

Intergroup Studies

POL005

Version 3.1

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1 PURPOSE

Intergroup trials are required to efficiently address key public health questions in large inclusive studies. Progress in rare tumors can only be achieved through intergroup collaboration.

Major scientific breakthroughs in human biology and oncogenesis offer unprecedented opportunities to improve cancer care using the increased understanding of the function of genes and gene products relevant to human cancer. To integrate these genomic research results into clinical practice and to define new state-of art treatments, high quality international clinical trials and translational research are necessary.

Advances in pharmacogenetics and genomics have had the implication that we now need to consider smaller subsets of specifically selected patients for a biochemically determined therapies. Large international collaboration is therefore necessary in order to reach accrual goals in trials investigating these innovative targeted therapies. Such international trials can often only be conducted successfully by combining the efforts of several research groups and networks which could span Europe, USA, Canada, Australia and elsewhere.

This document outlines the EORTC policy on intergroup studies that facilitate this type of collaboration.

2 DEFINITIONS

- ◆ **Group:** national/international network of investigators and/or institutions and/or groups or structure/agency working together.
- ◆ **Coordinating Group:** (synonymous with “leading”) group responsible for the scientific content of the study.
- ◆ **Collaborating Group:** other group participating to the study.
- ◆ **Clinical Trial Office (CTO):** clinical research infrastructure responsible for the management of the study.
- ◆ **Data Center (DC):** somewhat analogous to CTO, but differs from CTO in that it also includes data management capacity and a statistical office.
- ◆ **Coordinating Data Center (DC):** Data Center of the coordinating group or the one contracted by the coordinating group to conduct the study.
- ◆ **Study conduct:** the term that covers all the procedures necessary to design, initiate and manage the study as well as to publish its results.
- ◆ **Legal entity:** structure considered as “moral person” following the laws of the country where it is registered.
- ◆ **Sponsor:** an individual, company, institution or organization which takes responsibility for the initiation, management of a clinical study and/or financing of a clinical study.
- ◆ **Steering committee:** Committee of representatives of the collaborating groups, the representative of the coordinating Data Center and the study sponsor.
- ◆ **Study Coordinator of the group:** medical representative of the group responsible for the coordination of all issues related to the study that are of the resort of his group.
- ◆ **Outline:** the short proposal of the future study with rationale, design and the statistics.

3 POLICY

Intergroup collaboration at EORTC is based on three main principles:

- ◆ There can be only one protocol which must be used by all collaborating groups.
- ◆ There can be only one set of Case Report Forms (CRFs) by all collaborating groups.
- ◆ The data from all collaborating groups are collected in one independent Data Center (called coordinating) for entry into their database, which is centrally updated and used for the analysis.

Many major cooperative groups in Europe, the US and other parts of the world recognize these rules as international standards for intergroup collaboration.

The EORTC Board and EORTC Chairs Assembly accepted these in March 1996.

4 CRITERIA FOR INTERGROUP COLLABORATION

Any group is considered as a potential partner for intergroup collaboration. All groups wishing to collaborate with the EORTC (either participating to the study coordinated by an EORTC group or inviting an EORTC group to participate to their study) should work according to the following criteria:

- ◆ work in compliance with legal and ethical requirements in the countries where the group conducts the study and follow the ICH-GCP principles (as applied in the national law for EU countries);
- ◆ have a track record of clinical studies in this particular disease conducted as a group (or being advised by a more experienced group);
- ◆ have a system to monitor the quality of their centers (in terms of compliance to current ICH-GCP, the quality of delivered care, the compliance to the protocol and quality of data);
- ◆ be represented by a legal entity and have access to a Clinical Trials Office/Data Center which handles the administrative matters of the group as well as the data collection (when EORTC Headquarters is coordinating) and data management and analysis (when non-EORTC group is coordinating)

Prior to any new collaboration, the EORTC International Regulatory Affairs / Intergroup Office investigates whether or not these criteria are fulfilled by the group. If any of the above criteria are not met for justified reasons, the decision to accept the participation of such a group will be taken by the Director General.

