University of Hertfordshire

SPONSOR OVERSIGHT

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for the
Management and Organisational Oversight of University of Hertfordshire
Sponsored/Co-sponsored/CTSN adopted Clinical Trials

SOP Number: gSOP-11-02	**Effective Date:** 10/08/22
Version Number: v2.0	**Review Date:** 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire standard operating procedure. This document describes the procedures for the management and organisational oversight of University of Hertfordshire (UH) sponsored/co-sponsored clinical trials.

The UK policy framework for health and social care research (2017) requires that all health and social care research that is within the responsibility of the Health Research Authority (HRA) or the Devolved Administration's Health Departments has a formal sponsor, and sets out guidance on the expectations of Sponsors for all clinical research in the UK.

The sponsorship responsibilities for Clinical Trials of Investigational Medicinal Products (CTIMPs) are specifically described in the EU Clinical Trials Directive 2001/20/EC, further clarified in the Good Clinical Practice (GCP) Directive 2005/28/EC and transposed into UK law by means of the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments.

The sponsor shall ensure that the relevant trial oversight committees (Trial Management Group (TMG), Trial Team (TT), Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC) where applicable) are employed to ensure that the rights, safety and well-being of the trial participants are protected and to ensure that the trial is conducted, recorded and reported in accordance with the currently approved protocol and any amendments, SOPs, Good Clinical Practice and with the applicable clinical trial regulations.

For trials adopted by the UH CTSN the division of clinical trial related tasks will be recorded in a clinical trials delegation log.

2.0 PURPOSE

- To specify the decision process for which local management and organisational oversight groups should be in place for UH Sponsored/co-sponsored clinical trials.

- To outline the roles of the sponsor/co-sponsor, Clinical Trials Support Network (CTSN), and Chief Investigator (CI) (or Designated Individual (DI)) in the management and organisational oversight for UH sponsored/co-sponsored/CTSN adopted clinical trials.

- To outline the procedures for implementation and management of the respective oversight committee structures established for UH sponsored/co-sponsored/CTSN adopted clinical trials.

3.0 APPLICABLE TO

This applies to all staff involved in clinical research sponsored/co-sponsored by UH, including: Unit Heads, Chief Investigators (CI), Principal Investigators (PI), Consultants, Co-investigators, Clinical Trial Pharmacists, Research Managers, Statisticians, Research nurses, Allied Health Professionals, Trial Coordinators, CTSN, NHS R&D Department & Data Managers.

4.0 RESPONSIBILITIES

4.1 The **Sponsor** shall:

a) Maintain a database of all trials requiring oversight and their status.
b) Through the **Advisory Group on Research Governance for Clinical Studies** (AGRGCS) ensure that UH sponsored/co-sponsored/CTSN adopted clinical trials have the appropriate level of management and organisational oversight.
c) Through the AGRGCS monitor progress of all sponsored clinical studies.
d) Ensure reporting timelines are met and address any issues arising.
e) Review responsibilities as reported by the Clinical Trial Support Network Management Group (CTSNMG) where clinical trials are externally sponsored but adopted by the CTSN.

4.2 The **Clinical Trial Support Network Management Group (CTSNMG)** shall ensure that all UH sponsored/co-sponsored clinical trials adopted by the CTSN:

a) Have an appropriate level of management and organisational oversight, which will be determined before the trial commences.
b) Review the trial specific Risk Assessment and decide whether a trial specific Quality Management and Monitoring Plan (QMMP) and Safety Monitoring Plan (SMP) should be written.
c) Based on the Risk Assessment ensure, where relevant, a DMEC and TSC with an appropriate membership composition as outlined in the corresponding terms of reference is in place.
d) Are monitored to assess the progress of the trial by reviewing all reports/ recommendations produced by the DMEC and TSC.

