



CHaRT

Standard Operating Procedure book

Details:

Version number:	08
Lead authors:	CHaRT director, QA manager, CHaRT research managers, senior trial manager, deputy senior trial managers, senior IT development manager, senior statistician, senior health economist, process evaluation leads, PPIE coordinator
Issue date:	01/10/2024
Effective date:	01/11/2024
Review date:	01/10/2027

Approval:

Approved by:		
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Storage:

Location of document:	
Paper:	QA manager
Electronic:	Q-Pulse
Web:	www.abdn.ac.uk/hsru/what-we-do/trials-unit/chart-sops-556.php

A Standard Operating Procedure (SOP) is a detailed written instruction used to achieve uniformity when performing specific functions and is used to set out the way practice and procedures need to be performed. SOPs are written instructions and records of procedures agreed and adopted as standard practice.

The definitive version of the Centre for Healthcare Randomised Trials (CHaRT) SOP book appears online, not in printed form, to ensure that the up-to-date version is used. Hardcopy printouts are UNCONTROLLED COPIES. If you are reading this in printed form, check the version number and date to ensure you are working to the current version.

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT CHECKING IT IS THE LATEST VERSION.

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Version history:

Version number	Details/reason for change	Date approved
01	None, new procedure. Launch of SOP book	21/04/09
02	Review and update of all chapters and web links	24/06/10
03	Review and update of all chapters and web links, referencing the UoA-NHSG SOPs where appropriate and referencing to Q-pulse for all CHaRT specific templates & policies. Details of SOP authors on front page renamed to "Lead Authors" and listed by roles. The names are given in a new section "Lead Author History" below. More detailed chapter specific "Version History" sections have been added at the end of each chapter.	15/10/12
03.01	Minor typographical changes (approval not required)	28/11/12
04	Review and update of all chapters and web links, referencing the SOP-QA (formally UoA-NHSG-SOPs) where appropriate for locally sponsored studies and referencing to Q-pulse for all CHaRT specific templates & policies. The following chapters were renamed: Chapter 8 'Final Trial Reporting' to 'Trial publications and Dissemination', and Chapter 13 'Consumer issues' to 'Patient and Public Involvement'.	22/10/15
05	Review and update of all Chapters and web links; removal of word 'issues' from Chapter headings; removal of Health Psychology chapter (chapter 12); inclusion of Chapter on randomisation (chapter 11); inclusion of NEW Chapter on IT infrastructure (chapter 9); inclusion of NEW Chapter on embedded qualitative evaluations (chapter 14) and as a result the re-ordering of Chapters where required.	19/04/18
06	Review and update of all Chapters, hyperlinks and web links where required. All links to Q-Pulse have now been clearly highlighted & staff have been directed to use the software for accessing these. Any new templates, examples or guidance documents, relevant to CHaRT procedures, have been added. Significant changes have been made to Chapters 5, 6 and 10 to ensure all procedures, especially regulatory ones, are current and up-to-date, and Chapter 15 includes two new sections; these describe the process for supporting Patient and Public Involvement (PPI) partners and the best methods for documenting PPI.	05/05/20
07	Review and update of all Chapters, hyperlinks and web links where required. Any new templates, examples or guidance documents, relevant to CHaRT procedures, have been added. All links to local UoA/NHSG SOPs have been clearly	11/05/22

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	highlighted throughout this SOP book and hyperlinked to the appropriate webpage. The 'Cross references' section at the end of each chapter has been renamed to 'Related references and resources'. Chapter 14 title renamed from 'Embedded qualitative evaluations' to 'Embedded process evaluations'. Significant changes have been made to Chapters 5, 6 and 7 to ensure all procedures, especially regulatory ones, are current and up-to-date.	
08	Review and update of all chapters, hyperlinks and web links where required. Any new templates, examples, or guidance documents, relevant to CHaRT procedures, have been added. The review period for this SOP book has been changed from two to three years. Following HSRU's name change to Aberdeen Centre for Evaluation (ACE) in September 2024, any mention of HSRU has been updated and replaced with ACE as and where appropriate. Significant changes have been made to Chapters 7, 8, 10, 12 and 15 to ensure all procedures are current and up to date. These key changes are detailed in the chapter specific 'Version History' together with details of any other minor updates.	25/09/24

Lead authors' history:

Version number	Names of Lead Authors (Theme Leaders)	Date approved
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Version number	Names of Lead Authors (Theme Leaders)	Date approved
	health economist); who are grateful for the substantive contributions from other members of CHaRT/HSRU staff.	
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07	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Ruth Thomas (CHaRT research manager), Kirsty McCormack (CHaRT research manager), Seonaidh Cotton (senior trials manager), Suzanne Breeman and Lynda Constable (deputy senior trials managers), Mark Forrest (senior IT development manager), Lorna Aucott (senior statistician), Graham Scotland (senior health economist), Katie Gillies (HCA programme director), Katie Banister (PPIE coordinator); who are grateful for the substantive contributions from other members of CHaRT/HSRU staff.	31/05/22
08	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Ruth Thomas (CHaRT research manager), Kirsty McCormack (CHaRT research manager), Seonaidh Cotton (senior trials manager), Suzanne Breeman and Lynda Constable (deputy senior trials managers), Mark Forrest (senior IT development manager), Graeme MacLennan (senior statistician), Graham Scotland (senior health economist), Katie Gillies and Sharon McCann (process evaluation leads), Magda Rzewuska Diaz (PPIE coordinator); who are grateful for the substantive contributions from other members of CHaRT/HSRU staff.	25/09/24

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ABBREVIATIONS

ACE	Aberdeen Centre for Evaluation
ADE	Adverse Device Effect
CAG	Confidentiality Advisory Group
CAPA	Corrective Action and Preventative Action
C&C	Capacity and Capability
CE	European Conformity
CHaRT	Centre for Healthcare Randomised Trials
CI	Chief Investigator
CRF (eCRF)	Case Report Form (electronic Case Report Form)
CSO	Chief Scientist Office (part of Scottish Government Health and Social Care Directorates)
CTA	Clinical Trial Authorisation
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
DMP	Data Management Plan
DPIA	Data Protection Impact Assessment
DSUR	Development Safety Update Report
EME	Efficacy and Mechanism Evaluation Programme
EU	European Union
EudraCT	European Clinical Trials Database
FOI	Freedom of Information
FTS	File Transfer Service
GCP	Good Clinical Practice
GRP	Good Research Practice
HEAP	Health Economics Analysis Plan
HRA	Health Research Authority
HSDR	Health Services and Delivery Research
HSC-PBPP	NHS Scotland Public Benefit and Privacy Panel for Health and Social Care
HTA	Health Technology Assessment
IAHS	Institute of Applied Health Sciences
IB	Investigator's Brochure
ICH	International Conference on Harmonisation

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IMP	Investigational Medicinal Product
IMS	Integrated Management System database
IP	Intellectual Property
IRAS	Integrated Research Application System
ISF	Investigator Site File
IT	Information Technology
MDCI	Medical Device Clinical Investigation
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare products Regulatory Agency
MRC	Medical Research Council
NHS	National Health Service
NHSE	National Health Service England
NIHR	National Institute for Health and Care Research
NIHR CRN CC	NIHR Clinical Research Network Coordinating Centre
NIHR HTA	National Institute for Health Research Health Technology Assessment
PHR	Public Health Research
PI	Principal (local) Investigator
PIL	Patient Information Leaflet
PMG	Project Management Group
PPI	Patient and Public Involvement
PPIE	Patient and Public Involvement and Engagement
PIP	Protecting Information Policy
PWI	Project Website Initiation
R&D	Research and Development
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RfPB	Research for Patient Benefit
RN	Research Nurse
RSV	Randomisation Simulations Verification
QA	Quality Assurance
QALY	Quality Adjusted Life Year
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SmPC	Summary of Product Characteristics

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SOP	Standard Operating Procedure
SOP-QA	Standard Operating Procedure - Quality Assurance
SPSS	Statistical Package for the Social Sciences
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMP	Trial Monitoring Plan
TSC	Trial Steering Committee
TSD	Trial Service Definition
UAT	User Acceptance Testing
UKCA	UK Conformity Assessed
UKCRC	UK Clinical Research Collaboration
UoA	University of Aberdeen
USADE	Unanticipated Serious Adverse Device Effect
USM	Urgent Safety Measures

RELATED REFERENCES AND RESOURCES (Q-PULSE AND LOCAL SPONSOR SOPS)

Q-Pulse Within this document there are a number of associated documents that are accessed via Q-Pulse. The titles of these documents appear in the text coloured **red**. All CHaRT staff will have a specific login to Q-Pulse and have access to this software via their PCs.

Sponsor SOPs Links to locally Sponsored SOPs have been added to this document, where relevant. The SOP reference and title for each of these documents appear in the text coloured **blue**. The full list of Sponsor SOPs can be found here:
www.abdn.ac.uk/grampian-research-office/sops/index.php

Chapter 1: Standard Operating Procedure (SOP) details

CHAPTER 1: STANDARD OPERATING PROCEDURE (SOP) DETAILS

[\[v08.0100.08\]](#)

LEAD AUTHOR

CHaRT director.

BACKGROUND

The Standard Operating Procedure (SOP) for the design, conduct, analysis, reporting, documentation and quality assurance of randomised controlled trials (RCT) and other high quality trial designs in the Centre for Healthcare Randomised Trials (CHaRT) clinical trials unit (CTU), Aberdeen Centre for Evaluation (ACE), University of Aberdeen (UoA).

PURPOSE

The purpose of this chapter is to provide details of the aims of the SOP book; their structure (format, style, content); who is responsible for them and how they are maintained.

APPLICABILITY

- Essential for those members of staff involved in the production and maintenance of the SOP.
- Useful background reading for all members of staff observing the SOP in their work.

STANDARD OPERATING PROCEDURE (SOP) DETAILS

1.1 Overview of SOP [\[v08.0101.08\]](#)

Clinical trials are expected to be run to exacting ethical, regulatory and legal standards and it is paramount that all CHaRT clinical trials are conducted in compliance with: the trial protocol and CHaRT SOP book, the University of Aberdeen's Research Governance Handbook (www.abdn.ac.uk/staffnet/research/research-governance-304.php), the UK Policy Framework for Health and Social Care Research (www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/) and the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (SI1031: www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf) and any updates. For locally sponsored studies, the joint University of Aberdeen and NHS Grampian's sponsor SOPs (SOP-QA: www.abdn.ac.uk/grampian-research-office/sops/index.php) must be complied with and, where relevant, the Sponsor's Quality Management System Matrix should be completed documenting which of the Sponsor SOPs have been read. This should be held in staffs' training records (see [Section 16.3](#)). For externally sponsored studies, the relevant corresponding requirements, which may include local SOPs, may need to be integrated. International trials must conform to all relevant national requirements.

Currently, only Clinical Trials of an Investigational Medicinal Product (CTIMPs) are required to comply with the UK Medicines for Human Use (Clinical Trials) regulations. However, to ensure consistency of quality assurance across all clinical trials adopted by CHaRT, **all** trials (CTIMPs and non-CTIMPs) need to adhere to the appropriate regulations and are run in compliance with the principles of Good Clinical Practice (GCP). Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, and that the clinical trial data are credible.

This SOP book describes how CHaRT conducts its trials, covering all aspects including: the scientific issues of design and analysis; ensuring a trial is properly authorised; conducting

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studies to the principles of GCP; specific issues for disciplines that comprise the core competencies required for a multidisciplinary trial (trial managers, data coordinators, IT professionals, statisticians, health economists, qualitative researchers, clerical staff, clinical staff); ensuring quality throughout; describing the processes for documentation and archiving trial materials and training issues.

The aim of this SOP book is to have a simple core set of generic processes that need only routine minor review (every three years) and modification, with occasional update to respond to major external change in the ethical, regulatory and legal framework. For a specific trial, all the detail of the processes will be contained in the trial guidance (see [Section 5.5.1](#)), which will document any departure from the CHaRT SOP.

1.2 Style of SOP [\[v08.0102.01\]](#)

To facilitate ease of maintenance and readability, the SOPs appear in book form – that is, we do not have individual SOPs each formatted to an identical template. The book comprises chapters (covering a theme e.g. trial management issues), and chapters will comprise headings, which in turn will cover specific items.

1.3 Contents of SOP [\[v08.0103.03\]](#)

In general, a specific item and/or a chapter will be expected to cover:

- **Lead author:** State the role of the person responsible for leading the authoring of the chapter.
- **Background:** Briefly discuss the background to the SOP, referring to regulatory guidance, if applicable. Consider the driving forces or why the SOP is necessary.
- **Purpose:** Describe the procedure to be followed and the setting in which the SOP applies.
- **Applicability:** Define the scope of responsibility for the SOP.
- **SOP title:** Describe the procedures and specific items that relate to the chapter.
- **Related references and resources:** Include any additional publications, weblinks or further reading that is not already cross referenced within the chapter as appropriate.
- **Version history:** Summarise the significant changes made to the SOP chapter from the previous version.

1.4 Format of SOP [\[v08.0104.03\]](#)

To make the **Book > Chapter > Section** style workable, the following administration format is adopted.

- **For a chapter:**

Chapter X:

<Title> e.g. Chapter 10, Statistical issues

Version:

<Version number> e.g. xx.cc.ss.yy - where xx is the overall protocol 'counter', cc is the chapter identifier & ss the section identifier (always '00' for a chapter); yy is the version of this chapter.

- **For a section:**

Section C.XX:

<Title> e.g. 10.4: Randomisation (statistical issues)

Chapter 1: Standard Operating Procedure (SOP) details

Version: <Version number> e.g. xx.cc.ss.yy - where xx is the overall protocol 'counter', cc is the chapter identifier & ss the section identifier; yy is the version of this section.

1.5 SOP responsibilities [\[v08.0105.02\]](#)

The overall responsibility for the SOP book is held by the director of CHaRT. The CHaRT Quality Assurance (QA) manager will oversee the document control of this book and is responsible for managing and facilitating the SOP review, delegating responsibility for authoring chapters on a common theme (e.g. data management, statistics, trial management, and so on) to the appropriate theme leader (senior IT development manager, senior statistician, senior trials manager, and so on). Individual sections within these chapters, covering a specific item, may be delegated by the theme leader to individual staff members as appropriate.

1.6 SOP review [\[v08.0106.05\]](#)

The SOP book will be formally reviewed every three years from the issue date, or earlier should substantive changes in the external environment in which randomised controlled trials are conducted necessitate such a review. The CHaRT director and the SOP committee (see [Section 1.9](#) below for membership) are responsible for identifying new requirements, detecting obsolescence, and updating current material. The review of the chapters within the SOP book will be coordinated by the designated theme leader (lead author). The CHaRT QA manager is then responsible for collating and formatting the chapters of the SOP book, updating the version numbers for the various chapters and sections of the book (see [Section 1.4](#) for details) and updating the '[Version History](#)' section of the book.

Once finalised, the SOP book will be reviewed by the UoA/NHS Grampian research governance and QA managers to ensure local compliance. Thereafter, the CHaRT QA manager will arrange for the completed version of the SOP book to be reviewed by the director of CHaRT for final approval, will add the appropriate Issue Date; Effective Date and Review Date, and then the CHaRT director and QA manager will add wet signatures. The SOP issue date is the date the SOP book is issued and made available to all CHaRT staff. The effective date will be one month after the issue date to allow sufficient time for CHaRT staff to be trained.

1.7 SOP training [\[v08.0107.03\]](#)

CHaRT recognises that to ensure its staff are conversant and compliant with the SOP book, training is a key issue. All CHaRT staff are required to be familiar with the content of the SOP book (and relevant detail of the trial guidance (see [Section 5.5.1](#) for details) for all trials they have responsibilities for). The QA manager will organise general SOP overview training sessions which take place for new CHaRT staff. A note of this training is held by the QA manager. Training sessions, covering specific aspects of the SOP book, are usually managed in specialist groups e.g. statisticians, IT, trial managers, clerical staff, senior staff and in generalist groups for generic issues.

1.8 SOP location [\[v08.0108.03\]](#)

An electronic version of the currently approved **SOP book** is available on **Q-Pulse** and at www.abdn.ac.uk/hsru/what-we-do/trials-unit/chart-sops-556.php. The original signed copy of

Chapter 1: Standard Operating Procedure (SOP) details

the SOP book is held by the QA manager (or delegate) in a secure location within the CTU. The QA manager (or delegate) also has another hard copy that is available for controlled use and distribution. Superseded versions of the original copy and electronic copy of the SOP book will be archived as appropriate.

1.9 SOP committee [\[v08.0109.06\]](#)

The CHaRT SOP committee is responsible for all aspects of the specifications, authoring, maintenance, and distribution of the CHaRT SOP. The committee is chaired by the CHaRT director, who is responsible for the conduct of all CHaRT's activities, and comprises the QA manager, senior and deputy senior trials managers, senior IT development manager, research manager(s), senior statistician, senior health economist, process evaluation leads and Patient and Public Involvement and Engagement (PPIE) coordinator. Membership will be reviewed as a specific item every three years and is detailed in the '[Lead Authors' History](#)' at the start of the SOP book.

1.10 Standardisation [\[v08.0110.02\]](#)

CHaRT's philosophy is to demonstrate all processes used in its trials are of high quality and fit for their purpose. There is a commitment to re-use existing, proven tools, possibly customising them to new situations in new trials. Standardisation is therefore a key objective. A resource repository containing a number of templates and examples (protocols, patient information leaflets, case report forms, committee reports, statistical analysis plans) is managed and document controlled using quality management specific software (**Q-Pulse**) and should be consulted when planning a new trial.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Updated SOP details to include Lead Author & Version history; updated 1.6: SOP review to include details on sponsor oversight.	Jan 2012
04	Updated section 1.1 to include information on externally sponsored studies, section 1.6 to detail the issue and effective dates, and section 1.8 to amend the location of the SOP book from the Shared drive to Q-Pulse.	Aug 2015
05	Minor wording amendments, updated Section 1.9 to include addition of new lead authors.	Apr 2018
06	Minor changes to wording in section 1.1 including information on local Sponsor Quality Management System matrix.	Feb 2020
07	Updated section 1.1 to remove the reference to the IAHS Research Governance and QA policy and the Declaration of Helsinki, section 1.3 to change 'Cross references' to 'Related references and resources'. Minor changes to wording in section	Apr 2022

Chapter 1: Standard Operating Procedure (SOP) details

	1.7 to provide more clarity regarding training. Addition of deputy senior trials managers to the section 1.9.	
08	Updated the SOP review period from two to three years in sections 1.1, 1.6 and 1.9	Apr 2024

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CHAPTER 2: CHART DETAILS

[\[v08.0200.07\]](#)

LEAD AUTHOR

CHaRT director.

BACKGROUND

To describe the setting and environment in which CHaRT operates.

PURPOSE

The purpose of this chapter is to provide the context in which CHaRT conducts its business, as an academic clinical trials unit specialising in the design, conduct, analysis and reporting of publicly funded trials, within the setting of the University of Aberdeen. CHaRT achieved full registration as a UK Clinical Research Collaboration (UKCRC) Clinical Trials Unit in November 2007, which was renewed in 2012, 2017 and again in 2022.

APPLICABILITY

- It is not essential reading but should be useful background for all members of staff, particularly those involved in writing or maintaining the SOP Book.

CHaRT DETAILS

2.1 CHaRT setting

[\[v08.0201.02\]](#)

CHaRT is concerned with collaborating on all aspects of the design, conduct, analysis and reporting of randomised clinical trials of important healthcare questions and funded by the public sector.

CHaRT is part of the Aberdeen Centre for Evaluation (ACE) which is itself part of the Institute of Applied Health Sciences (IAHS), which is part of the School of Medicine, Medical Sciences and Nutrition in the University of Aberdeen.

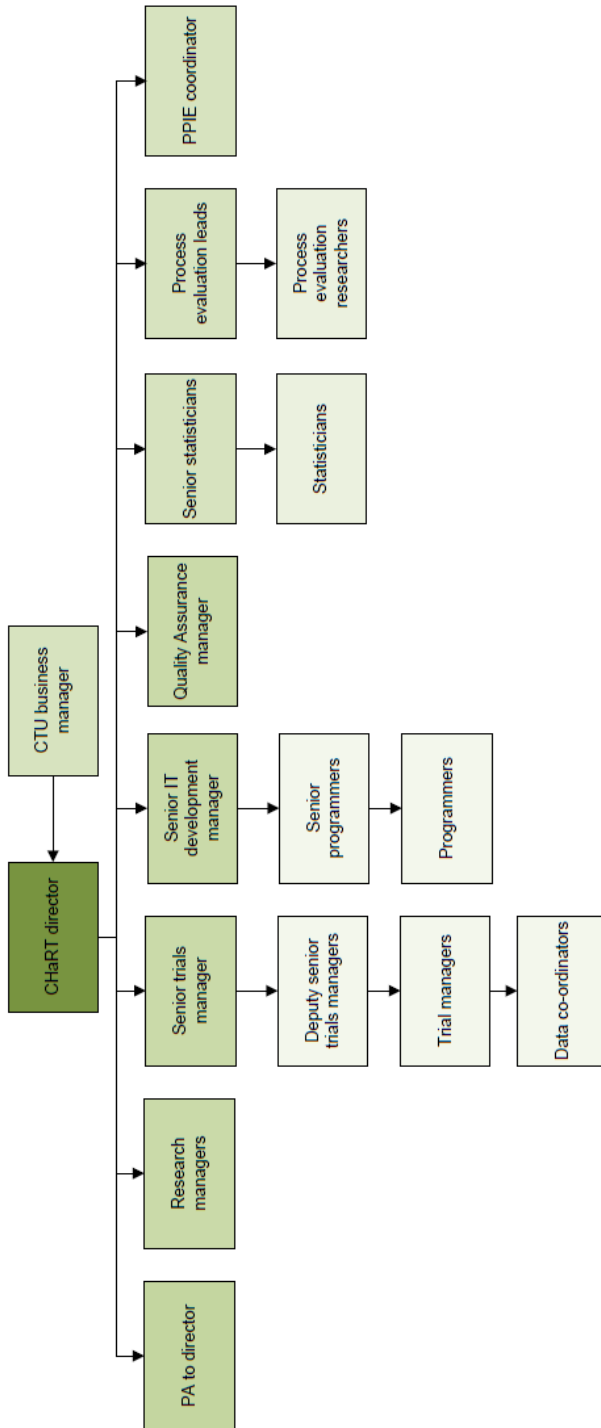
Members of CHaRT are therefore employed by the University of Aberdeen, and as such are subject to the rules and regulations of the University. CHaRT itself is likewise obliged to follow University policies and procedures. These policies include those governing:

- recruitment (including all employment laws)
- training (including professional development)
- research practices (including research misconduct)
- research governance and quality assurance
- intellectual property (IP)
- financial issues
- promotion procedures
- data confidentiality

This SOP book is written with these structures in mind. If any text within the SOP book is found to be in conflict with these University policies, it will be amended at the earliest opportunity.

2.2 CHaRT organisation Organogram of CHaRT

[\[v08.0202.07\]](#)



COPY

Organogram

CHaRT is part of ACE, and all its staff are members of ACE. A senior CHaRT management group comprises the senior trials managers, senior IT development manager, senior statistician, research managers, QA manager and CHaRT PA/secretary, and the CHaRT director to whom they report. Other members of CHaRT (trial managers, programmers and data co-ordinators) report to their line manager. The senior CHaRT management group receives input from senior leads in statistics, health economics, and clinical disciplines as required.

- **Trial management:**

The trial management function is managed by the senior and deputy senior trials managers who report to the CHaRT director. There are various models of engagement for the provision of trial management for CHaRT trials. Generically, these models involve either complete trial management support from CHaRT or a more supervisory, mentoring type role where an experienced CHaRT trial manager provides oversight and guidance to a trial manager who is not located within CHaRT.

- **IT/applications:**

The IT/applications programming function is approximately 80% CHaRT activity, the remaining 20% being non-CHaRT activity (e.g. web-based disease registries, observational studies) so for administrative convenience this whole function is run by CHaRT. The programming group is managed by the CHaRT senior IT development manager, with input from two senior programmers.

