Standard Operating Procedure (SOP)

Trial Oversight Committees

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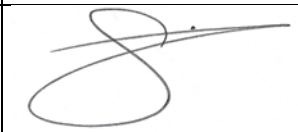
Signature of Authoriser			

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SOP Chronology		
SOP Version Number:	**Reason for Change:**	**Author:**
V1.0	Original Version	Ali Alshukry / Georgia Bullock

Associated JRES documents

SOPs	WPDs	Docs	LOGs
	JRESWPD0023 General Research Definitions	JRESDOC0119 Risk Assessment Tool JRESDOC0116 Trial Steering Committee Charter	

		JRES0116a Data Monitoring Committee Charter	

Contents

1. Background

All CTIMPs sponsored by St George's require oversight from several committees, as part of the monitoring strategy. These include a Data Monitoring Committee (DMC) and a Trial Steering Committee (TSC). Additional groups may also be required for some CTIMPs, such as a Trial Management Group (TMG).

DMC:

The DMC is a group of experts, independent of the study team, who review accumulating data from an on-going clinical trial. The remit of a DMC is to safeguard the interests of the trial participants by monitoring their safety and the treatment efficacy of the interventions during the trial. The DMC may also assess other aspects of a clinical trial such as efficacy, study integrity, design aspects, recruitment and some ethical considerations (such as early analysis and publication).

The decision to form a DMC will depend on the complexity, duration and end-points of the trial. The decision will be made by the CI and Sponsor with input from an independent statistician where relevant and will be considered as part of the Sponsor risk assessment questionnaire review. There may also be a requirement from the funding award body as a condition of funding.

TSC:

The TSC provides overall trial supervision and advice through its Chair, on behalf of the Sponsor. Its role is to ensure that the trial is conducted in accordance with the protocol, GCP, and relevant regulations. The TSC should include members who are independent of the trial investigators, their employing organisations, funders, and Sponsor. The TSC concentrates on the progress of the trial, adherence to the protocol, patient welfare, and considers new information of relevance to the research question. The TSC may meet at the beginning of the trial to approve the final protocol and, once active, considers any new relevant information, including recommendations from the DMC and other committees/groups or results from other studies. Based on any such information, the TSC may make recommendations to the Sponsor to change the trial documents (i.e. the protocol or patient documents) or to stop or extend the trial.

The decision to form a TSC will depend on the complexity, duration and end-points of the trial. The decision will be made by the CI and Sponsor and will be considered as part of the Sponsor risk assessment. All multi-centre CTIMPs (including device trials) should have a TSC.

2. Joint Research and Enterprise Services (JRES) Policy

All JRES SOPs will be produced and approved in accordance with the JRES SOP on SOPs and must be used in conjunction with local NHS Trust and University policies and procedures.

The JRES acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGHFT). St George's will be the official name used on all SOPs to represent either institution acting as Sponsor.

3. Scope

This SOP outlines the process to be followed in deciding on and assembling a DMC and TSC for CTIMPs sponsored by St George's. It also describes additional groups that may be required for the CTIMP, such as the TMG.

4. Definitions

For general research-related acronyms used in this SOP, refer to the General Research Definitions Working Practice Document (JRESWPD0023).

5. Responsibilities

This SOP is to be followed by the JRES Research Governance and Delivery Team (RGDT) and the Chief Investigator (CI) of the proposed study.

The Clinical Research Associate (CRA) will be responsible for completing the Risk Assessment Tool (JRESDOC0119) and for highlighting the need for a DMC and TSC with the CI.

The CI is responsible for documenting all trial committees within the protocol and setting them up prior to study green light.

The CI is responsible for establishing the relevant committees and groups and for ensuring that their charter is agreed, and a Chair is appointed. The JRES has templates for the DMC and TSC charters.

It is the CI's responsibility to ensure that all committee members are appropriately trained.

The committee Chairs are responsible for ensuring that the Clinical Research Associate (CRA) and the Research Development and Governance Manager (RDGM) receive copies of committee findings/reports/minutes on a regular basis in line with periodic meetings.