5 OPERATIONAL ASPECTS and RESPONSIBILITIES OF KEY PARTIES

5.1 Steering Committee

The Steering Committee is responsible for the scientific value of the study and decisions on eventual future utilization of the material, data and results pertaining to the study (within the limits defined by the Sponsor(s)).

The Steering committee should be in place from the moment collaboration is confirmed and collaborative agreement signed (or earlier) The Steering Committee consists of representatives (clinical and/or operational) of all participating groups and the study sponsor. In case of involvement of an industrial partner in the study (as sponsor or as support provider), the industry representative may be part of the Steering Committee, but without voting rights. The representative of the Data Center of the coordinating group or of the one used by the coordinating group to conduct the study may also be part of the steering committee

Responsibilities of the Steering Committee for a given study should be clearly described within an agreement or a charter.

5.2 Coordinating Group

The Coordinating Group should, as far as possible, involve all collaborative groups in the project development from very early stages (concept or outline stage) as this is essential for the success of the trial.

The Coordinating Group should be responsible for developing the scientific parts of the protocol and the CRFs, monitoring the status and the progress of the study, and writing the publication (in collaboration with other the parties).

The Coordinating Group should ensure that the project is independently peer reviewed.

The Coordinating Group should discuss and document (through a signed agreement) delegation of tasks and responsibilities with each of collaborating groups and other partners (industrial partners, CROs etc...). This agreement should cover all scientific, logistic and legal aspects of collaboration. The Coordinating Group may delegate this task to the Coordinating Data Center.

5.3 Coordinating Data Center

The responsibility of the Coordinating Data Center is to coordinate all issues related to the conduct of the study following the scientific protocol developed under the responsibility of the Coordinating Group. The Coordinating Group and Coordinating Data Center may be part of the same organization or may belong to different legal entities. In any case, the Coordinating Data Center should be either an academic partner or an independent structure (i.e., a CRO) directly contracted by the Coordinating Group.

The EORTC clinical group can be the lead group of an intergroup trial while EORTC Headquarters can handle all operational aspects and act as Coordinating Data Center.

EORTC Headquarters may also support coordinating activities and act as Coordinating Data Center for non-EORTC clinical groups who are leading the trial scientifically, but who are not necessarily supported by an operational platform.

The Coordinating Data Center should develop CRFs and the trials data base, perform the centralized registration / randomization, and perform the central data management as well as the statistical analysis.

Electronic systems (e.g. randomization, e-CRFs etc...) of the Coordinating Group / Data Center should be used as much as possible.

In order to comply with the main principles for intergroup collaboration, the Collaborating Group(s) and their Data Centers/CTOs should guarantee that:

- ◆ there will be no corrections/modifications done to the CRFs by the Collaborating Groups;
- ◆ only the coordinating Data Center will enter the data in the computer (unless sites are directly entering the data through a remote data capture system) and perform the quality control of data; when necessary, queries will be issued by the coordinating Data Center/CTO (i.e., the collaborative Data Center is not supposed to enter the data into the data base, nor validate the CRFs. If nevertheless they decide to do so, these databases will not be taken into account and no attempt at reconciliation will be made);
- ◆ there will be only one main analysis organized by the Coordinating Group based on the data handled by the Coordinating Data Center.

The Coordinating Data Center will perform all analyses (status reports, interim analysis, and final analysis) on the central Database and distribute the results as appropriate. The contents and timing of the analyses during the study should be agreed upon by the Steering Committee and described in the protocol.

In case the Coordinating Group uses an exterior Coordinating Data Center but has the necessary statistical resources, the final analysis can be performed by both parties in collaboration.

The Coordinating Data Center should support the Coordinating Group by doing any other tasks which require centralization.

5.4 Quality control and quality assurance

Data quality control should preferably be the responsibility of the Coordinating Data Center.

