

# EORTC Tissue Research Policy

**POL015**

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**Distribution**

Everybody

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## 1. General Principles for EORTC Tissue Research

The EORTC has a longstanding tradition and experience in conducting clinical trials in Europe and beyond. However, improvements in cancer care are possible not only by running trials with new treatment modalities, but also through performing basic science research.

Translation of recent advances in understanding the molecular and cellular pathology of cancer into patient benefit is one of the activities EORTC groups are performing. Translational research is possible through collection of tumor tissue from patients entered in EORTC trials.

Tumor sample collection and tissue research can be done prospectively, following the clinical trial, or, retrospectively, after the clinical trial has been closed.

Pharmaceutical companies or even non-EORTC groups can be involved as partners in tissue research, depending on the trial and translational research project.

However, regardless on how and where tissue collection is performed and laboratory analysis done, general principles of EORTC Tissue Research Policy are to be respected. This is to ensure that scientific and ethical principles under the EORTC legal framework are respected for all types of research conducted.

Therefore:

- ◇ in case of prospective material collection (new trials beginning after initiation of this policy), patients must be adequately informed about the translational research project (see 2.6)
- ◇ In cases where material has already been collected but there is no consent for secondary use of material (future research), reasonable efforts should be made to recontact the patient. If recontacting is not possible with reasonable efforts (e.g. patient died, lost to follow up), research projects on this material might, however, still be allowed by the EORTC under certain circumstances and conditions (in certain countries some national regulations foresee exceptions for the use of stored tissue) if the project has successively gone through an ethical and scientific review process.
- ◇ Ethical and scientific review is mandatory before any material can be made available for research (submission to EORTC TRAC and EORTC IRB).
- ◇ Once EORTC TRAC and IRB have reviewed the project, it should be submitted, for review, to the institutional IRB/EC from which the project originates. In cases where no such EC exists, the project will be submitted to one or two external IRB at institutions from which material was collected.
- ◇ any intellectual property rights acquired by using tissue samples of patients entered in the EORTC should lead to compensation to EORTC (see 2.5.4 and 2.6)
- ◇ publication rules according to EORTC policy must be respected (see 2.5.3)

## 2. EORTC Tumor Bank

### 2.1. Introduction

#### 2.1.1. Histology Review

Patients are included in EORTC clinical trials on the basis of a (local) pathological diagnosis.

Final pathological diagnosis is based on the review done by the pathologist experienced in the specific disease. This is not only for quality assurance purposes but also to assure the level of confidence in the pathology diagnosis.

### 2.1.2. Translational Research

Translational research studies are integrated clinical-laboratory investigations designed to improve the prevention, diagnosis and/or treatment of cancer. These studies involve both clinical and laboratory investigations or laboratory investigations on clinical material collected during clinical trials. Generally speaking translational research is disease-specific. Creative proposals for translational studies should emerge in EORTC groups from stimulating multidisciplinary collaboration between clinicians, pathologists and basic scientists.

The role of the pathologist in translational research is twofold: to promote an active role of pathologists with a proper background in the research of the EORTC groups (in co-operation with scientists from other groups), and to make (tumor) material accessible for research. Therefore, pathologists from institutes where material originates will be actively involved in the process of material release for a specific translational research project.

### 2.1.3. Purpose of the EORTC Tumor Bank

The Tumor Bank has been set up to improve and harmonize histological review in EORTC clinical trials by providing dedicated logistical support in collection and storage of paraffin block/slides(s), pathology forms and digital images.

The Tumor Bank will also support translational research in the context of EORTC trials, by providing rapid access to information (via VTB Website) and tumor tissues needed for side-studies.

In 2002, the EORTC Data Center also received a grant from the European Commission to participate in the 'TuBaFrost' project (2002-2005). The objective of the TuBaFrost project is to create a network of collections of well-documented, standardized frozen tumor samples for research stored in cancer centers and university hospitals across Europe.

The initial costs related to supporting the creation of the EORTC Tumor Bank came from the Partheon Trust (2000-2003) while the European Commission Grant covers the costs related to the new TuBaFrost project. Any remaining costs are covered by the EORTC funds.

## 2.2. Definitions

**Translational Research:** Integrated clinical-laboratory investigations designed to improve the prevention, diagnosis and/or treatment of cancer. Involves both clinical and laboratory investigations, or laboratory investigations on clinical material collected during clinical trials.

**Real Tumor bank:** EORTC Tumor Bank Office, which is located at the EORTC Data Center in Brussels. Glass slides and paraffin blocks, related to EORTC trials, will be collected and stored here.