- **Statistical input:**

The statistical group is managed by the senior statistician. CHaRT is configured in such a way that, in principle, it could obtain statistical support from other academic units (see [Section 12.11](#): Partnerships with external statisticians).

- **Health economic input:**

The provision of health economics expertise is approached on similar lines to statistical support: CHaRT has a close working relationship with the Health Economics Research Unit (HERU) in IAHS. CHaRT also collaborates with non-Aberdeen health economists (see [Section 13.8](#): Partnerships with external economists).

- **Clinical, methodological and other input:**

CHaRT receives input from various sources (e.g. from clinical and methodological leads) and more broadly from the IAHS and externally; including links through the UKCRC CTU network and their subgroups (trial management, QA, information systems, statistics, Patient and Public Involvement and monitoring). This input usually comprises assisting with understanding of clinical contexts and understanding of patient and public perspectives for trial participation, assessing evidence bases, helping with grant applications, and advertising on clinical networks and professional bodies.

- **Finance:**

To remain competitive in attracting funding, and to deliver trials consistently on time and budget, providing value for the public funders (the taxpayers), CHaRT has developed an internal costing model for its trials. The costing of a new trial and the subsequent management of the trial budget is a collaboration between senior CHaRT staff and the CTU business manager, and all other stakeholders.

RELATED REFERENCES AND RESOURCES

ukcrc-ctu.org.uk/

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Minor change to organogram to show “senior management group” and additional information on Clinical Input to 2.2: CHaRT organisation.	Jan 2012
04	Minor update to organogram and new section for programming group in section 2.2: CHaRT organisation.	Jul 2015
05	Updated Organogram, removal of text re health psychology; update to IT applications paragraph, and clinical, methodological and other input paragraph.	Apr 2018
06	No change.	Jan 2020
07	Minor wording update to ‘Purpose’. Organogram updated, minor wording updates to include all relevant UKCRC CTU network subgroups in ‘Clinical, methodological and other input’ section, and addition of weblink to UKCRC under ‘Related references and resources’.	Jan 2022
08	Minor update to the Background and section 2.1 to reflect the change from HSRU to ACE. The organogram has been revised to reflect the current organisational structure within CHaRT, and updates and clarifications have also been made regarding the functions and input from all groups.	Sept 2024

Chapter 3: Quality Assurance (QA)

CHAPTER 3: QUALITY ASSURANCE (QA)

[\[v08.0300.08\]](#)

LEAD AUTHOR

Quality Assurance manager.

BACKGROUND

Clinical trials rely on the goodwill of participants; are time consuming for the research staff; and tend to be expensive to fund. It is therefore a prerequisite that all trials in CHaRT are conducted to a high quality – to avoid putting participants at unnecessary or pointless risks, since a trial of an unimportant question or a trial conducted to a poor standard would not provide meaningful evidence; to allow the research staff to work efficiently in the knowledge that their efforts are combining to produce valuable insights; to reassure the funders that public money is being used appropriately and to good effect; and to demonstrate to the sponsor of the trial that their interests are safeguarded.

PURPOSE

To describe the rationale and processes for all quality assurance (QA) activities within CHaRT. QA is the set of processes by which CHaRT can demonstrate that its work has been carried out at or above the relevant required level of performance.

APPLICABILITY

- Essential reading for all CHaRT staff.

QUALITY ASSURANCE (QA)

3.1 Overview of QA in CHaRT [\[v08.0301.04\]](#)

The responsibility for all QA activity resides with the CHaRT QA manager. The QA manager is a senior member of CHaRT staff and has scheduled monthly QA meetings with the director of CHaRT. The QA manager also interacts regularly with the CHaRT senior management group (see [section 2.2: CHaRT organisation](#)).

The QA manager's primary responsibilities are:

- overseeing and advising on assessments of quality on CHaRT's projects (see [section 3.2: Internal assessment of QA procedures](#));
- overseeing CHaRT's co-operation with external auditors & monitors (such as NHS Grampian and NHS England), regulators (such as Medicines and Healthcare products Regulatory Agency (MHRA)), and so on (see [section 3.3: External audit and monitoring of QA procedures](#)) and;
- training (see [section 3.4: Training](#)).

The QA manager is also expected to facilitate any activity designed to detect or arising from the discovery of "Fraud and misconduct" (see [section 3.5](#)).

3.2 Internal assessment of QA procedures [\[v08.0302.06\]](#)

CHaRT's internal QA procedures operate at two levels (a) CHaRT generic procedures, and (b) trial specific procedures.

Chapter 3: Quality Assurance (QA)

3.2.1 CHaRT generic procedures

- (I) *Quality assurance of CHaRT staff:* The CHaRT director and line manager will ensure that staff have appropriate qualifications and experience to deliver their responsibilities by having: up-to-date CVs; complete and accurate training records; and a system of periodic annual review to identify training gaps.
- (II) *Quality assurance of buildings/work environment:* It is the responsibility of the University of Aberdeen's Estates Department's Maintenance Team to ensure that the building(s) that staff work in is maintained and fit for purpose.

All computing and IT equipment are supported and tested by IT services. Any other electrical office equipment is tested by Estates (or sub-contracted to an external company by Estates). Faults affecting any equipment are reported to the CTU business manager. All staff and students are trained on the use of equipment and provided with simple instructions as and when required.

The UoA's health and safety inspection and work-station assessments are carried out in accordance with the UoA Health & Safety Policy. Although staff routinely work in CHaRT offices, if they are required to work anti-social hours or in potentially uncontrolled environments e.g. home visit to a participant to collect outcome data via a face-to-face interview etc., care will be taken that staff understand potential risks and are able to follow procedures to minimise those risks e.g. taxi transport in anti-social hours; having a colleague present in an uncontrolled environment.

3.2.2 Trial specific procedures

The type of trials CHaRT engages in are usually long-term studies of complex interventions involving investment of considerable sums of public money. They are multidisciplinary in nature, involving core competencies such as experienced trialists, trial managers, IT professionals, statisticians, health economists, and qualitative researchers, interacting with clinical staff and participants. It is essential that trials are properly designed, conducted, analysed, reported and archived. The evidence that these procedures have been carried out to the required standard is through the production of trial documentation, which are developed using the repository of approved standardised templates available on [Q-Pulse](#). The trial Project Management Group (PMG) (see [section 5.12.1](#)) is then responsible for reviewing and commenting on any trial specific documentation. In addition, if any deficiencies are found, the senior trial managers will negotiate a correction plan with the responsible staff, including the QA manager and/or CHaRT director, and will monitor that its implementation has been successful. If the deficiency is generic or has ramifications for other trials, that will be addressed by the senior CHaRT management group.

As part of CHaRT's QA processes, the QA manager together with the senior trials manager(s) will review the final draft of each trial's **Trial Monitoring Plan** (TMP), available on [Q-Pulse](#), and any subsequent updates to the TMP thereafter. In addition, the QA manager/senior trials managers will carry out a review of the trial specific monitoring activities during the trial, as detailed in the TMP, and any observations will be noted, addressed and recorded in Q-Pulse (see [Section 5.12](#)). In addition, the QA and senior trials managers will perform a quarterly review of the trial specific deviation logs submitted to the local Sponsor to address any generic findings across studies, and implement a corrective and preventive actions (CAPA) plan, as appropriate (see [Section 6.8](#)).

Chapter 3: Quality Assurance (QA)

3.3 External audit and monitoring of QA procedures [\[v08.0303.05\]](#)

The QA manager will act as point of contact for all external audits and monitoring of CHaRT (for example, from NHS Grampian R&D and/or University of Aberdeen (refer to [SOP-QA-29: Audit](#) and [SOP-QA-28: Monitoring](#) for locally sponsored studies)), other non-Aberdeen Universities or NHS Trusts with whom CHaRT is collaborating; and regulatory bodies such as the UK MHRA (refer to [SOP-QA-30: MHRA Inspections](#) for locally sponsored studies) or NHS England.

The QA manager will facilitate CHaRT's response to such external audits, providing requested documentation, making sure staff are available, responding to requests during visits, and then co-ordinating CHaRT's response to any requirements identified in the auditor's report.

For all external trial specific monitoring, the QA manager will assist the trial office team: with any preparation for the visit; being available for the monitoring visit (if required); with coordinating the response to any findings raised in the monitor's report.

For both audits and monitoring visits, where generic (non-trial specific) 'Observations' or 'Non-conformances' have been reported and may affect or have an impact on other trials, the QA manager will liaise with senior trials manager(s) and/or CHaRT senior management group to ensure all trial teams are made aware of this. In addition, changes may need to be made to specific CHaRT processes. Refer to [SOP-QA-28: Monitoring](#) for details of how monitoring findings (observations and/or non-conformances) are documented, reported and addressed for locally sponsored studies.

3.4 Training [\[v08.0304.04\]](#)

CHaRT understands the need for a properly trained workforce, and that training is a constantly evolving requirement. It is therefore committed to identify, meet and document its staff training and development needs (see [section 16.3](#) for further information). All staff are expected to keep an up-to-date 'Staff Development Manual', or an equivalent, which will include their CV, annual review objectives, staff training courses attended.

The responsibility of the QA manager is to periodically review key training records (e.g. GCP, Information Governance, Research Integrity), and liaise with the CHaRT senior staff (such as the CHaRT director, the CHaRT senior trials manager, CHaRT senior IT development manager, and the senior statistician) to assure compliance, where applicable.

3.5 Fraud and misconduct [\[v08.0305.03\]](#)

If during any routine or ad-hoc inspection of trial documentation, or any correspondence or within any conversations with staff within or out with CHaRT, the QA manager (or delegate) has reason to suspect the possibility of fraudulent behaviour or behaviour which might amount to research misconduct, they must, without delay, inform the CHaRT director, in strict confidence. If the CHaRT director is potentially compromised in any way, they should alert the director of the IAHS (or their superior).

Chapter 3: Quality Assurance (QA)

CHaRT staff, as University employees, are required to be aware and abide by the University policies on issues of research misconduct. For further information, please refer to the UoA's Research Governance Handbook at www.abdn.ac.uk/staffnet/research/research-governance-10644.php#panel6326, the University's Policy & Procedure on Public Interest Disclosure (whistleblowing) www.abdn.ac.uk/staffnet/governance/policies-procedures-plans-and-guidlines-399.php and local Sponsor guidance on Study Management: Management and Monitoring www.abdn.ac.uk/clinicalresearchgovernance/study-management/management.php.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Further information added to section 3.2.1 on Quality assurance of buildings/work environment.	Jan 2012
04	Minor changes to title of section 3.2 to say 'assessment' instead of 'audit' and 3.3 to include 'monitoring'. Details of study-specific monitoring visits added. Minor changes & updates.	Apr 2015
05	Minor wording amendments and clarification regarding QA of CHaRT staff.	Apr 2018
06	Update to section 3.3 on feedback to CHaRT staff from any generic monitoring or audit findings, and update to weblinks in section 3.5.	Jan 2020
07	Minor update to section 3.3 to include link to Sponsor SOP-QA-28: Monitoring and add NHS Digital as potential auditors and renaming of 'Findings' to 'Non-conformances', and section 3.4 to clarify wording around review of key training records, giving examples.	Nov 2021
08	Minor wording updates to sections 3.1 and 3.2.1 to reflect changes from HSRU to ACE and other UoA changes regarding health and safety. Update to section 3.2.2 to provide information on CHaRT's internal processes for reviewing CHaRT trial monitoring plans and trial specific deviations, and addition of weblinks to UoA Research Governance handbook in section 3.5.	Feb 2024

CHAPTER 4: COLLABORATION

[\[v08.0400.04\]](#)

LEAD AUTHOR

Research managers.

BACKGROUND

CHaRT receives core funding from the University of Aberdeen and NHS Grampian, and competitive grant funding from many public funders such as: NIHR HTA, HSDR, PHR, EME, Research for Patient Benefit (RfPB), CSO, and other research councils, charities and commercial organisations. It is important that CHaRT has rigorous and transparent criteria for developing collaborations with research partners.

PURPOSE

To describe the criteria upon which CHaRT's engagement will be based.

APPLICABILITY

- Essential for all senior CHaRT staff involved in strategic decision making.
- Desirable background reading for all CHaRT staff.

COLLABORATION

4.1 CHaRT collaboration criteria [\[v08.0401.04\]](#)

The management of the selection of the trials adopted into the CHaRT portfolio is the responsibility of the CHaRT director and the CHaRT research managers. The criteria for selection of trials can be found at: www.abdn.ac.uk/hsru/what-we-do/trials-unit/planning-a-trial-553.php. When assessing the suitability of a trial for adoption into the CHaRT portfolio and the necessary work up for funding, the views from various stakeholders are solicited and discussed. Arrangements for CHaRT's engagement will vary for each trial depending on the collaboration sought.

Reflecting our academic remit, CHaRT primarily collaborates as an intellectual partner in the research, not as a service provider. It expects to lead the methodological design of the trial; to take responsibility for the management of the trial; and to use the most appropriate technologies for the analysis and reporting of the trial. Variations on this model of engagement are undertaken. However, in all instances CHaRT anticipates making a significant intellectual contribution to the research, and for its staff members to be recognised for their contribution as grantholders and authors as appropriate.

RELATED REFERENCES AND RESOURCES

[Chapter 2: CHaRT details](#)

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	

Chapter 4: Collaboration

03	Removed paragraph referring to strategy gap, detailed staff involved in CHaRT advisory group, and included sentence about arrangements for CHaRT's engagement.	Jan 2012
04	Minor changes to Background about funders.	Apr 2015
05	Minor wording amendments; clarification of portfolio target and frequency of advisory group meetings.	Apr 2018
06	Minor update to Background to reflect the current status of the CHaRT trial portfolio.	Feb 2020
07	Minor change to 'Background' to update list of funders and to section 4.1 to remove the CHaRT Advisory Group meetings timeframe.	Jan 2022
08	Removal of reference to core funding support from CSO in the Background, and update in section 4.1 to the process for assessing trial suitability for adoption into the CHaRT portfolio.	Mar 2024

CHAPTER 5: TRIAL INITIATION

[\[v08.0500.08\]](#)

LEAD AUTHORS

Senior and deputy senior trials managers.

BACKGROUND

The initiation (or set-up) phase of a trial is demanding. There are a number of legally required processes that need to happen (the authorisations – ethical, regulatory e.g. Clinical Trial Authorisation, financial e.g. insurance and indemnity, and site contracts). There is usually a relatively short, fixed time frame from being awarded the grant to starting recruitment (typically no more than six months). In addition to the obligatory authorisations, the multidisciplinary trial team must effectively organise the trial materials such as the protocol, the case report forms (CRF), patient information leaflets (PIL), the consent form and any other trial documentation; and the trial databases and IT applications (such as the randomisation system). This requires good communication and planning between the various groups – the clinicians, statisticians, programmers, trial methodologists, trial managers and so on. A trial manager usually plays a pivotal role in this phase.

Reflecting the diverse populations that the trials aim to serve is crucial for the validity and applicability of the results. Trial Forge (www.trialforge.org/improving-trial-diversity/) is a valuable resource that offers guidance on improving trial diversity. In particular, the INCLUDE Framework on Trial Forge provides a way of identifying challenges and opportunities to including diverse ethnic and socioeconomic backgrounds, as well as those with impaired capacity to consent. Members of the trial and site teams, and oversight committees may also provide suggestions for how to address some of these challenges. By integrating these approaches during trial initiation ([chapter 5](#)), during the recruitment and follow-up phases ([chapter 6](#)), publication and dissemination ([chapter 8](#)), within process evaluation ([chapter 14](#)) and in patient and public involvement ([chapter 15](#)), we aim to ensure our trials are more representative and the findings more universally applicable. This not only improves the quality of the research but also upholds ethical standards in clinical research.

PURPOSE

To describe the essential processes in developing a trial from successful grant proposal to first randomised participant.

APPLICABILITY

- Essential reading for all CHaRT staff involved in launching a trial, in particular the trial managers.

TRIAL INITIATION

5.1 Trial authorisations [\[v08.0501.08\]](#)

5.1.1 Sponsorship

All CHaRT trials need a sponsor (see the following link for a description of “sponsor” www.ct-toolkit.ac.uk/glossary/?letter=S&postcategory=-1). The sponsor(s) is usually the substantive employer of the Chief Investigator (CI). Therefore, for trials led from Aberdeen, this will usually be the University of Aberdeen and NHS Grampian as co-sponsors (refer to [SOP-QA-4: Applying for Sponsorship](#) for details on applying for sponsorship for locally sponsored studies). When the CI is based out with Grampian it is the trial manager’s responsibility to check with the CI that sponsorship has been obtained. It is usual (obligatory, if the

Chapter 5: Trial Initiation

University of Aberdeen and/or NHS Grampian is the potential sponsor) for an organisation considering taking on the role of sponsor to institute a risk assessment, to establish whether their responsibilities will be executed properly by the trial team. It is the trial manager's responsibility to liaise with the sponsor about the risk assessment. Where a sponsor requires the trial manager to complete a risk assessment, this should be done in consultation with the senior trial managers. A CHaRT **risk assessment** template is available on **Q-Pulse**. As indicated above, the sponsor's role is an important one in the configuration of a clinical trial. CHaRT as a trials unit will undertake to communicate promptly and effectively with the sponsor(s) to satisfy and reassure the sponsor(s) that the sponsor's obligations on the authorisations, the financing and the progress reporting (including emerging safety data) of the trial are being met. This will include providing information before the start of a trial for the purposes of risk assessment by the sponsor(s) and submission of core documentation to the sponsor(s) for sign off prior to submitting applications for regulatory approvals.

The trial manager should be satisfied that the appropriate insurance and indemnity is in place, by verifying this with the sponsor.

5.1.2 Ethics approval

The need for independent review of the ethics of medical research is obligatory.

CHaRT will always comply with the relevant process in force. Currently, for our UK trials within the NHS, this is the Health Research Authority (HRA) www.hra.nhs.uk/ and the Integrated Research Application System (IRAS) www.myresearchproject.org.uk/ who maintain the established UK-wide framework for review of research.

Prior to trial start-up, all trials must have favourable opinion from a Research Ethics Committee (REC), and recruitment must not start until a favourable opinion is in place. For studies that are neither a CTIMP or a combined IMP/device trial, the application form can be found at: www.myresearchproject.org.uk/. For studies that are a CTIMP or a combined IMP/device trial, please see [section 5.1.4](#) for more information. A trial manager will establish with the CI who is taking responsibility for preparing and submitting the ethics application. The trial manager must have a copy of the full ethics submission and approval, filed in the TMF. It is usual that each document submitted to REC with the initial submission is versioned as version 1. Any deviation to this should be documented on a version log. Please see [SOP-QA-10: Applying for Research Ethics Committee Opinion](#) for further information for locally sponsored studies.

In exceptional circumstances, a trial may fall out with the remit of HRA and as such ethical review should be sought elsewhere.

5.1.3 Management approval

Management approval (sometimes referred to as Capacity and Capability (C&C) or R&D approval) must be obtained from the appropriate bodies prior to any research commencing (this may be from the R&D department of an NHS Trust, R&D department of an NHS Board, primary care general practice, primary care dental practice, Research Network or similar depending on where the research is to take place). Similar to the ethics favourable opinion, no recruitment at a centre should take place until R&D approval is in place for that site. Please see [SOP-QA-10: Applying for Research Ethics Committee Opinion](#) for local procedures on applying for R&D approvals.

There are different mechanisms in place for seeking R&D approval between nations.

Links to further details of the coordinating centres in England, Scotland, Wales and Northern Ireland are given below:

1. England: With the introduction of HRA approval, individual sites will be required to confirm capacity and capability according to the HRA processes. www.hra.nhs.uk/planning-and-improving-research/best-practice/nhs-site-set-up-in-england/
2. Scotland: NHS Research Scotland Permissions Coordinating Centre. www.nhsresearchscotland.org.uk/services/permissions-co-ordinating-centre/permissions
3. Wales: Health and Care Research Wales Permissions. healthandcareresearchwales.org/researchers-support-and-guidance-researchers-obtaining-approval-run-study-uk/obtaining-approval
4. Northern Ireland: Health and Social Care Application Gateway. research.hscni.net/approval-research-hsc

5.1.4. Regulatory approval

It is not always obvious what is or is not a Clinical Trial of an Investigational Medicinal Product (CTIMP) under the EU Directive. It is the trial manager's responsibility to verify that each trial has been checked against the published algorithm: (assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf) and if there is any doubt, seek advice from the Sponsor.

Studies involving a device that is not European Conformity (CE) or UK Conformity Assessed (UKCA) marked may fall under the Medical Devices Regulations. See www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device for further information and how to apply. Queries as to whether a trial would fall under the Medical Devices Regulations can be directed to the MHRA.

If the research is a CTIMP, or a combined IMP/device trial, taking place in the UK, there is a single application route for clinical trial authorisation (CTA) from the MHRA, and REC approval. Detailed guidance on the application process is available at www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/combined-ways-working-pilot/. The application form is available at [Identity Gateway \(nihr.ac.uk\)](http://identity.gateway.nihr.ac.uk). It is usual for the CI to own this IRAS form, and for the trial manager to adopt the deputy role in IRAS.

It is vital that the CHaRT trial team work closely with the lead clinical trials pharmacist or appropriate team member(s) to ensure that all procedures and facilities are appropriate, and any pharmacies involved with the trial are fully informed and adhering to the specific trial criteria. Please see [SOP-QA-15: Management of Medicinal Products used in Research](#) for further information for locally sponsored studies.

5.1.5 Other approvals that may be required

Other approvals may be required for a project, for example Radiation Assurance, or approvals associated with the use of routine data (for example from NHS Scotland Public Benefit and Privacy Panel for Health and Social Care (PPB) or Confidentiality Advisory Group (CAG)). The requirement for any additional approvals should be agreed between the Sponsor, CI and trial team and sought as appropriate.

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5.1.6 International authorisations

If any international sites are involved within a trial, the trial manager should work with the CI and Sponsor to ensure that all relevant national authorisations are obtained and maintained as appropriate.

5.1.7 Legal and financial

There are usually a number of legal issues that need to be addressed in a multicentre clinical trial. It is also important that the financial arrangements are in place before the trial starts. Sub-contracts are issued between the sponsor and the appropriate Trust/Board, Practice, Care Home or other appropriate body, including details of any research funds available to the sites. It is the responsibility of the CI or his/her designated team member to instruct and monitor contract activity. Please refer to [SOP-QA-13: Generation of Contracts](#) for further information on the generation of contracts for locally sponsored studies. All financial and contractual details should be considered confidential. It is the CI's (or delegate's) responsibility to verify that contracts between the sponsor(s) and individual recruiting centres are in place and up to date and bring any queries and/or variations to the attention of the sponsor(s). Recruitment at an individual site should not commence until this signed agreement is in place.

Contracts with any third parties are also likely to be required, for example with companies supplying IMP or devices, or carrying out laboratory tests or providing licensed questionnaires or transcription services. Please refer to [SOP-QA-16: Selection and Management of Third-Parties](#) for further information for locally sponsored studies.

For high value purchases (£50,000 or more) the sponsor is likely to require a tendering process before procurement of goods or services. Examples of an **invitation to tender** and **single supplier justification** are available on [Q-Pulse](#). The sponsor procurement policy is likely to include financial thresholds above which quotes may be required (this may be for purchases of £1000 or more). For locally sponsored studies, contact the University of Aberdeen procurement team (www.abdn.ac.uk/staffnet/working-here/purchasing-procurement-1110.php).

If services or products are being provided free of charge by a company or organisation, a contract or agreement is likely to be required. For locally sponsored studies, contact the University of Aberdeen R&I team (www.abdn.ac.uk/business-info/research-innovation/).

5.2 Data protection [\[v08.0502.02\]](#)

In order to comply with the appropriate data protection legislation, consideration must be made as to whether a trial requires a data protection impact assessment (DPIA). Data protection legislation requires that a DPIA is undertaken for any proposal to use personal data that *may result in a high risk* to individuals' privacy. A DPIA is not necessary for all research studies involving personal data, but it is a statutory requirement if the trial meets one of the mandatory criteria.

