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Protocol Development Process, Selection and Approval Procedures for EORTC Studies

POL016

Version 3.0

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Table of Contents

1 OBJECTIVES 3

2 DEFINITIONS 3

3 POLICY..... 3

4 RESPONSIBILITIES 3

5 OVERVIEW 4

6 GENERATING A STUDY PROPOSAL..... 5

7 SUBMISSION OF STUDY PROPOSAL..... 5

 7.1 Strategic endorsement 6

 7.2 Scientific peer review..... 6

8 ASSESSMENT OF THE PRACTICAL FEASIBILITY 7

9 STUDY PROCESSING 7

10 DEVELOPMENT OF FULL PROTOCOLS 8

11 FULL PROTOCOL APPROVAL 8

12 COMPLIANCE TO MILESTONES AND TIMELINES 9

13 CONCLUSION..... 9

14 DOCUMENT HISTORY 9

1 OBJECTIVES

The present policy describes the milestones implemented by the EORTC Board and Executive Committee (ExCo) to select studies to be conducted by the EORTC.

EORTC resources for protocol development, implementation, management and analysis will be allocated to studies which carry the EORTC label. In general the EORTC is the legal sponsor for these studies. However, when these studies are carried out with external partners, the EORTC may delegate sponsorship to one of those partners. EORTC principles of independence will always apply.

The present policy focuses on the optimal steps for a study to be conceived and the role of the different EORTC committees in the selection / development process, on the criteria used at its different levels, as well as the optimal ways for submitting study proposal to the EORTC and developing them into full protocols with the goals to minimize delay until study activation process.

2 DEFINITIONS

- ◆ **EORTC Strategy:** the recommendations made by the EORTC Executive Committee (ExCo)/ Board for study parameters which will 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, which will ensure that a study can be efficiently performed within the EORTC Headquarters, the EORTC network, and within reasonable timeline.
- ◆ **Academic Fund:** a competitive source of money set up by the EORTC to support unfunded projects (and potential studies) and allocated by the EORTC Board.

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).

The EORTC must remain flexible and open in allowing projects to come from various sources, and the EORTC framework must remain adaptable to each specific situation.

4 RESPONSIBILITIES

- ◆ **The EORTC Group** will appoint a Study Coordinator for each proposed study.
- ◆ **The Study Coordinator** will submit the study outline to the EORTC Executive Committee / Board via EPOD and, if accepted, subsequently submit it to the Protocol Review Committee (PRC) to eventually develop the full protocol in cooperation with a designated EORTC Headquarters team.
- ◆ **The EORTC Headquarters** will assess the feasibility of all proposed studies and estimate EORTC resources to be allocated to the study. The EORTC Headquarters team will assist the Study Coordinator in developing and submitting the study outline(s) selected by the ExCo and thereafter in developing and submitting the full protocol for review by the PRC.

- ◆ **The EORTC Protocol Review Committee (PRC)** will review all proposed studies (on the basis of the submitted outline) 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 the 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 the PRC for implementation of translational research projects in EORTC clinical studies.
- ◆ **The EORTC Executive Committee (ExCo)** is responsible for the initial endorsement of studies to be supported by the EORTC (subsequent approval by the PRC is required), their practical feasibility, the EORTC resources necessary to the conduct the study, and the track record of the EORTC Group.
- ◆ **The EORTC Headquarters Protocol Help Desk (PHD) Officer** will assist the Study Coordinator and the Headquarters team to assemble the full protocol (after approval of the outline) according to a standard procedure.
- ◆ **EORTC Early Project Optimization Department (EPOD):** A team at EORTC Headquarters dedicated to actively participate in the development of Group strategy, offer project support and optimization, and conduct pro-active project development. Operationally, EPOD serves as the port of entry for new projects into the EORTC and helps manage these projects during their early phase.
- ◆ **EORTC Project and budget development department (PBDD):** provides budget estimations for EORTC Headquarters resources and negotiates with the Group officer concerning the group costs/site compensations. The Head of the PBDD will participate in the negotiations with the potential financial supporting body (Pharmaceutical Company or other partners) and assist the teams, after ExCo endorsement, to bring the project to PRC outline review. PBDD provides green light for protocol development once the budget has been secured
- ◆ **EORTC Translational Research Unit (TRU):** A unit at EORTC Headquarters that actively participates and supports TRAC in developing translational research activities at the EORTC. The TRU also participates and coordinates the review of proposals at several stages in protocol development thereby ensuring a quality assurance mechanism for translational research at the EORTC.

5 OVERVIEW

The ultimate objective of this policy is to guarantee the EORTC capacity of excellence, adherence to the EORTC scientific strategy, and ensure the principles of independence.