**Virtual Tumor Bank (VTB):** Images and information about the patients and material are stored in VISTA (EORTC Clinical database) and the VTB database

**Pathology Review:** This is review of the local diagnosis by a single central pathologist and/or a panel of pathologists

**Translational researcher:** A scientist who is involved in a laboratory research project and is interested in obtaining some material collected in a EORTC clinical trial(s).

**Digitization:** Creating digitized images from the glass slides (e.g. using a digital camera mounted on a microscope)

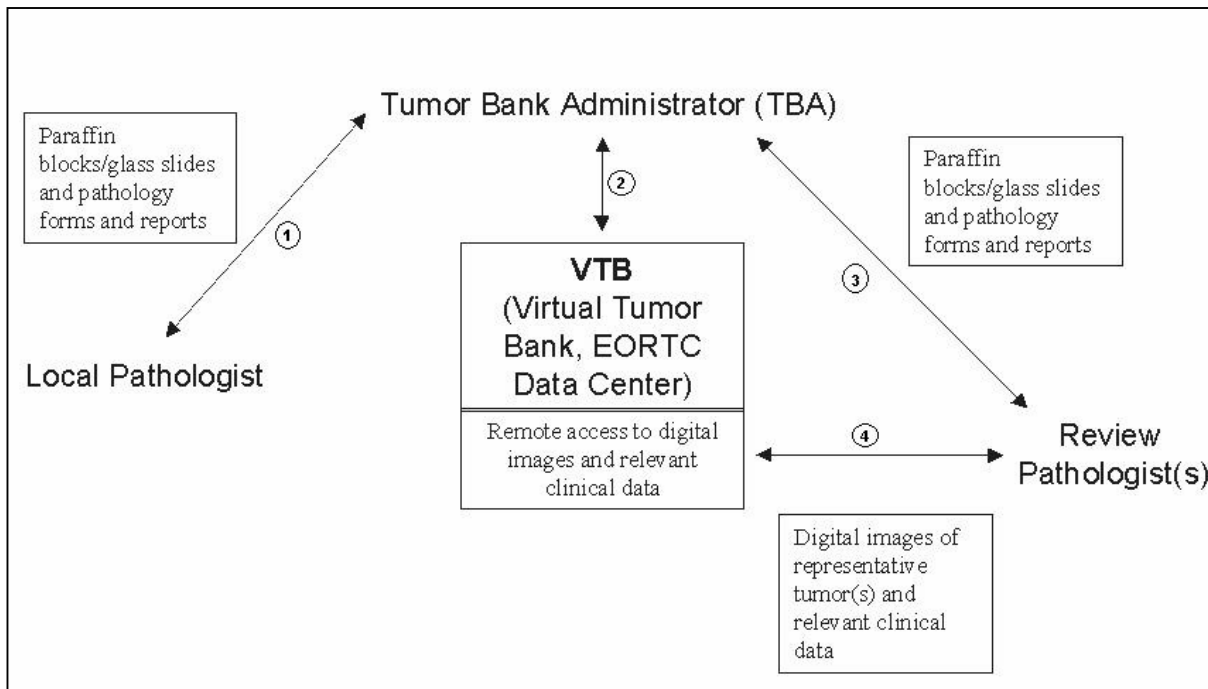
## 2.3. Objectives of the EORTC Tumor Bank

The EORTC Pathology Group and the EORTC Data Center started the Tumor Bank in September 2000. This has been initially set up as a three-year pilot project with future perspective to serve the whole EORTC.

The aims of the Tumor Bank:

