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Interacting with the IDMC through the IDMC Support Unit

ST-004-SOP
Version 2.2
ALWAYS REFER TO THE INTRANET TO CHECK THE VALIDITY OF THIS DOCUMENT

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1 PURPOSE

To describe how the Headquarters study team interact with the EORTC Independent Data Monitoring Committee through the IDMC Support Unit.

2 SCOPE

This procedure applies to all EORTC studies for which a formal interim analysis or any IDMC report is submitted to the EORTC Independent Data Monitoring Committee for their assessment.

3 POLICY

However, other IDMCs may be put in place for studies coordinated by other groups or per contractual agreement with a commercial sponsor who is supporting the full cost of the study, provided the general policy of IDMC independency is maintained.

The EORTC Policy 004 defines the EORTC Policy regarding Independent Data Monitoring Committees.

The functioning of the permanent IDMC for EORTC studies is also ruled by a Charter.

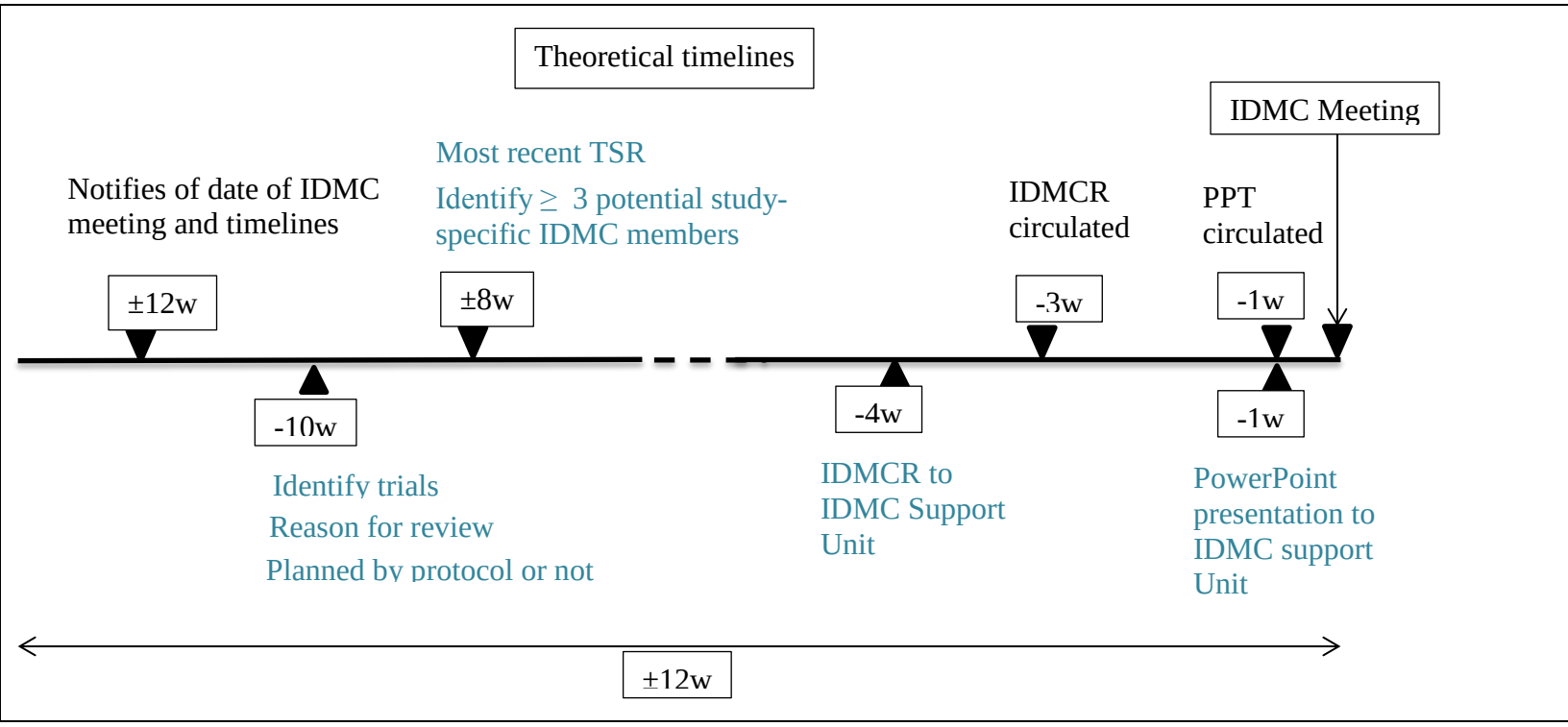
If by exception, another IDMC than the central EORTC IDMC is used for a study (for instance per contractual agreement with a commercial sponsor who is supporting the full cost of the study), it should fit with the general definition of independency set forth by the POL004 and a study IDMC charter must be signed by all IDMC members before their first meeting.