4.3 For trials adopted by the **CTSN**, the CTSN shall:

a) Review the oversight requirements as part of the governance checks and suggest requirements to the CI where necessary.
b) Ensure Terms of Reference for the relevant oversight committees are written and approved.
c) Ensure the QMMP or Monitoring Plan and SMP is completed as appropriate.
d) Ensure that the data in the trial database is analysed and a DMEC/TSC report is written 1 to 2 weeks prior to the DMEC/TSC meeting.
e) For CTIMPS ensure that the trial statistician writes the DMEC/TSC report.
f) Distribute the report to members of the DMEC/TSC as appropriate at least 1 week before the meeting.

g) Ensure they are available, to attend the DMEC/TSC meeting and guide the committees through the report if required.
h) Maintain records of activity of the oversight committee meetings and facilitate the review of the recommendations outlined by the respective oversight committee group by the CTNSMG.
i) Facilitate provision of any feedback from the CTSNMG to the CI and/or designee following review of the recommendations outlined by the respective oversight committee where required.
j) Attend Trial Management Group/research team meetings as appropriate to ensure governance issues are highlighted and complied with correctly. The CTSN will ensure that any potential serious breaches identified or discussed at these meetings are escalated to the AGRGCS where necessary.

4.4 The **Chief Investigator and/or Delegated Individual** shall ensure the following responsibilities are carried out:

a) That the required oversight committee structure is incorporated into the design of the study protocol.
b) That all persons involved in the trial including the Study Statistician, Trial Coordinators/Data Manager and the CTSN are made aware that a DMEC meeting has been organised.
c) Review the status of the study database at least 4 weeks before a scheduled DMEC meeting, and ensure that any required data locks have been completed at least 2 weeks prior to the DMEC meeting.
d) That the Study Statistician is made aware of any other relevant information for the DMEC report.
e) Facilitate the CTSN attendance during research team meetings/TMG meetings (as required).
f) Assist in facilitating the Organisational Oversight Committee's meetings in whatever ways are deemed necessary by CTSN.
g) Abide by any recommendations that the DMEC, TSC or sponsor/CTSNMG require.

4.5 Where responsibility for investigational product(s) accountability at the trial site has been delegated to the NHS Pharmacy Department, the **Clinical Trials Pharmacist** shall ensure the following responsibilities are carried out:

a) All records of the investigational product's delivery, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused product is maintained. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects.
b) That the investigational product is stored as specified in the protocol and in accordance with applicable regulatory requirement(s).
c) That the investigational product is only used in accordance with the approved protocol.

5.0 PROCEDURE

5.1 The CTSNMG will decide on the level of oversight required for each study using the Risk Assessment.

5.2 The CTSN/Trial Manager will complete a QMMP/Monitoring Plan and SMP as appropriate.

The CI/DI will set up the agreed oversight committees, prepare the Terms of Reference and a formal schedule of meeting dates.

1. A TMG – will provide day-to-day management of the trial, ensure all practical aspects of the trial are progressing well and identify potential issues. Membership, roles and responsibilities are detailed

in the TMG Terms of Reference (CTSN TP-34).

2. A TT - will be responsible for monitoring the progress of the study and address any key issues that arise. Membership, roles and responsibilities are detailed in the TT Terms of Reference (CTSN TP-36).
3. A TSC - will provide oversight of the trial and advice to the TT and CTSN. The Chair of the TSC should be independent of the study team. Membership, roles and responsibilities are outlined in the TSC Terms of Reference (CTSN TP-35).
4. A DMEC - The DMEC should consist of at least 3 independent members including one statistician and one appropriate clinician. Details of membership, roles and frequency of meetings are outlined in the DMEC Terms of Reference (CTSN TP-38).

5.3 The CTSN should ensure that records are maintained identifying the activity of study specific oversight committees. A member of the CTSN will attend research team meetings/scheduled TMG meetings (where required) to assist with the resolution of any governance issues that may occur.

5.4 The CI/DI should ensure that recommendations raised by the DMEC/TSC are responded to and address the issues raised in the recommendations.

5.5 A written acknowledgement will be issued following the review of the recommendations outlined by the DMEC to the CI by the CTSNMG and will detail any additional recommendations made by the CTSNMG to the CI. This written response should be maintained within the TMF by the CI and/or DI.