Collaborating Groups should receive regular updates about the general performance of their sites and to take action (if required by the Coordinating Group / Data Center) for poorly performing sites (if any).

When possible, the read-only access to the database can be given to the Collaborating Groups (restricted to the data of its sites) for the same purposes.

5.5 Endorsement by Collaborative Groups

Many clinical research networks have procedures in place to officially endorse the project. For example, within the EORTC, any project presented by EORTC groups or investigators needs to be endorsed by the EORTC Board (strategy review) and approved by the EORTC Protocol Review Committee (independent peer review).

It is recommended, provided that the Coordinating Group's protocol has already been reviewed and approved through an independent peer review procedure, not to repeat external reviews.

The EORTC has a process in place by which other peer review systems of other groups can be recognized by the EORTC, and external review will not be duplicated during the EORTC Protocol Review Committee review.

5.6 Publication

The Coordinating Group will write the final publication of the study results on the basis of the statistical analysis performed at the Coordinating Data Center. Before submission for publication, a draft manuscript will be circulated to all Collaborating Groups (via members of the Steering Committee if publication review is among the tasks of the Steering Committee) and any other co-author for review with a feasible deadline (not less than four weeks).

Interim publications or presentations of the study before the recruitment is discontinued may not disclose any results concerning therapeutic efficacy or any other primary endpoint of the study by treatment arm.

The authorship should be prospectively described in the protocol and agreements between parties. It should optimally include representatives of all Collaborating Groups unless prevented by specific authorship rules of a given journal. In any case, participation of all partners should be transparently and fairly recognized in the publication.

5.7 Data ownership and availability

The Database should be maintained centrally after the publication of results of the study, preferably by the Coordinating Data Center.

Sponsor(s), whether they are an academic organization or an industrial partner, are usually owners or co-owners of the data or at least that of the sub-set of patients under their responsibility. In case collaborating groups are not Sponsors of their members, they should have the license to use the data of the sub-set of patients randomized by their members, except otherwise agreed in writing.

The release of data of the sub-set of patients to any collaborating group should be considered by the Coordinating Data Center after the final analysis and the publication (at least upon request), provided it is not prohibited by any previous agreement.

The decision on the extent of the update of the Database after the main publication of the study should be taken prospectively by the Steering Committee or at least agreed with all Collaborating Groups.

For any use of data that do not belong to the Coordinating Group, the agreement of concerned Collaborating groups is mandatory, unless otherwise agreed.

6 JOINING A RUNNING STUDY

A group joining a running study from another group should accept the protocol and CRFs without any modifications (with the exception of the administrative section). The clinical representative from the group who started the study becomes the Study Coordinator, and the Data Center of his group becomes the Coordinating Data Center. The representative of the Coordinating Data Center should ensure that each collaborating group is contracted in order to properly fix the details of their participation. From then on, the study is considered as an intergroup study and follows the same guidelines as described for intergroup studies that were developed jointly.

7 EORTC PATIENT ACCOUNTING FOR MEMBERSHIP

EORTC has an international network. Within a given EORTC-intergroup protocol, participants might be members of the EORTC group and of the other collaborating national/international group(s). When participating through a non-EORTC group, the EORTC investigator can use the accrual for his/her EORTC group affiliation, if both, EORTC group and non-EORTC group collaborate in the same intergroup study.

8 DOCUMENT HISTORY

Version number	Brief description of change	Author	Date
1.0	Initial Release	Patrick Therasse	Oct 1999
2.0	Definitions and responsibilities of Coordinating group, Coordinating Data Center.	Patrick Therasse Anastassia Negrouk	10 Apr 2003
2.1	Transfer to new template; no further modification	Anastassia Negrouk	14 Feb 2005
Version number	Brief description of change	Author	Effective date
3.00	Merge of intergroup policies POL 005, 010 and 012 in one document. simplification and update to the current legal environment	Anastassia Negrouk	02 Mar 2012
3.1	Adapted to new organizational chart	Anastassia Negrouk	11 May 2015