The JRES Sponsor representative is responsible for ensuring the reporting outcomes from the relevant committees to the regulatory authorities, where appropriate. Where required, reports will be provided to the Research Governance Committee.

6. Procedure

6.1 Data Monitoring Committee (DMC)

A DMC must be established for trials that involve:

- subjects with life-threatening illnesses
- vulnerable populations and/or with significant potential risk of harm
- substantial unknown or uncertain risks

The CRA or RDGM must document and file in the TMF the decision and justification for not having a DMC.

The DMC will comprise at least three people, including clinicians and at least one statistician. All members should be independent of the investigators, funder / Sponsor, the host institution and the TSC. The CI or their designee will create a Charter for the DMC describing:

- Membership.
- Roles and remit.
- Permissible recommendations.
- Frequency and organisation of meetings.
- How decisions are reached, whether they are advisory or executive and who they report to (how and when).
- Who is responsible for maintaining DMC documentation.

Members must be asked to declare any conflict of interest. The Sponsor must not be present at meetings to ensure the independence of the committee.

During the trial, the DMC will review the trial's progress by:

- Reviewing whether there are any safety concerns on one or more treatment arms (by considering toxicity data, SAEs/SUSARs, deaths etc) or any ethical reasons why the trial should not continue.
- Reviewing the data to see if it shows significant benefit on one or more treatment arms or whether there is evidence that, should the trial continue, it would fail to show clear benefit on any treatment arm.
- Suggesting any additional data analyses (using unblinded data where necessary) where it is relevant for advising whether the trial should continue or be terminated early.
- Monitoring the sample size (including recruitment targets and losses to follow-up) and make recommendations.
- Advising on substantial protocol amendments that may impact upon data or safety, such as changing the primary end points.
- Considering any new information relevant to the trial, including reports from the TSC and any related external research.
- Making recommendations to the TSC and / or TMG whether to continue, modify or stop the trial.

The DMC will make recommendations to the Sponsor which may include recommending the termination of a trial for safety reasons, due to evidence of the trial's futility, or the trial's overwhelming statically proven benefit. This will be done directly with the CRA or RDGM, unless a TSC has also been set up, in which case the DMC may report to the TSC which in turn will report to the CRA or RDGM.

The ultimate responsibility for the trial is with the Sponsor and thus the responsibility for implementing any changes to the trial recommended by the DMC (eg: stopping the trial or a treatment arm, making changes to the trial design) will ultimately be the Sponsor's decision. However the Sponsor will justify and document any decision not to follow the DMC's recommendations.

6.2 Trial Steering Committee (TSC)

The CI and Sponsor (CRA and RDGM) will need to consider the risks associated with the IMP, any safety implications, unusual assessments being conducted, size of the trial, and complexity of the trial protocol. Where a TSC is decided on, the CI must ensure that the procedures are formalised in the protocol or in a TSC charter.

The documented procedures must include:

- Members and core quorum.

- Responsibilities of the TSC and key decisions.
- How meetings and decisions are documented and reported.
- To whom outputs are circulated.
- Responsibility for TSC documentation, including archiving.

The TSC will normally include:

- 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).
- An independent statistician (where possible and deemed necessary).

The trial Sponsor, trial statisticians, Data Manager, Trial Manager etc. can attend TSC meetings as appropriate.

6.3 Trial Management Group (TMG)

The formation of a TMG is at the discretion of the CI. The CI must notify the CRA or RDGM if a TMG is to be created and provide the terms of reference and membership. The role of the TMG is to monitor the day to day conduct and progress of the study and ensure that the protocol is adhered to. The TMG normally includes those individuals responsible for the day-to-day management of the study, such as the CI, statistician, study/trial manager, research nurse and data manager.

The Chief Investigator may able to perform the functions of a TMG in a small study.

The TMG should monitor all aspects of the progress and conduct of the trial. The Chief Investigator should retain copies of all meeting agendas, papers and minutes in the Trial Master File and copies of meetings minutes should be sent to the Sponsor to ensure Sponsor oversight.

7. References

ICH GCP.

https://www.ema.europa.eu/en/documents/scientific-guideline/questions-answers-data-monitoring-committees-issues_en.pdf

8. Appendices

None associated with this SOP.