Joint Research Management Office Standard Operating Procedure for:			
Trial Committees			
SOP Number:	**47**	Version Number:	**4.0**
Effective Date:	**14th November 2022**	Review Date:	**14th November 2025**

Authorship and Review:			
Author:	**Marie-Claire Good, Senior GCP and Governance Manager**		
Signature:	*The signed original is held within the JRMO office*	**Date**	
Reviewer:	**Rebecca Carroll, Quality Assurance Manager**		
Signature:	*The signed original is held within the JRMO office*	**Date:**	
Reviewer:	**Rupert Pearse, Clinical Director of Research & Development**		
Signature:	*The signed original is held within the JRMO office*	**Date:**	

Authorisation:			
Name/Position:	**Coleen Colechin, Senior Operations Manager (Pre-Award)**		
Signature:	*The signed original is held within the JRMO office*	**Date:**	

Purpose:

The role of trial committees is to give independent and expert oversight of the conduct of clinical trials. The purpose of this Standard Operating Procedure (SOP) is to define which committees are necessary and provide procedural guidance on the set-up and conduct of trial committees for studies that are sponsored by Barts Health NHS Trust (Barts Health) or Queen Mary University of London (Queen Mary).

This SOP also gives guidance on trial committee composition and committee charters.

Scope:

This SOP is mandatory for Clinical Trials of Investigational Medicinal Products (CTIMPs), Advanced Therapy Investigational Medicinal Products (ATIMPs), and Clinical Investigation Trials sponsored by Barts Health or Queen Mary.

This SOP should be considered best practice for all Queen Mary and Barts Health sponsored research and should be applied proportionately to other types of clinical research that do not fall within the scope above.

Abbreviations:

ATIMP	Advanced Therapy Investigational Medicinal Product(s)
Barts Health	Barts Health NHS Trust
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product

DMC	Data Monitoring Committee
EOT	End of Trial
GCP	Good Clinical Practice
HRA	Health Research Authority
JRMO	Joint Research Management Office
MHRA	Medicines and Healthcare Regulatory Agency
Queen Mary	Queen Mary University of London
REC	Research Ethics Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedures
SOG	Sponsor Oversight Group
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

Definitions:

Trial Management Group (TMG):

The role of the Trial Management Group (TMG) is to deliver the study, monitoring all aspects of the conduct and progress of the study, ensuring that the protocol is adhered to, and taking appropriate action to safeguard participants and the quality of the study itself. TMGs meet regularly but their frequency may vary depending on the phase of the study. The TMG normally includes those individuals responsible for the day-to-day management of the study, such as the Chief Investigator (CI), Statistician, Trial Manager and Data Manager. Every study should have a TMG but if the study increases in complexity and risk, additional committee or oversight mechanisms may be required. A template TMG remit can be found in *Associated Document 1: Further guidance for Trial Committees*.

Data Monitoring Committee (DMC):

An Independent Data Monitoring Committee (DMC) is a group of experts independent of the study team who review accumulating data from an on-going clinical trial. The DMC will monitor the safety and the treatment efficacy of the interventions during the study. The DMC is not necessary for all studies, it is the TSC decision.

Trial Steering Committee (TSC):

A TSC provides overall study supervision and advice through its Independent Chair, on behalf of the study sponsor and/or the funder. Its role is to ensure that the study is conducted in accordance with the protocol, Good Clinical Practice (GCP), and relevant regulations. The TSC should include members who are independent of the study investigators, their employing organisations, funders, and sponsor.

Independent:

The Chair should not be an employee of Barts Health or Queen Mary. They should not be named on any funding application associated with the study and should not have been involved in the study design or study planning stages. They should not be colleagues or close research collaborators of the trial team.

Charter:

A document which describes the role and function of the committee. The charter (also referred to as the "Terms of Reference") should also cover the committee's membership and quorum, how often it meets, how decisions are reached and whether they are "advisory" (which is the norm) or "executive.