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For locally sponsored studies, a completed [DPIA Requirement form](#) should be completed and submitted when applying for sponsorship. If a DPIA is needed, a template **DPIA form** is available on [Q-Pulse](#). Further information about DPIAs, including details of the mandatory criteria, is available at www.abdn.ac.uk/staffnet/governance/data-protection-6958.php#panel8628. You can also use the '[data protection checklist for researchers](#)' to help guide you through your data protection obligations.

5.3 Trial registration [\[v08.0503.05\]](#)

All trials will be registered on a publicly available registry. Currently these include:

- The International Standard Randomised Controlled Trial Number (ISRCTN) Registry (www.controlled-trials.com)
- The National Institute of Health Trials Registry (www.clinicaltrials.gov)
- Research registry (www.researchregistry.com/) – although this is not preferred for trials.

If a funder/sponsor has a policy for registration, usually that will prevail.

It is a requirement for publication by leading journals and by the RECs that the trial be registered before any participants are randomised.

At the end of the trial, there is usually a requirement to upload the results to the trials registry (see [section 5.1.4](#) and [section 7.2](#)).

In addition, most, if not all CHaRT trials will be eligible for National Institute for Health Research Clinical Research Network (NIHR CRN) portfolio support: www.nihr.ac.uk/researchers/collaborations-services-and-support-for-your-research/run-your-study/crn-portfolio.htm

5.4 External relations [\[v08.0504.02\]](#)

It is the duty of all CHaRT staff to maintain professional and courteous relations with all external bodies that CHaRT will collaborate with. This will include other University departments (within Aberdeen, across the UK and further afield), other CTUs, professional bodies, government departments, NHS bodies, charities, funding agencies, and regulators. CHaRT works hard to project and maintain an image of excellence and reliability, and it is important that CHaRT staff promote this image at all times by their attitude and conduct.

5.4.1 Funders

CHaRT's long-term sustainability rests in part on maintaining its successful and established partnership with major funders such as NIHR Health Technology Assessment (HTA), Medical Research Council (MRC) and Chief Scientist Office (CSO). It is therefore important that CHaRT staff establish and maintain good relations with funders and that they understand and meet their contractual obligations to the funder. It is particularly important that in the event of any difficulties or dissatisfaction expressed by the funder, senior CHaRT staff are made aware of the situation.

Both background and any potential foreground IP issues will be considered by the funder at trial start-up and throughout the project. Advice can be sought from the sponsor(s).

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5.5 Trial protocol [\[v08.0505.07\]](#)

All CHaRT trials are required to have a trial protocol. **Protocol (CTIMP and non-CTIMP)** templates are available on [Q-Pulse](#). For locally sponsored studies, please refer to [SOP-QA-3: Protocol Guidance for High Risk Trials and CTIMPs](#). For studies sponsored elsewhere, the sponsor should be consulted about their preferred protocol template. The trial protocol is a statement of the scientific objectives of the trial, with clear detail on the methods and conduct and with input from all relevant disciplines. The trial protocol is usually based on an extension of the final approved grant submission. Members of the trial Project Management Group (PMG) are usually expected to take responsibility for drafting the protocol.

Trial protocols should be published in a peer-reviewed journal (preferably in open access mode) and should include the SPIRIT checklist¹ items. CHaRT, in collaboration with the CI, will take responsibility for this. Refer to specific journal guidelines as to when protocol papers will be accepted (for example before recruitment closes or before analysis starts). See [Chapter 8: Trial publications and dissemination](#) for more detail.

5.5.1 Trial guidance

It is important to distinguish the trial protocol from the trial guidance (sometimes referred to as an operation's manual), the former is the scientific statement of the trial's aims and methods; the latter is a very detailed description of trial processes that deliver the trial. The trial guidance is intended to grow organically as the trial progresses, documenting problems and their solutions, and also ensuring their consistent implementation across centres in a trial.

5.5.2 Management of trial supplies

For details about procurement, please refer to [section 5.1.6](#). Details of the management of trial supplies (e.g. drug supply, devices, equipment etc), which may include storage, accountability, distribution, recall procedures, labelling and incident reporting, should be detailed in the individual trial protocol and/or trial guidance.

5.6 Case report form (CRF) [\[v08.0506.06\]](#)

For the purposes of the SOP a Case Report Form (CRF) encompasses clinical case report forms and also patient reported outcomes such as questionnaires, both of which may be paper or electronic (eCRF).

The CRFs record the trial data. Wherever possible, tried and tested formats from previous trials should be used or adapted when designing the CRFs for a new trial. A number of CRF templates are available in the CHaRT resources repository on [Q-Pulse](#). For validated tools, licence agreements may be required.

CRFs are developed alongside the trial protocol and dummy tables (if necessary CRFs may be modified after feedback). See [Section 6.10](#) for further details about amendment processes for key documents.

The development of the CRFs is a multidisciplinary task, needing input from:

- investigators
- those responsible for the data collection e.g. trial nurses
- statisticians

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- health economists (as appropriate)
- health psychologists (as appropriate)
- IT application programmers
- trial managers
- patient and public involvement (PPI) partners
- trial committees (Trial Steering Committee (TSC), Data Monitoring Committee (DMC))

CRFs need to be subject to systematic checks against the trial protocol and version controlled. CRFs must be clearly set out, the data being collected matching the trial dummy tables (see [section 12.1](#)). CRFs will be incorporated into training materials and the Investigator Site File (ISF) and sent out to the sites by CHaRT and/or maintained by CHaRT on the trial web portal.

All participant completed questionnaires should be submitted to REC for approval; CRFs are not usually submitted to REC unless explicitly requested.

The versions of the CRFs that are approved internally for use will be versioned as version 1. At the outset of a trial, the programming team will build version 1 of the eCRFs (see also [section 6.10](#) for amendments).

5.7 Informed consent [\[v08.0507.06\]](#)

Consent is an essential element for all participants in clinical trials. It is usual for participants to be informed of their role in the trial and consent to it by indicating their willingness to participate by signing and dating an informed consent form. Any deviation to this process will be documented in the trial protocol.

For most studies, the key requirements of this process are that the participant is able to give consent; that they do so voluntarily; that they understand what they are consenting to; and that the consent is properly documented (the **consent form** template is available on [Q-Pulse](#)). Please refer to [SOP-QA-9: Receiving Informed Consent](#) for locally sponsored studies.

Traditionally, the mechanism for imparting the information to a participant to give them the opportunity to start comprehending their potential role in the trial is the **patient information leaflet** (PIL; this template is available on [Q-Pulse](#), please also see www.hra.nhs.uk/planning-and-improving-research/best-practice/informing-participants-and-seeking-consent/ and www.hra.nhs.uk/about-us/news-updates/improving-information-people-taking-part-research/ for further guidance on the content of these leaflets). The time that potential participants will have to consider participation will be detailed within the protocol. They also need to be given adequate access to trial staff to discuss any concerns they have.

Once informed consent has been satisfactorily given, the participant must be given a copy of the consent form for their retention. The protocol should document whether or not signed copies of the consent forms are returned to the trial office. The original “wet-ink” signed consent form should be retained in the Investigator Site File (ISF) (see [section 5.10.2](#)). Informed consent forms are a very important component of the essential documentation of a trial.

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Particular attention needs to be paid when eliciting the consent of vulnerable groups; these include participants with temporary or permanent cognitive impairment (for example, trials in an emergency setting when a person might be unconscious; or trials in people with dementia or mental health conditions); trials in children; trials in people with learning difficulties or language issues; and so on. Refer to the relevant national guidance on incapacity (see www.hra.nhs.uk/planning-and-improving-research/best-practice/informing-participants-and-seeking-consent/). If consent is not possible and assent or verbal agreement is sought, this procedure will be fully detailed in the trial protocol together with the mechanism for subsequently gaining fully informed consent, where relevant.

For some trials it may be preferable to obtain consent electronically (e-consent), or at least to have e-consent as an option for obtaining consent. The process for delivering e-consent, which is managed via CHaRT's secure web-based trial management system, must be agreed with the Sponsor, CHaRT programming team and the trial PMG. Please see www.hra.nhs.uk/about-us/news-updates/hra-and-mhra-publish-joint-statement-seeking-and-documenting-consent-using-electronic-methods-econsent/ for further guidance.

5.8 Other documentation [\[v08.0508.01\]](#)

In addition to the documents described in [Sections 5.5](#), [5.6](#) and [5.7](#), other documentation will be required to be drafted prior to trial initiation. This may include covering letters for questionnaires or other trial supplies, advertising materials etc., Investigational Medicinal Product Dossier (IMPD), Investigator Brochure (IB), and drug labels etc.

5.9 Trial website [\[v08.0509.01\]](#)

In most trials run through CHaRT, the data will be recorded via a trial website which is developed by the CHaRT programming team. The trial website may have a patient facing component (containing information about the trial), communication tools, and other functionality to assist with trial management activities. The trial team will complete the Project Website Initiation document (see [Section 10.2.1](#)) which the programmers will use to set up the initial trial website. The trial team will also complete the Trial Service Definition document which specifies the functionality (see [section 10.2.1](#)).

5.10 Essential documentation [\[v08.0510.06\]](#)

5.10.1 Trial master file index (TMF)

The trial master file index (TMF) must include all essential documentation related to the trial and can be a hard copy, electronic or a hybrid system. The Sponsor may require the trial holds a hard copy TMF, and Sponsor requirements should be confirmed at trial start. A **TMF index** template is available on [Q-Pulse](#). The index should be very clear about what essential documents are held as hard copy (and their location) and what essential documents are held electronically (and their location; for example, on the shared network or the trial website). Any essential information or documents missing must be explained in a **file note** (a template can be found on [Q-Pulse](#)) or within the **TMF index**. Maintenance of the essential trial documentation is the responsibility of the trial manager(s).

5.10.2 Investigator site file index (ISF)

The trial's investigator site file index (ISF), like the TMF, can be a hard copy, electronic or a hybrid system. An **ISF index** template is available on [Q-Pulse](#). The ISF index, should be very clear about what essential documents are held as hard copy (and their location) and

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what essential documents are held electronically (and their location). The ISF must include all essential documentation related to the trial relevant to the individual site. Any missing information or documents or deviations must be explained in a **file note**. It is the responsibility of the trial manager (or member of the trial team) to provide each site with an initial ISF and thereafter any updated documents. Sites who maintain a hard copy of their site file must take responsibility for keeping their ISF up to date.

Please refer to [SOP-QA-7: Trial Master File](#) and [SOP-QA-8: Investigator Site File](#) for further details on establishing and maintaining a TMF and ISF for locally sponsored studies.

5.11 Site selection and initiation [\[v08.0511.06\]](#)

Sites are identified in a variety of ways, such as those listed in the grant application, sites CHaRT or the CI has worked with before, and new sites. Efforts should be made to engage sites that serve diverse populations. When considering selection of sites, the trial manager should document communication about the suitability of the site. A trial site **expression of interest form** template, which may include recruitment target, is available on [Q-Pulse](#) and can be used for this purpose. For locally sponsored studies, please also refer to the [SOP-QA-40: Multi-Centred Site Selection](#).

It is important that sites recruiting participants into a trial are prepared sufficiently to transact the trial processes competently and efficiently. It is usual for CHaRT to provide training to site staff in trial processes, including informed consent, randomisation, CRF completion, data entry on a trial web portal, adverse event reporting and query receipt and resolution and other issues as appropriate. The **pre-site initiation questionnaire**, which is available on [Q-Pulse](#), may be a helpful tool to inform discussion during the site initiation. All CRFs and trial procedures should be reviewed with particular emphasis given to consenting procedures.

Roles and responsibilities of individual site team members should be included in the trial's **site delegation log** (a template can be found on [Q-Pulse](#)). It is essential that those with delegated responsibilities are fully aware of their responsibilities (e.g. informed consent, randomisation, data entry, clinic visit scheduling, adverse event reporting, query processing, etc). A copy of the signed delegation log should be kept in the ISF and TMF. For locally sponsored studies, refer to the [SOP-QA-6: Study Start-Up](#).

Site visits/training can take place prior to appropriate legislative procedures being in place but no participant recruitment can start until all necessary approvals have been issued. Site initiation may be carried out by either visiting sites, holding central trial training days or by telephone/video conferencing/pre-recorded webinars to train trial staff at the recruitment sites in the trial processes. This should be undertaken before the first participant is recruited into a trial at the site. **Guidance on training for trial sites** is available on [Q-Pulse](#).

It is emphasised that training may need to be repeated over a long trial, or as and when needed (e.g. when new staff join a centre). Any training gaps identified, are to be rectified as soon as practicable.

Prior to visits/training, the trial manager will try to ensure that local team members involved in the trial have the opportunity to familiarise themselves with the protocol and all essential documentation ([see section 5.10](#)). Any procedures that are not clear can be discussed during the site visit training or, where training is given via pre-recorded webinars, by email or during a telephone or online Question and Answer session. If possible, all those involved in

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the trial locally (e.g. PI, recruitment officer, research nurse, physiotherapist, pharmacist etc.) should attend the relevant sections of the initiation meeting/training session or watch the appropriate pre-recorded webinars. After the visit/training, the trial team may want to consider forwarding the CHaRT online site initiation **training evaluation form** for site staff to complete: <https://forms.office.com/e/dunSmF3ej2>.

5.12 Trial monitoring [\[v08.0512.07\]](#)

The sponsor usually conducts a risk assessment for randomised controlled trials. The risk assessment contributes to the creation of a CHaRT trial specific monitoring plan. For locally sponsored studies, a CHaRT **trial monitoring plan** (TMP) template is available on **Q-Pulse**. For studies sponsored elsewhere, the sponsor may provide a template. The CHaRT TMP should be reviewed by the senior trials manager and/or deputy senior trials managers and the QA manager before being finalised ([see Section 3.2.2](#)). This plan should be reviewed and updated when appropriate throughout the trial.

The CHaRT TMP details the scope, the level of data checking (e.g. all consent forms, all primary outcomes, 10% of a selected minimisation covariate, 10% of questionnaires) and the type of checking (e.g., source data verification or accuracy of data entry) with a responsive plan depending on what was found (e.g. >3% error would trigger more extensive checks).

In addition, the CHaRT TMP describes the trial oversight, training and central monitoring arrangements. We may use monitoring solutions (for example during the preparation of DMC reports) which identify spurious or unusual data patterns in accruing data. This central monitoring indicates potentially problematic centres and allows investigation and targeted monitoring in a proactive rather than reactive manner.

In some studies, it may be agreed with the senior trials manager and/or deputy senior trials managers and the QA manager that a CHaRT TMP is not required and if so, this will be documented in the TMF accordingly.

The Sponsor may also have a separate monitoring plan detailing the monitoring that they will undertake.

5.12.1 Trial oversight

The five main groupings that contribute to the oversight and governance arrangements for each trial are: the funder(s), the sponsor(s), the Project Management Group (PMG); an independent Trial Steering Committee (TSC); an independent Data Monitoring Committee (DMC). The membership and remit of these committees, including frequency of meetings and expected progress reports, will be referenced in the trial **protocol** and detailed in the **TSC** and **DMC charters**. Templates of these documents are available on **Q-Pulse**. Please refer to [SOP-QA-17: Project Committees](#) for further information on creating the necessary management and oversight committee for locally sponsored studies.

- The **funder** is likely to require regular progress reports and will provide guidance on issues encountered within the trial (see [section 5.4.1](#)).
- The role of the **sponsor** (see [section 5.1.1](#)) is to have ultimate responsibility for the trial and ensure that trial is being conducted in accordance with the principles of GCP and the relevant regulations.

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- The **PMG** will consist of the grantholders, those responsible for the day-to-day management of the trial (usually the trial manager) and can include a Patient and Public Involvement (PPI) representative.
- The role of the **TSC** is to monitor and supervise the progress of the trial. The membership usually consists of an independent chair, together with at least two other independent members. It is also usual to have independent PPI representation on the TSC. The CI (or an appropriate deputy) is also a member. Whilst it is normal that members of the PMG are invited to the TSC meetings (in particular the trial manager and statistician), it should be noted that their role at these meetings is to purely report on trial progress and/or answer questions the independent TSC members may have. Therefore, not everyone from the PMG is required to attend, and consideration should be given to ensure that the number of PMG members in attendance does not dominate the meeting. The CHaRT **TSC charter** template, which can be found on [Q-Pulse](#), was developed using the MRC CTU template TSC Charter version 1.02, 13-Mar-2006.
- The role of the **DMC** is to monitor accumulating trial data during the course of the trial and make recommendations to the TSC as to whether there are any ethical or safety issues that may necessitate a modification to the protocol or closure of the trial. CHaRT has adopted the DAMOCLES charter for DMCs and suggests to the independent DMC members that they adopt the Terms of Reference. A copy of the CHaRT **DMC charter** template can be found on [Q-Pulse](#). It is important that closed progress reports to the DMC, since they may contain unblinded analyses, are held in strict confidence and are only accessed by authorised personnel. In general, they should not be seen by other members of CHaRT or the individual trial team, including the CI, the trial manager, and so on. Closed reports, and minutes from the closed session should be securely archived by the statistician preparing the report, for later inspection if the need arises. An open DMC progress report is frequently prepared, and this can be seen by all members of CHaRT and the individual trial team. If there is no requirement for a DMC (for example in a non-randomised trial), this should be documented in the protocol and the TSC are likely to assume the ethical and safety monitoring role.

The independent members of the TSC and DMC should meet to agree their terms of reference. The Funder or Sponsor will determine whether this should be prior to the first randomisation.

5.13 Patient and Public Involvement (PPI) [\[v08.0513.03\]](#)

A crucial aspect of the design of CHaRT trials is that the question being investigated is of importance to potential participants and uses outcomes that measure dimensions of the condition that matter to the person with the condition or their families/carers. The most effective way of ensuring that these conditions are maximized is to involve people with everyday lived experiences (i.e. individuals who are able to contribute a patient and/or wider public perspective) in the design and delivery of the trial (see [Chapter 15: Patient and Public Involvement](#) for more detail). CHaRT has an unambiguous commitment to the involvement of members of the public in as many of its trial processes as possible. Such involvement will be sought as early as possible in the development process for the trial – ideally from the grant application stage. PPI input should be sought on at least the patient facing documents prior to seeking REC approval. Membership of specific trial committees such as the PMG and the TSC are also recognised ways of involving patients and/or the public.

RELATED REFERENCES AND RESOURCES

Trial timeline (2023; available on [Q-Pulse](#))

¹www.spirit-statement.org/

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Total revision and re-ordering of this chapter; particularly to sections 5.1, 5.4 and 5.7.	Jan 2012
04	Updates to sections 5.1, 5.6, 5.7 and 5.8. Further clarity on section 5.4.2 Case Report Form; including updates to relevant web links	Apr 2015
05	Updates to sections: 5.1.3. R&D approval paragraph to include information on the different R&D procedures across the UK; 5.1.4. addition of paragraph on studies using devices; 5.1.5. merging of Legal and Financial paragraph. Addition of two new sections 5.7 other documentation and 5.8 essential documentation (previously within Chapter 6).	Apr 2018
06	Minor clarifications to sections 5.1.2, 5.1.4, 5.4.1, 5.5, 5.8 and 5.10. Revision of text to reflect C&C procedures (5.1.3); addition of text about tendering procedure and services/products (5.1.5); addition of text about uploading results at the end of study and revision of text in relation to CRN function (5.2); revision of text around publication of trial protocol (5.4); revision to text to clarify version of consent to be retained in the ISF, clarification around consent in vulnerable groups (5.6); revision of text around delegated responsibilities (5.9); addition of text around funder progress reports, revision of text around role of the DMC and timing of agreeing terms of reference for TSC and DMC (5.10.1).	Mar 2020
07	Updates to text in sections 5.1.2 and 5.1.4 to provide guidance on the new HRA Combined review process, section 5.11 on new methods for delivering site training, and section 5.12 to provide more clarity on both the CHaRT trial monitoring plan requirements and the membership of the TSC. Paragraph referring to registering the trial on the EMA has been removed from section 5.3. Additional text added to section 5.7 to provide information on the e-consent process. Three new sections added: 5.2 Data protection; to provide information and guidance on potential data protection requirements, specifically data protection impact assessments (DPIAs), 5.9 Trial website; to provide information on setting up the trial website, and 5.5.2 Management of trial supplies. Reference to the trial timeline included.	Apr 2022
08	Updates to the Background to include more information as well as guidance on improving trial diversity. Addition of two new sub-section, 5.1.5 on Other approvals and 5.1.6 on International	Apr 2024

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	<p>authorisations (Legal & financial changed from 5.1.5 to 5.1.7). Updates to text (section): information on completing a risk assessment if required (5.1.1), to provide more detail on local procedures regarding Data protection (5.2), to include a minor clarification regarding protocols for external sponsor (5.5); regarding Sponsor requirements for maintaining a TMF (5.10); to include some information about engaging sites that serve diverse populations and to provide information about evaluating site training (5.11) and to provide further clarification about when a CHaRT trial monitoring plan may or may not be required (5.12).</p>	
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Chapter 6: Trial conduct and management

CHAPTER 6: TRIAL CONDUCT AND MANAGEMENT

[\[v08.0600.08\]](#)

LEAD AUTHOR

Senior and deputy senior trials managers.

BACKGROUND

Although trial design is of fundamental importance (an important question investigated with optimal methodology) it is said that a successful trial is “10% science, 90% process”. Having established and proven techniques for conducting the trial is therefore crucial.

PURPOSE

To describe the CHaRT processes in conducting a trial from the first randomisation (or screening) through to the last participant, last follow-up, and document generic issues for trial management of CHaRT trials.

APPLICABILITY

- Essential reading for all CHaRT staff involved in trial conduct, in particular the trial managers and data coordinators.

TRIAL CONDUCT AND MANAGEMENT

6.1 Good Clinical Practice [\[v08.0601.03\]](#)

Good Clinical Practice (GCP) is an ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve participation of human subjects. Compliance with the principles of this standard provides public assurance that the rights, safety and well-being of trial subjects are protected. It is imperative that all staff working within CHaRT have appropriate training in GCP (a level of knowledge that reflects their exposure to the principles). For CTIMPs and medical device clinical investigation, staff will be required to attend a GCP specific training course; in addition, staff should refer to www.legislation.gov.uk/uksi/2004/1031/part/4/made for further information on GCP in clinical trials relating to the Medicines for Human Use Regulations 2004. For non-CTIMPs, staff are required to attend the local Good Research Practice (GRP) training course. Also refer to [SOP-QA-34: Good Clinical Practice/Good Research Practice Training](#) for locally sponsored studies.

For non-CHaRT staff working on CHaRT trials e.g. Principal Investigators (PIs), Research Nurses (RNs) etc., GRP or GCP training should be commensurate with the local team members' roles and responsibilities and the type of trial they are working on.

6.2 Trial monitoring [\[v08.0602.05\]](#)

The CHaRT trial monitoring plan as detailed in [Section 5.12](#) should be followed, and trials may be subject to internal review ([see Section 3.2.2](#)). In addition, trials may be monitored and/or audited by external bodies (e.g. R&D Departments, MHRA; [see Section 3.3](#) for more information and refer to [SOP-QA-28: Monitoring](#), [SOP-QA-29: Audit](#) and [SOP-QA-30: MHRA Inspections](#) for locally sponsored studies).

Chapter 6: Trial conduct and management

6.3 Governance arrangements [\[v08.0603.04\]](#)

Research Governance applies to everyone working in health care research (including CIs, PIs, RNs, laboratory staff and CHaRT staff). For further details, refer to the relevant sponsor's guidance. For studies sponsored by the University of Aberdeen, refer to the University of Aberdeen / NHS Grampian web pages for research governance issues related to clinical research studies: www.abdn.ac.uk/grampian-research-office/, and the UoA's Research Governance Handbook: www.abdn.ac.uk/staffnet/research/research-governance-304.php.