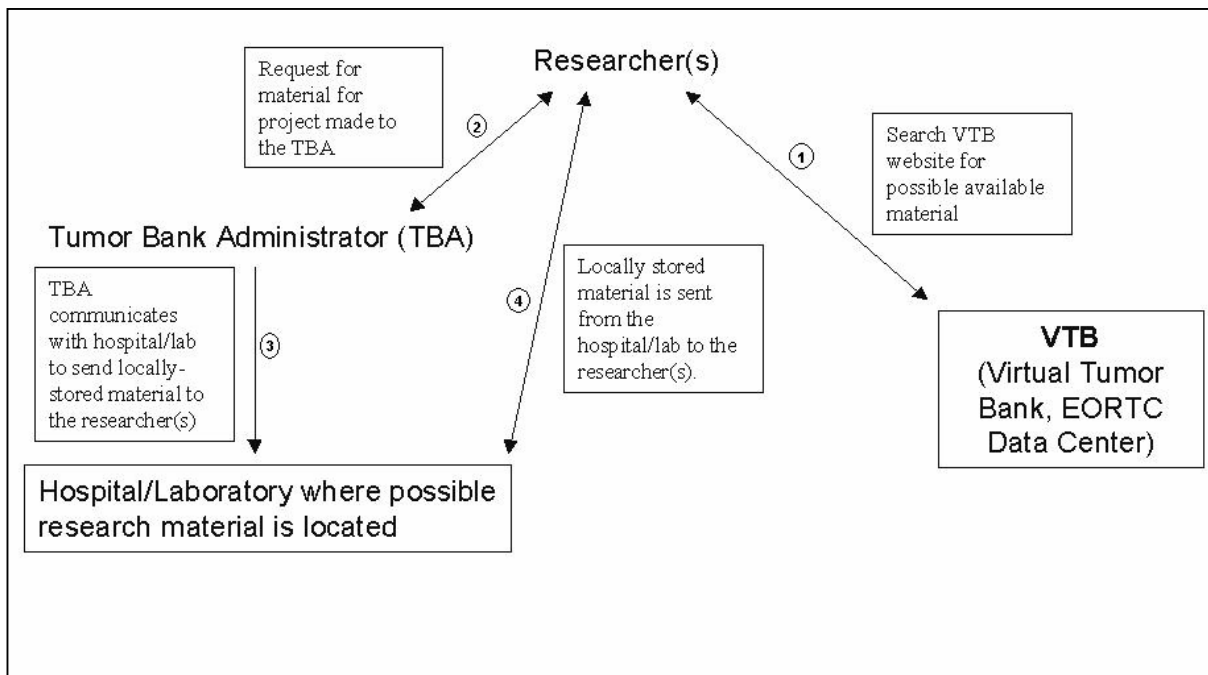
1. Improve and harmonize the histological review in EORTC clinical trials (using telepathology)

The diagram below shows how the flow of material (slides/paraffin blocks), forms and images is carried out in the review process of EORTC trials supported by the EORTC Tumor Bank:



2. Facilitate the translational research in the context of EORTC trials, by providing rapid access to the tumor tissues needed for side-studies (using an online search engine).

The diagram below illustrates the communication and flow of information and material between the entities involved in translational research involving the EORTC Tumor Bank:



Details on the rules and process involved in the above diagram are explained in further detail in section 2.5.2.

For these aims to be accomplished, the following activities will take place:

- ◇ collection and centralized storage of paraffin blocks/slides (real tumor bank)
- ◇ collection of pathology forms (virtual tumor bank)
- ◇ collection of material related information (decentralized collection of paraffin blocks, glass slides and frozen material) (virtual tumor bank)
- ◇ collection (online) of digital images (virtual tumor bank)
- ◇ development of an online Virtual Tumor Bank (VTB) website where pathologists and researchers can:
  - ◇ access the information on local and review diagnoses, site of disease etc.
  - ◇ access the material information (staining, tumor type, fixation, current location etc.)
  - ◇ access the digital images (overview [low magnification] and representative [high magnification])
  - ◇ facility for pathologists (involved in specific trials) to upload digital images and diagnoses online into the patient case

Experience coming from the pilot phase will serve as a basis for full implementation in EORTC trials as a whole.

## **2.4. Responsibilities**

### **EORTC Tumor Bank Executive Committee (ETBEC)**

The EORTC Tumor Bank is managed by the EORTC Tumor Bank Executive Committee (ETBEC). This committee is composed of members of the EORTC Data Center and the EORTC Pathology group:

- ◇ EORTC Tumor Bank Administrator (TBA)
- ◇ EORTC Tumor Bank Coordinator
- ◇ Chair of the EORTC Pathology group
- ◇ Chair of the EORTC Tumor Bank
- ◇ Chair of the Telematics subcommittee of the EORTC Pathology Group

The committee meets monthly in a teleconference to discuss the progress of the pilot phase and the next necessary actions to take in its development.

### **External support to the Tumor Bank Project**

- ◇ EORTC Executive Committee
- ◇ EORTC Protocol Review Committee (PRC)
- ◇ EORTC Translational Research Advisory Committee (TRAC)
- ◇ EORTC Institutional Review Board (IRB)
- ◇ Chairman of the EORTC Laboratory Research Division
- ◇ Representatives of the EORTC IT unit
- ◇ EORTC Data Center Legal Advisor

## **2.5. Material Use**

### **2.5.1. For review/diagnostic purposes**

As the patients are randomized into clinical studies, a request will be made from the EORTC Tumor Bank Office to the local pathologist to send the material (paraffin blocks/glass slides), completed local pathology form and institutional pathology report to the EORTC Tumor Bank Office in Brussels.