4 DEFINITIONS

- **Independent Data Monitoring Committee (IDMC):** an independent committee of clinicians and statisticians whose task is to review the status of a clinical trial and make recommendations to the clinical research group concerning the trial's continuation, modification and/or publication.
- **Permanent IDMC for EORTC studies (EORTC IDMC):** a permanent committee of experts including at least: a medical oncologist, a radiation oncologist, a surgical oncologist and a biostatistician.
- **IDMC Chair:** the person elected by the EORTC Board to chair the IDMC.
- **IDMC Support Unit Officer ("IDMC secretary"):** the EORTC Headquarters staff assigned to provide administrative support to the EORTC IDMC Support Unit.
- **Head of IDMC Support Unit:** a member of the EORTC Statistics Department assigned to organize and supervise the functioning of the EORTC IDMC and the IDMC Support Unit Officer. The Head of IDMC also provides methodological support to the IDMC members and reviews and approves all the interim unblinded analysis reports prepared by EORTC statisticians to inform the trial reviews of the IDMC.
- **IDMC report (IDMCR):** confidential report on an interim statistical analysis issued before data maturity for review by the IDMC.
- **Study Management Group**: For an EORTC study the study management group consists in the EORTC Headquarters core team in charge of running the study (clinical research physician, statistician, project manager and data managers) and the principal study coordinator.
- **Study Steering committee (SSC)**: The committee that provides the overall supervision of the study and has the executive power. The SSC should monitor study progress and conduct and give advice on

scientific credibility. Membership of the SSC shall, as a minimum, include the study coordinators, the representatives of collaborative groups involved, as third parties and at least one representative of the EORTC Headquarters and the representative of the sponsor. When EORTC is the sponsor, the EORTC study clinical research physician is the representative of EORTC as sponsor. In some protocols the SSC may sometimes be named differently, such as Study Executive Committee, or Study Executive Board for instance. When no SSC has been formally set up for an EORTC study, SSC in this study will then refer to the study coordinators (principal and co-coordinators) and the Chairperson of the EORTC groups involved in the study, and there will be at least one member of the EORTC Headquarters team (usually the EORTC study Clinical Research Physician) in charge of the study at the EORTC Headquarters plus the representative of the study sponsor

5 PROCEDURE



Legend: delays are expressed in number of weeks (w) in relation to the IDMC meeting date

5.1 Notification of IDMC Meeting

IDMC meetings are planned on a quarterly basis.

Approximately **12 weeks** prior to the next meeting, the IDMC Support Unit Officer:

- notifies the statisticians and clinical research physicians of the date of the next meeting and provides deadlines for receipt of the required information.

The Statistician provides to the IDMC Support Unit Officer:

- approximately **ten weeks** prior to the meeting: a list of protocols to be reviewed and the reason for the review.
- approximately **eight weeks** prior to the meeting: the names of potential external reviewers (after discussion with the Study Coordinator and Clinical Research Physician) and trial specific administrative information and documents.

