the clinical study will discuss research findings with the research participant. The investigator takes due care to protect confidentiality of the patient and respect his/her right not to receive such information.

If the results are linked to any hereditary finding (on cancer genes or incidental findings), the principle investigator will immediately inform EORTC, producing a report of the hereditary findings. EORTC will share the report with the patient's clinician, according with the EORTC Policy "Reporting of genetic results and incidental findings" (POL022).

10 TRANSPARENCY

Full list of EORTC studies is publicly available on its website.

According to EORTC Publication Policy POL009, where possible, EORTC publishes results of its research in peer reviewed journals, including negative results. Practice changing results may also be communicated via the EORTC newsletter, made available on the EORTC website, and/or distributed to patient organizations.

Sharing research data is governed by EORTC Data Sharing POL008.

EORTC clinical research results (including agglomerated data, which do not include individual patients' data and/or anonymized data) are made publicly available via the European/national clinical trials data base(s) as required by the applicable legislations.

Coded patient data can be made public and/or uploaded to publicly available data platforms/repositories only provided patients gave specific consent to do so or that such release is permitted by the applicable legislation and/or is ethically acceptable. In any case, no such release will take place prior to EORTC formal confirmation that all relevant safeguards are in place and all steps are successfully completed in order to comply with all applicable legislations.

11 MEASURES TO ENSURE COMPLIANCE

The EORTC Board delegates to the Chief Executive Officer all responsibility for monitoring the compliance of institutions with the above-mentioned procedures on patient information. The Chief Executive Officer puts in place appropriate verification procedures.

The Chief Executive Officer has a full authority to take appropriate corrective actions (including temporary or permanent suspension of institutions from registration/randomization) whenever non-compliance with these procedures is suspected or proven.

12 REFERENCES

- ◆ Guideline for ICH-GCP (Good Clinical Practice)
- ◆ Declaration of Helsinki
- ◆ EU Directive 2001/20/EC (Clinical Trials Directive) and EU Clinical Trials Regulation as it becomes applicable (CTR, EU 536/2014)
- ◆ EU Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice
- ◆ EU General Data Protection Regulation (GDPR, EU 2016/679)

13 DOCUMENT HISTORY

Version N°	Brief description of change	Author	Effective date
1.0	Initial Release	Denis Lacombe	
1.1	Deletion of OHRP chapter and few small changes in the Introduction chapter	Ivana Teodorovic	04 May 2004
2.0	Complete revision of all chapters	Ullrich Bethe	06 Sep 2006
2.01	Update to the current legal framework & clarifications	Anastassia Negrouk	02 Mar 2012
2.1	Update according to new organization chart.	Anastassia Negrouk	11 May 2015
2.2	Various updates related to the release of the POL021, clarifications.	Anastassia Negrouk	15 Jun 2018
2.3	Minor changes to align to the new structure of the organization and the new governance	Roxana Albu	19 July 2021