These forms and material are then relayed to the review/reference pathologist for the study.

If panel review is to take place within the study, the EORTC Tumor Bank Office will contact the members and instruct them to use the VTB website to review the patient case and images and submit their diagnoses.

Material (paraffin blocks/glass slides) will be permanently stored in the EORTC Tumor Bank Office unless the local pathologist has specifically requested return of some or all of the material. In the latter situation, all the material requested will be sent back to the local pathologist.

As soon as pathology review has been completed for the patient case, the EORTC Tumor Bank Office will distribute, to all the pathologists involved in reviewing of the patient case, a copy of all the review pathology forms.

### **2.5.2. For Translational Research**

#### **2.5.2.1. Prospective**

The description of translational research and type of material required for translational research for the study will be found in the PRC/TRAC-approved protocol. The EORTC Tumor Bank Office will send the material (paraffin blocks/slides) required for the study's translational research to the laboratory performing translational research.

For distribution of frozen material (this is never stored in the EORTC Tumor Bank Office), this will be evaluated and discussed on a case-by-case basis between the EORTC TB Office and the Group taking into account of the financial status, logistical organization, and time frames.

It will be the responsibility of the EORTC Tumor Bank Office to retrieve the unused material back from the laboratory performing translational research.

#### **2.5.2.2. Retrospective**

##### **2.5.2.2.1. EORTC Group/single EORTC institute requesting material from own trial**

The responsible scientist (as mentioned in the protocol) will send the full project with a list of material required to the EORTC Tumor Bank Office. The EORTC Tumor Bank Office will then forward this to the EORTC Tumor Bank Executive Committee (ETBEC), the Translational Research Advisory Committee (TRAC) and the EORTC Institutional Review Board (IRB).

TRAC has an advisory role especially related to scientific matters. IRB is involved in approving the ethical aspects and will make the final approval of the project.

After approval, the EORTC Tumor Bank Office will send the material (in case of paraffin blocks/slides stored in the EORTC Tumor Bank Office) or will contact the relevant institution where the respective material (locally stored paraffin blocks/glass slides and frozen tissue) is stored. The latter will then be sent directly to the laboratory responsible for trial translational research. The TBA will receive a copy of the material form that is sent and returned with the locally stored material.

In case there is disagreement in approving the project and use of material, the EORTC Executive Committee will mediate discussion between TRAC, IRB and the responsible scientist.

#### 2.5.2.2.2.EORTC Group/single EORTC institute requesting material from another EORTC Group

The responsible scientist (as mentioned in the protocol) will send the full project with a list of material required to the EORTC Tumor Bank Office. The EORTC Tumor Bank Office will then forward this to the EORTC Tumor Bank Executive Committee (ETBEC), the Translational Research Advisory Committee (TRAC), EORTC Institutional Review Board (IRB) and the chairman of the group where the material originated. The chairman(s) of the group(s) must approve release of material.

TRAC has an advisory role especially related to scientific matters. IRB is involved in approving the ethical aspects and will make the final approval of the project.

After approval, the EORTC Tumor Bank Office will send the material (in case of paraffin blocks/slides stored in the EORTC Tumor Bank Office) or will contact the relevant institution where the respective material (locally stored paraffin blocks/glass slides and frozen tissue) is stored. The latter will then be sent directly to the laboratory responsible for trial translational research. The TBA will receive a copy of the material form that is sent and returned with the locally stored material.

In case there is disagreement in approving the project and use of material, the EORTC Executive Committee will mediate discussion between TRAC, IRB, chairman(s) of the group(s) and the responsible scientist.

#### 2.5.2.2.3.Request from Academic Institute/Organization outside the framework of EORTC

Academic institutes/organizations could request access to tissue samples for their research work. In these situations, they could take the opportunity of using tissue samples from the EORTC Tumor Bank following approved agreement/contract described under 2.5.4.

The responsible scientist (as mentioned in the project) will send the full project to the EORTC Tumor Bank Office. The EORTC Tumor Bank Office will then forward this to the EORTC Tumor Bank Executive Committee (ETBEC), the Translational Research Advisory Committee (TRAC), EORTC Institutional Review Board (IRB) and the chairman of the group where the material originated. The chairman(s) of the group(s) must approve release of material.

TRAC has an advisory role especially related to scientific matters. IRB is involved in approving the ethical aspects and will make the final approval of the project.

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In case there is disagreement in approving the project and use of material, the EORTC Executive Committee will mediate discussion between TRAC, IRB, chairman(s) of the group(s) and the responsible scientist.