6.4 Finance [\[v08.0604.01\]](#)

The trial manager, supported by the senior CHaRT team, the CI and colleagues in the sponsor's finance team, is responsible for reviewing the trial budget, considering current expenditure, and forecasting costs to the end of the study. The sponsor's finance team is usually responsible for providing financial reports to the funder. Permission to vire between budget headings should be sought from the funder.

6.5 Requests for information [\[v08.0605.02\]](#)

At some point in a trial, you may receive a request to share information. Requests may be as a result of a Freedom of Information (FOI) request, it may come direct from one of the trial participants or it may be for another reason. The University of Aberdeen has guidelines about data sharing available at www.abdn.ac.uk/staffnet/governance/data-protection-6958.php#panel12616.

If the request specifically relates to data sharing (e.g., data sets for additional analysis or individual participant data meta-analysis) please see [section 8.5](#).

6.5.1 FOI requests

The Freedom of Information (FOI: Scotland) Act 2002 gives individuals a general right to access recorded information held by Scotland's public authorities, promoting greater openness and accountability across the public sector. This legislation applies to the University of Aberdeen. Please refer to the University's webpages for details regarding FOI: www.abdn.ac.uk/staffnet/governance/freedom-of-information-254.php. If you are asked to respond to a FOI request, please consult a member of the senior CHaRT team or the CTU business manager in the first instance. You will be provided with advice about how to proceed.

Please note that not every request will explicitly state it is a FOI request. If you feel that any request for information is outside of normal trial information flow and requires to be handled sensitively, please consult with a member of the senior CHaRT team or the CTU business manager to get advice.

6.5.2 Participant requests

Participants may request a copy of their study data or other information that relates to their participation in the study. Before sharing any data or information that specifically relates to them, please discuss with the senior trial manager/QA manager. Careful consideration should be given to the verification of participant identify before sharing any information.

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6.5.3 Other requests

Other requests for information may come from journalists or campaign groups. Before sharing information that is not in the public domain, discuss with the senior trial manager, QA manager or senior IT development manager.

6.6 Progress reporting [\[v08.0606.07\]](#)

The funder of the trial will have a format and timeline for reporting. It is the responsibility of the trial manager and CI to know when progress reports are due and in which format. The report to the funder should be delivered on time, addressing all issues, particularly any areas of concern.

For CTIMPs, it is the sponsor's responsibility to prepare and submit the annual Development Safety Update Report (DSUR) to the Medicines and Healthcare products Regulatory Agency (MHRA), but this may be delegated to the CI (and any such delegation should be documented in the (co-)sponsorship agreement and/or the trial protocol). If delegated, the sponsor may require to review the DSUR before submission. The trial manager is usually involved in preparing the DSUR. Please refer to www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues for details on submitting a DSUR using the MHRA Portal. Please also refer to www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/ to confirm if the DSUR should also be copied to the REC (along with a copy of the CTIMP's Safety Reporting form). The MHRA submission details should be used as evidence of the DSUR submissions and should be retained in the TMF and forwarded to the sponsor. Please refer to the [SOP-QA-21: APRs and DSURs](#) for details on preparing and submitting DSURs for locally sponsored studies; examples of recent **DSUR reports** are available on [Q-Pulse](#).

The DSUR preparation may highlight if there is a requirement for a substantial amendment to update the reference safety information (SmPC or IB). Please refer to [SOP-QA-14: SmPC, Investigator Brochure and IMP Dossier](#) for details about the use of these regulatory documents. Reconciliation of the Serious Adverse Event (SAE) log against the SAEs recorded on the trial website should be undertaken before preparing the line listings for the DSUR. Consideration should be given to MedDRA coding of SAEs prior to preparing the line-listings. In order to access the MedDRA coding you will need a MedDRA ID before logging in to their website tools.meddra.org/wbb/. Please liaise with the senior and deputy senior trials managers for details on accessing MedDRA.

The trial manager should also comply with any requests from local R&Ds for individual progress reports.

Projects with a Confidentiality Advisory Group (CAG) approval (see [Section 5.1.6](#)) will require to submit an annual review report. Please refer to www.hra.nhs.uk/approvals-amendments/managing-your-approval/progress-reports/ for further details.

6.7 Safety reporting [\[v08.0607.07\]](#)

Serious Adverse Event (SAE) procedures (including who is responsible for reporting) must be detailed within the trial protocol for all interventional studies (including both CTIMPs and non-CTIMPs). The local PIs, CI or their medically qualified deputies are usually responsible for assessing seriousness, relatedness (causality), severity and expectedness. See the HRA

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guidance for clarification on definitions and reporting procedures/timelines for both CTIMPs and non-CTIMPs: www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/.

All SAEs that require to be recorded as part of the trial protocol should be recorded on the appropriate SAE form. A CHaRT **SAE form** template is available on **Q-Pulse**, but some sponsors will require their own SAE form to be used. For locally sponsored studies, please also refer to the [SOP-QA-22: Adverse events in CTIMPs](#) for further details on identifying, recording and reporting SAEs in CTIMPs and [SOP-QA-39: Adverse Events in Medical Device Clinical Investigations](#) for AEs, SAEs, Adverse Device Effects (ADEs), Serious Adverse Device Effects (SADEs), Unexpected Serious Device Effects (USADEs) in medical device clinical investigations (MDCIs).

All electronic SAEs recorded remotely in CHaRT trials are automatically flagged to relevant members of the trial team (which may include the CI, trial manager and senior CHaRT management) to ensure appropriate follow-up. CHaRT may facilitate the CI in the reporting of an SAE to the relevant parties (e.g. sponsor, DMC, TSC, REC, regulator) in the appropriate timescale, once it has been generated and assessed. The details of such arrangements should be stated in the trial protocol and fully specified in the trial guidance/operations manual and associated legally binding contracts.

6.8 Deviation and breach reporting [\[v08.0608.07\]](#)

Breaches of the conditions and principles of GCP or the trial protocol should be recorded on the CHaRT **breach report form** which can be found on **Q-Pulse**. Possible breaches should be discussed with the trial CI, Senior trials manager or the CHaRT director, or outwith CHaRT (e.g. with NHS R&D director or sponsor) as appropriate, as soon as it becomes apparent that a possible breach has occurred. Please refer to [SOP-QA-25: Deviations and Breaches](#) for further information on the reporting of breaches for locally sponsored studies.

An initial assessment of seriousness should be made by the CI. A serious breach is one which is likely to affect, to a significant degree, the safety or physical or mental integrity of the subjects of the trial or the scientific value of the trial. The CHaRT **guidance on deviations and breaches** can be found on **Q-Pulse**.

If the breach is potentially serious it should be reported to the sponsor as soon as possible (within 24 hours of being identified). The sponsor, together with other key stakeholders (e.g. the CI, trial manager, R&D director/manager) will undertake an assessment and consider whether a corrective and preventive action (CAPA) plan is required. If the breach is confirmed as serious, the sponsor, or delegated research team member, will notify the REC within 7 days of becoming aware of the serious breach. For CTIMPs, the MHRA should also be informed within 7 days of confirmation of the serious breach. The Notification of Serious Breaches of GCP or Trial Protocol Form should be used to inform both the MHRA and the REC – www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#report-a-serious-breach

For locally sponsored studies, please see [SOP-QA-43: Suspected Serious Breaches](#) for further information on the notification of serious breaches of GCP and/or the trial protocol in all studies defined as interventional by the Sponsor.

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If the breach relates to a data protection issue, the data breach should also be reported to the Sponsor's Data Protection Officer as soon as possible (usually within 24 hours). Please see website for full details: www.abdn.ac.uk/staffnet/governance/data-protection-6958.php#panel8626.

For locally sponsored studies, there is also a requirement to document deviations and report these on a quarterly basis to Sponsor. Deviations are defined as any change, divergence, or departure from the study design, procedures defined in the protocol, research project documentation, SOPs, confidentiality and data protection or GCP that does not significantly affect a subject's rights, safety, or well-being, or study outcomes. Please refer to [SOP-QA-25: Deviations and Breaches](#) for further information. As part of CHaRT's QA processes, the QA manager together with the senior trials manager(s) will, following submission to the local Sponsor, collectively review the CHaRT deviation logs (see [section 3.2.2](#)), address any generic findings across CHaRT trials, and implement a corrective and preventive action (CAPA) plan, as appropriate.

6.9 Urgent safety measures [\[v08.0609.02\]](#)

An Urgent Safety Measure (USM) occurs when a research participant or participants are identified as being at risk of harm in relation to their involvement in a research project and urgent action, which deviates from the approved protocol, is required to manage the event and protect the participant(s). In such circumstances, the sponsor, CI or any PI may make changes to the conduct of a trial without first giving notice to the REC or obtaining a favourable opinion. If a USM is implemented, the sponsor should be notified immediately. The REC should also be informed by telephone, ideally within 24 hours. Notice in writing should follow to the REC within 3 days.

For CTIMPs, a USM can be implemented without giving notice to the MHRA first. However, the MHRA should be informed by telephone, ideally within 24 hours of the measure being taken. Notice in writing should follow within 3 days. A substantial amendment covering the changes made as part of the USM should be submitted within two weeks of the notification to the MHRA.

Where a USM requires amendment to trial documentation, this should be submitted to REC (and MHRA if applicable) as soon as possible and marked as being in response to a USM.

Refer to [SOP-QA-42: Urgent Safety Measures](#) for locally sponsored studies. Further information on dealing with a USM is available from the HRA (www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/) and MHRA (www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues).

6.10 Amendments [\[v08.0610.07\]](#)

Any changes/updates to trial documentation must be agreed through informed discussion and minuted at appropriate trial meetings.

Refer to the funder's contract to review whether any proposed amendment requires their approval before submission to sponsor and / or REC. Sponsor(s) will review and approve any

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proposed amendments prior to submission. [SOP-QA-19: Amendments](#) provides further details on how to process and submit amendments for locally sponsored studies.

The amendment tool and full guidance, which can be found at www.myresearchproject.org.uk/help/hlpamendments.aspx, should be used for all amendments for project-based research. The tool categorises the amendment and provides tailored guidance on which review bodies the amendment needs to be sent to, based on the changes that are being made to the trial. An **amendment checklist** is available on **Q-Pulse**, providing prompts of the potential tasks to be actioned when submitting an amendment.

The locked version of the amendment tool can then be submitted to the appropriate review bodies. It also provides detailed information about the amendment to participating sites. The amendment tool, together with all the supporting documents, should be submitted using the online IRAS amendments submission platform: www.myresearchproject.org.uk/help/hlpamendments.aspx.

In a CTIMP, if the amendment requires submission to the MHRA, this should be made through the MHRA Portal which can be found at mhrabpm.appiancloud.com/suite/sites/MHRA_Submissions. Further guidance on submitting an amendment using the MHRA portal is available on **Q-pulse: Guidance for submitting an amendment using the MHRA portal**. In a device trial, the amendment is emailed to CI-amendments@mhra.gov.uk (see www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device#amendments for further information).

The R&D approval processes vary depending on the geographic location of participating sites. See www.myresearchproject.org.uk/help/hlpnhshscr.aspx for further details.

The amendment shall only be implemented once all the necessary approvals have been received. The trial manager should ensure that the processes and timing of amendment notification/approval are implemented. Rather than submitting multiple amendments in close succession, one amendment covering all changes may be preferable.

For CTIMPs, if a substantial amendment is being made to the protocol, take the opportunity to ensure that the reference safety information (SmPC/IB) is reviewed and updated if appropriate. Please refer to [SOP-QA-14: SmPC, Investigator Brochure and IMP Dossier](#) for details of the use of these regulatory documents. Any change that the trial team wish to make (in terms of the version of the reference safety information) is considered a substantial amendment. Changes to the version of the reference safety information may have implications as to how any safety events are assessed during that DSUR reporting period and therefore consideration should be given to the implementation date of any change to the reference safety information (see MHRA blog for more details; mhrainspectorate.blog.gov.uk/2016/03/02/reference-safety-information-for-clinical-trials/ and mhrainspectorate.blog.gov.uk/2017/01/18/reference-safety-information-ii/).

An **amendment log** (available on **Q-Pulse**) should be maintained in the TMF summarising the key changes, together with new version numbers and dates of any revised documents.

Following the receipt of relevant approvals, at the point of implementation, amended documents should be distributed to appropriate sites and made available on the trial website.

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Sites will be instructed to destroy any unused hard copies of older versions and mark any hard copy versions in their ISF as superseded. New versions will be incorporated in training materials.

Any planned changes to CRFs or questionnaires should be discussed with the programming and statistics teams so that the trial database and Statistical Analysis Plan (SAP) can be updated as required (see [Section 10.2.5](#) for details on Change Management in relation to databases). A **change request form**, available on [Q-Pulse](#), is required for any changes to the data collection tools built on the trial website. All changes to the protocol, questionnaires or the CRFs should be consistent. If there are any changes to REC approved documents (for example questionnaires), approval of the new version must be obtained before these are implemented.

6.10.1 Amendment processes for key documents

The first version of documents submitted for regulatory and/or ethical approval should be Version 1 (see [section 5.1.2](#)). Amendments made subsequent to or as a condition of regulatory/ethical favourable opinion (as applicable) will generate a new version, incrementing in whole numbers. A **version control document**, available on [Q-Pulse](#), should be used to record changes made to key documents and can be made available to sites.

6.11 Error correction [\[v08.0611.04\]](#)

Error correction on a hard copy paper CRF is undertaken by crossing through the incorrect data with a single line, adding the correct data and signing/initiailling and dating the change in permanent ink. Justification of why the correction has been made (such as a copy of a letter from an investigator clarifying data) may be attached to the CRF or noted on the electronic CRF (eCRF). Under no circumstances is correction fluid (e.g. Tippex) to be used. The CHaRT **guidance on the completion of CRFs** document can be found on [Q-Pulse](#). For locally sponsored studies, please also refer to [SOP-QA-27: Good Documentation Practice](#). There is an electronic audit trail for all amended electronic data on CHaRT trial databases.

Any personal identifiable data that is received by CHaRT centrally and does not form part of the content of a CRF form in completed CRFs will usually be obscured at the time of data entry or prior to archiving (e.g. if a participant writes their name or other identifying information on a CRF, this is covered over upon receipt by pen and/or sticker). There are cases where personal identifiable data should not be redacted (e.g. a letter written by a participant to the trial team, a prescription). These should be discussed on a case-by-case basis. Please refer to the [SOP-QA-12: Case Report Forms](#) for local sponsored guidance on managing research data in CRFs.

6.12 Query processing [\[v08.0612.03\]](#)

The frequency that queries are generated is dependent on the size of the trial and data collected. The standard method of data entry by trial personnel is via a dedicated software programme or trial web portal, hosting a remote data capture application authorised by CHaRT. Some validation can be built into the data capture application whereby the data entry person will be asked to clarify or confirm impossible or improbable entries at the point of entry. Care should be taken in respect of the amount and the range of validation that is included, so as not to restrict users. To clean the data, further queries will be generated at specific times (e.g. weekly, monthly, or at important milestones; such as several weeks before a database

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lock for a DMC Report). In the newer trial websites, data queries can be generated within the trial website. The resulting queries will be distributed to the responsible person (PI, nurse or recruitment officer etc.) at each centre, who will investigate and attempt to resolve the query, and update and correct via the trial web portal, or via the trial office at CHaRT.

In addition, it is also possible to request a specific report from a trial database that is not one of the pre-defined standard reports already set up on the trial database. Please refer to the **guidance on requesting a new database report** which can be found on [Q-Pulse](#) for information on how to do this.

6.13 Filing [\[v08.0613.04\]](#)

With the large volume of documentation required for each trial a satisfactory filing system of both hard copy and electronic data is essential. It is the responsibility of all CHaRT staff to ensure that data are held securely and confidentially and can be easily retrieved.

Access to all electronic trial data must be restricted to authorised team members. Hard copies of CRFs should also be stored securely.

6.14 Trial meetings [\[v08.0614.04\]](#)

Trial meetings, whether 'in-house', PMG, TSC or DMC should have a designated chair. Constitution of these committees is described in [section 5.12.1](#). For significant meetings an agenda should be made available to all attendees in advance and should be referred to during the meeting to ensure that all items are systematically reviewed as required. Meetings should be organised in sufficient time to maximise attendance. It may be appropriate for meetings to be held via tele- or video-conference e.g. Microsoft (MS) Teams or Zoom. **Guidance on using MS Teams for e-meetings** is available on [Q-Pulse](#). For in-person meetings, clear details will be sent to attendees with regard to location and, when appropriate, travel options.

It is common practice within CHaRT to hold regular (e.g. fortnightly) 'in-house' meetings for trials that are in start-up, with reduced frequency while the trial is ongoing, increasing in frequency again during the close-out phase. Membership of the 'in-house' group will include appropriate CHaRT personnel.

Minutes of meetings should be taken by the data co-ordinator, trial manager, or another team member, and distributed and filed appropriately.

6.15 Site contact/follow-up [\[v08.0615.01\]](#)

Recruitment and clinical follow-up at sites can go on for many months or years within an individual trial. Building and maintaining good relationships with site staff is essential. Strategies to improve and enhance these relationships and maintain lines of communication should be adopted whenever possible, in agreement with the PMG. Common strategies include newsletters, teleconferences and, where there is allowance in the budget, providing trial specific merchandise such as pens and post-it note pads. See **guidance on maintaining site and participant motivation** document on [Q-Pulse](#) for further information. Opportunities may arise to research different strategies to maintain site contact and build good relationships. These may require the approval of the relevant trial committees, sponsor, funder, REC and so on.

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6.16 Participant contact [\[v08.0616.04\]](#)

The protocol will describe the process for initial approach to participants and how subsequent contact is made. Local contact is covered during the initial site training and detailed in the trial operations manual. Contact by central CHaRT personnel will normally be following participant consent and is also documented in the protocol and / or trial guidance.

All CHaRT staff must be aware of their duty of confidentiality and will maintain a professional approach to all participant contact. Contact may be made via post, telephone, text message and email by designated team members. If a trial participant has a query that the team member cannot answer (e.g. a clinical query), the team member is responsible for passing that query to a relevant person for resolution.

Where research involves NHS patients, data or facilities, in addition to requiring NHS R&D permission for the trial, members of the trial team may need to be covered by an appropriate Human Resource agreement with the NHS organisation hosting their research. The NHS Research Passport algorithm, which can be found at www.hra.nhs.uk/planning-and-improving-research/best-practice/research-passport/, provides guidance on whether CHaRT personnel will require an honorary NHS contract or letter of access depending on the level of patient contact they have throughout the trial. In addition, NHS R&D departments may also provide guidance.

6.17 Participant follow-up [\[v08.0617.06\]](#)

6.17.1 *Within trial*

Participant follow-up is detailed within the trial protocol (see [Section 5.5](#)). Participant contact preferences may be recorded such that correspondence is delivered by for example, post and email. When questionnaires are sent from CHaRT, it is normal practice that participants who fail to return them will be sent reminders approximately three weeks following the initial distribution (although this time-frame may be shortened in some trials). Second reminders (by post, telephone or email) may also be used. It may be appropriate to adopt, or research, other strategies to enhance retention and response to questionnaires. The automated Interactive Voice Response (IVR) may also be used for participant follow-up. It is important that all such methods of contact with participants, and their frequency, is pre-specified in the trial protocol and any relevant approvals (e.g. REC) obtained.

Before generating any participant contact (for example questionnaires or end of trial results letter) the trial website should be updated with any known changes to patient status (e.g. withdrawal from follow-up or death).

We will aim to accommodate the needs and requests of trial participants, e.g. that a CHaRT member of staff telephone them to complete questionnaires. **Guidance for data collection by telephone** is available on [Q-Pulse](#). This document outlines the issues to consider before contacting the participant, as well as the process for collecting the data by telephone and for recording the data on the trial database.

Depending on the trial design/population and length of follow-up, it is important to keep participants informed of progress and CHaRT encourages trials to issue newsletters and a lay summary of results to the trial participants when available. The sponsor and / or the REC should be consulted as to whether such correspondence requires approval before distribution.

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6.17.2 Long-term follow-up

In some trials, long-term follow-up would not be appropriate, for example, short-term interventions with no perceived safety or effectiveness issues in the long-term.

Some CHaRT trials will seek to obtain funding to collect long-term follow-up data. Long-term follow-up is potentially for many years or decades after the participant has reached the primary trial outcome – for example, a trial of knee replacement may have its primary outcome as quality of life at two years post-operation, but it may look at the device failure at 10 years post-operation. Long-term follow-up is usefully differentiated between that which requires further patient contact (whether by post, telephone, clinic or home visit, which may be supplemented with data on individual patients from hospital or GP records) and that which can be completed solely by record linkage (remote capture of further participant data on all participants from natural registries). Some studies may involve both types of long-term follow-up. Long-term follow-up that involves further patient contact is usually more expensive and requires considerable organisation. Whatever the nature of the follow-up, the following three requirements are key:

- REC favourable opinion for the long-term follow-up, specifying the nature and frequency of participant contact, must be obtained, and it is strongly advised to obtain these permissions, and the consent of the participant, at the beginning of their involvement i.e. on the original consent form (prior to randomisation).
- Adequate funding needs to be secured to guarantee the viability of the follow-up, the quality of data captured and the analysis and reporting of the data.
- The project needs to be set up and documented on the assumption that the long-term follow-up will not be carried out by the original trial team. It should be assumed that no-one will be available with direct knowledge of the original conduct of the trial. It is therefore the responsibility of the original team to specify the long-term follow-up protocol in such a way that this critical knowledge is passed on, in so far as possible, in writing.

A **long-term follow-up checklist** to help consider what actions might be required is available on [Q-Pulse](#).

6.18 The role of the Chief Investigator (CI) [\[v08.0618.03\]](#)

The Chief Investigator has overall responsibility for the trial. The responsibilities of the CI are documented in the delegation of responsibilities appended to the sponsorship/Co-sponsorship agreement.

6.18.1 CI absence

If the CI is temporarily absent (e.g. on short periods of annual or sick leave), a suitably qualified delegate should be identified to provide cover for any essential tasks.

For absences which are known or expected to be longer (e.g. sabbatical or maternity leave), consideration should be given that an acting or new CI is appointed. The sponsor and/or funder should be consulted for advice on the most appropriate approach. If a new CI is appointed, a substantial amendment will be required.

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6.18.2 CI leaves or retires

If the CI is leaving to work at another institution either a new CI would be appointed or the existing CI would continue in this role, subject to the approval of the funder, sponsor(s) and the old and new employing institutions. This would involve significant consultation and agreement of the sponsor(s) and funder.

If the CI is retiring, a new CI would usually need to be appointed, though there may be exceptions to this. This would involve significant consultation and agreement of the sponsor(s) and funder, and a formal appointment process may be required. A change of CI would constitute a substantial amendment.

For locally sponsored CTIMP or medical device clinical investigations, please refer to the [SOP-QA-24: Managing a Change in Chief Investigator of a CTIMP or Medical Device Clinical Investigation](#) for further details on managing a change in CI.

6.19 The role of the Principal Investigator (PI) [\[v08.0619.02\]](#)

The Principal Investigator has overall responsibility for the trial at site. The responsibilities of the PI are documented in the site delegation log and the site agreement.

6.19.1 PI absence

If the PI is temporarily absent (e.g. on short periods of annual leave or sick leave), a suitably qualified delegate should be identified to provide cover for any essential tasks. R&D offices at NHS sites should be notified about cover arrangements for absent PIs.

