Trial Steering Committee Charter

Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke

Trial Identifiers

Sponsor:	University of Nottingham
Sponsor's reference:	31350 and 08093
NRES reference:	08/H1102/112
EudraCT number:	2007-006749-42
MHRA reference:	03057/0027
ISRCTN	ISRCTN47823388
Clinical trials.gov reference:	N/A

TSC Members:

1. Chair:	Helen Rodgers and Clinical Professor of Stroke Care, Associate Director SRN
2. Chief Investigator:	Philip Bath and Stroke Association Professor of Stroke Medicine, Associate Director SRN
3. Deputy Chief Investigator	Nikola Sprigg and Associate Professor, Regional Lead SRN
4. Statistician:	Stuart Pocock and Professor of Medical Statistics
5. Member:	Hugh Markus and Professor of Neurology
6. Member:	Tom Robinson and Professor of Stroke Medicine, Deputy Director SRN
7. Member:	Graham Venables and Consultant Neurologist and Clinical Director
8. Member:	Stan Heptinstall and Former Head of Cardiovascular Medicine
9. Independent Member:	Ahamad Hassan and Consultant Neurologist and Stroke Physician, Local Investigator
10. Independent Member	William Toff and Senior Lecturer in Cardiology (belongs to the same institution as one of the applicants)
11. Independent Member:	Chibeka Kasonde and Lay member
12. Independent Member:	Christine Roffe and Consultant in Stroke Medicine, PI, Regional Lead, SRN
13. Member:	Rob Dineen and Clinical Associate Professor, Radiology
14. Member:	Lelia Duley and Professor of Clinical Trials Research
15. Member:	Marilyn James and Professor of Health and Social Economics Policy
16. Independent Member:	Craig Smith and Stroke Physician

TSC Roster:

Chair of Independent Data Monitoring Committee (IDMC) as applicable:
Professor Ian Ford

TSC Coordinator: Mrs Sally Utton

Approval signatures

The following individuals, by providing their signatures, indicate their understanding of and willingness to comply with the roles and responsibilities assigned to them in this Charter.

	Role	Signature	Date
Helen Rodgers	Chair		
Professor Ian Ford (as applicable)	Chairman IDMC		
Philip Bath	Chief Investigator		
Nikola Sprigg	Deputy Chief Investigator		
Stuart Pocock	Statistician		
Mrs Sally Utton	TSC Coordinator		
Hugh Markus	TSC Member		
Tom Robinson	TSC member		
Graham Venables	TSC member		
Stan Heptinstall	TSC member		
Ahamad Hassan	Independent TSC member		
William Toff	Independent TSC member		
Chibeka Kasonde	Independent Lay TSC member		
Christine Roffe	Independent TSC member		
Rob Dineen	TSC Member		
Lelia Duley	TSC member		
Marilyn James	TSC member		
Craig Smith	Independent TSC member		

I Scope of Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke Charter

The role of the TSC is to provide overall supervision for a trial on behalf of the Trial Sponsor and Trial Funder and to ensure that the trial is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care, the ICH Good Clinical Practice guidelines and in accordance with all applicable laws and statutes. It should be noted that the day-to-day management of the trial is the responsibility of the Chief Investigator, and as such the Chief Investigator may wish to set up a separate Trial Management Group (TMG) to assist with this function.

The objective of the TSC Charter is to outline the specific purposes and functions of the TSC and those supporting its activities.

II Composition of the Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke TSC

The definition of independent is as follows:

- Where possible not part of the same institution as any of the applicants or members of the project team
- Not related to any of the applicants or members of the project team
- For the Chair only – not an applicant on a rival proposal

The membership should be limited and include:

- An **independent** Chairperson (UK based and/or holding a substantive UK based appointment and not involved directly with the study other than as a member of the Steering Committee)
- Two or more other **independent** expert members with relevant expertise (clinical and/or methodological)
- The Chief Investigator
- Where possible a lay/consumer representative who is able to contribute a patient and/or wider public perspective.
- Statisticians/epidemiologists/diagnosticians with relevant expertise

The study manager, study statistician etc. should attend meetings as appropriate. Observers from the Sponsor and /or Host Institution should be invited to all meetings.

Helen Rodgers will serve as Chairman of the TSC. The Sponsor, University of Nottingham, and the funder, the Department of Health, will approve all TSC members.

The Chair and members to sign and maintain a log of potential conflicts and/or interests: Ideally TSC members must not have a conflict of interest that would bias their review of trial data (e.g. TSC members must not have a financial interest that could be substantially affected by the outcome of the study, strong views on the relative merits of the study drug, relationships with individuals in trial leadership positions that could be

considered reasonably likely to affect their objectivity, or involvement in any potential competing trial).