For further details on the definitions of Trial Committees, see *Associated Document 1 Further guidance for Trial Committees.*

Relevant SOPs:	
SOP 9	Sponsorship of Clinical Investigations and other MHRA-regulated Medical Device Studies
SOP 11a	Sponsorship of MHRA regulated studies (Process for Researchers)
SOP 27	JRMO Internal Filing Process

SOP Text:		
	Responsibility	**Activity**
1.	CI	**All CTIMPs must have a TSC.** All CTIMPs, ATIMPs and Clinical Investigations must have a TSC. For details of the TSC purpose, composition and general guidance see *Appendix A*. It is the CI's responsibility to set-up a TSC. All TSCs should include a non-voting Joint Research Management Office (JRMO) Governance section member as a Sponsor representative (for CTIMPs, ATIMPs and Clinical Investigation Trials this is usually a GCP manager). For further detailed guidance, see the National Institute for Health Research (NIHR's) Trial Steering Committee and Study Steering Committee Guidance
2.	CI and named study statistician	**Assess the need for a DMC.** For all CTIMPs, ATIMPs and Clinical Investigations, a justification from the named statistician and CI should be provided at the study design stage to ascertain if a DMC is needed. The CI should consider whether the funder has any requirements during this decision-making process. For details of the DMC purpose, composition and general guidance see *Appendix B*. For Clinical Investigations, the decision of whether to include a DMC should be based on the study risk assessment. This should be discussed with the allocated GCP manager at study design
3.	CI	**All CTIMPs, ATIMPs and Clinical Investigations require a TMG**. It is best practice for all studies to have a TMG. It is the CI's responsibility to set-up a TMG. For details of the TMG purpose, composition and general guidance see *Appendix C*.
4.	CI	**Trial committees must be documented within the protocol.** All CTIMPs, ATIMPs and Clinical Investigations must outline their trial committees within the protocol. Individuals should not be named but committee roles (i.e., Chair, Statistician, etc.) should be indicated in the protocol. For all committees convened the following should be produced and retained: • Charter *(Associated Documents 2 and 3);* located within Sponsor Oversight File and the Trial Master File (TMF) • Conflict of Interest Declarations from all members and attendees *(Associated Documented 4: Competing Interests Form);* located within Sponsor Oversight File and TMF • CV and GCP training (all members); located within TMF only
5.	CI	**Committees should be set up prior to study activation.**

		Membership of committees should be agreed, the charter drafted, and first meeting scheduled prior to the sponsor issuing confirmation of sponsorship with permission to activate sites. (See *SOP 9 Sponsorship of Clinical Investigations and other MHRA-regulated Medical Device Studies* and SOP 11a: Barts Health/Queen Mary Sponsorship of MHRA regulated studies) Committees should continue to meet until the End of Trial (EoT) Notification is submitted, in accordance with the protocol and charter.
6.	CI	**All members of any committee should receive appropriate GCP training**. This can be the JRMO's GCP training or the NIHR's online GCP course. Barts Health and Queen Mary committee members are welcome to attend the JRMO training at no cost. For Clinical Investigations, committee members should have appropriate ISO 14155 training. (See the JRMO website for booking details or email: research.governance@qmul.ac.uk) It is the CI's responsibility to ensure all committee members are appropriately trained. **EXCEPTION:** Any consumer / public / patient representatives on the committee do not need to attend a certified GCP/ISO14155 course, but the CI should ensure they are given a level of understanding of the research environment and GCP/ISO14155. This training should be documented within the TMF.
7.	CI or delegate	**All meetings and critical decisions must be documented.** All meetings (blinded sections and unblinded), discussions and decision-making must be documented and retained in the TMF. Blinded reports, and discussions surrounding blinded reports, must be retained by the independent committee chairman until the study team is formally unblinded. After this point, the chairman must ensure the blinded documentation is added to the TMF prior to archiving. For CTIMPs, ATIMPs and Clinical Investigation *only*, minutes should be sent to the GCP team. The timing of this will vary depending on the type of reporting a team is performing. Minutes will either be attached to quarterly reports and/or disseminated as part of the main minute's distribution list.
8.	Clinical Trial Monitors	**Minutes should be chased, reviewed (where appropriate), saved and filed appropriately (As per *SOP 27 JRMO Internal Filing Process*).** The timing of the distribution/receipt of minutes should be agreed at the final governance meeting or when confirmation of sponsorship is issued. Minutes will be chased at each monitoring visit and/or on receipt of summary monitoring reports. Failure to submit minutes will be escalated and/ or items from minutes via GCP manager to Sponsor Oversight Group (SOG) Where possible, or where concerns are raised, minutes will be reviewed by a member of the GCP team. Minutes will be saved.

