EORTC European Organisation for Research and Treatment of Cancer The future of cancer therapy	**Policy on Independent Data Monitoring Committees**		
Document owner	Scientific Direction	Version number	1.1
Effective date	2023-05-03	Identifier	J-01-POL-01

1 Purpose

The purpose of this document is to describe the EORTC policy for the use of Independent Data Monitoring Committees (IDMC) in EORTC sponsored studies. It can be used as a reference document for studies sponsored by non-EORTC organizations if of interest for the conduct of such studies.

2 Scope

The policy is applicable to any prospective clinical study sponsored by EORTC.

3 Policy statement

IDMC review is mandatory:

- for all phase III and phase II studies that require **a protocol planned IDMC review**; or where formal interim analyses and early stopping rules are planned and described upfront in the protocol; or for complex studies with planned adaptions of the study sample size or design that are based on interim analysis of the un-blinded study data.
- on a yearly basis as **periodic IDMC review** for all phase III studies and other selected studies. The protocol review committee (PRC), the disease-oriented group (DOG) or other EORTC committees can suggest including a study in the yearly review. The IDMC chair makes the final selection of other studies to be reviewed every year. Periodic IDMC reviews are to stop at primary study analysis but can be extended beyond that point in time by decision of the IDMC.
- whenever safety signals are identified during the study medical review in a study for which no IDMC was originally planned, and there is a need for independent assessment of the data, an **emergency IDMC review** may be created upon request of the study team, and upon decision of the IDMC chair.

4 Changes since last version

Process step	**Changes since last version**
Scope	Clarification of a discrepancy between purpose and scope. Scope updated: clinical studies sponsored by EORTC instead of involving EORTC.

5 Policy

5.1 IDMC charter

The functioning of the IDMC is ruled by a charter that describes the membership, terms of reference, roles, responsibilities, authority, decision-making and relationships of the IDMC, including the timing of meetings, methods of providing information to and from the IDMC, frequency and format of meetings, statistical issues and relationships with other committees. Study-specific charters are developed from the master EORTC IDMC charter and contain additional study specific information.

Permanent members sign the master IDMC charter.

Study-specific members (including patient partners, if any) sign a study-specific IDMC charter upon agreeing to join an IDMC. Study-specific IDMC charters are fully aligned with the master IDMC charter.

5.2 Terms of reference for the IDMC

For periodic IDMC reviews, the IDMC shall:

- Monitor evidence for treatment harm (e.g., toxicity, serious adverse events and serious adverse reactions, toxic deaths)
- Be informed about data completion and cleaning rates, as performed by the study sites and EORTC headquarters
- Recommend modifications to be made to the study protocol with regards to the observed risk/benefit ratio
- Recommend actions to be taken by the study team regarding issues identified with protocol compliance, study feasibility and/or quality
- Monitor compliance with previous IDMC recommendations.

The following topics can also be within the terms of reference for each study. Whenever deemed necessary, IDMC may also:

- Monitor evidence for treatment differences in the main efficacy outcome measures, in particular in relation to protocol specified early stopping rules, if any; this activity can amount to an unplanned interim efficacy test, and requires a strong rationale to be undertaken
- Assess the impact and relevance of external evidence
- Recommend whether the study should continue to recruit participants or whether recruitment should be terminated either for everyone or for some treatment groups and/or some participant subgroups
- Recommend whether one should present or publish the results of all or some of the study endpoints earlier than anticipated, i.e., prior to study maturity per protocol
- Recommend if follow-up should be continued in all or subgroups of patients

- Make recommendations on planned study adaptions, in particular when they require interim assessment of un-blinded treatment effects (such as in randomized phase II continuing or being expanded to phase III studies or for adaptive sample size re-estimation)
  Advise on protocol modifications proposed by investigators or sponsors (e.g. to inclusion criteria, study endpoints, or sample size);
- Suggest additional data analyses.

