EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

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Protocol Development Process, Selection and Approval Procedures for EORTC Studies

POL016
Version 3.3

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

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1 PURPOSE

The present policy describes the protocol development process and the selection and approval procedures for EORTC studies.

The present policy focuses on the role of the different EORTC committees in the study selection and development, on the criteria used at different milestones, and on the process for submitting study proposals to EORTC and developing them into full protocols.

2 DEFINITIONS

- **EORTC Strategy**: the recommendations made by the EORTC Board for study parameters in order to ensure that the study concepts developed by EORTC Groups are in line with the missions of the organization.
- **Feasibility**: the process of consultation, whether internal or external to EORTC Headquarters (HQ), in order to ensure that a study can be performed within reasonable timelines by the EORTC HQ and the EORTC network of investigators.

3 POLICY

EORTC projects must be channeled through specific procedures to guarantee that they are in line with the EORTC mission. The procedures must be efficient while preserving EORTC independence and scientific excellence. Without exception, all EORTC Groups or Task forces must adhere to the same principles. The development of all EORTC studies is governed by the current policy (POL016).

4 RESPONSIBILITIES

- **The EORTC Group** will appoint a Study Coordinator for each proposed study.
- **The Study Coordinator** will submit the study concept to the EORTC Board and, if endorsed, subsequently submit the study protocol synopsis to the EORTC Protocol Review Committee (PRC) for approval, before proceeding to protocol development in cooperation with a designated EORTC HQ team.
- **The EORTC HQ** will assess the feasibility of all proposed studies and estimate the required EORTC resources. The EORTC HQ team will assist the Study Coordinator through protocol synopsis and study protocol development and review.
- **The EORTC Protocol Review Committee (PRC)** will review all proposed studies based on the submitted protocol synopsis and assess their scientific value in grading their originality, interest, methodology, and feasibility.
- **The EORTC New Drug Advisory Committee (NDAC)** will advise the EORTC Groups and PRC for EORTC participation in new drug development programs in cooperation with industrial partners.
- **The EORTC Translational Research Advisory Committee (TRAC)** will advise the EORTC Groups and PRC for implementation of translational research projects in EORTC clinical studies.
- **The EORTC Cancer in the Elderly Task Force (ETF)** will advise the EORTC groups and PRC for specific aspects regarding the treatment of elderly patients in EORTC clinical studies.

- **The EORTC Board** is responsible for the strategic endorsement of studies to be supported by EORTC (subsequent approval by PRC is required) and assess their feasibility.
- **EORTC Project Management** supports the teams in the operational set-up of studies. Project Management, in close collaboration with the Accounting and Finances reporting unit, provides the resource estimations for EORTC HQ and negotiates with the Group officers concerning the group and site compensation.

5 OVERVIEW

The objective of this policy is to guarantee the adherence to the EORTC scientific strategy and the application of the principles of independence, aiming to maintain the capacity for scientific excellence.

The EORTC principles of independence include:

- The study protocol synopsis is reviewed and approved by the independent PRC.
- The database of EORTC studies is handled by EORTC HQ or an equivalent independent organization until at least primary endpoint maturity.
- EORTC HQ or an equivalent independent organization has primary responsibility for the final study analysis and publication.

In addition, a charter must regulate IDMC and biological material storage and rules for access.

EORTC study concepts may be generated through several routes.

Most frequently, an EORTC Group generates a proposal that is then processed through the various steps, as indicated below.

- An EORTC partner, cooperative group, or pharmaceutical company approach the EORTC Group or HQ.
- The EORTC HQ generates an idea based on scientific strategy review or its active contacts with the commercial sector.

In all cases, the key elements for rapid acceptance and optimal development of the project by the EORTC are for the EORTC Group and HQ to collaborate very early on and, when applicable, uniformly approach the EORTC partners. Efficiency of the EORTC processes can be ensured when the complementary expertise of the Group and HQ are combined.

6 GENERATING A STUDY PROPOSAL

The EORTC HQ team, in particular the Medical representative (MR), the Statistician, provide early guidance and assistance, especially technical expertise, to all EORTC Groups and Task Forces. Medical representative may support a Group to optimize selection of agents and serve as an interface with the relevant committees, such as TRAC, NDAC and ETF, or facilitate interactions across Groups.

7 SUBMISSION OF STUDY PROPOSAL

A Group will appoint a Study Coordinator who will be the main driver of the study on behalf of the Group. The EORTC procedures ensure strategic endorsement as well as independent peer review for the methodological, scientific, and medical validity. The Study Coordinator will be the main actor on behalf of the Group for the following steps.

7.1 Strategic endorsement

The strategic endorsement is the early review, based on preliminary study parameters, objectives, and key feasibility information, of the study concept, in order to verify that it is within the scope of the EORTC scientific strategy. This step involves submitting the study concept to the EORTC Board, under the guidance and support of the EORTC HQ team, in order to maximize the chance of success.

