Cambridge Clinical Trials Unit Operational Manual

Key messages
- The Cambridge Clinical Trials Unit (CCTU) offers the services of expert personnel.
- The CCTU is an NIHR UKCRC CTU network registered unit.
- The CCTU works across the Cambridge BRC and the CUH partnership to facilitate high quality research.
- This document outlines the functional relationships between the CCTU and researchers.

Summary
The CCTU is able to offer a broad range of expertise and resources for Investigators undertaking clinical research, including study design, regulatory and GCP compliance requirements, trial set-up, coordination, data management, statistics, pharmacovigilance, quality assurance, quality control and monitoring; analysis.

The CCTU encourages Investigators planning a clinical trial to contact the unit at the earliest possibility for assistance and guidance to set up their trial.

Staff in the CCTU work across a range of specialities:
- Trial Coordination
- Study Design
- Regulatory Applications
- GCP and Regulatory Requirements
- Data Management
- Statistics
- Health Economics
- Quality Assurance
- Monitoring
- Pharmacovigilance
- Document Control (SOPs, guidance and templates)

1 Scope
This document applies to any staff collaborating with the Cambridge Clinical Trials Unit (CCTU).
2 Purpose

This document outlines the expertise and resources available to investigators involved in randomised controlled trials and other well designed studies within CUH partners, Cambridge BRC and beyond.

3 Definitions

3.1 Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Trust-Sponsored</td>
<td>Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH) or sponsored by CUH jointly with The University of Cambridge</td>
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3.2 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
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<tr>
<td>CCTU</td>
<td>Cambridge Clinical Trials Unit</td>
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<td>NIHR</td>
<td>National Institute for Health Research</td>
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<td>R&amp;D</td>
<td>Research and Development</td>
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<td>CTIMP</td>
<td>Clinical Trials of Investigational Medicinal Products</td>
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<td>DMC/DMEC</td>
<td>Data monitoring (and Ethics) Committee</td>
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<td>TSC</td>
<td>Trial Steering Committee</td>
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<td>ReDA</td>
<td>Portfolio Management data base</td>
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<td>BRC</td>
<td>Biomedical Research Centre</td>
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<td>CUH</td>
<td>Cambridge University Hospitals</td>
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4 Introduction

The CCTU works in partnership with investigators to deliver the highest quality clinical trials and clinical research. The unit’s portfolio covers a broad range of therapeutic areas, mirroring the vast spectrum of research interest of Cambridge University Health Partners and the Cambridge BRC.

In addition, the CCTU has been delegated to conduct sponsor oversight responsibilities for Trust and University Sponsored CTIMPs including regulatory affairs, amendments, monitoring, pharmacovigilance and quality assurance.

Grant independent core funding is provided by the Cambridge BRC, to support a critical mass of experienced core staff. The CCTU has a clinical Director, operationally; staff are managed by the Director of Operations. The CCTU has been established to provide expert guidance for researchers running CTIMPs and other well designed trials and studies. The CCTU employs Clinical Trial Coordinators to be assigned to a project on behalf of Chief Investigators.
5 Responsibilities

The Cambridge University Hospitals NHS Foundation Trust Research Board oversees overall strategy and clinical governance of the CCTU. The Director of the CCTU is a medically qualified clinician and investigator; clinical input is also provided by the NIHR Cambridge Biomedical Research Centre Executive, the R&D Director, CCTU Clinical Director and CCTU steering committee. The CCTU has clinical speciality theme leads – notably vasculitis, paediatrics, cancer, cardio-vascular, radiology, mental health and surgery. The CCTU senior management group reviews all proposed trials at the outline stage to provide scientific input and critique and will recommend whether the study requires a TSC and/or DMC.

The members of the CCTU steering committee consist of an independent chair, clinicians covering a wide range of clinical disciplines and representatives from the MRC Biostatistics Unit, the Institute of Public Health (Epidemiology), the Cancer Research UK Cambridge Institute and Cambridge and Peterborough Foundation Trust (Mental Health).

6 Range of Staff and Resources

6.1 Grants Officer

The Clinical Trials Grants Officer can provide expert guidance and support to investigators in the preparation, submission and effective management of research grant proposals involving the CCTU. They can help identify suitable funding stream(s) and determine the requirements of the funder (application deadlines, eligibility for costs etc.). The Grants Officer can also provide CCTU costing (i.e. staff salaries, administration and travel costs etc.) based on the resources and expertise required for the proposal.

Investigators planning a clinical trial or study should contact the CCTU by email (cctu@addenbrookes.nhs.uk) as soon as possible; ideally at the very early stages before any grant applications are made to evaluate the scope of the planned trial and any support the CCTU can offer.

6.2 Clinical Trial Coordinators

By using of a set of SOPs, templates, forms and guidance notes, the CTCs are responsible for the set-up, conduct, the day to day management of their designated clinical trials from start up to closure and archiving. Good communication and routine monitoring ensures oversight of the status and progress of trials coordinated and managed by the unit.

