Protection of Human Subjects Participating in Clinical and Translational Research

POL002
Version 2.1
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| Director General on Behalf of the Board
Denis Lacombe | | |

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Table of Contents

1 PURPOSE ................................................................................................................................................... 3
2 DEFINITIONS ............................................................................................................................................ 3
3 POLICY ....................................................................................................................................................... 3
4 PROTOCOL APPROVAL .......................................................................................................................... 4
5 ADEQUATE INFORMATION TO PATIENTS ........................................................................................ 4
  5.1 Patient Information Sheet and Informed Consent Form ................................................................. 4
  5.2 Obtaining informed consent from each patient ............................................................................ 5
6 PHARMACOVIGILANCE: DRUG/TREATMENT SAFETY .................................................................. 5
7 MEASURES TO ENSURE COMPLIANCE ............................................................................................ 5
8 PRINCIPLES APPLYING TO TRANSLATIONAL RESEARCH ........................................................... 6
  8.1 Consent ................................................................................................................................................. 6
  8.2 Translational research specified in the study protocol ..................................................................... 6
  8.3 Storage of HBM for future not yet defined research .................................................................... 6
  8.4 Withdrawal of consent for use of HBM in research ...................................................................... 6
9 FEEDBACK OF INDIVIDUAL RESULTS TO PARTICIPANTS ........................................................... 7
10 CONFIDENTIALITY AND DATA PROTECTION ............................................................................. 7
11 EORTC COLLABORATION WITH NCI COOPERATIVE GROUPS .................................................. 7
12 REFERENCES ........................................................................................................................................ 8
13 ABBREVIATIONS ............................................................................................................................... 8
14 DOCUMENT HISTORY .......................................................................................................................... 8
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 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 Policy 020 to and ensures homogeneous conduct of studies involving biological material from patients who have participated in EORTC clinical trials.

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 Headquarters 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): 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 59th World Medical Assembly, Seoul, Korea, October 2008). The EORTC policy on HBM collection, storage and use is also applicable to clinical studies involving research on HBM.

In addition to the guidelines of the Declaration of Helsinki, EORTC adheres to the principles expressed in ICH-GCP (International Conference on Harmonization - Good Clinical Practice, July 2002). ICH-GCP defines the standards of conduct for clinical research to be followed by EORTC and EORTC investigators.
All, the CPMP/ICH/135/95 note from the European Medicines Agency (EMA) and Directives 2001/20/EC and 2005/28/EC, laying down principles and detailed guidelines for good clinical practice, apply.

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 must be conducted in compliance with the principles of the Declaration of Helsinki.

EORTC protocols provide treating physicians/investigators 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) and by the leading and/or local ethics committee(s) (as specified by national regulations). Proof of protocol approval by the ethics committee(s) and competent authorities has to be provided to the EORTC Headquarters prior to site authorization.

5 **ADEQUATE INFORMATION TO PATIENTS**

5.1 **Patient Information Sheet and Informed Consent Form**

EORTC has developed informed consent templates in English which are regularly reviewed by the EORTC Headquarters Institutional Review Board (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 the protocol documents (though physically managed as separate document).

A copy of the translated and version-controlled PIS/IC in the local language is reviewed by 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 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.

A copy of the final approved document must be provided to the EORTC Headquarters. Only after receipt of this document can an institution be authorized to enter patients in a particular trial.
5.2 Obtaining informed consent from each patient

In compliance with ICH-GCP, patients in EORTC trials are adequately informed prior to any trial participation. In particular, all patients are informed about the voluntary nature of his/her participation in any trial, confidentiality and protection of his/her data, potential risks and benefits of participation in any trial, 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 registered/randomized in a study. At registration/randomization EORTC Headquarters registers 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 on-site monitoring.

6 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.

7 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.
8 PRINCIPLES APPLYING TO TRANSLATIONAL RESEARCH

8.1 Consent

HBM can only be collected, stored and used with the appropriate consent of the patient. This is mandatory in order to comply with the high ethical standards of EORTC clinical studies (Declaration of Helsinki, ICH GCP, the European Clinical Trials Directive 2001/20/EC and national laws).

8.2 Translational research specified in the study protocol

Study protocols may foresee that the patient authorizes storage of and access to his/her HBM for a defined research project specified in the protocol. This can be requested as a mandatory or optional adjunct to the clinical trial. Thus, the patient is free to join any proposed research project fully or only in part, depending on the nature of each project. Specific mandatory wording is foreseen in the EORTC PIS/IC templates.

In compliance with applicable legislation, approval by an ethics committee of the clinical study protocol including the specified research project with the HBM is obtained before the actual start of any such research.

8.3 Storage of HBM for future not yet defined research

It is possible that HBM is stored for future, not yet defined research. If this is the case, the general scope of such research is clearly described in the protocol.

Storage and use of HBM for future not yet known research with a predefined scope project needs to be specifically authorized by each patient.