All TSC members are expected to serve from study start until the study is completed. Should it be necessary for a member to resign, the member must submit the effective date of resignation in writing to the Department of health funder, Sponsor, TSC Chairman, and Chief Investigator. In the event a member resigns, the Sponsor, TSC Chairman and Chief Investigator, will initiate the process to identify a replacement member with approvals as above.

III TSC Contacts and *ad hoc* Consultants

TSC contacts and *ad hoc* consultants are not considered to be members of the TSC. The official TSC contacts are named on the TSC roster and will be appointed as follows:

The Sponsor, University of Nottingham, will assign a TSC Coordinator who will provide administrative, logistical, and coordinating services to the TSC. The TSC Coordinator will serve as the primary administrative point of contact for communications with the TSC members and TSC-related issues and will interface with the Sponsor and the operational leads on the project team, as appropriate.

The Sponsor will assign a trial statistician who will generate data and reports for the TSC to review. In addition, this individual will be available to the IDMC where applicable, to provide consultation regarding the information presented within the IDMC reports.

The Chair of the Trial Steering Committee will serve as a primary contact person for the IDMC and IDMC issues. The Chief Investigator will be copied into correspondence.

The TSC may, with prior approval from the Sponsor, contact and involve selected expert consultants who may provide additional, relevant insight or expertise to the TSC, regarding any specific issues that may arise.

As a rule, TSC contacts and consultants must not attend closed sessions of TSC Data Review Meetings with the exception that the IDMC may elect to involve the unblinded Biostatistician in closed session meetings.
Attendance at TSC/SSC meetings by non-members is at the discretion of the Chair.

IV Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke
TSC responsibilities

Terms of Reference
The minimum quoracy for a meeting to conduct business is 67% of appointed members with at least three Independent Members.
Specifically, the TSC members are authorised and expected to perform the following functions:

- To monitor and supervise the progress of the study towards its interim and overall objectives

- To concentrate on progress of the trial, adherence to the protocol, patient safety and the consideration of new information of relevance to the research question
- To review at regular intervals (annual / bi-annual / quarterly) relevant information from other sources (e.g. other related studies)
- To provide advice, through the Chair, to the Chief Investigator(s), the Trial Sponsor, the Trial Funder, the Host Institution and any Contractor on all appropriate aspects of the trial
- To provide advice to the investigators on all aspects of the trial
- To consider the recommendations of the Data Monitoring Committee (DMC) where one exists as defined by the Sponsor organisation based on an assessment of risk
- Consider the need for additional unscheduled reviews of study data.
- Ensure the confidentiality of all information received relating to the trial.
- In the event of further funding being required, to provide to the Sponsor and funder(s) appropriate information and advice on the data gathered to date in a manner that will as far as possible protect the integrity of the study.
- Participate in and vote on TSC recommendations bearing in mind the fact that ethical considerations are of prime importance. Only appointed members will be entitled to vote and the Chair will have a casting vote
- Make clear recommendations to the Sponsor and to the Independent Data Monitoring Committee (as applicable).
- To agree proposals for substantial protocol amendments and provide advice to the Sponsor and funder regarding approvals of such amendments

Although there may be periods when more frequent meetings are necessary, the TSC/SSC should meet at least annually

- Meetings should be scheduled to follow shortly after DM(E)C meetings so that reports from that group can be considered
- Minutes of meetings should be sent to all members, the Sponsor, the funder and the filed in the trial master file

The responsibility for calling and organising TSC/SSC meetings lies with the Chief Investigator, in association with the Chair.

Throughout the trial, the TSC Chairman will serve in a leadership role and will be authorised and charged with the following additional responsibilities:

The Role of the Chair of TSC

- The Chair's responsibilities include:
- Arranging an inaugural meeting to finalise the protocol and to set up a schedule of meetings to align with the project plan
- Establishing clear reporting lines – to the Funder, Sponsor, etc.
- Being familiar with relevant guidance documents and with the role of the IDMC
- Providing an independent, experienced opinion if conflicts arise between the needs of the research team, the funder, the Sponsor, the participating organisations and/or any other agencies
- Leading the TSC to provide regular, impartial oversight of the trial, especially to identify and pre-empt problems
- Ensuring that changes to the protocol are debated and endorsed by the TSC; letters of endorsement should be made available to the project team when requesting approval from the funder and sponsor for matters such as changes to protocol

- Being available to provide independent advice as required, not just when TSC/SSC
- meetings are scheduled
- Commenting on any extension requests and, where appropriate, providing a letter of recommendation to accompany such a request
- Commenting in detail (when appropriate) regarding the continuation or termination of the project
- Chair all TSC meetings.
- Ensure that all relevant data have been reviewed by the TSC members and that all issues have been addressed.
- Ensure that only the members of the TSC are present during TSC deliberations, when TSC recommendations are discussed and TSC voting procedures are conducted.
- Arrange for consultation(s) and/or request additional data, as deemed necessary.