For absences which are known or expected to be longer (e.g. sabbatical or maternity leave), consideration should be given that an acting or new PI is appointed. The sponsor and/or relevant R&D department should be consulted for advice on the most appropriate approach. In a CTIMP, if a new PI is appointed, an amendment will be required.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Total revision and re-ordering of this chapter; particularly to sections 6.6 and 6.7.	Jan 2012
04	Substantial changes to section 6.4, 6.5, 6.6, 6.8, 6.15 and new Section 6.16: the role of the Chief Investigator (CI); including updates to relevant web links.	Aug 2015
05	Updates to sections 6.4, 6.8; 6.10; and 6.15.1 Addition of new section 6.7 on urgent safety measures; and 6.17 on the role of the PI. Essential documentation moved to Chapter 5, Section 5.7.	Apr 2018
06	Minor clarification to sections 6.15 and 6.16.2. Addition of GRP and removal of reference to Declaration of Helsinki (6.1); update to the	Mar 2020

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	UoA's Research Governance Handbook (6.3); clarification that substantial amendment may require updating RSI, addition of text around MedDRA coding (6.4); removal of reference to internal safety reporting policies and link to HR guidance added (6.5); addition of text about reporting data breaches (6.6); clarification of process for USMs in CTIMPs (6.7); text updated to include information regarding the new amendment tool being used for all project based research, clarification of text around RSI in CTIMP, and amendments to CRFs (6.8); addition of text regarding personal identifiable information that should not be redacted (6.9); clarification of process for CI absence (6.16.1) and PI absence (6.17.1).	
07	Addition of a new section (6.4 Request for Information), to provide information on the process around FOI, participant and any other types of data requests. Minor wording amendments to sections 6.5 to include details about the MHRA amendment portal (replacing CESP); 6.6 regarding completion of SAE forms. Section 6.7 (previously 6.6) renamed from 'Breach reporting' to 'Deviation and breach reporting' and additional text given to provide information of the procedures for reporting deviation and breaches locally. Minor updates to Amendments (6.6) to reflect regulatory change to process, Query processing (6.11) to include information on requesting database reports, Filing (6.12), Trial meetings (6.13) to include relevant CHaRT guidance, Participant follow-up (6.16) to include information about using automated Interactive Voice Response and collection of patient data from medical records.	Apr 2022
08	Addition of a new section 6.4 on Finance. Updates to text (section): to cross-reference to section 3.2 regarding internal review of trial monitoring plans (6.2), on how to deal with requests for information (6.5); removal of text about the completion and submission of APRs as this is no longer an HRA requirement and clarification to CHaRTs process for preparing and submitting a DSUR (6.6), referencing local SOPs on safety reporting in CTIMPs and device studies (6.7), to describe internal review of deviations (6.8); relating to discussion of amendments at appropriate trial meetings addition of process for device studies and addition of links to relevant internal Q-Pulse documents (6.10).	Sept 2024

CHAPTER 7: TRIAL CLOSE-OUT

[\[v08.0700.08\]](#)

LEAD AUTHOR

Senior and deputy senior trials managers.

BACKGROUND

All clinical trials will end at some point, either having reached their scheduled milestones and finished at the expected time, or unexpectedly due to safety concerns, for overwhelming evidence of benefit sooner than expected, or for other reasons (e.g. it is futile to continue, or other competing trials make it impossible to continue). The end of a trial must be anticipated and planned for accordingly from its start.

PURPOSE

To document CHaRT processes for the management of trial close-out.

APPLICABILITY

- Essential reading for all CHaRT staff involved in the close-out phase of a trial.

TRIAL CLOSE-OUT

7.1 Close-out procedures [\[v08.0701.08\]](#)

Usually, a close-out is scheduled. Procedures for a scheduled close-out should be discussed and documented by the trial team prior to close-out beginning. Information on trial close-out procedures can be found at: www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/. A **close out checklist for end of study or early termination of study** and a **site close-out form**, together with **guidance on closing out a trial site**, are available on **Q-Pulse**. It is the ultimate responsibility of the sponsor (may be delegated to Chief Investigator (CI)) to ensure that proper procedures are in place, and are then undertaken (please refer to the [SOP-QA-31: Research Project Closure](#) for details on the procedure for formally closing a trial for locally sponsored studies).

Although undertaken as an ongoing process, it is essential that the TMF is checked for completeness and any personal identifiable information from questionnaires or interviews have been checked for anonymity (when appropriate). Any outstanding errors and inconsistencies should be resolved and, if they cannot be resolved, the reasons for this are documented (for example in a **file note** or within the trial website).

In a scheduled close-out, there is sometimes the opportunity to close-out in a staggered timetable. The trial manager will develop centre specific plans for close-out which will include:

- The date of closure of the randomisation system. Confirmation of the date of closure should be documented.
- Timing of the closure of emergency unblinding, if relevant, should be agreed in advance. Closure of any unblinding process will often post-date closure of randomisation and/or the active treatment period.
- Resolution of any outstanding data queries.

Chapter 7: Trial close-out

- Organisation of transmission of appropriate data, either electronic or paper, using secure measures where appropriate to CHaRT.
- Confirmation of which records are to be archived, in what format (hard copy, electronic), where they will be archived, and for how long (refer to original IRAS, protocol and site agreements).
- Return or disposal of all equipment (e.g. computers, clinical kit), as appropriate and arrangements for closing down dedicated office space, removal of publicity material, decommissioning dedicated phone lines, closing trial web portals and so on. In certain circumstances, equipment may be gifted to the research site rather than it being returned to the trial office. This should be discussed with the CI and with the contracts team to ensure that appropriate agreements are in place.
- Completion of all contractual issues with a centre, including final payments for services.

On occasion, a trial may be terminated early (see [section 7.3](#)) or suspended for a short period. In such cases the plan for close-out or suspension should be discussed, documented, and updated as the situation develops. Prior to a decision to terminate early or suspend a trial, the Sponsor, Funder, TSC and/or DMC should be consulted. They should be involved in ongoing discussions and planning.

7.2 Timelines for notifying stakeholders of scheduled trial termination [\[v08.0702.05\]](#)

- **For CTIMPs:** the competent authority (in the UK, the Medicines and Healthcare products Regulatory Agency (MHRA)), the Research Ethics Committee (REC) and the sponsor(s) should be notified of the end of trial within a specific time (currently 90 days) of the end of trial as defined by the protocol by completing a Declaration of the End of Study form (found at www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/) Please refer to www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues for details on submitting the end of trial declaration, which is completed via the MHRA Portal. A copy should also be sent to the local R&D office(s) if they have requested a copy. The appropriate final trial report should be submitted to the REC within 12 months of end of the trial.

For CTIMPS that were previously registered on EudraCT, the clinical trial summary results will need to be reported to EudraCT within six or 12 months depending on the type of trial. Summary results should be published in the public register (or registers) where the trial is registered. The MHRA should be emailed (via CT.Submission@mhra.gov.uk) to inform them that the trial results have been posted to EudraCT (see www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial for details).

- **For non-CTIMP trials:** the trial manager should ensure that the end of study notification is made to the appropriate REC and sponsor within 90 days using the necessary form (found at www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/). A copy should also be sent to the local R&D office(s) if they have requested a copy. The final trial report should be submitted to the main REC within 12 months of the end of trial as defined in the protocol.

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7.3 Early termination of a trial [\[v08.0703.06\]](#)

Any decisions about early termination should be discussed initially with the trial sponsor and funder, and if appropriate with the DMC and TSC. If the trial is still in the recruitment phase and early termination is required, the randomisation system must be closed and staff at recruitment sites informed of this by adding information to the randomisation line and/or the randomisation section of the trial website and/or contacting staff at sites directly.

Regardless of why the study is terminated (for example, futility, safety, funding, etc) in the event that participants are still “on treatment” (e.g. still taking trial medication, undergoing surgery or part way through a behavioural intervention), a comprehensive plan is required detailing what actions need to be taken in terms of ceasing (or continuing) treatment. This should be agreed with the CI and the sponsor in the first instance, and then communicated to participants and investigators. Consideration should also be given to any agreements in place for the trial, for example supply agreements, and these should be discussed with the sponsor’s contract team before contact is made with the third party.

It may be helpful to refer to CHaRT’s **guidance for significant major study events** on **Q-Pulse** to consider what actions might need to be addressed.

Once this is achieved, the plan for the scheduled close-out should then be exacted.

- **For CTIMPs:** the MHRA and REC should be notified within 15 days of an early termination of a trial. Please refer to [section 7.2](#) for details of the process for CTIMPs. Local R&D office(s) should also be informed.
- **For non-CTIMPs,** the REC, should be notified within 15 days of an early termination. Please see [section 7.2](#) for details of the process for non-CTIMPs. Local R&D office(s) should also be informed.

7.4 Temporary suspension of a trial [\[v08.0704.04\]](#)

Possible reasons for a temporary suspension include to investigate a Suspected Unexpected Serious Adverse Reaction (SUSAR), because there is a product recall, a major external event such as a pandemic, or it might be that a sponsor suspends the trial to deal with funding or insurance issues. In such circumstances, it may be necessary to suspend the randomisation system temporarily with the intention to restart once the issues have been resolved. The trial sponsor should be involved in any discussion about a potential temporary suspension. If dealing with a temporary suspension, please refer to CHaRT’s **guidance for significant major study events** available on **Q-Pulse**.

- **For CTIMPs,** the MHRA, funder and REC should be informed within 15 days from when the trial is temporarily suspended. This should be made as a substantial amendment, using the notification of amendment form and clearly explain what has been halted (e.g. stopping recruitment and/or interrupting treatment of participants already included) and the reasons for the temporary halt www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#suspend-or-terminate-a-trial. Depending on the reason for the suspension, it may also be appropriate to inform the TSC and DMC.
- **For non-CTIMPs,** apart from the MHRA notification process, all other relevant notifications and procedures as for CTIMPs apply.

Chapter 7: Trial close-out

To restart a trial that has been temporarily halted, the request is made to the MHRA (for CTIMPs), sponsor and the REC as a substantial amendment using the notification of amendment form and providing evidence that it is safe to restart the trial. If the decision is taken not to restart a trial that has been temporarily halted, the MHRA (for CTIMPs), sponsor and REC should be notified within 15 days of this decision, using either the 'Declaration of End of Trial form' or the 'Declaration of End of Study form' as appropriate and the procedures for early termination should be followed as described in [Section 7.3](#).

7.5 Trial reporting [\[v08.0705.01\]](#)

Whether the trial was fully completed or terminated early, the trial manager should ensure that all pertinent trial reports are issued (see [section 8.1](#) for further details) and participants are notified of the results (if applicable). In addition, all relevant registers (see [section 5.3](#)) should be updated as appropriate. For locally sponsored studies, please refer to [SOP-QA-31: Research Project Closure](#).

7.6 Finance [\[v08.0706.01\]](#)

The trial manager should work with the sponsor's finance team, together with a member of the senior CHaRT team and the UoA research accountants in Research Financial Services (post-award team), to ensure that any end of trial financial procedures have been considered and completed and, where appropriate, funds for dissemination activities are held back.

7.7 Archiving [\[v08.0707.05\]](#)

The CI is responsible for liaising with the sponsor's named archivist to ensure the TMF and all trial data are archived. The named archivist is then responsible for ensuring this data is stored securely, retrieved, destroyed and recorded appropriately (see SOP-QA-32).

CHaRT ensures that the TMF is complete, properly labelled before being sent to be archived. Most documentation within the TMF will not be identifiable; however, there are exceptions to this (e.g. consent forms, prescriptions and associated documentation, letters from participants).

Unless otherwise agreed and documented, CHaRT also ensures that the final database on which the analysis and publication is based is complete, properly labelled and securely archived. See CHaRT's [guidance on archiving and top tips](#), which is available on [Q-Pulse](#), for details of various archiving requirements.

The sponsor and/or funder will advise on the retention period for the TMF and trial data at the outset of the trial. This is usually documented in the protocol, the Integrated Research Application System (IRAS) application and site agreements. It is a requirement that trial documentation can be accessed by appropriate senior CHaRT staff and therefore archived data must be retrievable within a reasonable timeframe. The University of Aberdeen has an archiving policy (see [SOP-QA-32: Archiving](#) for details relating to archiving for locally sponsored studies). The trial manager should ensure that, for studies sponsored out with University of Aberdeen/NHS Grampian, archiving arrangements and procedures are clearly documented in the protocol, IRAS, site agreements or elsewhere in the TMF.

If the CI leaves or retires during the period that the TMF or data is in archive, arrangements must be made for its ongoing safekeeping and security.

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With regards to the Investigator Site File (ISF), it is a site’s responsibility to archive the ISF for the time period specified in the site agreement and/or in the REC application. Consideration should be given as to how sites can maintain access to documents that were held electronically on the trial website and not held as hard copy in the ISF. If studies adopted an electronic or hybrid ISF, arrangements should have been made during trial close-out to provide the site with copies of documents held in the electronic ISF that would no longer be available to them when the trial website is archived. It is a site’s responsibility to archive the ISF regardless of whether they recruited participants or not. If a site did not receive R&D approval and was not opened for recruitment, the sponsor would not normally require the ISF to be archived at site but this should be confirmed with the sponsor. However, this should be documented appropriately in a file note within the TMF.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	More clarification to procedures for trial close-out and two new sections: 7.2 Timelines for notifying stakeholders of study termination and 7.4: Temporary suspension of a trial.	Jan 2012
04	More detail added to Section 7.1, 7.2, 7.3 and 7.4 including updates to relevant web links.	Apr 2015
05	Updates to all sections.	Apr 2018
06	Minor update to section 7.1 around procedures for a scheduled close-out, plus additional text to clarify the processes for early termination and trial suspension (7.1); clarification around identifiable information and archiving of database (7.5).	Mar 2020
07	Addition of links to Q-Pulse guidance documents in sections 7.1, 7.3 and 7.5. Section 7.2 updated to include details for submitting end of trial declaration via MHRA portal (no longer CESP) and the applicable processes for reporting trial results. Rewording of section 7.3 to provide more clarity on the process, section 7.4 to acknowledge the effect of an external event (pandemic), and section 7.5 to detail the responsibilities and processes for trial sites archiving their ISFs.	Apr 2022
08	Addition of two new sections: Trial reporting (7.5) and Finance (7.6) with respect to trial close-out. Minor updates to text in sections: 7.1 to specify additional close-out tasks regarding return or disposal of trial equipment, 7.2, to clarify the process for trial close-out in CTIMPs, and 7.7 to clarify the responsibilities of the CI and named archivist when archiving.	Sept 2024

Chapter 8: Trial publication(s) and dissemination

CHAPTER 8: TRIAL PUBLICATION(S) AND DISSEMINATION

[\[v08.0800.08\]](#)

LEAD AUTHOR

CHaRT director and senior trials manager.

BACKGROUND

There is an obligation to full and open publication of trial results, whatever the findings. All trials must be reported fully, regardless of findings, this includes: trials with perceived null results, trials which failed to recruit to target and trials which were unexpectedly terminated. In so far as possible, trials should be reported to their planned intentions. Moreover, trials need to be reported as soon as is practicable and within the time frames specified by funders and/or regulatory bodies.

PURPOSE

To describe CHaRT's policies for ensuring trials are properly reported in both a timely and accurate manner.

APPLICABILITY

- Essential reading for all CHaRT staff involved in publishing trial findings.
- Useful background reading for all CHaRT staff with research interests.

TRIAL PUBLICATION(S) AND DISSEMINATION

8.1 Trial publication(s) and dissemination [\[v08.0801.04\]](#)

It is the responsibility of the CI, in conjunction with the CHaRT lead, where appropriate, to be aware of the requirements of the stakeholders in the trial (the funder, the sponsor, ethics, regulatory, consumer groups, and so on) in respect of final trial publication(s) and dissemination, and to ensure that these are delivered in a timely and appropriate manner (see [Section 7.2](#) for more details). Please refer to the [SOP-QA-33: Research Project Publications and Dissemination](#) for further information for locally sponsored studies on drafting publications and dissemination.

8.2 Publication [\[v08.0802.06\]](#)

All studies managed by CHaRT have a commitment to publish the findings of the research.

8.2.1 *Minimum requirements*

It is mandatory that the results of every trial appear in the public domain in a timely fashion. For the majority of CHaRT trials, it is anticipated that there will be a results paper published in a peer-reviewed medical/scientific journal. Particular attention should be paid in ensuring it is followed for trials which failed to meet their objectives either in terms of failing to recruit; terminating early due to safety issues, or futility concerns; or failing to demonstrate a clinically worthwhile treatment effect. If the trial is a CTIMP and was previously registered on the EudraCT website, there is an obligation to register the findings on the EudraCT website (please refer to [section 7.2](#) for details of this process).

In addition, many trials also publish a design and/or baseline characteristics paper in a peer-reviewed journal (ideally any design paper should be accepted for publication before final database lock).

Chapter 8: Trial publication(s) and dissemination

8.2.2 Authorship

The protocol should include a clear statement of authorship. Authorship should include all individuals who have made a substantial academic contribution according to the guidance and recommendations of the International Committee of Medical Journal Editors (ICMJE)¹. Where possible the **CHaRT authorship policy**, which can be found on **Q-Pulse**, should be used, but in certain instances CIs based elsewhere may use their host institution's authorship policy.

8.2.3 Acknowledgements

All individuals who have made a substantial contribution to the research project without fulfilling the authorship criteria should be clearly acknowledged, usually in an 'Acknowledgments' section, detailing their contributions. See **acknowledgements checklist** available on **Q-Pulse**.

The funder should be acknowledged in any publications. If other organisations have contributed to the study (for example by providing study medication, loaning equipment or providing supplies at a reduced price), it is likely that the Supply Agreement will include a statement as to how their support should be acknowledged in any publication. The Supply Agreement may also provide them with the advance notice of any publication and/or the opportunity to review before submission. The Sponsor's contracts team can advise on interpretation of such clauses where required.

8.2.4 Dissemination

It is important that as well as a commitment to peer reviewed medical/scientific publication, trial results and methodology are disseminated to an appropriate level at scientific meetings (e.g. Society for Clinical Trials Conference, workshops, invited lectures). There should also be a commitment to disseminate material from the trial internally within the IAHS in lunchtime research meetings, study days and so on, and to professional and lay publications when appropriate.

As detailed in the HRA guidance, which can be found at <https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/#informingparticipants>, participants should be informed of the final trial results as detailed in the protocol and in the Integrated Research Application System (IRAS) application (see [section 5.1](#) for more detail). The research findings should be disseminated to both study participants and the wider public in an easily understandable format. This may involve offering simplified explanations of results in Plain English, utilising visual tools such as infographics, or employing various creative methods. A **trial results letter** template, together with examples of infographics, is available on **Q-Pulse** for use.

8.3 Patient and public involvement in dissemination [\[v08.0803.02\]](#)

A plain English summary is required for some publications and reports. It is best practice to have patient and public involvement (PPI) in the development of such a summary (see [sections 15.2](#) and [15.3](#)). Their contribution to developing the summary should be acknowledged.

Patient and public research partners who meet the criteria for authorship¹ should be offered a co-authorship of scientific outputs, recognising them as equal partners in the study. Otherwise, a general acknowledgment should be given.

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Where possible, PPI should be included in the development of any documentation detailing the final trial results that is to be shared with participants.

8.4 Conflicts of interest [\[v08.0804.02\]](#)

The key CHaRT policy with regard to actual or potential conflict of interest is open disclosure. It is very seldom, if ever, that a potential conflict would stop participation in an activity, or preclude a major journal from publishing. Identified conflicts of interest are discussed at the project management group (PMG: see [section 5.12.1](#)) level on a case-by-case basis. If the perceived conflict is openly disclosed, it can usually be discounted when weighed against the researcher's reputation and track record. Likewise, institutional conflicts of interest (for example, the source of CHaRT funding) can be dealt with similarly by open disclosure.

It should be noted that, in general, to maintain their strict independence, independent members of the Trial Steering Committee and Data Monitoring Committee should not gain any academic credit by being a co-author on trial publications. Their role should be gratefully acknowledged and their agreement to this should be obtained before accepting this role (see [section 5.12.1](#) for further details).

8.5 Data sharing [\[v08.0805.01\]](#)

Requests for information may include requests for data sets for additional analysis or individual participant data meta-analysis. Before sharing information that is not in the public domain, discuss with the senior trial manager, QA manager or senior IT development manager. Please refer to the **data sharing policy** available on [Q-Pulse](#) for information about CHaRT's data sharing process. Further information can also be found at www.abdn.ac.uk/hsru/what-we-do/trials-unit/data-sharing-1115.php

RELATED REFERENCES AND RESOURCES

Guidance to authors: Study outputs

Final report preparation timetable and checklist

RefWorks ProQuest - guidance on sharing documents

(all the above documents can be accessed via [Q-Pulse](#))

¹Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals. (www.icmje.org/#authors)

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Renaming of Chapter from "Trial Reporting" to "Final Reporting and Publication" and further information in sections 8.1 and 8.3.	Jan 2012
04	Renaming chapter from 'Final Reporting and Publication' to 'Trial Publications and dissemination'; Changes to sections 8.1 and 8.2.	Jun 2015

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05	Minor wording amendments.	Apr 2018
06	Minor change to section 8.1 to remove the word 'grantholder' as CHaRT lead would be a grantholder and deletion of CTIMP specific text as SOP-QA-33 is now relevant to all studies. Update to section 8.2.2 to clarify that CIs based elsewhere may use a different authorship policy.	Feb 2020
07	Update to Lead Author to include senior trials manager. Addition of new sub section on Acknowledgments (8.2.3); and new PPI section to include detail of PPI in reporting (8.3). Include references to relevant Q-Pulse guidance documents and templates.	Apr 2022
08	Addition of new section 8.5 on Data Sharing. Updates to text (section): to provide information around accessibility and dissemination to patients and public (8.2.4); to include guidance on acknowledging patient and public research partners (8.3). Minor clarifications in 8.2.1 regarding current EudraCT reporting for CTIMPS and 8.2.3 to include link to relevant Q-Pulse template. Updates to all relevant references (guidance documents and templates) available on Q-Pulse.	Apr 2024



Centre for Healthcare Randomised Trials

Chapter 9: IT infrastructure

CHAPTER 9: IT INFRASTRUCTURE

[\[v08.0900.04\]](#)

LEAD AUTHOR

Senior IT development manager

BACKGROUND

IT Infrastructure forms the backbone of CHaRT's online data management websites and applications that support clinical trials. Many different pieces of hardware and software are used by the Programming Team but are managed by the University of Aberdeen's (UoA) IT Services. There is a constant interface between UoA IT Services and CHaRT's Programming Team and CHaRT in general. The Programming Team also interface with many servers and services owned and operated by IT Services.

PURPOSE

To describe CHaRT's policies and procedures for IT infrastructure.

APPLICABILITY

- Essential reading for all CHaRT technical staff (including programmers, IT professionals, and statisticians) and all CHaRT staff using the information systems (including trial managers and data co-ordinators).
- Desirable background reading for all other CHaRT staff, particularly those who interact with CHaRT IT systems.

IT INFRASTRUCTURE

9.1 Receipt and installation of new hardware and software [\[v08.0901.04\]](#)

New hardware and software are installed and configured by the UoA's computer services unit, hereafter called IT Services, who are responsible for the management, operation and support of the University's networks, server infrastructure, software and hardware. Pre-approved software is available from the System Centre Configuration Manager (SCCM) Software Centre and can be installed by any user. The user reviews and accepts the new system. Programmers have elevated privileges that allows them to install some software without getting permissions from IT services.

9.2 Modification to existing hardware and software [\[v08.0902.02\]](#)

Requests for modification to hardware or software can be made by the senior IT development manager to IT Services if the upgrade is to improve performance or functionality. IT Services will make the modifications if they have the resource to support them.

Requests for modification to CHaRT software are made via email to support.chart@abdn.ac.uk or directly logged in the support section by users via the trial website. Requests may require completion of a Change Request Form (see [Section 10.2.5](#)).

9.3 Description of redundancy features [\[v08.0903.01\]](#)

Redundancy features for the CHaRT's critical systems are managed by IT Services.

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9.4 System decommissioning [\[v08.0904.01\]](#)

Hardware and software decommissioning will be handled by IT Services.

9.5 System and data back-up [\[v08.0905.01\]](#)

Routine server and individual PC backup are managed by IT Services.

9.6 Preventative maintenance [\[v08.0906.01\]](#)

Hardware and software maintenance are handled by IT Services. They will arrange warranties and support at the time of purchase.

9.7 System or application patch installation [\[v08.0907.01\]](#)

Notification of new patches will be received from IT Services. New patches will be installed remotely if considered necessary.