6.0 RELATED DOCUMENTS

- Risk Assessment template (CTSN TP-30)
- Quality Management and Monitoring Plan (QMMP)
- Safety Monitoring Plan (SMP)
- Data Monitoring and Ethics Committee Terms of Reference (CTSN TP- 38)
- Trial Steering Committee Terms of Reference (CTSN TP-35)
- Trial Management Group Terms of Reference (CTSN TP-34)
- Trial Team Terms of Reference (CTSN TP-36)
- TSCD/DMC Report Template (CTSN TP-33)
- gSOP-02 Adverse Event Reporting
- gSOP-06 TMF/Site File
- gSOP-10 Serious Breaches
- gSOP-33 Risk Assessment
- CTSNMG Terms of Reference
- AGRGCS Terms of Reference
- UK Framework for Health and Social Care Research (2017)
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7.0 APPENDICES

- Appendix 1 - Definitions

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
02	10/08/22	Scheduled review

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date 23/07/2022**

Pro Vice-Chancellor (Research & Enterprise) Approval
Professor J M Senior

Signature  **Date 08/08/2022**

10.0 AGREEMENT

Please detach and retain in your training files

I have read and understood the contents and requirements of this SOP (gSOP-11-02) and accept to follow UH policies implementing it.

Recipient

Signature: ……Date: ……..

Name & Position: ……..

Appendix 1: Definitions

Adverse Event (AE)
Any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

Chief Investigator (CI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial
A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)

A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Data Lock Point
This should be the last day of the one year reporting period and the DSUR should be submitted to the MHRA and the REC no later than 60 days after the data lock date.

Data Monitoring and Ethics Committee (DMEC): A group of experts (including Clinical experts, Statisticians and if appropriate Ethicists and Patient Advocates) not associated with the trial that monitor safety and efficacy data while a trial is ongoing. The role of the Data Monitoring Committee is to review the accruing trial data and to assess whether there are any safety issues that should be brought to participants attention or any reasons for the trial not to continue. The DMC may comprise of UH staff who are independent from the study, but specialists who are independent from UH can also be included. As a minimum, an Independent Chair, Statistician and Clinician to the study should be present during DMC meetings.

Delegated Individual (DI)
An individual delegated by the PI to carry out their task(s).

Good Clinical Practice (GCP)
As defined in the Regulations.

International Conference on Harmonisation (ICH)
The ICH produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as (ICH-GCP).

Investigational Medicinal Products (IMP)
A pharmaceutical form of an active substance or placebo being tested, or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

(b) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
(c) used for an indication not included in the summary of product characteristics under the authorisation for that product, or
(d) used to gain further information about the form of that product as authorised under the authorisation

Principal Investigator (PI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has responsibility for the conduct of the trial at a host site.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)
Any untoward medical occurrence or effect that at any dose results in:
- Death
- Is life-threatening*
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly or birth defect
- Is an important medical event

* "life-threatening" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

The Regulations
Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Management Group (TMG): The Trial Management Group for each trial is set up to oversee the clinical and practical aspects of the day to day management of the trial. The TMG normally includes individuals such as the Chief Investigator, Trial Physician(s), Statistician, Trial Coordinator, Research Nurse, and Data Manager(s)..

Trial Master File
The Trial Master File (TMF) will be held at the principal site by the sponsor, Chief Investigator or at the co-ordinating Centre. The TMF should contain all essential documents defined as documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. A Trial Master File should be set up at the beginning of a trial and maintained up-to-date throughout the trial until trial conclusion.

For trials currently running, it is recommended that Section 8 of the ICH-GCP Guideline is followed as guidance in order to meet statutory requirements. However, some of the documents listed may not be available or applicable in many non-commercial trials. The appropriate documentation will vary according to the trial and sponsor requirements.

Trial Steering Committee (TSC): The role of the Trial Steering Committee is to provide overall supervision and monitoring of the trial towards its interim and overall objectives and to oversee adherence to the protocol and patient safety. The Trial Steering Committee should accept the approved trial protocol and agree on subsequent amendments to the study protocol before they are submitted to the sponsor. In addition, the TSC should provide advice to the investigators on all

aspects to the trial. A Trial Steering Committee should have
members who are independent of the investigators (i.e. independent to the study). Decisions about continuation or termination of the trial or substantial amendments to the protocol are usually the responsibility of the Trial Steering Committee, taking into account reports/advice of the DMEC.

Trial Team: The Trial Team is responsible for monitoring the progress of the study, addressing key issues that may arise and reporting to the Sponsor and funder.