The EORTC scientific strategy primarily focuses on clinical studies which aim at changing practice and/ or developing knowledge on the biology of the disease and mechanisms of actions of tested strategies.

The EORTC principles of independence are based on the acceptance of

- ◆ The study concept by the independent Protocol Review Committee.
- ◆ The database of EORTC studies is handled by EORTC Headquarters or an equivalent independent organization until at least primary end-point maturity.
- ◆ EORTC Headquarters 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 which is then processed through the various steps, as indicated above.*
- *An EORTC partner, cooperative group, or pharmaceutical industry organization approach the EORTC Group or Headquarters.*
- *The EORTC Headquarters generates an idea based on scientific strategy review and/or its active contacts with the commercial sector.*

In any case, the key elements for rapid acceptance of the project by the EORTC and for guarantying the optimal development are for the EORTC Group and Headquarters 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 Headquarters are combined.

An early interaction will allow the following aspects to be efficiently evaluated

- ◆ Compliance to scientific strategy
- ◆ Internal and external feasibility
- ◆ Optimization of the multidisciplinary expertise available at EORTC
- ◆ Budget and resources evaluation
- ◆ Early project management and timelines

6 GENERATING A STUDY PROPOSAL

The role of EPOD is to provide early guidance to all EORTC Groups and Task Forces in cooperation with the Group specific EORTC Headquarters team and, in particular, the Clinical Research Physician (CRP) and Statistician.

EPOD is advisory and supportive to the Group through the Group specific EORTC Headquarters team. EPOD may provide guidance on a specific concept but is mostly involved when a concept requires technical expertise. EPOD may support a Group to do a thorough disease or organ related strategic analysis to identify unmet needs and key clinical questions in order to generate a protocol which is consistent with the EORTC scientific strategy. EPOD may optimize selection of agents and serve as an interface with the relevant committees such as TRAC or units such as TRU or facilitate interactions across Groups.

EPOD is therefore a catalytic tool to embrace the overall strategy and expertise and place a scientific concept in optimal position for success. In this, EPOD identifies at an early stage all of the parameters which need to be addressed to ensure successful study implementation.

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 (ExCo) as well as an independent peer review for the methodological, scientific, and medical validity (PRC). 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 to be developed in order to verify that it will meet the principles of the EORTC scientific strategy. This step is ensured by submitting the information to ExCo after an optional advisory step through EPOD. This early advisory review allows the EORTC Groups to streamline their efforts and optimally develop projects in order to guarantee chance of success and circumvent an unnecessary workload on the EORTC Headquarters' teams.

7.2 Scientific peer review

Scientific peer review is ensured by submitting an extended study outline to the EORTC Protocol Review Committee (PRC).

For each study proposed by an EORTC Group, an outline should be submitted to the PRC Secretariat via the outline submission procedure. The outline should specify the classification of the project according to the EORTC Scientific Strategy as assessed by the Group. The outline should briefly describe the rationale for the principal parameters of the study (objectives, principal eligibility criteria, therapeutic interventions, end-points, statistical design, companion studies...). This will enable the PRC to assess the scientific value of the proposed study. The outline should also identify a Study Coordinator appointed by the EORTC Group(s) and possible non EORTC partners.

Groups are encouraged to submit the outline as soon as 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 Headquarters team. All outlines to be submitted must be endorsed by the EORTC Group Chair.

For studies that contribute to a new drug development project or a Translational Research project, NDAC and/or TRAC will be consulted (and often also the Cancer in the Elderly Task Force). The Groups are advised to consult the NDAC and/or TRAC respectively before the outline submission. Eventual remarks from the NDAC or TRAC should be notified at the time of outline submission.

All submitted outlines will be reviewed by the PRC.

If there is a disagreement with the classification provided by the Group, the PRC will reclassify the study proposal according to the EORTC Scientific Strategy.

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:

- ◆ The study proposal is accepted. (Minor comments and suggestions may be issued and sent for information. The authors may consider them to improve the project.)
- ◆ The outline should be modified and resubmitted. (Major comments must be implemented and/ or discussed.)
- ◆ The study proposal is rejected in case of major problems.

PRC decisions are based on the independent review of the outline by several experts (members of the PRC and external reviewers who have no conflict of interest).

When appropriate, comments of the NDAC and/or the TRAC may be issued and forwarded to the Group as suggestions.

When major comments are issued by the PRC, the Study Coordinator is asked to resubmit an outline incorporating PRC suggestions. In case of major disagreement between the author and the PRC, a teleconference or a meeting with the PRC Chair will be organized. If the disagreement remains, the ExCo will make the final decision.

The PRC Chair issues a decision letter which is sent to the Study Coordinator, Group Chairman, and the involved EORTC Headquarters team members.