#### 2.5.2.2.4.Request from Pharmaceutical Industry

Pharmaceutical companies may wish to perform tissue research to support their drug development and registration process within the framework of cooperation with EORTC.

The responsible scientist (as mentioned in the project) will send the full project to the EORTC Tumor Bank Office. The EORTC Tumor Bank Office will then forward this to the EORTC Tumor Bank Executive Committee (ETBEC), the Translational Research Advisory Committee (TRAC), EORTC Institutional Review Board (IRB) and the chairman of the group where the material originated. The chairman(s) of the group(s) must approve release of material.

TRAC has an advisory role especially related to scientific matters. IRB is involved in approving the ethical aspects and will make the final approval of the project.

After approval, the EORTC Tumor Bank Office will send the material (in case of paraffin blocks/slides stored in the EORTC Tumor Bank Office) or will contact the relevant institution where the respective

material (locally stored paraffin blocks/glass slides and frozen tissue) is stored. The latter will then be sent directly to the laboratory responsible for trial translational research. The TBA will receive a copy of the material form that is sent and returned with the locally stored material.

In case there is disagreement in approving the project and use of material, the EORTC Executive Committee will mediate discussion between TRAC, IRB, chairman(s) of the group(s) and the responsible scientist.

### **2.5.3. Methodology of Publication/Publication Policy for results of side-studies related to translational research**

Results of side studies related to translational research may be published or presented to the medical community before trial maturity and publication of the primary endpoint (final results) of the trial, provided the data related to those side studies are mature and provided there is no direct relationship between these results and the primary trial endpoint.

Such publications must be reviewed, authorized and approved by the statistician and coordinating physicians in charge of the trial, chairman of group and study coordinator (along which material has been collected).

A list of authors must be created at start of project/side-study so that unnecessary conflicts do not occur

The EORTC group(s) concerned by the data transfer will be clearly acknowledged and the EORTC trials will be referenced with their official number and title.

Inclusion of the pathologists (who provided respective material for research) and EORTC Data Center representative(s) as co-authors will be considered for each project on a case by case basis with respect to the extent of their involvement in the project

### **2.5.4. Contracts and Legal Documents**

For all types of translational research, a contract must be created for each project whether it is between academic laboratories or pharmaceutical companies.

This contract will address specific conditions for use of material and results coming from this research (benefits, patenting and any possible drug registration).

This contract will guarantee appropriate compensation for EORTC research for any intellectual property rights acquired. Any intellectual property rights must be discussed with the EORTC Executive Committee on a case by case basis.

## **2.6. Patient Information Sheet - Informed Consent (PIS-IC)**

Patient must receive complete and adequate information regarding the translational research project (aims, storage, data protection, voluntary aspects, approval system, etc.). This is mandatory to comply with high ethical standards in the scope of EORTC clinical trials (Helsinki Declaration, ICH GCP, national laws and in future European Directive on clinical trials). Therefore EORTC foresee standard PIS templates:

- ◇ in case of translational research project, which is an optional part of a prospective clinical trial, patient will consent for a clinical trial, and in a separate consent form for the translational research on tissue (biological material)
- ◇ in case of translational research project, which is a mandatory part of a prospective clinical trial, patient will consent together for the clinical trial and translational research on tissue (biological material)

In cases where material has already been locally collected but there is no consent for secondary use of material (future research), reasonable efforts should be made to recontact the patient. If recontacting is not possible with reasonable efforts (e.g. patient died, lost to follow up), research projects on this material might, however, still be allowed by the EORTC under certain circumstances and conditions (in certain countries some national regulations foresee exceptions for the use of stored tissue) if the project has successively gone through an ethical and scientific review process.

It cannot be excluded that results from use of patient's biological material could lead to an acquisition of intellectual property rights by the EORTC. Patients will not receive any financial return. Should there be any financial return for the EORTC, it will be reinvested only in cancer research to improve cancer care.

### 3. List of abbreviations

EORTC EC:	EORTC Executive Committee
ETBEC:	EORTC Tumor Bank Executive Committee
IRB:	Institutional Review Board
PIS-IC:	Patient Information Sheet-Informed Consent
PRC:	Protocol Review Committee
TBA:	EORTC Tumor Bank Administrator
TRAC:	EORTC Translational Research Advisory Committee
VTB:	Virtual Tumor Bank

### 4. Appendices and references

Document title	Reference (file name)
World Medical Association Declaration of Helsinki	
International Conference on Harmonisation – Good Clinical Practice	ICH GCP