Specific mandatory wording is foreseen in the EORTC PIS/IC templates. Ethics committees, as appropriate (and/or other regulatory body if applicable), are approached by the principal investigator of the research project with the collaboration of EORTC Headquarters. The appropriate Ethics Committee(s) or other appropriate body review and approval of the project is done prior to the start of any future research project on the patient’s stored HBM. Whether or not the patient needs to be contacted in order to obtain his/her consent for a future research project is determined individually by the appropriate Ethics Committee(s), i.e., for each future research project, in compliance with applicable legislation. All complimentary information about HBM storage and use in research projects is consulted in the EORTC policy on Human Biological Material Collection, Storage and Use of biological materials (POL020).

For storage and use of biological material in research for purposes not foreseen in the study protocol (secondary use of HBM), please refer to the EORTC policy on Human Biological Material Collection, Storage and Use (POL020).

8.4 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, data and information already generated at the time of withdrawal will continue to be used. HBM linked to the concerned participant is identified using the code (in accordance with privacy and confidentiality principles) and HBM is returned to the originating clinical site 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.

All other results are made available to the public via the European/national clinical trials data base(s) as per applicable legislation.

Practice changing results may also be communicated via the EORTC newsletter (publicly available through the EORTC web site) and distributed to patient organizations if pertinent.

10 CONFIDENTIALITY AND DATA PROTECTION

The EORTC constantly checks all of its procedures so that compliance with the EU Directive 95/46/EC on the protection of personal data is guaranteed. Personal data are defined as any information related to an identified or identifiable natural person (data subject). The EORTC adheres to the principles of this directive which are transparency, legitimate purpose and proportionality. In order to keep a patient’s identity confidential, clinical/personal or other health data collected by the EORTC are coded, but not anonymized. The clinical/personal data are processed for the explicitly specified and legitimate purpose defined by the study protocol, i.e., the data are used only for the purpose for which they were collected.

11 EORTC COLLABORATION WITH NCI COOPERATIVE GROUPS

Within the scope of its guidelines for international trials, NCI-CTEP (Cancer Therapy Evaluation Program) requires that EORTC Headquarters complies with some requirements of the National Cancer Institute (NCI) and the US Office for Human Research Protection (OHRP), in addition to all applicable European and national legislation.

Among these requirements is the need for the EORTC Headquarters to hold an OHRP - approved assurance (currently called a Federal Wide Assurance-FWA). This assurance allows performance of trials for which the EORTC exchange data with the NCI supported cooperative groups or otherwise benefit from NCI resources.

Since 2000, EORTC Headquarters has held CPA T4631 which was replaced by a new registration: FWA00004444 (which is linked to the EORTC Headquarters Institutional Review Board: IRB00003305).

The EORTC Headquarters Institutional Review Board meets at least annually to review all projects in collaboration with US groups as required by NCI-CTEP and OHRP.
12 REFERENCES

♦ Guideline for Good Clinical Practice (Note for Guidance on Good Clinical Practice CPMP/ICH/135/95)
♦ Declaration of Helsinki
♦ EU Directive 2001/20/EC (Clinical Trials Directive)
♦ EU Directive 95/46/EC

13 ABBREVIATIONS

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CTEP</td>
<td>Cancer Therapy Evaluation Program (of NCI)</td>
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<td>CPA</td>
<td>Cooperative Project Assurance (of NCI)</td>
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<td>EU</td>
<td>European Union</td>
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<tr>
<td>FWA</td>
<td>Federal Wide Assurance (of NCI)</td>
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<td>ICH-GCP</td>
<td>International Conference on Harmonisation – Good Clinical Practice</td>
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<td>IDMC</td>
<td>Independent Data Monitoring Committee (of EORTC)</td>
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<td>NCI</td>
<td>National Cancer Institute (United States of America)</td>
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<td>OHRP</td>
<td>Office for Human Research Protection (United States of America)</td>
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<tr>
<td>PIS/IC</td>
<td>Patient Information Sheet / Informed Consent</td>
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14 DOCUMENT HISTORY

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<td>1.0</td>
<td>Initial Release</td>
<td>Denis Lacombe</td>
<td></td>
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<tr>
<td>1.1</td>
<td>Deletion of OHRP chapter and few small changes in the Introduction chapter</td>
<td>Ivana Teodorovic</td>
<td>04 May 2004</td>
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<tr>
<td>2.0</td>
<td>Complete revision of all chapters</td>
<td>Ullrich Bethe</td>
<td>06 Sep 2006</td>
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<tr>
<td>2.01</td>
<td>Update to the current legal framework &amp; clarifications</td>
<td>Anastassia Negrouk</td>
<td>02 Mar 2012</td>
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<td>2.1</td>
<td>Update according to new organization chart.</td>
<td>Anastassia Negrouk</td>
<td>11 May 2015</td>
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