7.2 Scientific peer review

For each study proposed by an EORTC Group, a protocol synopsis should be submitted to the PRC. The protocol synopsis should briefly describe the rationale for the principal parameters of the study (objectives, principal eligibility criteria, therapeutic interventions, end-points, statistical design, translational research studies, etc.), enabling the PRC to assess the scientific value and integrity of the proposed study. The protocol synopsis should also identify a Study Coordinator appointed by the EORTC Group(s) and possible intergroup and commercial partners.

Groups are encouraged to submit the protocol synopsis after the essential parameters of the study have been discussed and agreed upon by the potential investigators. Submission will be done jointly by the Study Coordinator and the EORTC HQ team. All protocol synopses to be submitted must be endorsed by the EORTC Group Chair.

The PRC evaluation involves requesting review by PRC and external reviewers for all studies and TRAC, NDAC and ETF as applicable.

The PRC grades the following parameters:

- Originality
- Interest / relevance
- Methodology
- Feasibility

According to the following scale:

- A: Excellent
- B: Good
- C: Fair
- D: Not acceptable

The PRC makes one of the following decisions, which is communicated to the Study Coordinator, Group Chair, and the involved EORTC HQ team members:

- The study proposal is accepted. Minor comments and suggestions may be issued and sent for information. The authors may consider them in the development of the protocol to improve the project.
- The protocol synopsis should be resubmitted. Major comments must be discussed or implemented and an updated protocol synopsis submitted.
- The study proposal is rejected.

PRC composition:

PRC consists of 25-30 members and 10-15 phase I/II experts. Members commit for a three-year term, renewable once. In addition, the PRC routinely consults external experts as needed, under the coordination of the PRC chair.

The Chair of PRC reviews the composition of the PRC upon appointment, and proposes new members to the EORTC Board. A turnover of approximately one third of PRC members is recommended to maintain a good balance between continuity and new expertise in PRC reviews, i.e. not all members should be renewed at the time of change of Chair.

PRC decisions are based on the independent review of the protocol synopsis by several experts (members of the PRC and external reviewers who have no conflict of interest). In the case of major disagreement between the Study Coordinator and the PRC, a teleconference or a meeting with the PRC Chair will be organized. If the disagreement remains, the EORTC Board will make the final decision.

8 ASSESSMENT OF THE FEASIBILITY

This is a responsibility of the EORTC HQ team. The feasibility assessment (HQ greenlight) usually occurs after PRC approval of the study protocol synopsis, as described in the EORTC HQ standard operating procedures (SOPs).

The feasibility includes methodological feasibility, applicability to EORTC policies and SOPs, availability of resources and adequate financing, and patient access at the treatment sites. It is the responsibility of EORTC HQ to alert the Group, and if needed the EORTC Board, if the study feasibility is not assured.

9 DEVELOPMENT AND APPROVAL OF FULL PROTOCOLS

After HQ greenlight, the EORTC HQ team will initiate the protocol development process, harmonize the work of the different contributors, circulate all relevant information, and inform the Group Chair in case of problems.

The protocol document is assembled at EORTC HQ based on templates adapted by the Study Coordinator, other members of the writing committee, and the EORTC HQ team.

Study protocols must be a faithful development of the information approved in the protocol synopsis. Significant modifications of the study parameters or design after PRC approval will need to be approved by the PRC. Modifications impacting on the required resources need to be approved by the EORTC HQ Budgets and Contracts Unit in order for the study to be conducted by EORTC.

Study protocol review is performed at EORTC HQ by an internal panel of reviewers that does not include members of the study team. The following aspects will be carefully examined:

- Adherence to the approved protocol synopsis.
- Compliance with EORTC policies and SOPs.
- Clarity and lack of inconsistencies that may affect the conduct or management of the study.

Once comments have been addressed and inconsistencies resolved the protocol is approved.

Full protocol approval is communicated to the Study Coordinator, the Group Chair, and the HQ team.

10 COMPLIANCE TO MILESTONES AND TIMELINES

EORTC HQ has a commitment to keep protocol development timelines under control. This is continually evaluated as part of EORTC processes. All critical steps of study development are logged and benchmarked to acceptable standards of conduct. This allows rapid identification of delays or emerging obstacles so that immediate corrective measures can be taken.

11 DOCUMENT HISTORY

Version N°	Brief description of change	Author	Effective date
1.0	Initial release	Martine Van Glabbeke	16 Apr 2004
2.0	Integration of the EORTC scientific strategy	Martine Van Glabbeke	07 Nov 2005
3.0	Implementation of updated EORTC HQ procedures.	Denis Lacombe	19 Apr 2011
3.1	No reference to EORTC Executive Committee anymore. Update according to current EORTC HQ organizational chart Add PRC composition Clarification of the process	Vassilis Golfinopoulos	22 Apr 2014
3.2	No reference to EPOD, reference to clinical scientists instead; No reference to the TRI department; Replacement of COD by Budgets and Contracts Unit for financial green light; Language editing for clarity	Vassilis Golfinopoulos	26 Apr 2017
3.3	Adaptation to the reflect the new organigram (Project Management replaces Clinical Operations Department, Medical Representatives in place of Clinical Scientists and Clinical Research Physicians) Terminology update: protocol synopsis in place of outline. HQ greenlight replaces confirmation of funding availability to start protocol development activities.	Vassilis Golfinopoulos	25 Jun 2020