Change control

This section outlines changes from version 3.0 to version 4.0

Section changed	Summary and description of changes
Throughout	Addition of device requirements
Associated document	Removal of associated document 1 in place of hyperlink
Associated document	New associated document for more detailed guidance on committee definitions and template TMG remit.

List of appendices

Appendix ref.	Appendix name
Appendix A	Trial Steering Committees Guidance
Appendix B	Data Monitoring Committee Guidance
Appendix C	Trial Management Group Guidance
Appendix D	References, Related External SOPs, Web links

List of associated documents

Document number	Document name
Associated Document 1	Further guidance for Trial Committees
Associated Document 2	Sample DMC Charter template
Associated Document 3	Damocles Charter for DMCs template
Associated Document 4	Competing Interests Form

Appendix A

Trial Steering Committees (TSC)

The role of the TSC is to provide overall supervision of the study on behalf of the study Sponsor and study funder and to ensure that the study is conducted in accordance with the principles of GCP and relevant regulations. The CI is responsible for convening an appropriate TSC. The CI is also responsible for liaising with the funding body to ascertain whether they require a TSC or have committee guidance as a funding condition.

Composition:

The TSC will normally be limited to:

- An independent chair (mandatory).
- At least two other independent members, usually representing clinical areas under study.
- One or two Principal or Co-investigators.
- Two service / patient representatives (where possible).
- Independent statistician (where possible and deemed necessary).
- A sponsor representative
- Where required, a funder's representative

Study Statisticians, Data Manager, Study Manager etc. should attend TSC meetings as appropriate.

Document the TSC membership in the protocol

Prior to commencement of study

- Meet and agree roles and responsibilities. This meeting may be held jointly with the DMC.
- Review and agree the final study protocol before regulatory submission.
- Agree an appropriate timescale for meetings, at least annually.
- Agree the minimum quoracy for meeting to conduct business (see *Associated Document 2: Damocles Charter* for more details).
- Agree data that should be presented at each meeting.
- Create and agree a committee charter.

During the study

The TSC will meet according to its charter (at least annually) in order to:

- Monitor the progress of the study.
- Monitor adherence to protocol.
- Review available information relating to patient safety.
- Consider new information of relevance from other sources.
- Make executive decisions about the study as suggested by the TMG (e.g., protocol amendments where practical).
- Consider and act on the recommendations of the DMC, Research Ethics Committee, and competent authority (Medicines and Healthcare Regulatory Agency (MHRA)) as appropriate, including the termination the study.

If the TSC charter identifies a need for statistical reports to be prepared in order to advise the committee, it is the CI's responsibility to ensure the TSC receives this information. It is the responsibility of the statistician named on the protocol to advise the CI on data to be presented at the TSC meetings and appropriate timescales, so that there is sufficient time to check the data and carry out the analysis before circulation to the committee.

Appendix B

Data Monitoring Committee (DMC)

The role of the DMC is to review unblinded accruing study data and is the only body that has access to unblinded data. The DMC may also be asked by the TSC, Study Sponsor or Study Funder to consider data emerging from other studies. The DMC should advise the TSC. The DMC should be independent of the investigators and the funder / sponsor.

The CI is responsible for liaising with the funding body to establish if they require a DMC as a condition of funding (or have guidance on such committees), and where appropriate liaising with the study statistician and / or sponsor to determine the need for a DMC. Where it is necessary or appropriate for the study to have a DMC, the CI is responsible for identifying appropriate members. The membership of a DMC, or a justification of why a DMC has not been formed, should be documented in the protocol.

Composition

- Small, usually 3-4 members, all independent.
- At least one clinician experienced in the clinical area.
- At least one expert study statistician.
- A chair with previous experience of serving on DMCs.
- All members should be independent of the investigators, funder / sponsor, the host institution and the TSC.

Prior to commencement of the study

- Meet and agree a DMC charter. This meeting may be held jointly with the TSC.
- Review study protocol.
- Determine a schedule of meetings at least annually and timed so that reports can feed into TSC meetings.
- Agree the minimum quoracy for meetings to conduct business (see *Associated Document 3: DAMOCLES Charter* for more details).
- Agree a DMC charter specific to the study (see *Associated Document 2: Sample DMC Charter Template*).
- Provide the study team with details of any potential conflicts of interest for each committee member (or confirmation that no such conflicts exist) and a copy of their CV and evidence of GCP training.