6.3 Data Managers

Data Managers guide the development and structure of case report forms, perform validation checks for data entry, and provide overall data management guidance.
6.4 **Statisticians**
The CCTU can provide statistical support for but not limited to, specification of endpoints, randomisation, statistical analysis, interim analyses, missing data, sample size and a detailed statistical analysis plan.

6.5 **Database Programmers**
Database programmers control database system security and work with trial teams to agree a database specification, then design, build and validate the system following processes defined in CCTU SOPs. Programmers also carrying out data downloads as requested by the trial teams and configure reports.

6.6 **Clinical Trial Officers**
For Trust and/or University Sponsored CTIMPs the CCTU will provide a dedicated Clinical Trial Officer to guide the trial team through the set up and approval process for all trial submissions, this will include the trial level risk assessment, initial application, amendments, annual reports and end of trial documentation.

6.7 **Clinical Trial Monitors**
For Trust and/or University Sponsored CTIMPs a Clinical Trial Monitor will create a monitoring plan based on the initial and subsequent on-going risk assessments. The monitoring plan will determine the activity and frequency of monitoring and includes, but is not restricted to: source data verification, review of CRFs. Trial Master Files and/or Investigator Site Files laboratory arrangements and facilities, staff training records (CVs and GCP), pharmacy arrangements, trial team SAE management and close out monitoring to ensure all essential documents are archived.

6.8 **Pharmacovigilance Manager**
For Trust and/or University Sponsored CTIMPs the Pharmacovigilance Manager will work with the trial team to provide guidance to ensure that all necessary PV activities are undertaken by the trial team as appropriate. This may include support for developing trial specific reporting forms and PV training.

6.9 **Quality Assurance**
The QA Manager can offer guidance for writing trial level SOPs and designing forms for investigators. CCTU documents for use by trial teams are available on the clinical trials web site.


6.10 **Health Economist**
The CCTU can provide expertise in incorporating economic endpoints into a clinical trial (cost effectiveness analysis), as well as evidence synthesis and decision analytic modelling prior to a study to determine the economic case for a proposed future trial.
6.11 IT resources

6.11.1 Quality Management System: Q-Pulse
Q Pulse is used in the CCTU as a quality management system to enable version control of CCTU SOPs, forms, guidelines, and templates. It is also used to manage CCTU staff training and training records. The system is hosted on the local CUH servers.

6.11.2 Database Management: MACRO by Elsevier
MACRO is an electronic data capture system for clinical trials. MACRO is used as the CCTU default database development environment for CTIMPs. Elsevier host and support the MACRO database and are responsible for database backups.

6.11.3 Database Management: Cambridge University Clinical School Servers
Virtual Windows servers on the Cambridge University’s Clinical School network can be used by CCTU programmers for bespoke database development to support trial teams where MACRO is unsuitable, e.g. for storage of personal identifiable data. These servers host both public and secure websites. Databases containing personal identifiable data are hosted within the University's Secure Data Hosting Service.

6.11.4 Randomisation Systems
The CCTU can provide web-based randomisation systems. At the time of writing the preferred supplier is Sealed Envelope although other systems are also utilised as required. The CCTU can advise and document the study-specific user requirements, organise user acceptance testing and provide ongoing support for a randomisation system during the course of a study.

6.11.5 CCTU Portfolio Management System: ReDA
ReDA is used in the CCTU as a comprehensive portfolio management tool to track the progress of trials and studies. ReDA provides a data trail for auditing, recall of amended data, amendment details when changes were made and by whom, accurate and up-to-date information about the status of individual trials, and the activities of participating sites. It is also used for the storage of trial level documents and SOPs.

6.12 CCTU Committees
Within the unit there are monthly team meetings between the groups, coordinators, data managers, QA/QC, and statisticians to communicate workload etc. The outcomes from these meetings are fed up to the monthly team meeting.

Outcomes from the monthly team meeting are fed up to the Senior Management group and from there to the Management Board.

6.12.1 CCTU Management Board
CCTU/INF008 Terms of reference
6.12.2 CCTU Senior Manager Group
CCTU/INF007 Terms of Reference

6.12.3 Annual Management Review Group
The AMRG meets annually to review the Quality Management System and set the quality indicators for the year according to CCTU/SOP042 Procedure for Management Review

7 Monitoring Compliance with and the Effectiveness of this Document
a. Process for Monitoring Compliance and Effectiveness
As part of routine monitoring visits, audit and inspection
b. Standards/Key Performance Indicators
This process forms part of a quality management system. Documents are reviewed every two years

8 References
The Cambridge Clinical Trials Website

9 Associated documents
None

10 Equality and Diversity Statement
This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

11 Disclaimer
It is your responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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