Guideline notes on - Trial Steering Committee (TSC)

Trial Steering Committee (TSC)

The Trial Steering Committee is a committee whose role is to monitor and supervise the progress of the trial and ensure that it is being conducted in accordance with the principles of GCP and the relevant regulations. The Trial Steering Committee should agree the trial protocol and any protocol amendments and provide advice to the investigators on all aspects of the trial. A Trial Steering Committee may have members who are independent to the investigators, in particular an independent chairperson. Decisions about continuation or termination of the trial or substantial amendments to the protocol are usually the responsibility of the Trial Steering Committee. A TSC normally acts on behalf of the Sponsor and Funder(s).

Terms of Reference - Guideline

1. To monitor and supervise the progress of the trial towards its interim and overall objectives;
2. To review at regular intervals relevant information from other sources (e.g. other related trials);
3. To consider the recommendations of the Data Monitoring and Ethics Committees (DMC & REC);
4. In the light of 1, 2 & 3 to inform the funder on the progress of the trial;
5. To advise the funder on publicity and the presentation of all aspects of the trial.

Membership of TSC Guideline

The Chief Investigator (CI) must inform the sponsor/funder of the TSC composition from the before their first meeting. The membership should be limited and include an independent Chairman (not involved directly with the trial other than as a member of the TSC), two or more other independent expert members and the Chief Investigator. Where possible the membership should include a lay/consumer representative. A Senior Statistician should be invited to all meetings, in the role of observer. The trial manager, trial statistician etc should attend meetings as appropriate. Observers from the funder and Host Institution (Sponsor if different from the Host Institution) should be invited to all meetings.

Guidance Notes

Meetings

Before the trial starts, the CI should organise a meeting of the TSC to finalise the protocol, which should then be sent to the funder/sponsor. The TSC should then meet at least annually, although there may be periods when more frequent meetings are necessary. Meetings should be organised by the CI. Papers for the meeting should be circulated in advance. Accurate meeting minutes should be prepared by the CI and agreed by all the members, and a copy sent to the sponsor/funder.

Trial Steering and Management

The role of the TSC is to provide overall supervision of the trial on behalf of the sponsor/funder. In particular, the TSC should concentrate on the progress of the trial, adherence to the protocol, patient safety and consideration of new information. Day to day management of the trial is the responsibility of the CI. The CI may wish to set up a separate Trial Management Group to assist with this function.

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Good Clinical Practice

The TSC should endeavour to ensure that the trial is conducted at all times to the standards set out in the Guidelines for Good Clinical Practice (GCP).

Patient Safety

In all the deliberations of the TSC the rights, safety and well being of the trial participants are the most important considerations. The TSC should ensure that freely given informed consent is obtained from each trial participant. The TSC should advise the investigators on the completeness and suitability of the patient information provided.

Progress of the Trial

It is the role of the TSC to monitor the progress of the trial and to maximise the chances of completing the trial within the agreed time scale. At the first TSC meeting, targets for recruitment, data collection, compliance etc should be agreed with the CI. Based on these targets, the TSC should agree a set of data that should be presented at each meeting (see template).

The CI is required to submit an annual report to the funder/sponsor based on the template suggest at the end of these notes. The report should be endorsed by the TSC, should be stand alone, and contain sufficient information to enable the funder/sponsor to assess the progress of the trial without the need to refer back to the original grant application. The annual report should inform the funder/sponsor of any new information that has a bearing on safety or ethical acceptability of the trial or any significant complaints arising, with a justification of the decisions taken.

In exceptional circumstances the sponsor/funder will consider proposals for extension of grants for clinical trials. If progress on the trial suggests that an extension may be necessary, the TSC should notify the sponsor/funder at the earliest opportunity. The sponsor/funder will require evidence from the TSC that all practicable steps have been taken to improve recruitment and keep within the agreed duration of the grant. Information would be required on the availability of data collected to date (from this and other studies) and advice on the likelihood that continuation of the trial will allow detection of an important effect. This should be done using methods that do not un-blind the trial.

Adherence to Protocol

The full protocol should be presented and agreed at the first TSC meeting. Any subsequent changes to the protocol must be approved by the TSC, MHRA (if applicable), the REC, the funder/sponsor and acknowledged by the NHS R&D Dept (when acting as the host institution).

Data Monitoring

At its first meeting, the TSC may establish a Data Monitoring Committee (DMC), particularly for double blinded studies. The DMC should meet regularly to review the un-blinded data and results of any interim analyses. Members of the DMC should be independent of both the trial and TSC (so as not to bias or un-blind the study).

Consideration of New Information

The TSC should consider new information relevant to the trial including reports from the DMC. It is the responsibility of the CI, the Chairman and other independent

members to bring results from other studies that may have a direct bearing on future conduct of the trial to the attention of the TSC.

On consideration of this information the TSC should recommend appropriate action, such as changes to the protocol, additional patient information, or stopping the trial. The rights, safety and well-being of the trial participants should be the most important consideration.

It is the responsibility of the CI to notify the TSC, DMC and relevant regulatory authority (if applicable) immediately of any unexpected serious adverse events occurring during the course of the trial.

Template for Trial Steering Committee Agendas and Reports

The funder requires that an independent Trial Steering Committee (TSC) is set up for every multi-centre trial. The TSC should meet at least once a year and submit an annual report to the funder. The table below outlines the information that should be provided by the CI at each meeting. This template should be used as a basis for the agenda of TSC meetings and a template for the annual report. These headings may not be appropriate at every stage of an individual trial or for all trials.

Name of Trial and Grant Number

Please include a graph plotting the cumulative target and achieved recruitment numbers against time since start of recruitment

	Target (date target set)	**Achieved** (date achieved)
Sample size sought		
Date recruitment started		
Proposed date for end of recruitment		
Actual recruitment rate versus target rate (by month/quarter)		
Acceptance rate, as a proportion of i. those invited to participate ii. all eligible participants, if known		
Quarterly/monthly forecasts of recruitment for the planned remainder of the **trial**		
Losses to follow-up i. as a proportion of those entered ii. per month/quarter		
Number still being followed-up successfully and number who have completed follow up		
Completeness of data collected		
Any available results (pooled)		
Any organisational problems		
Issues specific to the **trial** (as specified by the TSC)		