The IDMC Support Unit Officer:

- checks the correspondence received at the secretariat since the past meeting in order to identify the other matters (i.e., requests for additional interim looks, follow-up on former reviews) that need to be discussed at the next meeting.
- prepares the draft agenda and submits it to the IDMC Chair and Head of IDMC support unit for review and approval.
- obtains the approval of the IDMC Chair for the choice of external reviewers proposed by the group. The IDMC Support Unit Officer collects conflicts of interest declarations of the proposed external reviewers and checks FDA debarment list against any names of US experts proposed as external membership so as to reject any expert who would appear on that list. In that instance, the IDMC Support Unit Officer informs the IDMC Chair of the proposed name and reason why the person cannot be selected. The IDMC Support Unit Officer also forwards any potential conflicts of interest to the Chair of the EORTC IRB for resolution.

Once a protocol has been selected for review, the IDMC Support Unit Officer:

- notifies the group Chair and Study Coordinator and asks them to provide any comments that they might have.

Whenever the IDMC meeting agenda is available, the IDMC Support Unit Officer

- notifies the study coordinators and group chairs of each trial of the date and time of the review and arranges that the IDMC can reach them, if necessary, during the open session of the IDMC pertaining to their respective studies.

5.2 IDMC Report (IDMCR)

The (unblinded) trial Statistician prepares the IDMC Report according to ST-006-SOP and provides it to the Head of IDMC Support Unit approximately **four weeks** prior to the meeting. The interim analysis and validation of the primary endpoint are done in accordance with EORTC procedures ST-003-SOP.

For blind studies, the Statistician and the Clinical Research Physician remain blinded. The unblinded statistician and unblinded clinical research physician (pharmacovigilance physician) prepare IDMC reports that involve unblinded results. The blind is not broken unless according to the corresponding EORTC procedure (CM-011-SOP).

The IDMC Report is signed off by the Statistician and the Clinical Research Physician who prepared it. It is reviewed and approved by the Head of IDMC Support Unit (ST-004-AF-01).

The IDMCR, it is then circulated to the permanent and study specific IDMC members. This is done approximately **three weeks** prior to the meeting.

Comments from all IDMC members should be returned to the IDMC Support Unit Officer approximately **one week** prior to the meeting. Should the IDMC request any additional data analyses, these are forwarded to

the (unblinded) trial Statistician by the IDMC Support Unit Officer, if the Head of the IDMC Support Unit considers that the requested information is necessary to the IDMC review and that is feasible for the (unblind) statistician to produce the extra information and make it available during the IDMC meeting.

A PowerPoint file summarizing the IDMCR is provided by the trial Statistician approximately **one week** prior to the meeting for forwarding to the IDMC members.

5.3 IDMC Meeting

The IDMC Support Unit Officer:

- drafts the meeting agenda approximately two weeks prior to the meeting and circulated to the IDMC Chair and Head of IDMC for review and approval.
- distributes the final agenda to the IDMC members and to the Statistician and Clinical Research Physician of the trials scheduled for review between ten days and one week prior to the meeting.
- shares the written comments received from the study-specific IDMC members to the permanent IDMC members.

The IDMC Chair decides if the meeting is to be held face-to-face or by means of a webex/teleconference.

The IDMC Support Unit Officer reserves the meeting room and organizes the webex/teleconference.

The agenda of the meeting follows the guidance specified in the POLICY 004.

Only the trial unblinded Statistician and unblinded Clinical Research Physician may attend the confidential session of the IDMC meeting on behalf of the Headquarters Team. For non-blinded studies the statistician and CRP attend. The trial Statistician (unblinded statistician for blinded trials) presents a 15-minute summary of the IDMC during the confidential session of the meeting; focusing on the questions being asked to the IDMC.

The Head of IDMC Support Unit takes notes during the meeting in order to draft the confidential minutes of the meeting but does not actively take part in the discussion of the IDMC unless asked by the IDMC. During the IDMC meeting, the Head of IDMC Support Unit ensures that the main message of the recommendation letter is drafted by the committee, so that the Head of IDMC Support Unit can prepare the draft recommendation letter shortly after the meeting.

For blinded trials, a member of the IDMC is charged with this task and the Head of IDMC Support Unit does not participate in the closed session.

