EORTC
Avenue E. Mounierlaan 83 / 11
Brussel 1200 Bruxelles
België - Belgique
Tel : +32 2 774 16 11
Fax : +32 2 772 35 45
E-mail : eortc@eortc.be
Web : http://www.eortc.be

EORTC Principles for Investigational Sites Activation

POL018

Version 1.2

ALWAYS REFER TO THE EORTC INTERNET WEBSITE TO CHECK THE VALIDITY OF THIS DOCUMENT

Author: *Head Quality Assurance and Control Unit* Christine de Balincourt	Signature:	Date:
Authorized by: *Director General on Behalf of the Board* Françoise Meunier	Signature:	Date:

Table of Contents

1 PURPOSE

The objective of this policy is to describe the principles for investigational site participation to EORTC studies. It defines the guidelines by which EORTC will grant authorization to sites to join a particular study and to monitor site activities until the first patient is included. Alongside these principles, it defines the level of authority and decisions which can be taken towards non performing sites early on in the process of study activation investigational sites.

The process of getting a clinical study up and running is considered to be a limiting factor for the compliance to the overall expected timelines. The steps to bring all sites on board for a clinical study are multifold and complex to be achieved simultaneously. These steps are at the corner of project management, regulatory and ethical procedures. Improvement in the efficiency of the start up of clinical studies requires the dedication of all involved parties. These steps which require optimal coordination deserve full attention and cooperation from the joining investigational sites.

2 DEFINITIONS

- **Feasibility form:** first notification and call for interest and site feasibility to the EORTC Group members
- **Confirmation of Interest by principal investigator form:** Trough this document the investigator will confirm the site participation to the study, whether he has or not a conflict of interest, give site contact details and if applicable declare sub-site to the EORTC Headquarters.
- **Initiation package:** Package sent to all investigators who confirmed their participation. It includes all necessary documents for initial submission to the Ethics Committees by the investigators and for authorizing their site to participate in the study.

3 POLICY

Extensive regulatory work is nowadays to be performed to activate countries and sites to join a clinical study. The administrative process and compliance is now strictly regulated in EU member states since the implementation of the European directive 2001/20/EC. The complex regulatory procedures do have a direct cost to be achieved and executed but also submission costs to competent/regulatory bodies are more the rule than the exception. Insurance costs have also risen. In some countries, absence of patient entry within 1 year of study authorization will lead to authoritative closure of the study by the competent authorities. Taking all this environment into account, EORTC has implemented a specific process to control as closely as possible the activation of sites.

4 CALL FOR INTEREST AND SITE FEASIBILITY

Preliminary participation and feasibility will be done by circulation of the PRC-approved outline document to the relevant EORTC site network with request to complete the feasibility form.

It will capture study population / study process specific information in order to have an objective assessment of the feasibility per site. The form must be completed through the web application within 2 weeks. An extension of maximum 2 weeks will be considered.

Sites returning the form after the deadline will be logged on a waiting list. Depending on the expected and documented feasibility they might be taken on board from the start or at later stage to replace sites not fulfilling activation procedures adequately.

This first step, though preliminary is critical as it will serve for the initial budget assumption to run the study. However, significant deviation to the initial assumption criteria may lead to budget re-evaluation

Based on the outcome of this feasibility, the Headquarters will investigate if any quality or regulatory issue might hamper site participation.

The proposal of sites and countries participating with eventual strategies for resolving/addressing feasibility issues is discussed with the Disease Oriented Group Steering Committee and the Study Coordinator.

Final site selection will be provided to the company and/or collaborative group(s) for consideration, if applicable.

Site(s) not considered for participation will be contacted by the Headquarters.

5 INITIATION PACKAGE

Upon approval of the full protocol, a confirmation of interest by the principal investigator is requested to the selected sites. Based on this confirmation, the initiation package is sent. It contains all necessary documents for an initial submission of the trial by the investigators to their Ethical Committee(s) and other relevant regulatory bodies (Hospital Management Board, Hospital Direction, etc…) and fulfillment of all administrative requirements for site authorization.

The Headquarters will follow-up on the local process at each institution on a regular basis and at least every month after initiation package distribution. If deemed necessary, an additional reminder can be issued 4 months after initiation package distribution.

Failure at 6 months after receipt of the initiation package to provide complete and thorough information or to show that the process is actively addressed will lead to site interruption and replacement by a site on the waiting list.

6 SITE ACTIVATION

Upon receipt of all required regulatory documents from the site, Ethics Committee and Competent Authority's approvals and/ or any other central approval, along with the signed site contract, the site is authorized for patient recruitment.

Entry of the first patient is closely followed up by the EORTC Headquarters.

In absence of patient recruitment at 3 months after authorization, the Headquarters will investigate if any limiting factor can be actively addressed to overcome recruitment difficulties.

At month 6 from authorization, sites failing to prove that adequate screening procedures are in place and not documenting recruitment failure will be considered no longer interested and will be closed to patient entry and replaced by sites on the waiting list.

It is important to note that replacing sites is not only a costly process, but also creates substantial administrative burden (regulatory amendment). If site replacement exceeds 25%, a complete study feasibility re-assessment and budget re-evaluation is recommended.

While the decision to close sites will always be looked at on a case by case approach jointly with the relevant EORTC network/group officers, the EORTC reserves the right not to activate a site which is the only site in a given country unless a clear motivation and/or past commitment data are available.

7 SUMMARY

	Aim of the process	Initial deadline	Last deadline
Feasibility form	Initial feasibility based on study outline	2 weeks	2 additional weeks
Confirmation of interest	Confirmation of participation , initial regulatory steps	3 weeks	3 additional weeks
Initiation packages	Full scientific and regulatory packages for local procedures	on a regular basis and at least every month	6 months
1st patient included	Assess site commitment and control study timelines	3 months	6 months

8 DOCUMENT HISTORY

Version number	Brief description of change	Author	Effective date
1.0	Initial release	Denis Lacombe	27 March 2007
1.1	Implementation of updated EORTC Headquarters procedures.	Denis Lacombe	06 April 2011
1.2	Update and clarification of the definition of confirmation of interest, the contents of the initiation package, and the conditions for site activation.	Christine de Balincourt	04 April 2014