During the study

The DMC will meet regularly in accordance with the agreed protocol and charter. It is the responsibility of the CI / delegated study staff to provide DMC with a comprehensive report for each meeting as agreed in the DMC charter. It is the responsibility of the statistician named on the protocol to advise the CI on data to be presented at the DMC meetings and appropriate timescales, so that there is sufficient time to check the data and carry out the analysis before circulation to the committee. The DMC will review the studies progress which may be through the following information:

- Review whether there are any safety concerns on one or more treatment arms (by considering e.g., toxicity data, Serious Adverse Event (SAE)/ Suspected Unexpected Serious Adverse Reaction (SUSAR), deaths), or any ethical reasons why the study should not continue.
- View whether the data shows significant benefit on one or more treatment arms.
- Whether there is evidence that, should the study continue, it would fail to show clear benefit on any treatment arm.

- Suggest any additional data analyses (using unblinded data where necessary) where it is relevant to advising whether the study should continue or be terminated early.
- Monitor the sample size (including recruitment targets and losses to follow-up) and make recommendations.
- Advise on substantial protocol amendments that may impact upon data or safety, such as changing the primary end points.
- Consider any new information relevant to the study, including reports from TSC and any related external research.
- Make recommendations to the TSC and / or TMG whether to continue, modify or stop the study.

Additional considerations

- In conjunction with the Study Manager / Coordinator, the DMC chair may prepare reports for the TSC and open reports for the DMC, in accordance with the agreed charter or terms of reference.
- The DMC may arrange for any interim statistical analysis to be carried out by a statistician independent of the study and assist as appropriate.
- If an unblinded interim statistical analysis is required by the DMC this should be undertaken by a qualified statistician independent of the study. There are various ways that this can be arranged; it is acceptable for this person to be an independent statistician within the sponsor's organisation.
- It is the responsibility of the CI to arrange regular meetings of the DMC and it is the Chair's responsibility to retain copies of the minutes for future reference.
- Copies of open DMC minutes should be filed in the TMF and the Statistical Master File along with a note of who holds the closed report and minutes.
- It is the responsibility of the CI to circulate copies of the minutes to the sponsor (JRMO) and to the funder if required.

Format of the DMC meeting

The format of the DMC meeting may have two parts:

1. **Open DMC session** which all TMG members (blinded and unblinded) may attend to review general study progress and pooled data.
2. **Closed DMC sessions** to review unblinded results (see *Associated Document 2: Sample DMC Charter Template*). During the closed session, blinded members (e.g., investigators) cannot be present.

Attendance of the CI or co-investigators at the open session of the DMC meetings should only be at the invitation of the DMC Chair.

Appendix C

Trial Management Group (TMG)

The role of the TMG is to deliver the study and monitor all aspects of the conduct and progress of the study, and to ensure that the protocol is adhered to, and that appropriate action is taken to safeguard participants and the quality of the study itself. The TMG should meet as frequently as is required by the progress of the study, and as determined by the members of the group.

The TMG should:

- Ensure the protocol is adhered to and take action as necessary to remedy any difficulties.
- Consider and act on the recommendations of the TSC and DMC, Health Research Authority (HRA), Research Ethics Committee (REC) and competent authority (MHRA) as appropriate.
- Consult co-investigators prior to protocol amendments in a timely and efficient manner.
- Refer any possible protocol amendments to the TSC.

It is the CI and TMG groups' responsibility to inform the sponsor (and where applicable the funder) of decisions made by the TSC or DMC.

Appendix D

References, Related External SOPs, Web links

With thanks and acknowledgements to:

- Pragmatic Clinical Trials Unit SOP on trial committees
- Barts Clinical Trials Unit SOP on trial committees
- Centre for Experimental Cancer Medicine SOP on trial committees
- Committee for medicinal products for human use , Guideline on data monitoring committees, July 2005
- ICH Topic E6 (R2) Guideline for Good Clinical Practice, 14 June 2017. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002874.pdf
- ISO 14155:2020 Clinical investigation of medical devices for human subjects — Good clinical practice
- DAMOCLES study group. A proposed charter for clinical trial data monitoring committees: helping them to do their job well. Lancet, 2005. 365: 711-22.
- Clinical Trials Toolkit: http://www.ct-toolkit.ac.uk/glossary

Medical Research Council. MRC Guidelines for Good Clinical Practice in Clinical Trials 1998. Available from: http://www.mrc.ac.uk/documents/pdf/good-clinical-practice-in-clinical-trials/