9.8 Servers: start up and shut down [\[v08.0908.01\]](#)

All server start-ups and close-downs will be managed by IT Services.

9.9 System monitoring: capacity management [\[v08.0909.01\]](#)

System space capacity will be monitored by IT Services. If additional space is required for a particular system, new space will be purchased or will be extended by expanding system volume space.

9.10 Support desk and problem resolution [\[v08.0910.02\]](#)

IT Services will provide a first line support service. Requests for support will be via email (servicedesk@abdn.ac.uk). Support requests are tracked until resolved and accepted by the user.

Support requests for CHaRT software will be made via the relevant trial website (where appropriate) or by email to support.chart@abdn.ac.uk.

9.11 System failure register [\[v08.0911.02\]](#)

IT Services will document such problems as server shut-downs, disk space issues which have resulted in a loss or reduction of service, serious system problems flagged via internal support requests, web service attacks and virus infections. CHaRT will document any randomisation service downtime. The senior IT development manager and CHaRT Support is alerted of any server failure via automated emails from central IT Services.

9.12 Third party networks: interfacing of local networks to wide area networks [\[v08.0912.01\]](#)

Network topology diagrams will be documented by IT Services. Copies of server details used by CHaRT are available in the **server diagrams (JPEG)** document on **Q-Pulse**.

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9.13 Distribution of software upgrades [\[v08.0913.01\]](#)

IT Services will manage software upgrades if they provide additional functionality that may be of use, or the upgrade includes error fixes required to ensure system integrity or the current version becomes obsolete.

9.14 Maintenance of virus protection and handling of virus alerts and infections [\[v08.0914.01\]](#)

IT Services will manage virus protection software upgrades. If a virus is suspected, then IT Services must be notified immediately (servicedesk@abdn.ac.uk).

9.15 Security management – user account management, passwords and access rights [\[v08.0915.03\]](#)

IT Services will ensure that users will be assigned a unique username and will be allocated to a staff group. Usernames will be deleted when they are no longer required. IT Services will provide guidance about passwords (see www.abdn.ac.uk/staffnet/working-here/passwords.php) which must be kept confidential. Passwords must not be written down.

Usernames and passwords to log in to trial websites will be requested by the trial manager or data co-ordinator and then will be actioned by the CHaRT programming team. Usernames for CHaRT websites consist of the first initial followed by the surname (all lower case). If this username already exists for someone else, then an integer will be appended to the name. Passwords will be at least 8 characters, using a mix of upper and lower case and numerical values. On first login to the trial website users will be prompted to change the password to something more memorable. CHaRT use their in-house system called SPoT (Single Point of Trust) to issue logins and passwords for trial websites. A user will have a single login and will be given access rights for studies as appropriate. Once a trial user (including both CHaRT trial staff and trial site staff) leaves, all access to the trial website will be removed accordingly.

Programmers will run a report every three months on users not accessing the system for longer than 6 months. Trial managers will then review the reports and will then utilise the user account management system to remove permissions and accounts where required (see the **quarterly users' review** document available on **Q-Pulse**).

9.16 Network security [\[v08.0916.01\]](#)

Network security and the physical security of the network are managed by IT Services.

9.17 Server environmental monitoring [\[v08.0917.01\]](#)

IT Services is responsible for monitoring the environment where servers are housed to prevent overheating of equipment.

RELATED REFERENCES AND RESOURCES

None.

Chapter 9: IT infrastructure

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
05	New chapter.	Apr 2018
06	Minor updates to Background and sections 9.1, 9.2, 9.10, 9.15.	Sep 2019
07	Minor updates to section 9.1 regarding installation of non-approved software, section 9.11 regarding server failure alerts and section 9.15 regarding removal of 90 day password updates as no longer a UoA requirement	Oct 2021
08	Minor word changes to sections 9.1, 9.14, 9.15 and 9.17	Apr 2024

CHAPTER 10: DATA MANAGEMENT

[\[v08.1000.08\]](#)

LEAD AUTHOR

Senior IT development manager.

BACKGROUND

High quality data (usually defined by completeness and accuracy) are of fundamental importance to the scientific integrity of any clinical trial. Trial data are expensive to collect, so it is imperative that there are tried and trusted processes for the collection, storing, back-up, and archiving of trial data. Trial data are often confidential and potentially sensitive, so data security is essential. Staff need to be trained in the safe and efficient use of IT systems.

PURPOSE

To describe CHaRT's policies and procedures for handling trial data.

APPLICABILITY

- Essential reading for all CHaRT technical staff (including programmers and IT professionals, and statisticians) and all CHaRT staff using the information systems (including trial managers and data co-ordinators).
- Desirable background reading for all other CHaRT staff, particularly those who interact with CHaRT IT systems.

DATA MANAGEMENT

10.1 Data Management Plans [\[v08.1001.04\]](#)

A Data Management Plan (DMP) describes and defines all data management activities for a trial. A DMP should consider the following requirements:

- Map of file server arrangements.
- Details of trial personnel involved with the trial and data access roles assigned to each.
- A complete set of finalised case report forms (CRF).
- Database design
 - Software, hardware and database location.
 - Detailed description of database structure (data dictionary).
 - Detailed description of data entry system.
- Data entry procedures
 - Method of data collection – paper CRF, electronic devices.
 - Type of data entry - double or single data entry with checking (entry and verification).
 - Data preparation before entry onto electronic system.
- Data query rules
 - Automated checks must be specified in enough detail to enable set up of data entry screens and validation programs. Checks that can be done automatically e.g., making sure a test value is in range, during or after data entry should be clearly identified.
 - Data validations must be specified in the CRF.
 - Data flow and tracking to ensure optimal data completion and to facilitate reporting.
- Query handling
 - How queries will be tracked.
 - Expected resolution time for data queries.

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- Who is responsible for making required changes to the data.
- Who is responsible for ensuring all queries are resolved before data is locked for analysis.
- Quality Assurance plan should include:
 - Audit trail checks.
 - Sample checks of critical data.
- Data review checks to ensure monitoring has been performed consistently.
- Training plan and log for data entry systems if required.
- Electronic data transfer rules.
- Back-up and recovery procedures.
- Archiving and security arrangements.
- Reporting progress.

It is the responsibility of the senior IT development manager to ensure that the DMP is in place before the first randomisation to the trial. These tasks may be delegated to the CHaRT trial specific trial manager and applications programmer to produce, from standard templates located in the Programming Team shared drive.

The DMP for each trial does not exist as a single document. The various constituent parts of the DMP can be found across multiple files. Some are standard documents that apply to all, for example, the server diagram, and some are trial specific, for example, CRFs. All of the required information can be found within the trial specific shared folder areas in use by the CHaRT programming team.

10.2 Development standards [\[v08.1002.08\]](#)

All programmers will be competent in the development of web applications for clinical studies and work to CHaRT guidelines for software development and will receive on the job training to achieve this competence.

In-house software which is resident on a secure server is developed according to a quality framework which encompasses the following:

- Controlled access.
- Full audit trails and traceability.
- Modular structure with re-usable elements to maximise portability and maintainability.
- In-built logical and consistency checks where appropriate.
- Encryption of personal identifiable data.
- Testing using test data before system goes live.
- Automatic back-up of data.
- Trial specific user guides.

10.2.1 Software design

Requirements will be discussed with relevant parties in the research team, by senior members of the programming team, including end users of the software solutions (see [section 5.9](#)). The CRFs will form part of the specification together with the protocol and data flow diagram (see [section 5.6](#)).

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Interpretation of CRF and questionnaire structures is made in Form Generator, which is used to create the bulk of the system user interface (UI) and code. See the **Form Generator – Authoring Metadata** document in [Q-Pulse](#).

During development a review of progress will be undertaken at appropriate stages. This will include review of design, source code and testing. Validation will include user testing and acceptance. Testing will include comparison of the software requirements, defined in the Trial Service Definition (TSD) and CRFs against the software developed and component testing to ensure correctness. Changes made to software in line with changing trial design, CRF and questionnaire design, additions of feature (Change Management) will be in accordance with [section 10.2.5](#).

A **trial service definition (TSD)** document available on [Q-Pulse](#) will be completed by the trial team, this will detail all requirements for the secure area of the trial website. This document will be used as reference during development and through to testing.

A **project website initiation (PWI)** document available on [Q-Pulse](#) will be completed by the trial team, this will detail all requirements for the public area of the trial website. This document will be used as reference during development and through to testing.

10.2.2 Software development

Software development is primarily initiated and managed using Form Generator. Please see the **Form Generator – DB objects and code generation** document available on [Q-Pulse](#).

Software and the underlying databases are developed in line with the **Coding standards** document on [Q-Pulse](#).

10.2.3 Software testing

Testing will be performed using Form Generator. This will be done in accordance with the software validation plan and test plans which will describe the actions to be taken, the expected results and the observed results. See the **Form Generator – Testing** document available on [Q-Pulse](#).

Internal testing is performed against the TSD, CRFs and/or questionnaires. Any changes, before 'go live', to requirements as a result of testing is reflected in the TSD document by the application programmer.

Before 'go live', the software will be supplied to trial staff who are required to perform live testing against the requirements in the TSD. This is referred to as User Acceptance Testing (UAT). UAT documentation is prepared by the programming team and provided to trial staff which, in turn, is passed back to the application programmer to review and make further amendments as required. Confirmation of completion of the UAT is documented by way of the **website green light form**. This form can be found on [Q-Pulse](#).

UATs may also be required for software involving complex design or where dynamic requirements exist. The final user acceptance tests must be signed off by a senior programmer or senior IT development manager.

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All UAT documentation is kept in the programming team shared folders for the trial.

An “All site test” will be performed before “go live” against the requirements set out in the TSD.

Any additional development during the mid cycle of a trial, e.g. when a new CRF or participant questionnaire has been developed and approved, will require the same process to be followed. This is not, however, the process for existing CRFs or questionnaires. Under these circumstances the change management process should be followed; see [section 10.2.5](#) for more details.

10.2.4 Go live

Before a trial system can go live the actions contained in the **Website green light form** found on **Q-Pulse** must be confirmed. A date for ‘go live’ is discussed and agreed by senior members of the programming team together with the appropriate trial manager.

The test data in the system, including participants, CRF, questionnaires and e-Consent data must be deleted.

10.2.5 Change management

Changes made during the initial development of a trial website will not require a formal change request.

Any change to existing CRFs or questionnaires, as a result of an amendment (see [section 6.10](#)), that either requires ethical approval or will require a change to the database in terms of new forms or updated field sets after first version release must be documented and will require completion of a **change request form**. This form can be found on **Q-Pulse**.

First version release of any data collection form is defined as active participant data being entered for that form and any change request should be discussed with the Project Management Group (PMG) and be signed off by two members of the CHaRT senior management team. Only in exceptional circumstances (e.g. to amend safety procedures) can a change request be submitted without the approval of the PMG. If authorisation for a change is not approved, then the reason must be documented.

It is the responsibility of the research team to ensure that any corresponding paperwork updates have the appropriate approval as described in [section 6.10](#).

Throughout the life of a trial, the programming team will receive requests for trial related technical assistance. Any requests for assistance, termed ‘Support requests’, are made directly through the trial website via a ticket system and often made by the trial manager or person with delegated authority; although a support request can be submitted by any trial staff who has a website login. Authorisation may be sought by a senior member of the programming team prior to work being undertaken. Questions related to determining the content for a future support request or urgent enquiries can be directed to the Programming team’s shared mailbox, support.chart@abdn.ac.uk.

These support requests follow the development and testing procedure to ensure all the data management procedures are followed. Once the ticket is actioned, the trial team

member/requestor is notified of the change and given enough time to test the request and revert back in case of further amendment or errors.

10.2.6 Data dictionary

The CRFs and questionnaires will form part of the TSD together with the protocol and the data dictionary.

The data dictionary is metadata (data used to describe the data being collected) defined in the extended properties of each column of the database tables and is mainly used for user defined reports and the generation of data queries. It records the question text, any contextual information e.g. the text of a primary question, and response options where these are needed.

When CRFs and questionnaires are generated using Form Generator this metadata is generated by that tool. However, when making manual modifications to CRFs and questionnaires, it is important that programmers update this metadata in the database for each column, and in the Form Generator.

10.2.7 Data queries

Data queries are questions made by trial management staff to site staff regarding the state of completion and content of data provided in electronic CRFs. The system provides a 'Missing data' report which forms the basis for data queries.

The definition of the Missing data report is undertaken by programmers based on the advice provided by trial managers. Typically, a senior member of the programming team will ask the trial manager to identify which questions are mandatory and qualify constraints i.e. if question X = response A then question Y is mandatory. If this information is not provided, the programmer will make each response mandatory.

Changes to the definition of the 'Missing data' report can be made by a support request or a Change request.

10.2.8 Database locking and data archival

For each interim DMC report, a copy of the database will be taken and preserved so that the report may be re-produced if required at a later date. Any data cleaning performed on the copy must be reflected in the live database. Live databases may continue to be used after final analyses if the trial then enters long-term follow-up.

When a trial terminates, the database must be archived to a secure network drive with adequate back-up procedures in place for the length of time stipulated by the funder.

The trial manager will complete the **project website archival (PWA) form** (available on **Q-Pulse**). Upon receipt of the completed PWA, the programming team will ensure all electronic data relating to that trial website and associate programming files are zipped up and archived securely in a restricted archive area. The database is detached from the database server (MS SQL Server), and the trial website is decommissioned from the web server and replaced with a simple holding page. The archived elements include the database, trial website, trial source code and trial documentation, SQL server jobs and SQL server reports. Only the senior IT development manager and senior programmers will have access to the archive area, permissions can be granted to other programmers on request.

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Databases must be archived in a format such that they may be recreated if necessary. It is the policy of the University that database software in production use is version N – 1, as such the database software will be upgraded incrementally as required to do so. To ensure compatibility with historic database archives, tests will be performed to ensure a database can be restored on the new software version as it is introduced. In the cases where restoration fails, an upgrade method will be identified and documented.

10.3 Data transfer [\[v08.1003.07\]](#)

10.3.1 Data issued from CHaRT

Electronic data transferred to an external location should be anonymised and the data only identified by a unique study number. If this is not practical (e.g. for data linkage to such institutions as Information Services Division) then the data should be encrypted, and password protected. The transfer must be made using a secure file transfer service (FTS); currently ZendTo which is available at zendto.abdn.ac.uk/.

All data transfers should be approved by the PMG using the **data request form** found on **Q-Pulse**. Once approved, the data transfer form should be completed and signed by the CHaRT staff member transferring the data. The **data transfer form** should be countersigned by the recipient and then returned to CHaRT. Further details of the data transfer procedures and required form can be found on **Q-Pulse**.

Please refer to the NHS Information Governance Toolkit (digital.nhs.uk/data-and-information/looking-after-information/data-security-and-information-governance/data-security-and-protection-toolkit) for further information regarding the handling of information.

10.3.2 Data received from the NHS

Strict guidelines have been issued by NHS England (NHSE) that specify requirements for the secure storage and management of NHSE data. Please refer to the [UoA NHS England Data management SOP](#), authored by UoA staff, which provides information and instructions for researchers on the control of access, secure storage and management of NHSE data to ensure compliance with the UoA NHS England Data Sharing Framework Contract. NHSE data must be kept secure and tightly controlled so requests for access and deletion can be completed in the appropriate manner.

Access to the data and requests for deletion, are under the control of the NHSE gateway manager and the gateway manager deputy: nhsgateway@abdn.ac.uk. These processes are important to prevent misuse of NHSE data and the NHSE data access, storage and management SOP be adhered to whenever personal or sensitive patient related data is provided by the NHS for research purposes. Any queries on this procedure should be directed to the NHS Gateway Manager at nhsgateway@abdn.ac.uk

10.4 Information security [\[v08.1004.03\]](#)

Information security management provides an enabling mechanism for information sharing, which ensures the protection of information and computing assets. Information security management has three basic components:

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- 1) Confidentiality - protecting sensitive information from unauthorised disclosure.
- 2) Integrity - safeguarding the accuracy and completeness of information and computer software.
- 3) Availability - ensuring that information and vital services are available to authorised users when required.

The University security policy applies to all staff and students of the University, and hence CHaRT, and covers the operation and uses of all IT systems and facilities administered by the University. It has been developed with reference to the University Colleges and Information Systems Association (UCISA) Information Security Toolkit. The information security policy can be viewed at:

www.abdn.ac.uk/staffnet/governance/policies-proceedures-plans-and-guidlines-399.php

Any serious incidents resulting from non-compliance with Information Security Policies will be dealt with by Human Resources and may result in disciplinary action. The CHaRT security policy builds on the University of Aberdeen's policy and includes specific clinical trial issues/processes.

Access to information on University computers is controlled by allocating all staff and students a unique username and password. This is done by IT Services. Access to websites set up for randomised trials is controlled by allocating a unique username and password to trial staff and users who require access to the sites. This is done by the CHaRT programming team. These usernames and passwords are not the same as the ones managed by UoA IT Services and apply only to the trial websites each person is allowed to access. Passwords must be kept confidential and must not be written down.

Within the trial website, the individual trial sites have centre- and feature-based role restrictions to ensure that site staff can only access the areas for which they have been delegated permissions for. The trial manager or data coordinator is responsible for what roles (feature access) and centres are requested. The programming team checks the correctness of the request before granting access to user.

10.5 Data Protection Act [\[v08.1005.03\]](#)

Personal information (including patient and staff information) relating to living individuals held on a computer or manual system is safeguarded by the UK [General Data Protection Regulation \(UK GDPR\)](#) and the [Data Protection Act 2018](#), which replaces the Data Protection Act 1998, both of which came into effect on 25 May 2018. This places obligations on those who record or use information, while at the same time giving specified rights to people about what information is held. Data Protection protects the right of the individual about what information is obtained, shared, processed or supplied whether via a computer or manual paper records.

All data handling processes carried out by CHaRT must conform to the current legislation and all personnel are made aware of this document as part of their induction checklist by reading and signing the ACE **protecting information policy (PIP)** which can be found on [Q-Pulse](#).

Any breach of the current legislation may result in the University, as the registered 'Data Controller', being liable in law for the consequences of the breach. This liability may extend to the individual processing the data and their Head of School under certain circumstances (see www.abdn.ac.uk/staffnet/governance/policies-proceedures-plans-and-guidlines-399.php).

10.6 Back up [\[v08.1006.01\]](#)

The security and safety of electronic trial data is a primary concern. Procedures exist which ensure that the data will be safe and intact if anything goes wrong with any element of the database system. Procedures fit in with corporate policies implemented by the IT services and are not a CHaRT-specific responsibility.

All data is stored on the University of Aberdeen's storage area in a password protected secure area. Access both physically and electronically is restricted.

10.7 Business continuity / disaster recovery [\[v08.1007.02\]](#)

The University of Aberdeen has drawn up a business continuity plan (www.abdn.ac.uk/staffnet/governance/business-continuity-352.php#panel5528). The contact details of the CHaRT director and senior IT development manager are included in the plan. The document outlines the response to a partial or complete loss of the building, including IT and communication systems. Central IT recovery solutions have been implemented to ensure business continuity within specified timescales.

The IT recovery schedule for central resources states:

- Emergency web communication will be enabled in less than four hours.
- Emergency email capability will be enabled within four hours.
- The CHaRT randomisation service will be operational within 24 hours and the service will be diverted to a mobile or different extension number initially.
- Up to 24 hours of data may be lost (since the last backup).

Since most trial data entry systems are now web-based there may be some delay in restoring these systems but essential correspondence between the trial office and sites or participants should be enabled within four hours of a critical incident. Access to a PC connected to a central server, a telephone and a recovered dataset will be the only immediate requirements.

The CHaRT randomisation service will provide all users with a suggested alternative randomisation plan for use in the event of a critical incident. The senior IT development manager is responsible for holding a list of all customer details that is kept off-site along with paper copies of randomisation details for emergency randomisation. Customers will also be instructed how to perform a local randomisation if no contact can be made with the trial office.

10.8 Encryption [\[v08.1008.03\]](#)

There are two levels of encryption for electronic data, these are:

Level one: Routine e-mail correspondence, with non-confidential attachments (e.g. trial meeting minutes) – no encryption required.

Level two: Highly confidential and/or sensitive information (e.g. randomisation codes, patient identifiable data, data monitoring reports)

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For level two data, staff must use the University File Transfer Service (FTS), ZendTo which is available at zendto.abdn.ac.uk/. Please contact the CHaRT senior IT development manager or senior trials managers if you need advice or need to encrypt any data.

RELATED REFERENCES AND RESOURCES

[SOP-QA-20: Data Management](#)

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Further information and revisions to sections 9.2.2, 9.3, 9.7 and 9.9.8.	Jan 2012
04	Minor changes and updates to sections 9.1, 9.2, 9.3, 9.4 (username and passwords to access trial websites).	Jul 2015
05	Update to DMP information in 10.1, new information about NHS digital in 10.3; additions made to paragraphs 10.2 programming standards; 10.2.2 Software testing; 10.2.3 Change management; Removal of Randomisation section; added as a new Chapter (Chapter 11).	Apr 2018
06	Added reference to TSD and PWI (10.2.1), minor updates and embedded links fixed in sections 10.2.2, 10.2.3, 10.2.4, 10.2.5, new archive section added (10.2.6), minor updates to 10.3.1, 10.4, 10.5, 10.7, and more detail around the levels of encryption & further examples given (10.8).	Oct 2019
07	Minor updates to sections 10.2, 10.3.1 and 10.8. Further detail about process for receiving NHSD data given in section 10.3.2. New paragraphs added to section 10.2.2 about the process to follow if there are additional developments of the trial database mid trial, section 10.2.3 about process around support requests, and section 10.4 regarding centre and trial staff database access depending on their role.	Oct 2021
08	Addition of four new sub sections: 10.2.2 Software development, 10.2.4 Go live, 10.2.6 Database design dictionary and 10.2.7 Data Queries. Wording changes and new sentences added to 10.1, wording changes to 10.2, text removed from 10.2.3, wording changes to 10.3.1 and 10.8.	Dec 23

Chapter 11: Randomisation

CHAPTER 11: RANDOMISATION

[\[v08.1100.04\]](#)

LEAD AUTHOR

Senior IT development manager

BACKGROUND

Randomisation is the process used for assigning subjects in a clinical trial to intervention groups without introducing human bias due to external factors. Random allocation ensures that any differences between the groups at trial entry are due to chance alone and that each individual has the same chance (after considering intervention ratios) of receiving each intervention.

PURPOSE

To describe CHaRT's policies and procedures for handling randomisation, blinding in clinical trials and to describe the documentation of these procedures.

APPLICABILITY

- Essential reading for all CHaRT technical staff (including programmers and IT professionals; and statisticians)
- Desirable background reading for all other CHaRT staff; particularly those who interact with CHaRT IT systems.

RANDOMISATION

11.1 Responsibilities

[\[v08.1101.01\]](#)

The grantholder statistician will discuss the randomisation specification with the senior statistician and senior IT development manager, Chief Investigator and possibly other senior staff (e.g. the CHaRT director, the senior trials manager, or other CHaRT CTU staff that are grantholders).

The senior IT development manager will advise the applications programmer of the specification for a randomisation system.

It is the responsibility of the trial manager to ensure that all trial personnel who are authorised to randomise participants are properly trained in the use of the randomisation system.

11.2 Specification

[\[v08.1102.02\]](#)

The specification of the randomisation design is the responsibility of the grantholder or senior statistician or the senior IT development manager. The type of randomisation method used will be trial specific and must attempt to reduce the chance of imbalance between treatment groups (e.g. simple, block, minimisation).

The randomisation methods and parameters of the randomisation process (e.g. stratification variables, inclusion and exclusion criteria) must be described fully in the protocol and entered into the Trial Service Definition (TSD).

Chapter 11: Randomisation

For non-CHaRT trials, anyone who approaches the programming team to request a randomisation service will communicate this specification in writing by completing a **randomisation service request form** which can be found on [Q-Pulse](#).

11.3 Implementation [\[v08.1103.01\]](#)

The applications programmer will be responsible for developing the randomisation specification.