When formulating its recommendations, the IDMC shall be careful to:

- Maintain confidentiality of all study information that is not in the public domain
- Consider the ethical implications of all recommendations
- Protect the integrity of the study.

5.3 Confidentiality, conflicts of interest and financing

5.3.1 Confidentiality

The deliberations and documents related to the study reviews by the IDMC are strictly confidential. The IDMC members should not discuss issues relating to their involvement in the study at all times.

5.3.2 Conflicts of interest

All IDMC members function in accordance with the EORTC policy on “Conflict of Interest, Bribery and Confidentiality”.

EORTC HQ asks the permanent IDMC members to update their potential conflicts of interest every year.

Study-specific IDMC members (including patient partners, if any) complete and sign the EORTC confidentiality agreement and interest disclosure form upon agreeing to join an IDMC and prior to each review.

In addition to the terms of EORTC policy on “Conflict of Interest, Bribery and Confidentiality”, the following circumstances shall be regarded as conflicts of interests for IDMC members, and exclude them from a study requiring an IDMC review:

- Being a permanent member of other EORTC review committees such as the EORTC protocol review committee, the EORTC scientific audit committee, and/or the EORTC board.
- Being member of other bodies involved in the study such as but not limited to: protocol writing committee, endpoint adjudication committee or any central review committee of the study
- Serving, at the time of the study review, as an officer of the EORTC group or taskforce leading the study.

- Recruiting and treating patients in the study being reviewed. If a member works in a department or institution that recruits patients in the study, he/she shall declare it in the conflicts of interest form, and the IDMC chair shall decide whether the involvement is such that it requires his/her exclusion.
- Being the principal investigator of a competing study to the one being reviewed.
- Being or having served on advisory boards either (a) for the same drug as the study drug, or (b) for the same pharmaceutical company AND the same indication as in the study, if not the same drug.
- US experts included in the Food and Drug Administration debarment list.

If the IDMC chair is conflicted for a study, then another IDMC member is appointed as an acting chair for that study.

Conflicts of interest to be declared, but that do not justify exclusion:

- Members who previously acted as external (occasional) reviewers (e.g. for EORTC protocol review committee) for the study being reviewed;
- Members who have served on advisory boards for the same pharmaceutical company as the one involved in the study, if any, but for a different drug and a different indication.

5.3.3 Financing of the IDMC

IDMC members shall receive no financial remuneration for their time spent in reviewing the studies. Travel expenses, if any, are reimbursed by EORTC.

5.4 Follow-up on IDMC recommendations

The final decision to act on the recommendations of the IDMC is the responsibility of the study steering committee.

The IDMC would generally expect that its recommendations would be endorsed.

In case of disagreement with the recommendations of the IDMC, the study steering committee can reach out to the IDMC in order to reach a consensus.

6 Definitions

- **Independent data monitoring committee** (IDMC): An independent data-monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical study, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a study.
- **IDMC analysis report (IDMCR):** Interim statistical report issued for IDMC review
- **Study steering committee (SSC) (also named Study executive committee, or Study executive board):** committee that supervises the study overall. Competences and composition to be defined per study in a steering committee charter.

- **Patient partner:** a cancer patient, caregiver, patient representative or a patient advocate who joined the IDMC to provide his/her patient's perspective on the study.

7 References

- DAMOCLES study group. A proposed charter for clinical trial Data Monitoring Committees: helping them to do their job well. The Lancet 2005; 365:711-722.
- European Medicines Agency. Guideline on Data Monitoring Committees. EMEA/CHMP/EWP/5872/03 Corr
  Guideline on Data Monitoring Committee (europa.eu) January 2006.
- European Medicines Agency. Questions and answers on Data Monitoring Committees issues EMA/CHMP/470185/2020.
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  Food and Drug Administration. Guidance for Clinical Trial Sponsors Establishment and Operation of Clinical Trial Data Monitoring Committees.
  http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf.
  2006.

8 Signature

This document will be electronically signed.
The signatories acknowledge that electronic signature is legally binding and equivalent to a handwritten signature.

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