5.4 After the IDMC meeting

Within five business days following the meeting, the Head of IDMC Support Unit drafts the recommendations for each study with the IDMC Chair. The IDMC Support Unit Officer sends them to the IDMC members for their final comments or approval.

After the comments have been received, the Head of IDMC Support Unit finalizes the recommendations.

The IDMC Support Unit Officer gets them approved and signed by the IDMC Chair.

The IDMC Support Unit Officer sends the signed letter of recommendation to Study Management Group with copies to the Headquarters Methodology Director, Medical Director and Director General, and IDMC Chair.

The Project Manager then forwards the recommendations to the any relevant external partners (other groups, sponsors, ...), to the Team at large (DM, PVU, ..) . The PM also informs all relevant head of units, when the recommendation impacts on study duration or continuation.

When an amendment follows from IDMC recommendation, the IDMC recommendation letter is sent to the PRC alongside the amendment document or included in the rationale for the amendment.

The confidential minutes are finalized after the formalization of the trial recommendations, and these minutes are approved and signed by the IDMC Chair.

The IDMC Support Unit Officer follows up on any IDMC recommendations where actions are required as well as any urgent matters that might arise between scheduled meetings.

6 FILING AND ARCHIVING

All official correspondence pertaining to the IDMC review of studies are saved in the IDMC Support Unit Officer electronic Mailbox.

All official IDMC documents including the agenda, Conflicts of Interest, confidential IDMC Reports, PowerPoint summary of the IDMC, comments of external reviewers and IDMC members, electronic copies of the signed trial recommendations and minutes are stored in a protected subdirectory of J:\UNIT\ IDMC where they remain confidential until final archiving of the study.

The trial recommendation letters are also filed in the statistics section of the e-Trial Master File.

All documents pertaining to the actual programming of the statistical analysis and its validation and the confidential IDMC Reports and its approval are stored in a restricted access subdirectory of the statisticians drive/STAT/trialnumber in accordance with statistics department procedures, or in the corresponding blinded trial folder if the trial is blind.

7 RACI MATRIX

Functions / Activities	Head IDMC Support Unit	IDMC Support Unit Officer	IDMC Chair	Stat	PM	(unblinded) Stat	(unblinded) CRP
Informs IDMC on study and reviewers				A			
IDMC report	A					R	R
Decides on agenda and format of IDMC meetings	I	R	A				
Organises IDMC meetings and distributes documents to IDMC	A	R	I				
Signs and approves minutes and recommendation letters	R	I	A				
Distributes recommendations to TMG	A	R	I				
Distributes recommendations					A		

Functions / Activities	Head IDMC Support Unit	IDMC Support Unit Officer	IDMC Chair	Stat	PM	(unblinded) Stat	(unblinded) CRP
Files IDMC documentation		A					
Files data and programs used to generate the IDMCR						A	

8 REFERENCES

- Committee for Medicinal Products for Human Use (CHMP). Guideline on Data Monitoring Committees. EMEA/CHMP/EWP/5872/03, July 2005.
- Guidance for Clinical Trial Sponsors. Establishment and Operation of Clinical Trial Data Monitoring Committees. Food and Drug Administration, March 2006

9 ASSOCIATED DOCUMENTS

Document title	Reference (file name or path)
IDMC report approval form	ST-004-AF-01

10 DOCUMENT HISTORY

Version N°	Brief description of change	Author	Effective date
1.00	Initial release superseding WP5201 version 1.1	Richard Sylvester	03 Apr 2009
2.0	Update of scope. Update to reflect new timelines and process simplification.	Laurence Collette	26 Mar 2013
2.1	Minor revision to change the terms (IDMC coordinator → head of IDMC), implement the IDMC charter if contractually agreed and the adaption of the process for double blind trial. Various clarifications	Laurence Collette	24 Oct 2013
2.2	New SOP template with RACI. Adapt definitions to POL004 and IDMC charter as well as new version of ST-006-SOP (IAR becomes IDMCR)	Laurence Collette	23 Feb 2016