11.4 Testing and simulations [\[v08.1104.03\]](#)

The applications programmer will be responsible for producing simulations data and completing the **randomisation simulations verification (RSV)** document (available on [Q-Pulse](#)). The number of simulations will be based on target recruitment across target centres.

A CHaRT CTU statistician for the trial will then check the RSV against the randomisation design in the protocol and sign off the RSV after checking the simulation results are correct.

Supporting documentation and datasets for all simulations should be held in the programming common drive for the trial.

11.5 Non-CHaRT trials [\[v08.1105.02\]](#)

As well as being used for all CHaRT trials, the randomisation service is made available on a selective basis as a discrete consultancy level service. This is paid for by the client. Similar processes are followed as in [section 11.2](#). The senior IT development manager will send details of all new external randomisation systems to the relevant University of Aberdeen Research and Innovation Business Development Officer so that Service Level Agreements can be issued before randomisation commences.

A formal assessment by the client's statistician as to the methodological appropriateness of the proposed randomisation scheme should be done before they provide it to us.

11.6 Unblinding [\[v08.1106.02\]](#)

The trial statistician, programmer and DMC may have access to unblinded data during the course of the trial. These staff members must not be involved in any other aspects of trial conduct. The rest of the research team will only have access to unblinded data after the end of the trial when final analyses have been completed (also refer to [section 12.5: Unblinding](#)).

If emergency unblinding of individual participants data due to safety concerns is required, then a trial specific 'Unblinding Procedure' will be created and kept in the Trial Master File (TMF). Emergency unblinding may be offered through the Telephone Randomisation Service or Web-based unblinding function where logging of such events is automated and alerts will be automatically sent to the appropriate people (which may include CI, trial manager, manufacturer and sponsor). Please see [SOP-QA-35: Unblinding](#) for further details on unblinding procedures for locally sponsored studies.

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11.7 Quality Assurance [\[v08.1107.03\]](#)

- A trial randomisation solution will be prospectively tested before going live (see [section 11.4](#)).
- Once the system is live, the properties of the trial randomisation solution will be checked at approximately 20% and 50% of the randomisation recruitment target, and also at the end of the trial, by the trial statistician (or another suitable qualified person or a senior member of the CHaRT programming team). Please refer to [SOP-QA-18: Randomisation & Blinding for Controlled Trials](#) for further information on randomisation and blinding for locally sponsored studies. This only applies to full CHaRT trials. Trials that are just using the randomisation service will only be validated at the start of the process unless specifically requested and paid for.

11.8 Training [\[v08.1108.01\]](#)

Randomisation applications will be used routinely by non-CHaRT personnel, usually trial coordinators, research nurses, and clinicians engaged as site staff. Although the randomisation applications are inherently simple and have been designed to be user friendly and easy to operate, nevertheless it is of paramount importance that all staff involved in the randomisation process (a) understand that process and (b) are trained in the facilitation of those processes – for example, in how to successfully complete a randomisation using the trial randomisation application. Every trial will have a section “Randomisation Procedures” in their trial guidance (see [Section 5.5.1](#)).

It is the responsibility of the trial manager to ensure that all trial personnel who are authorised to randomise participants are properly trained in the use of the randomisation system. Multicentre studies can vary considerably in the number of authorised users of the randomisation application, from a handful at a few sites, to perhaps several hundred across dozens or more sites. The length of time a recruitment application is live also varies considerably, from as little as a few weeks to several years. As a result, training needs to be flexible in terms of both content and mode of delivery. Flexibility in content is required because users will be from many different backgrounds and may have none to extensive experience of randomisation. Flexibility in delivery is required because over a long recruitment window in dozens of sites, there will usually be significant turnover in authorised randomisation staff. CHaRT have therefore developed as standard:

- Randomisation procedures in trial guidance (available on trial portal).
- Instructor-led demonstration of randomisation system at trial training day(s) at start of trial and as required.
- Remote one-on-one training (via phone or video link).
- All users should be given the opportunity to complete a successful ‘dummy’ randomisation prior to full authorisation.
- Telephone User Guide for telephone randomisation systems.
- Web User Guide for web randomisation systems.

11.9 Failures and unexpected occurrences [\[v08.1109.02\]](#)

The CHaRT randomisation system is automated, and so relies on either telephone or internet access being available. It therefore could potentially happen that a randomisation cannot be made via the telephone or web-based randomisation system. When the service is denied to

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all users (in all trials) by a breakdown in Aberdeen, all users will be notified as soon as possible and will be given a mobile telephone number to contact. In general, randomisations will be done manually by contacting Aberdeen staff until the automated service is resumed. If this is inconvenient (e.g. time zones for international studies) local randomisation may be permitted.

Full details of specific arrangements will be documented in a Trial Randomisation Specification for each trial in the randomisation service operations manual (a physical folder) and held with the programming team. The same procedure will operate when the denial of service is caused by a local problem at the site (i.e. not a systems failure in Aberdeen). All extraordinary randomisations will be documented and communicated to CHaRT (via the trial manager or senior IT development manager for non-CHaRT studies) at the earliest opportunity.

The systems are designed in such a way that if a transaction fails midstream, the transaction is cancelled. It is only at the point a randomisation ID and/or treatment assignment is issued that the transaction is considered complete.

11.10 Misuse & unauthorised use [\[v08.1110.01\]](#)

If an authorised user attempts to randomise the same person twice, the application issues a warning. This is usually when the user believes that the initial randomisation has failed, and immediately attempts to randomise the participant again. (Note: This only happens if the trial identifier is collected at time of randomisation. In other cases, double randomisations may not be readily identified).

As with all our secure web systems, unauthorised users are denied access through the use of access control via user ID management and passwords.

If a user attempts to access the web system and fails to use the correct user ID/password, they are locked out after three failures. Users will be alerted on screen that they have been locked out and they will have to email the support desk (support.chart@abdn.ac.uk) to have their account unlocked.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
05	New chapter; this Chapter used to be a sub section of Chapter 10: Data Management, and is now a stand-alone chapter; and reverted to version 01, e.g. [v05.11ss.01].	Apr 2018
06	Background text updated, minor updates and clarifications to sections 11.2, 11.4, 11.5, 11.6, and 11.9, particularly with respect to the role of the statistician. More detail provided regarding when the properties of the study randomisation solution will be checked (11.7).	Oct 2019

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07	New sentence added to section 11.7 to clarify the difference in the randomisation QA checks for 'full' CHaRT trials versus trials that are just using the randomisation service.	Oct 2021
08	Minor text changes to section 11.2, 11.3, 11.4, 11.6, 11.7, 11.9	Dec 2023

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Chapter 12: Statistics

CHAPTER 12: STATISTICS

[\[v08.1200.08\]](#)

LEAD AUTHOR

Senior statistician.

BACKGROUND

The application of rigorous statistical principles to every stage of the clinical trial – from optimal design, to pre-specification of analysis plans, to informative progress reporting of maturing data to Trial Steering Committee (TSC) and Data Monitoring Committee (DMC) in collaboration with the Trial team, to timely and accurate analysis and interpretation of the final data – is of fundamental importance to delivering a high quality trial that will provide reliable evidence.

PURPOSE

To document requirements for all statistical aspects of CHaRT's trials.

APPLICABILITY

- Essential reading for CHaRT statisticians, and any statistician involved in a CHaRT trial.
- Useful reading for any staff interacting with statistical staff.

STATISTICS

12.1 Methodology

[\[v08.1201.02\]](#)

CHaRT is committed to designing and delivering trials that are methodologically sound. Where CHaRT is responsible for the statistical aspects of a trial, a CHaRT statistician will be involved at the initial design stage to assess the most appropriate primary outcome, trial structure and sample size. This process is formally summarised along with relevant references and then verified by another member of the statistics team specifically for the sample size calculation which should be replicable from the information given in the application. Please refer to the **Sample size verification for grant applications checklist** available on [Q-Pulse](#).

Once a trial starts the assigned trial statistician will contribute to the trial setup phase with the development of the protocol, CRFs and other instruments for data collection (including dummy tables), ensuring the correct data is collected in the right format to answer the research question (see [section 5.6](#)). A CTU statistician will also check the randomisation process (see [section 12.5](#)).

12.2 Data manipulation

[\[v08.1202.01\]](#)

For any interim analyses, data cleaning or final analysis, the trial statistician will request or directly extract a datacut from the main database transferring it into the preferred analytical software (see [section 12.8](#)).

Derived outcomes (e.g. EQ-5D and other PROMS) will use validated code or bespoke code verified by another CTU statistician and referred to in the SAP (see [section 12.3](#)).

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12.3 Statistical analysis plans [\[v08.1203.05\]](#)

All CHaRT trials will have a statistical analysis plan (SAP; see [SOP-QA-23: Statistical Analysis Plans for Clinical Trials](#) for further details on the purpose and content of a SAP for locally sponsored studies). A **SAP template** is available on [Q-Pulse](#). This document will specify the statistical analyses for the trial. It will be a comprehensive statement of the trial hypotheses, and the methodology to be employed in addressing these hypotheses. It will be largely drafted early in the trial using dummy tables generated at the CRF design stage where relevant, will evolve reflecting any trial design amendments and generally be finalised towards the trial end before any unblinded information has been seen (except by the DMC). Although at present the SAP is not usually formally published, it would be expected to be available (for example, on the trial website) to interested researchers and may be required at submission of a paper on related work to a journal. It is authored by the trial statistician and approved by the Chief Investigator (CI) on behalf of the TSC (and grantholders) and a senior statistician. The DMC would usually be invited to comment on a draft.

12.4 Pilot / feasibility studies [\[v08.1204.01\]](#)

Increasingly, definitive trials of complex interventions, as well as drug trials, need to demonstrate feasibility (in terms of theory-based interventions, and measurable outcomes), an ability to recruit sufficient participants from interested centres, as well as demonstrate that adequate resource have been requested to complete the trial on time. Therefore, many studies require comprehensive pilot and/or feasibility work to be undertaken.

From a statistical perspective, such preliminary studies are often challenging, since by definition they face increased uncertainties, the resolution of which is the object of the trial. The design, conduct and analysis of such pilot and feasibility studies requires commensurate attention and commitment from the statistical team.

12.5 Randomisation (statistics) [\[v08.1205.03\]](#)

Randomisation is of fundamental importance in a RCT. All CHaRT RCTs utilise a proven, automated, centralised randomisation application. This is accessed by telephone or via the internet, e.g. through a desktop workstation, a handheld computing device or a mobile phone. The randomisation application is capable of employing a variety of designs, usually incorporating a minimisation algorithm, or stratification, or a mixture of the two. The randomisation procedure is tested for robustness prior to randomising the first participant (see [section 11.4](#)). It is the responsibility of a senior statistician, or delegated CTU statistician, to check that the randomisation method is what is specified in the protocol. Checks should be made that the correct minimisation or stratification variables have been used and that the correct levels have been specified. The simulations should be examined to confirm that randomisation is balanced for these variables. The randomisation sequence for each centre should also be inspected and any unusual allocation sequences investigated. Ad hoc monitoring of the randomisation procedure should be undertaken (such as during interim reports).

12.6 Unblinding [\[v08.1206.04\]](#)

For open trial designs of non-drug, complex interventions conducted by CHaRT it is usually not useful to insist on blinding the trial statistician or the DMC to allocation during trial analyses (since it is obvious from the data reported which intervention arm a participant is in).

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In trials where there is some element of blinding, consideration will be given as to whether it is appropriate for the trial statistician to be blinded to treatment allocation. There are mechanisms of dummy coding treatment allocations resolved by another statistician in the IAHS (but not on the trial team) should the DMC team feel the need to know.

Throughout the conduct of the trial no persons except the trial statistician, the CHaRT programmer and the DMC will have access to unblinded data. Should the trial require the analysing statistician to be blinded up until the final analysis (for instance if the trial were a CTIMP), this will be detailed in the trial specific SAP. At trial analysis, the data will be unblinded to the rest of the research team only when final analyses have been formally conducted in accordance with the agreed SAP. Please see [SOP-QA-35: Unblinding](#) for further details on unblinding procedures for locally sponsored studies.

12.7 Statistical reports [\[v08.1207.03\]](#)

The trial statistician has overall responsibility for the production of all statistical reports for a trial, though it will usually involve liaison with a number of trial personnel such as trial manager, data coordinator or programmer.

12.7.1 *Blinded/aggregate reports*

Blinded or aggregate reports are usually made available for PMG or TSC meetings and will typically involve a description of current recruitment rates, questionnaire response rates and missing data items in key variables.

12.7.2 *Unblinded reports*

Unblinded reports are only written for DMC meetings and only the trial statistician and programmer will author and have access to the report(s). As above (see [section 12.6](#)), if the trial statistician requires to remain blinded this will be detailed in the trial-specific SAP.

12.7.3 *Final trial reports*

The trial statistician is responsible for the execution and reporting the agreed SAP for the final trial reports. (See [Chapter 8](#) for details on trial publications and dissemination).

12.8 Statistical programming [\[v08.1208.02\]](#)

There is no single prescribed statistical package for CHaRT trials, rather there is an expectation that the package should be proven and fit for purpose. Stata and WinBugs are the most commonly used packages. Irrespective of the package used, a common file structure is required for the management of the statistical analyses in the SAP.

12.9 Statistical quality control [\[v08.1209.02\]](#)

Quality control of statistical aspects of CHaRT trials is highly important. All CHaRT trials will have at least two statisticians involved in the trial – a senior statistician to take overall management responsibility for the statistical aspects of the trial and a second statistician (called the trial statistician in this documentation) to be responsible for the day-to-day performance of all statistical aspects. The analysis of the primary outcome(s) will always be verified by a second statistician. To facilitate the handover of statistical analyses to other CHaRT statisticians due to any unforeseen staff changes (such as illness or staff retention) or for replication of the primary result, a common file structure is required.

Chapter 12: Statistics

All CHaRT statisticians must undergo appropriate Good Clinical Practice (GCP)/Good Research Practice (GRP) training (see [section 6.1](#)).

12.10 International Conference on Harmonisation (ICH) statistical principles

[\[v08.1210.01\]](#)

All statisticians working on CHaRT trials are expected to read the ICH Tripartite Guideline Statistical Principles for Clinical Trials E9 (see: database.ich.org/sites/default/files/E9_Guideline.pdf). Whilst recognising that the majority of CHaRT trials are non-drug or complex intervention studies that are not directly covered by this document, the document provides useful guidance on good statistical practice in trials. CHaRT does not, however, advocate an uncritical application of all the principles in the document.

12.11 Partnerships with external statisticians [\[v08.1211.01\]](#)

For CHaRT trials there is an expectation during the development of a trial proposal that a senior CHaRT statistician will be involved in the process and whenever possible the statistical aspects will be conducted by statisticians within CHaRT. However, it is recognised that, dependent upon the proposed design of the trial and the trial subject area, an external statistician may be more appropriate to maintain levels of academic rigour. In such circumstances, the external statistician will liaise with a senior CHaRT CTU statistician throughout the trial design, conduct and analysis and will be expected to apply the appropriate CHaRT statistical SOPs.

12.12 Interaction with Data Monitoring Committee [\[v08.1212.03\]](#)

The trial statistician will have responsibility for creating the reports to the DMC. Generation of the report will involve liaising with the trial programmer. Occasionally the trial statistician may not be the statistician who attends the DMC meeting and answers statistical queries in the interpretation of the data. In such circumstances this will be documented in the meeting papers, minutes and may be specified in the DMC Charter.

12.13 Statistical archiving [\[v08.1213.01\]](#)

During the Trial, each interim DMC report(s), analyses code, and a copy of the database will be preserved so that the report may be re-produced if required at a later date.

Once the final analyses are completed and the results published, all interim and DMC statistical reports (open and closed) will be securely archived by the trial statistician(s), for later inspection if required.

RELATED REFERENCES AND RESOURCES

[SOP-QA-18: Randomisation & Blinding for Controlled Trials](#)

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	

Chapter 12: Statistics

02	N/A	
03	Revision to section 10.11 in line with DMC Charter and addition of link to SOP-QA on Statistical Analysis Plans in section 10.1.	Jan 2012
04	Changes to wording of sections 10.2 and 10.8.	Jun 2015
05	Update to section 12.5 and minor wording amendments.	Apr 2018
06	Minor wording changes to Background text and section 12.2. More detail added to section 12.4 to describe the randomisation method checks in line with section 11.6. Updates to sections 12.5 and 12.11 to reflect current practice regarding blinding and implications for a closed DMC meeting.	Mar 2020
07	Minor update to section 12.4 to provide clarity on responsibility of senior statistician for checking the randomisation method. Updates to text in section 12.2 to include Q-pulse link to SAP, and sections 12.5 and 12.6.2 to provide guidance on the local process should the trial statistician be required to remain blinded.	May 2022
08	Addition of two new sections: 12.2 on Data manipulation and 12.13 on Statistical archiving to meet UKCRC requirements. Major updates to text in section 12.1 to provide more information around CHaRT's statistical role in the design stage of a trial including sample size calculations, development of trial protocol and CRF design. Minor update to section 12.8 to clarify the most common statistical packages used	Sept 2024

Chapter 13: Health economics

CHAPTER 13: HEALTH ECONOMICS

[\[v08.1300.06\]](#)

LEAD AUTHOR

Senior health economist.

BACKGROUND

Health economics plays a critical role in bringing together information on the effectiveness and resource implications of health care interventions within clinical trials. This chapter covers the generic issues in the conduct of an economic evaluation.

PURPOSE

To document generic issues for health economists involved in CHaRT trials.

APPLICABILITY

- Essential reading for all health economists involved in CHaRT trials.
- Useful background for all staff that interact with health economists.

HEALTH ECONOMICS

13.1 Methodology

[\[v08.1301.02\]](#)

CHaRT is committed to designing and delivering trials that are methodologically sound.

The economic evaluations conducted as part of such trials should as a minimum conform to guidelines for the design, conduct and reporting of economic evaluations.^{1,2}

On some occasions, cross-cutting methodological work will arise from the conduct of a trial. Such work should be agreed with the project management group (PMG) and Trial Steering Committee (TSC), and it is the economist's responsibility that all necessary permissions and ethical approvals are obtained to use the trial data for a methodological purpose. Some form of written independent peer review should be obtained prior to the commencement of the methodological work.

13.2 Development of care pathways

[\[v08.1302.01\]](#)

It is good practice for every economic evaluation to formally consider the care pathway that would be followed by patients receiving the trial interventions. The care pathway, as described in [Table 13.1](#), should describe the care and events that may be expected to occur following randomisation. The care pathway informs decisions about what data are required for the economic evaluation, how it might be collected and valued.

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Table 13.1 Constructing a care pathway for an economic evaluation

Care pathway	Example
Clinical event	Stroke
↓	↓
Clinical event management + subsequent clinical events	Acute care and rehabilitation + sequelae and complications of treatment
↓	↓
Resources used to manage events and outcomes of events	Length of hospital stay, intensity of rehabilitation therapy, management of sequelae and complications (e.g. bleeding from secondary prophylaxis) and health outcomes associated with each stage
↓	↓
Cost of resources used and utilities of outcomes	Valuation of resources using health care (and other) pay and prices and valuation of outcomes using quality adjusted life years (QALYs)/willingness to pay (WTP)

13.3 Economic analysis plans [\[v08.1303.04\]](#)

All CHaRT trials, where the health economics is being led from the University of Aberdeen, should have a **health economics analysis plan (HEAP)**, a template is available on [Q-Pulse](#). This document will specify the economic analyses for the trial, including any modelling that might be conducted to extrapolate results or place the results of the trial within the wider body of evidence.

The HEAP is a comprehensive statement of the trial's health economic aims and objectives, and the methodology to be employed in addressing these aims and objectives. It will be developed as the trial proceeds based on the plans recorded in the protocol, and in conjunction with the development of the CRFs (see [section 5.6](#)), such as the **surgical form**, and other instruments for data collection, such as the **participant time and travel costs questionnaire**; both templates are available on [Q-Pulse](#). The HEAP will generally be finalised towards the end of trial before analysis of the data commences. It will specify the importance of the questions (e.g. primary, secondary or tertiary outcomes) and will, outline the plans for estimation of between group differences in costs, relevant outcomes and cost-effectiveness. It will also specify the methods to be used to characterise uncertainty around these estimates and will pre-specify what, if any, subgroup analyses will be undertaken. A set of 'dummy tables' (these are *a priori* agreed tables illustrating how the final trial results will be reported) is expected to be included. The HEAP is likely to be closely related to the statistical analysis plan (SAP: see [section 12.3](#)) and should, as far as possible, follow the procedures set out in that analysis plan for natural and clinical outcomes. Where the HEAP deviates from the statistical analysis plan this should be documented, and a rationale provided.

It is expected that the HEAP should be available to interested researchers (for example, on the trial website). It is authored by the trial economist and approved by the (CI) on behalf of the TSC (and grantholders) and the senior economist.

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13.4 Pilot studies and pre-trial modelling [\[v08.1304.01\]](#)

Data collection tools should always be piloted before use within trials. Consideration should also be given to the development or conceptualisation of a model prior to the start of the trial, should resources allow, to identify information needs and key areas for further data collection within the trial. Such a model should be conducted following the principles of good practice for modelling studies^{2,3}.

13.5 Economic reports [\[v08.1305.01\]](#)

The trial economist has overall responsibility for the production of all economic reports, though it will usually involve liaison with a number of trial personnel such as trial manager, data co-ordinator or programmer. Due to the nature of an economic analysis, which requires interventions to be costed, all reports will be unblinded and only prepared for the final trial report.

13.6 Economic programming [\[v08.1306.03\]](#)

There is no single prescribed package for economic evaluation alongside CHaRT trials, rather there is an expectation that the package should be proven and fit for purpose (e.g. should a decision model form part of the trial analysis, an appropriate package such as Treeage or Excel would be used).

For within trial analyses, Stata is currently the most commonly used package. The within trial economic analysis should follow the guidance set out for the (SAP) and statistical programming ([sections 12.3](#) & [12.8](#)) respectively. However, analysis models for certain variables may be different to meet the requirements of the economic evaluation – in which case this should be clearly justified.

13.7 Economics quality control [\[v08.1307.02\]](#)

Quality control of economic aspects of CHaRT trials is highly important. All CHaRT trials will ideally have two economists involved in the trial – a senior economist to take overall management responsibility for the economic aspects of the trial and a second economist responsible for the day-to-day performance of all economic aspects and who will draft the analysis plan. In such circumstances where this work is performed by just one experienced economist, a more senior economist, who may not be directly involved with the trial, will provide appropriate health economic oversight, guidance and support. All economists involved in CHaRT trials must undergo appropriate GCP/GRP training (see [section 6.1](#)).

13.8 Partnerships with external economists [\[v08.1308.01\]](#)

For CHaRT trials involving an economic evaluation, a senior economist will be involved in the development of a trial proposal and, whenever possible the economic aspects will be conducted by a more junior economist allocated to the trial. However, it is recognised that, dependent upon the proposed design of the trial and the trial subject area, an external economist may be more appropriate. In such circumstances, the external economist will be expected to apply the appropriate CHaRT SOPs including those relating to the production of a HEAP ([section 13.3](#)), the piloting of trial instruments ([section 13.4](#)), the production of economic reports ([section 13.5](#)), and the quality control of economic data collection and analyses ([section 13.7](#)).