Sponsor responsibilities

The Chief Investigator, on behalf of the Sponsor, will have the following responsibilities with respect to the Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke TSC:

- After the funder's confirmation, provide final approval of the TSC Chairman and Members to serve on the TSC.
- Ensure relevant clinical or other data on the safety of study interventions are provided to the TSC.
- Ensure that TSC members are informed of trial progress and issues every 6 months.
- In preparation for meetings, ensure that the TSC receive a general summary of the status of the trial and any relevant clinical issues.
- Provide representation at all open and final sessions of TSC meetings, as needed.
- Provide final approval of minutes of meetings.
- Arrange for fair and reasonable reimbursement to TSC members for their Committee activities (any study-related travel costs, such as transportation, lodging, and meals).
- Provide a primary contact representative to receive recommendations from the IDMC.
- Maintain ultimate responsibility for safe study conduct.

Trial Statistician responsibilities

The Chief Investigator, on behalf of the Sponsor, will provide a trial statistician in support of the TSC process. The responsibilities of the statistician are as follows:

- Provide approval for and operate in accordance with the specifications outlined in this Charter.
- Work with TSC members to determine the data that are necessary for the TSC Stats Reports.
- Create computer programmes to generate the TSC Stats Reports and transfer those reports to TSC members in a secure and confidential manner.

- Ensure that the content of the reports or details of discussions at TSC meetings are treated in the strictest confidence and are not revealed to any non-TSC member prior to study closedown, without the written approval of the TSC Chairman.
- Maintain a secure and confidential archive of electronic copies of datasets and related programs provided to the IDMC Statistician.
- Provide consultation regarding the information presented in the TSC Stats Reports, as requested by TSC and/or IDMC members.

TSC Coordinator responsibilities

The Chief Investigator, on behalf of the Sponsor, will provide a TSC Coordinator. The TSC Coordinator will provide administrative, logistical and coordinating support to the TSC members. The TSC Coordinator will be charged with the following responsibilities:

- Provide approval for and operate in accordance with the specifications outlined in this TSC Charter.
- Serve as the primary, administrative point of contact for the TSC members and as the main liaison between the Triple Antiplatelets For Reducing Dependency After Ischaemic Stroke
- operations teams and the TSC members.
- Coordinate the implementation of the schedule for preparation and distribution of paperwork to TSC members.
- Follow-up to verify that all data required by the TSC is provided according to an agreed timeframe.
- Coordinate arrangements for all TSC meetings and TSC ad hoc meetings, as outlined in this charter.
- Maintain a central file of all key TSC-related correspondences.
- Receive and arrange payment of TSC member invoices and expense reports.

V TSC Member involvement in protocol review and training

All TSC members will have the opportunity to review and comment on the study protocol and any proposed amendments to the protocol. The TSC Chairman will attend an investigator training meeting prior to the study start. The Chief Investigator will respond to all queries from the TSC on details of the protocol or proposed amendments.

VI Records Retention

The TSC Chairman will return a copy of the TSC file (i.e., copies of all reports reviewed by the TSC and copies of final minutes of all sessions of any TSC meeting) to the Chief Investigator after the end of the study. It will be the responsibility of the Chief Investigator, on behalf of the Sponsor, to arrange for long-term archiving.

VII Indemnification and Liability

The Sponsor shall indemnify, defend and hold harmless each TSC member, from and against any and all losses, damages, liabilities, reasonable attorney fees, court costs, and expenses (collectively "Losses") resulting or arising from any third-party claims, actions, proceedings, investigations or litigation relating to or arising from or in connection with the performance of responsibilities by such TSC member contemplated herein, except to the extent any such Losses have resulted from a breach of such TSC member's obligations hereunder or from any wilful or intentional misconduct of the TSC member seeking indemnity hereunder.

References

1. NIHR Health Technology Assessment programme Trial Steering Committee (TSC) or Study Steering Committee (SSC) guidelines, April 2012

Appendix 1: Contact details

TSC members:

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