8 ASSESSMENT OF THE PRACTICAL FEASIBILITY

This is a responsibility of the EORTC Headquarters team. The feasibility assessment occurs parallel to the above activities and is further developed in the EORTC Headquarters standard operating procedures (SOPs).

The feasibility assessment is multifold and aims at ensuring several parameters which are critical to the successful performance of a clinical study.

It includes methodological feasibility, applicability to EORTC policies and SOPs, availability of internal resources, external feasibility for sites and patient access, and budgetary feasibility.

It is the responsibility of EORTC Headquarters to alert the Group, and if needed the Executive Committee, if the feasibility is not ensured. The parameters are assessed after the approval of the outline by the EORTC Protocol Review Committee following EORTC SOPs.

9 STUDY PROCESSING

Following PRC review of the outline, a PRC decision letter is issued.

Protocol development can then start immediately provided that PBDD has confirmed that external funding is secured as evidenced by a “letter(s) of intent” from the funder(s) or that academic funding has been granted.

All study proposals approved by the PRC which do not have adequate financial support are submitted for application to the competitive academic fund. Review of academic fund applications is done once a year. The selection committee consists of the members of the EORTC Board. The following information will be provided to the EORTC Board. The final selection of studies will be based on these elements.

- *The classification of the study according to the EORTC Scientific Strategy (according to the Group and according to the PRC).*

- *A copy of the final outline as approved by the PRC.*
- *The final four grades allocated by the PRC.*
- *The final estimation of the required EORTC resources and information about any financial support being allocated to the study.*
- *A short report from the EORTC Headquarters team summarizing the track record of the Group in terms of studies portfolio, scientific output, on-going studies supported by EORTC, eventual problems encountered with previous studies....*
- *Eventual feasibility problems identified by the EORTC Headquarters that are not yet solved.*
Studies having external funding will not be opened to recruitment unless the contract, securing adequate resources, has been signed.

10 DEVELOPMENT OF FULL PROTOCOLS

Selected study proposals will be developed into full protocols in conjunction with the EORTC Protocol Help Desk (PHD).

As soon as the outline is accepted, the EORTC Headquarters team will select one of its members as “contact person” with the PHD. This person 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 final document is assembled at the Headquarters by the PHD officer on the basis of “modules” adapted either by the Study Coordinator (and other eventual members of the writing committee) or members of EORTC Headquarters. All modules are developed according to templates and guidelines provided by the PHD.

11 FULL PROTOCOL APPROVAL

Full protocols must be the faithful development of outlines. Significant modifications of the study outline after its approval will need to be endorsed by the PRC. Modifications having an impact on the resources to be allocated by the EORTC need to be approved by the EORTC ExCo / Board in order that the study may be conducted by EORTC.

The first version of the full protocol will be submitted to PRC Secretariat to initiate the review process.

The review is performed at EORTC Headquarters by an internal independent panel of reviewers. The following aspects will be carefully examined:

- ◆ Adherence to the approved outline.
- ◆ Compliance with EORTC policies and Headquarters SOPs.
- ◆ Lack of clarity or inconsistencies that may affect the conduct and/or the management of the study.

The outcome of the internal review will be as follows:

- ◆ No problems are identified and the protocol is approved;
- ◆ Minor problems are identified and the protocol will be accepted pending modifications;
- ◆ Major discrepancies with the original outline and/or unresolved problems are identified and the protocol must be resubmitted to the PRC.

EORTC Headquarters reviewers communicate the result of their review to the PRC Secretariat. If the protocol is accepted, the Head of Protocol Development Unit issues and signs the letter giving the green-light to the study team to move forward to the activation process.

12 COMPLIANCE TO MILESTONES AND TIMELINES

EORTC Headquarters has a commitment to keep protocol development timelines under control. This is permanently evaluated as part of the internal process referred to as Streamline Simplify Harmonize under the supervision of the Quality Control Unit and conducted by the Project Management Unit.

All key and 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.

13 CONCLUSION

The increasing complexity of multidisciplinary clinical studies now extends to integrated disciplines such as imaging, laboratory expertise, and pathology, and this is occurring in a constantly evolving and more regulated environment that raises project development challenges. These challenges are exacerbated by the increased pressure from the various stakeholders and patients to more rapid therapeutic improvement. Therefore, the EORTC is constantly revisiting and upgrading its approaches to protocol development to ensure international and multidisciplinary efficiency while maintaining its capacity of excellence and ability to function within a reasonable timeframe.

14 DOCUMENT HISTORY

Version number	Brief description of change	Author	Effective date
1.0	Initial release	Martine Van Glabbeke	16/04/2004
2.0	Integration of the EORTC scientific strategy	Martine Van Glabbeke	07/11/2005
3.0	Implementation of updated EORTC Headquarters procedures.	Denis Lacombe	19/04/2011