Chapter 13: Health economics

RELATED REFERENCES AND RESOURCES

¹[Petrou S, Gray A. Economic evaluation alongside randomised clinical trials: design, conduct, analysis and reporting. BMJ 2011;342:d1548.](#)

²[Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting BMJ 2011;342:d1766.](#)

³[Caro JJ, Briggs AH, Siebert U, Kuntz KM; ISPOR-SMDM Modeling Good Research Practices Task Force. Modeling good research practices--overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force--1. Value Health. 2012 Sep-Oct;15\(6\):796-803. doi: 10.1016/j.jval.2012.06.012](#)

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Clarification of peer review requirements prior to the commencement of methodological work.	Jan 2012
04	Minor update to section 11.8: further clarification on the expectations of external economists	Jun 2015
05	Modification to text in paragraph 13.3 (economic analysis plans) to accommodate the need for a separate economic analysis plan where and when required.	Apr 2018
06	Update to section 13.3: more detail regarding the Health Economics Analysis Plan (HEAP) and minor changes to section 13.6 to update economic programming packages used.	Feb 2020
07	Clarification of working practices to section 13.7. Very minor updates to the rest of the chapter.	Apr 2022
08	Updates to text (section): to include reference to HEAP, and what information around expected content, and links to other HE templates available of Q-pulse (13.3) and to provide further clarification on economic programming and analysis (13.6). Additional reference added on the principles of good practice for modelling studies.	Apr 2024

Chapter 14: Embedded process evaluations

CHAPTER 14: EMBEDDED PROCESS EVALUATIONS

[\[v08.1400.04\]](#)

LEAD AUTHORS

Process Evaluation Leads

BACKGROUND

The aim of embedded process evaluation research is to identify any challenges during the internal pilot relating to design or conduct that can then be addressed and modified before progression to the full trial. This may include changes to the way the trial information is presented, recruitment consultations are framed or requirements for staff training.

PURPOSE

To document generic issues for researchers working on the process evaluations involved in CHaRT trials.

APPLICABILITY

- Essential reading for all process evaluation researchers involved in CHaRT trials.
- Useful background for all staff that interact with the process evaluation research team.

EMBEDDED PROCESS EVALUATIONS

14.1 Methodology [\[v08.1401.03\]](#)

CHaRT is committed to designing and delivering trials that are methodologically sound. It is likely that embedded process evaluations are more appropriate in some trials than others (e.g. those with very different interventions, surgery vs medical management) and the extent of the work planned may also vary across trials depending on the perceived challenges. However, each trial approaching CHaRT will be assessed by the CHaRT director and research managers (and further with the CHaRT Advisory Group), prior to consultation with the CHaRT Process Evaluation Lead before a judgement is made about inclusion of an embedded evaluation. If appropriate, a bespoke package of work will be developed accordingly and written up in a protocol as an appendix to the main trial protocol.

Researchers will be involved in all meetings and discussions regarding trial work up. The work required will be costed accordingly into any proposed grant application.

14.2 Process evaluation analysis plans [\[v08.1402.02\]](#)

The analysis for the proposed process evaluation work will be specified within the trial protocol. Established pragmatic approaches to analysis will be taken in order to support delivery of the trial.

14.3 Process evaluation reports [\[v08.1403.02\]](#)

Data from the embedded process evaluations will be developed into reports and fed back to the trial team and specific sites as appropriate. Reports will focus on indicators such as recruitment, retention, and crossovers. Explanatory data that facilitates fuller understanding of the process of these indicators will be presented at key points in trial delivery.

Chapter 14: Embedded process evaluations

14.4 Process evaluation quality control [\[v08.1404.01\]](#)

Quality control of process evaluation aspects of CHaRT trials is highly important. All CHaRT trials will have at least two process evaluation researchers involved in the trial – a senior researcher to take overall management responsibility for the process evaluation aspects of the trial, and a second researcher to be responsible for the day-to-day conduct of process evaluations in trials. As with all CHaRT teams, to facilitate the handover of process evaluation data and analysis to other CHaRT process evaluation researchers due to any unforeseen staff changes (such as illness or staff retention) a common file structure is advocated.

All CHaRT process evaluation researchers must undergo appropriate Good Clinical Practice (GCP)/Good Research Practice (GRP) training (see [section 6.1](#)).

14.5 Partnerships with external researchers [\[v08.1405.03\]](#)

For CHaRT trials involving an embedded process evaluation, a senior researcher will be involved in the development of a trial proposal and, whenever possible the process evaluation aspects will be conducted by a Research Fellow allocated to the trial. However, it is recognised that, dependent upon the proposed design of the trial and the trial subject area, an external researcher may be more appropriate.

RELATED REFERENCES AND RESOURCES

See [Guidance on roles and responsibilities - embedded studies](#) on Q-Pulse.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
05	New Chapter	Apr 2018
06	Update to the methodological process in sections 14.1 and 14.4.	Feb 2020
07	Chapter title updated from 'Embedded qualitative evaluations' to 'Embedded process evaluations'. 'Qualitative' either removed from Chapter text or replaced with 'process' or 'process evaluation'. Reference added to a related guidance document.	Oct 2021
08	Addition of a second lead author to this chapter: Process evaluation lead. Addition of new section 14.4 Process evaluation quality control.	Apr 2024

Chapter 15: Patient and public involvement

CHAPTER 15: PATIENT AND PUBLIC INVOLVEMENT

[\[v08.1500.07\]](#)

LEAD AUTHOR

PPIE coordinator

BACKGROUND

Patient and Public Involvement (PPI) is used as a wider term to cover a range of interactions that patients and the public have with the NHS, in service improvement, service delivery and feedback. The NIHR defines public involvement in research as research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them¹. This includes, for example, having patients and members of the public working with research funders to prioritise research, offering advice as members of the trial team or trial steering group, commenting on and developing research materials. The importance of involving patients and the public in this way as PPI partners in guiding the design and conduct of research (including trials) has been recognised in the literature and is widely accepted as best practice. PPI may take various forms, from the sharing of information and opinion to joint decision-making power and responsibility. CHaRT has an unambiguous commitment to the involvement of PPI partners in as many of its trial processes as possible.

UK Clinical Trial Units have an important role to play in supporting recruitment, signposting and coordinating PPI. Identifying challenges and key success indicators in this context is crucial, and these can be detailed in existing literature, for instance².

PURPOSE

To detail the type, level and timing of PPI in CHaRT trials.

APPLICABILITY

Essential reading for all CHaRT staff

PATIENT AND PUBLIC INVOLVEMENT (PPI)

The ACE Patient and Public Involvement and Engagement (PPIE) coordinator is available for any queries relating to patient and public involvement (PPI) in research studies, including CHaRT trials. An ACE level Public Involvement Partnership Group made up of local members of the public, which can provide input and feedback on general or specific elements of the research process, is available through the PPIE coordinator (see [section 15.7](#) for more information).

The NIHR is a major provider of guidance on PPI in the United Kingdom. They offer resources, support, and frameworks to promote the involvement of patients and the public in health research, for example:

- www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371 (Briefing note two)
- www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435

Chapter 15: Patient and public involvement

15.1 Who should I involve? [\[v08.1501.03\]](#)

In the context of CHaRT, we identify PPI partners (also referred to as 'patient and public research partners') as people with personal experience of the health condition being studied (e.g. as a patient, family member or carer), those who advocate for people with the health condition being studied or interested members of the public. Examples of the type of people who might provide PPI input to the design and delivery of CHaRT trials could therefore include:

- Members of organisations that represent people who have a lived experience of the condition under study (e.g. a disease specific patient support group).
- Individuals with a personal experience of the condition under study (or similar) either as a patient, family member or carer.
- Members of the public

It is helpful to draft a PPI plan of who will be identified (patients, carers, public), how many PPI partners are likely to be involved and how they will contribute during the research cycle (e.g. within an advisory group, project management group, trial steering committee, one-off consultation, questionnaire survey). A free NIHR online tool is available at plan4ppie.com/ to help plan PPI activities. This can be reviewed regularly during the trial by the trial team and the PPI partners.

15.2 Identifying appropriate PPI partners [\[v08.1502.05\]](#)

When identifying PPI partners, it is helpful to consider the likely location of any face-to-face meetings and how the PPI partners will be involved. It is not always straightforward to identify appropriate PPI partners.

The NIHR emphasises the value of combining various approaches to PPI, such as collaboration, co-production, and consultation, while ensuring a diversity of voices. They provide examples like involving one or two service users as collaborators throughout a project, with a broader group being consulted on specific aspects. It is often considered good practice to involve, where possible, two PPI collaborators rather than one, to maintain balanced perspectives and to avoid overburdening or isolating a single partner. Refer to 'Briefing note seven' for more information: www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371

There are often dedicated support organisations for patients who may be able to facilitate identifying potential PPI partners. Individual patients may be identified through direct contacts with the sites involved in the trial.

There are also other national organisations/resources dedicated to the involvement of PPI partners in research who can provide advice on appropriate PPI, for example:

- NIHR: www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435
- The UK Directory of Self-Help Groups (www.selfhelp.org.uk/) which is a free directory that lists self-help groups, support group and charities in the UK.
- People in research, where opportunities can be advertised nationally (www.peopleinresearch.org/).

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Additional opportunities to identify PPI Partners also exist through community outreach:

- Scottish Health Research Register (SHARE) - note that there may be a cost attached to this.
- Volunteer organisations (e.g. Volunteer Aberdeen www.acvo.org.uk) – which may be appropriate if a more generic health experience/perspective is required, or to help with advertising.
- Volunteer Scotland, which offers a Scotland-wide reach: [Advertise your opportunities - Volunteer Scotland](#)
- Social media (e.g. Facebook, Twitter, etc).

When identifying PPI Partners through established patient groups, it is important for the trial team to identify any funding source for the group and judge whether there could be any potential conflicts of interest depending on the nature of that funding. e.g. pharmaceutical companies. It may be important to explicitly clarify any potential conflicts with the trial funder.

It may be helpful to develop an advert (see the **advert for TSC PPI partner** example on [Q-Pulse](#)) and a role descriptor (please see the **role descriptor for PPI partner co-applicant** document available on [Q-Pulse](#)) to advertise or provide information about potential opportunities for PPI partners. It may also be helpful to clarify the mutual expectations of researchers and PPI partners. If a PPI partner is not meeting the agreed expectations, please consider referring to the **difficult conversations with public research partners** guidance, which is available on Q-Pulse, on how to explore and address the issue.

We recognise a number of benefits of involving experienced public research partners, for example the ACE Public Involvement Partnership group (see [section 15.7](#)), **in addition to** PPI partners, for example an individual with a personal experience of the health condition being studied, who are potentially inexperienced and less familiar with PPI:

- they are more familiar with methodologies, data interpretation, and the nuances of research design;
- they are likely to foresee challenges and suggest viable solutions based on their past experiences;
- they often have established networks that can facilitate broader engagement, collaboration, and dissemination of research findings;
- they are typically more adept at recognising and navigating ethical issues and cultural sensitivities;
- they can mentor and guide less experienced researchers or partners, sharing their knowledge and insights to build capacity within the research team;
- their experience allows them to critically assess research processes and outcomes, contributing to higher quality and rigor in the research;
- with their experience, they are often more skilled in advocacy and can be instrumental;
- they often bring a long-term perspective to research projects, understanding the implications and potential trajectories of research findings in a broader context.

15.3 Range of input from PPI partners [\[v08.1503.06\]](#)

PPI partners can contribute to the design, delivery, interpretation and dissemination of a randomised controlled trial in numerous ways.

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For CHaRT trials, involvement of PPI Partners includes activities across the life of a trial, from design stage to publication. These include but are not limited to:

- Advising on the appropriateness of the trial question and proposed trial outcomes (see [section 5.5](#))
- Commenting on the research proposal and protocol (see [section 5.5](#)).
- Advising on how to effectively recruit participants to improve enrolment and the representativeness of the trial
- Identifying potential challenges in maintaining participant engagement throughout the study
- Commenting on the IRAS form as appropriate.
- Commenting on written information materials e.g. PILs and consent forms (see [section 5.7](#)).
- Commenting on (and testing) the questionnaires to be used to collect patient outcomes.
- Advising on how best to conduct the consent process (see [section 5.7](#)).
- Serving as a member of trial governance committees (see [section 6.3](#)).
- Contributing to scientific output – authorship/review (see [section 8.3](#)).
- Advising on appropriate engagement with participants, patients and the public (e.g. via social media, newsletter, email etc.)
- Contributing to dissemination e.g. conference presentation, lectures, workshops at patient support groups, dissemination to patients and the public (see [section 8.3](#)).
- Advising on how to manage long-term participant engagement.

If the PPI partners identify any training or support needs across these objectives, these will be addressed accordingly. PPI partners may also serve as full co-applicants on the research proposal. In this case a helpful introductory document is **how does the research proposal process work?** available on [Q-Pulse](#).

15.4 Remuneration of PPI partners [\[v08.1504.04\]](#)

It is widely acknowledged that PPI partners should be remunerated for their time and contribution to research. For CHaRT trials, we adhere to the principles laid out in the NIHR guidance (www.nihr.ac.uk/documents/payment-guidance-for-researchers-and-professionals/27392/) and ensure appropriate costs (e.g. out of pocket expenses and honoraria) for PPI involvement are requested within the trial funding proposals. There may be processes required to set up such payments depending on the sponsoring organisation. For detailed information, please refer to the ACE's internal **guidance on payment to PPI partners** available on [Q-Pulse](#). While it is not CHaRT's responsibility to advise research volunteers of any impact reimbursement may have on their income tax or benefits, CHaRT staff should be aware that the NIHR has a benefits advice service to support members of the public whose welfare benefits may be affected by payment for involvement, further information can be found at : sphr.nihr.ac.uk/news-and-events/nihr-benefits-advice-service-for-public-involvement-in-research/

15.5 Support for PPI partners [\[v08.1505.02\]](#)

It is best practice for the trial to identify a trial team PPI lead who will be the named contact for any PPI partners. This ensures a clear communication pathway for PPI partners. It should be noted that contact details (including email) for PPI partners should not be shared within the trial team without prior consent of the PPI partner.

Prior to the first meeting it is helpful to have a one-to-one phone call or meeting with new PPI partners so they can ask any questions about the trial and their role. Summary documents

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about the trial, e.g. the plain language summary, trial website, PIL, as well as CHaRT's **how does the research proposal process work?** and **PPI jargon buster** documents (both available on [Q-Pulse](#)) may all be helpful resources. At intervals through the trial, PPI partners may require additional support to understand the research process and their role within it. A template **PPI feedback form** is available on [Q-Pulse](#) to help identify these needs. It is also helpful to consider the needs of any partners in the research when planning patient and public involvement - for example location, access requirements, vision, hearing, dietary, carers, timing of meetings, IT access, native language, any needs relating to the health condition being studied.

NIHR offers comprehensive guidance on creating inclusive research communities and fostering effective public involvement in health and care research www.nihr.ac.uk/documents/being-inclusive-in-public-involvement-in-health-and-care-research/27365. It covers topics like understanding power dynamics, valuing diversity, using inclusive language, considering locations for involvement, and building effective relationships. Should PPI partners want support outside of the research team they can be directed to the PPIE coordinator who may be able to facilitate this.

The entire research team plays a significant role in shaping the experience of PPI partners. The dynamics, communication, and interaction within the team can greatly influence how PPI partners engage, contribute, and perceive their role in the research process. Therefore, the team should consistently use understandable language and maintain a welcoming demeanour when interacting with PPI partners. It is crucial to show genuine interest in their views, acknowledging and taking their contributions seriously. When disagreements arise, acknowledge them empathetically and address thoughtfully. This approach fosters a supportive environment where PPI partners feel valued and heard, enhancing the overall effectiveness and collaboration of the team. For an insightful perspective from a PPI partner in a clinical trial about what matters to them, we suggest reading this brief article: trialsjournal.biomedcentral.com/articles/10.1186/s13063-023-07254-8.³

15.6 Documenting and reporting PPI [\[v08.1506.02\]](#)

There is an expectation that PPI will be clearly documented throughout the lifetime of the trial. Documentation of PPI may be included within the funding proposal, trial protocol, trial authorisations, trial registration, funder documents, PILs, newsletters, publications and other dissemination activities; see [Chapter 5](#) and [Chapter 8](#).

It is increasingly recognised as standard practice to provide in a scientific article describing study findings at least a brief description of the PPI activities involved in a study. The GRIPP2-SV reporting checklist suggests aspects to consider when designing this description. It can be provided as a concise summary within the main text, or a GRIPP2-SV completed and uploaded in a supplementary material. This approach ensures transparency and clarity about PPI involvement in the research. Examples of how GRIPP2-SV aspects have been described in previous research studies can be found in Table 2 of the article by Weschke et al. (2023)⁴:

15.7 ACE Public Involvement Partnership Group [\[v08.1507.01\]](#)

The ACE Public Involvement Partnership Group can provide input and feedback in the development of a proposal for funding (unfunded development), which ensures that the research addresses real-world needs and enhances the quality and applicability of the

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research outcomes. The Public Involvement Partnership group can also offer strategic input to the PPI activities and assist with trial-related tasks, such as participating in recruitment panels, and in education/dissemination activities, leveraging their experience in presenting study findings and promoting involvement. Members of the ACE Public Involvement Partnership group can be involved in individual research projects as co-applicants, members of trial steering committees, or as part of public/patient research partner panels. The PPIE coordinator can be contacted to identify individuals in the group with the relevant experience.

In line with the universally recognised need to diversify voices among public research partners, the group includes people from a broad spectrum of backgrounds and a wide range of lived experiences, including representations of marginalised communities.

RELATED REFERENCES AND RESOURCES

¹www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371#briefing-note-two-what-is-public-involvement-in-research

²[Selman, L.E., Clement, C., Douglas, M. et al. Patient and public involvement in randomised clinical trials: a mixed-methods study of a clinical trials unit to identify good practice, barriers and facilitators. *Trials* 22, 735 \(2021\). https://doi.org/10.1186/s13063-021-05701-y](https://doi.org/10.1186/s13063-021-05701-y)

³[Graham, M., Goodman, K. Commentary on my personal experience of patient and public involvement in the TOPSY trial. *Trials* 24, 228 \(2023\). https://doi.org/10.1186/s13063-023-07254-8](https://doi.org/10.1186/s13063-023-07254-8)

⁴[Weschke S, Franzen DL, Sierawska AK, et al Reporting of patient involvement: a mixed-methods analysis of current practice in health research publications using a targeted search strategy *BMJ Open* 2023;13:e064170. doi: 10.1136/bmjopen-2022-064170](https://doi.org/10.1136/bmjopen-2022-064170)

Additional references:

[Bagley H et al. A patient and public involvement \(PPI\) toolkit for meaningful and flexible involvement in clinical trials – a work in progress. *Research Involvement and Engagement* \(2016\) 2:15.](https://doi.org/10.1186/s13063-021-05701-y)

www.abdn.ac.uk/hsru/what-we-do/ppie/index.php

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	New section added: 13.4 – Remuneration of consumers	Jan 2012
04	Change from ‘Consumer issues’ to ‘Patient and Public involvement’; more detail added to ‘Background’ and section 13.4	Jun 2015
05	Updates to 15.2, 15.3 and 15.4, in particular addition of information on identifying PPI Partners Applicability amended to ensure that the chapter is ‘Essential reading for all CHaRT staff’	Apr 2018
06	Updates to all sections to reflect changes in CHaRT processes and links to new templates available on Q-Pulse (15.1 – 15.4); addition	Feb 2020

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	of two new sections to provide information on Supporting PPI partners and the best methods for documenting PPI (15.5 and 15.6).	
07	Further detail added in section 15.3 on PPI input	Oct 2021
08	Updates to the Background sections to include more information on PPI involvement in clinical trials in general and within CHaRT. Addition of new section 15.7 ACE Public Involvement Partnership Group. Major updates to all other sections (15.1-15.6) to ensure the procedures detailed align with CHaRT's current processes and guidance, to provide further detailed information on the identification of, input from, payments to, support for PPI partners, as well as documenting and reporting PPI, and to provide information around the inclusion of ACE's public involvement partnership group. Additional related references added.	Apr 2024



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Chapter 16: CHaRT Staff Training

CHAPTER 16: CHaRT STAFF TRAINING

[\[v08.1600.07\]](#)

LEAD AUTHOR

Senior trials manager/QA manager

BACKGROUND

The successful delivery of high-quality trials over a sustained period requires highly trained staff following tried and tested processes. Relevant and timely training of staff is a key component of CHaRT's ability to deliver these high-quality trials.

PURPOSE

To document the expectations for CHaRT staff in terms of requirements for, receipt of, and documentation of training needs and solutions. These may be gained from training courses, workshop, attendance at conferences etc.

APPLICABILITY

- Essential reading for all CHaRT staff.

CHaRT STAFF TRAINING

16.1 General

[\[v08.1601.05\]](#)

CHaRT staff are required by their job specifications to possess at minimum the appropriate experience and qualifications for their responsibilities. On appointment, all staff are assigned an appropriate buddy and given an induction pack, which includes the ACE staff handbook, as a basis for familiarisation and initial training. Part of this induction process includes a general Standard Operating Procedure (SOP) overview training session (see [section 1.7](#)). In addition, further training will be provided or offered as appropriate for the role: for example, an external course on a specific statistical technique for a statistician analysing a clinical trial; or a University internal course on time management for a trial manager; or a professional development course on team management.

Each member of the CHaRT staff has their training needs discussed regularly and at least once a year during their annual review. Training needs are identified according to the person's experience and responsibilities and solutions to those needs (e.g. on-the-job training and mentoring from CHaRT colleagues; internal training on the University staff development courses; and external training on courses or at conference workshops) identified. Training requests should be submitted via the 'Conference and Training Notification Form' link of the Integrated Management System (IMS) database on the '**Staff only**' webpage accessible from the ACE homepage www.abdn.ac.uk/hsru/.

16.2 Good Clinical Practice

[\[v08.1602.01\]](#)

It is a minimal requirement that **all** CHaRT staff – including trialists, trial managers, statisticians, IT programmers, secretaries, data co-ordinators, research managers, health economists, qualitative researchers, clinicians, clerical staff – have appropriate up to date GCP (or GRP) training (see also [Section 6.1](#)). For locally sponsored studies, refer to the [SOP-QA-34: Good Clinical Practice/Good Research Practice Training](#) on GCP training requirements.

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16.3 Training records [\[v08.1603.06\]](#)

It is the responsibility of all staff to document their training by keeping their dedicated staff development manual, or equivalent, up to date and accurate (see [section 3.4](#)). This would, for example, include a copy of their current CV, current job description, any promotion/regrading/contribution award application(s), annual review objectives, as well as copies of certificates of attendance (if available) and/or outline of course content (e.g. hand-outs and agendas) etc. as evidence of appropriate training, and a cumulative training log to maintain an ongoing record of all internal and external training. The **training log** template can be found on [Q-Pulse](#) (for locally sponsored studies refer to the [SOP-QA-2: Training Record](#)).

In addition, training on relevant sponsor SOPs and any trial specific processes should be recorded and filed together with your CV and GCP within the appropriate section of the Trial Master File (TMF) for the trial(s) you are working on. For locally sponsored studies, the [Sponsor's Quality Management System Matrix](#) (TMP-QA-44) should be completed by the CI and trial staff documenting which of the Sponsor SOPs have been read.

Training records should be available for any annual reviews, audits, monitoring visits and inspections. When a trial finishes or when a staff member leaves, a copy of their essential training documents (e.g. CV, GCP certificates) should be retained by CHaRT within the appropriate TMF for the trial they worked on.

16.4 Training feedback [\[v08.1604.03\]](#)

Training can be expensive and time consuming, particularly in the external market; and there are often limited suitable training courses available. CHaRT staff may proactively seek training opportunities that represent good value for money and should feedback on these training experiences they have had. Training feedback may be formally requested by your line manager via the IMS database. If feedback has been requested, an automated email will be sent direct to the member of staff asking them to complete a short evaluation.

RELATED REFERENCES AND RESOURCES

None.

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
03	Further clarification regarding need for retention of training records.	Jan 2012
04	Minor changes	April 2015
05	Minor wording amendments	Apr 2018
06	Removal of text about centralised training records (16.1); minor addition of reference to GRP (16.2); and further detail of what to file in training records regarding award applications (16.3).	Mar 2020
07	Minor wording changes to section 16.1 about submitting training requests, section 16.3 includes reference to recording any training	Nov 2021



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	on relevant Sponsor SOPs, and section 16.4 includes more detailed information about the new training feedback process.	
08	Update to section 16.3 about the recording and filing of any relevant sponsor SOP training as well as the completion and filing of the local sponsor SOP training matrix if applicable.	Feb 2024

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