

Protection of Human Subjects Participating in Clinical and Translational Research

POL002

Version 2.2

ALWAYS REFER TO THE INTRANET TO CHECK THE VALIDITY OF THIS DOCUMENT

<p>Author</p> <p><i>Head international Policy Office</i></p> <p>Anastassia Negrouk</p>	<p>Signature:</p>	<p>Date: (ex: 10-Feb-2017)</p>
<p>Authorized by:</p> <p><i>Director General</i> <i>On Behalf of the Board</i></p> <p>Denis Lacombe</p>	<p>Signature:</p>	<p>Date: (ex: 10-Feb-2017)</p>

This document is the property of EORTC.

No release of this document is granted for any use without the written agreement of the EORTC.

Table of Contents

1 PURPOSE.....3

2 DEFINITIONS3

3 POLICY.....3

4 PROTOCOL APPROVAL.....4

5 CONFIDENTIALITY AND DATA PROTECTION4

6 ADEQUATE INFORMATION TO PATIENTS4

 6.1 Research participant information and consent.....4

 6.2 Patient Information Sheet and informed Consent Form (PIS/IC).....5

7 PHARMACOVIGILANCE: DRUG/TREATMENT SAFETY5

8 PRINCIPLES APPLYING TO TRANSLATIONAL RESEARCH6

 8.1 Translational research specified in the study protocol6

 8.2 Storage of HBM for further not yet defined research6

 8.3 Withdrawal of consent for use of HBM in research6

9 FEEDBACK OF INDIVIDUAL RESULTS TO PARTICIPANTS6

10 TRANSPARENCY6

11 MEASURES TO ENSURE COMPLIANCE7

12 REFERENCES.....7

13 DOCUMENT HISTORY.....7

1 PURPOSE

This policy provides guidance on how to ensure the 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 are a particular focus of this policy. Moreover, this policy is complementary to the Policies 020 and 021 and ensures 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 Board:** the steering and executive body which advises the EORTC General Assembly on new activities and formulates proposals to be ratified by the EORTC General Assembly.
- ◆ **EORTC Headquarters:** the central trial management unit of the EORTC. It provides scientific, logistic and administrative support for the conduct of EORTC trials.
- ◆ **EORTC Human Research Participant Protection Panel (HRPP; former Institutional Review Board- IRB):** a panel responsible for safeguarding the rights and welfare of subjects participating in clinical trials conducted with the support of the EORTC Headquarters. It validates the informed consent templates used in EORTC trials and ensures that EORTC activities are conducted without conflict of interest, according to EORTC Policy "Conflict of Interest - Confidentiality" (POL001).
- ◆ **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 the EORTC is performed in compliance with the principles laid down in the Declaration of Helsinki (last amended by the 59nd World Medical Assembly, Seoul, Korea, October 2013), unless other version apply by virtue of any national law. The EORTC policy on HBM collection, storage and use 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, CTR) 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 and detailed guidelines for good clinical practice, Clinical Trials Regulation (EU No 536/2014, as it becomes applicable, GDPR) apply to clinical trials.

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 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 the EORTC state that research is conducted in compliance with the principles of the Declaration of Helsinki and all applicable EU and national laws.

EORTC protocols provide treating physicians/investigators and their staff with information to ensure that a study is 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. The work of the EORTC Protocol Review Committee is governed by the "Protocol Development Process, Selection and Approval Procedures for EORTC Studies" (POL016).

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

5 CONFIDENTIALITY AND DATA PROTECTION

EORTC ensures that all safeguards are in place to minimize any eventual risk of breaches and complies otherwise with requirements of GDPR as implemented in its policy on data protection (POL021). The EORTC regularly checks all its procedures relevant to the processing of personal data, so that it ensures privacy by design and compliance with GDPR.

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 his/her participation, confidentiality and protection of his/her 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 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) before he/she is inclusion in any study or project. At registration / randomization, EORTC Headquarters document 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 choice during the information and consent process, EORTC records choices made in order to ensure they are respected in the scope of any relevant processing activity.

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 scope/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 GDPR, 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 by the EORTC IRB/HRPP (each new version is reviewed prior to its use). These templates ensure that EORTC documents for patient information comply at all times 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 patient. 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 the 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 the patient's representative. In countries where the EORTC has a liaison office, these activities may be performed and/or coordinated by the EORTC liaison office.

All written, visual and any non-oral form of information provided to the patients within the framework of EORTC projects is approved by the competent Ethics Committee(s) and (if applicable) by the Competent Authorities as per applicable legislation.

The 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

The protection of human subjects is also promoted by adequate monitoring of drug/treatment safety. The Pharmacovigilance Unit at EORTC Headquarters 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 Headquarters 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, the EORTC is confident that 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.

The EORTC ensures that Ethics Committees are kept informed of the trial progress with an emphasis on the safety information via yearly reports. All comments and questions of Ethical 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 project may foresee that the patient authorizes storage of and access to his/her HBM for a defined research project specified in the protocol. HBM linked to the concerned participant is identified using the code (in accordance with privacy and confidentiality principles).

Research projects may be mandatory (e.g. integrated into the clinical study), optional or can constitute a stand-alone prospective research project. EORTC clearly specify if proposed research is optional or mandatory and provides appropriate justification for mandatory research. Specific wording is foreseen in the EORTC PIS/IC templates. In compliance with applicable legislation, 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 further research, which cannot be described at the time of the initial collection. If this is the case, the general scope of such research is described in the protocol. Specific mandatory wording is 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 needs to be contacted in order to obtain his/her consent for a specific research project, is 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 of 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 relevant Ethics Committee (s).

EORTC policy on Human Biological Material Collection, Storage and Use of biological materials (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 notifies EORTC Headquarters. 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 at the time of withdrawal will continue to be used (except for further research). Left over HBM is either returned to the originating clinical site, fully anonymized or destroyed.

9 FEEDBACK OF INDIVIDUAL RESULTS TO PARTICIPANTS

If the research gives rise to findings of analytical and clinical validity as well as clinical utility on the current or future health or quality of life of individual research participants, the principle investigator of the clinical study will discuss, if required, these results with the involved participant. The investigator takes due care to protect confidentiality and respect the right of the patient not to receive such information.

10 TRANSPARENCY

Full list of EORTC studies is publically available on its web site.

It is the EORTC policy, where possible, to publish results of its research in peer reviewed journals, including negative results. Practice changing results may also be communicated via the EORTC newsletter, made available through the EORTC web site and/or distributed to patient organizations.

It is the EORTC policy, to share research data. Any such sharing is done in compliance with EORTC Policy 008, provided compliance with the scope of the patient consent (unless any exception would legally apply) and only after confirmation that all relevant safeguards are in place and all steps are successfully completed in order to comply with all applicable legislation (and specifically, but not exclusively GDPR).

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

Coded individual 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 legislation (and specifically, but not exclusively GDPR).

11 MEASURES TO ENSURE COMPLIANCE

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

The Director General has full authority to take the appropriate corrective action (including temporary or permanent suspension of institutions from registration/randomization) whenever non-compliance with these procedures is suspected or proven. The EORTC Headquarters Institutional Review Board is informed directly about corrective actions taken by the Director General.

12 REFERENCES

- ◆ Guideline for Good Clinical Practice (Note for Guidance on Good Clinical Practice CPMP/ICH/135/95) and specifically its chapter 2.
- ◆ 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