CHaRT

Standard Operating Procedure book

Details:

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Lead authors:	CHaRT director, QA manager, CHaRT research managers, head of trial management, senior trials managers, senior IT development manager, senior statistician, senior health economist, process evaluation leads, PPIE coordinator
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Approval:

Approved by:

Graeme MacLennan		23 April 2026
CHaRT director	**Signature**	**Date**
Samantha Wileman		23 April 2026
QA manager	**Signature**	**Date**

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A Standard Operating Procedure (SOP) is a detailed written instruction designed to ensure uniformity in performing specific functions and to define how practices and procedures should be carried out. SOPs are written instructions documenting procedures agreed and adopted as standard practice.

The definitive version of the Centre for Healthcare Randomised Trials (CHaRT) SOP book is maintained 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.

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

	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
09	Relevant sections of the CHaRT SOP book have been updated to reflect and align with the new ICH-E6(R3) guidelines; these updates are detailed in the chapter specific 'Version History'. In addition, 'Q-Pulse' has been rebranded to 'Ideagen Quality Management (IQM)' and as such, all references to Q-Pulse have been updated. Other changes include; swapping the 'Background' and 'Purpose' paragraphs around for all Chapters to have 'Purpose' sit first and, updates to, and clarification of, the senior trials manager role. Since the updates in this revision of the CHaRT SOP book do not affect or impact local sponsor processes, it has been agreed by the CHaRT director and QA manager that the UoA/NHSG research governance and QA managers do not need to review it for local compliance prior to final approval.	18/09/25
10	A thorough review and update of the CHaRT SOP book to reflect and align with the new Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, and the adoption of the ICH-E6(R3) guidelines. In addition, all hyperlinks, web links and cross references have been checked and updated where required. Any new templates, examples or guidance documents, relevant to CHaRT procedures, have also been added. As a result of the new regulations, significant changes have been made to Chapters 4 (new section on Quality Control), 5, 6, 7, 10,12 (new section on handling secure external data), 13 (new section on handling secure external data and archiving). These changes are detailed in the chapter specific 'Version History' section, together with details of any other minor updates.	16/04/2026

Lead authors' history:

Version number	Names of Lead Authors (Theme Leaders)	Date approved
01	John Norrie (CHaRT director), Samantha Wileman (Quality Assurance manager), Alison McDonald (senior trials manager), Gladys McPherson (senior IT manager), Graeme MacLennan (senior statistician), Marion Campbell (HSRU director), Jill Francis (senior health psychologist), Luke Vale (senior health economist).	21/04/09
02	Jen Burr (CHaRT director), Samantha Wileman (Quality Assurance manager), Alison McDonald (senior trials manager), Gladys McPherson (senior IT manager), Graeme MacLennan (senior statistician), Marion Campbell (HSRU director), Jill Francis (senior health psychologist), Luke Vale (senior health economist).	24/06/10
03	John Norrie (CHaRT director), Samantha Wileman (Quality Assurance manager), Alison McDonald (senior trials manager), Gladys McPherson (senior IT manager), Graeme MacLennan (senior statistician), Marion Campbell (HSRU director), Jill Francis (senior health psychologist), Paul McNamee (senior health economist).	15/10/12
04	John Norrie (CHaRT director), Samantha Wileman (Quality Assurance manager), Alison McDonald (senior trials manager), Gladys McPherson (senior IT manager), Graeme MacLennan (senior statistician), Marion Campbell (HSRU director), Jill Francis (senior health psychologist), Paul McNamee (senior health economist); who are grateful for the substantive contributions from other members of CHaRT/HSRU staff.	05/08/15
05	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Ruth Thomas (CHaRT research manager), Kirsty McCormack (CHaRT research manager), Alison McDonald (senior trials manager), Seonaidh Cotton (deputy senior trials manager), 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.	12/04/18
06	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Ruth Thomas (CHaRT research manager), Kirsty McCormack (CHaRT research manager), Alison McDonald (senior trials manager), Seonaidh Cotton (deputy senior trials manager), 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	12/03/20

Version number	Names of Lead Authors (Theme Leaders)	Date approved
	are grateful for the substantive contributions from other members of CHaRT/HSRU staff.	
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/ACE staff.	25/09/24
09	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Seonaidh Cotton (head of trial management), Suzanne Breeman and Lynda Constable (senior trials managers), Mark Forrest (senior IT development manager), Graeme MacLennan (senior statistician). *Note: the list of authors for this revision is limited to just the authors whose chapters needed updating with relation to the new ICH-E6(R3) guidelines and where key changes have been made.*	18/09/25
10	Graeme MacLennan (CHaRT director), Samantha Wileman (Quality Assurance manager), Ruth Thomas (CHaRT research manager and PPIE coordinator), Kirsty McCormack (CHaRT research manager), Seonaidh Cotton (head of trial management), Suzanne Breeman and Lynda Constable (senior trials managers), Mark Forrest (senior IT development manager), Graeme MacLennan (senior statistician), Graham Scotland (senior health economist), Sharon McCann (process evaluation leads); who are grateful for the substantive contributions from other members of CHaRT/ACE staff	01/04/2026

TABLE OF CONTENTS

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
CtQ	Critical to Quality
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
HSC-PBPP	NHS Scotland Public Benefit and Privacy Panel for Health and Social Care
HSDR	Health Services and Delivery Research
HTA	Health Technology Assessment
IAHS	Institute of Applied Health Sciences
IB	Investigator's Brochure
ICH	International Conference on Harmonisation

IMP	Investigational Medicinal Product
IMS	Integrated Management System database
IP	Intellectual Property
IQM	Ideagen Quality Management
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
MOID	Modification of an Important Detail
MRC	Medical Research Council
NHS	National Health Service
NHSE	National Health Service England
NIHR	National Institute for Health and Care Research
NIHR RDN	NIHR Research Development Network
NIHR HTA	National Institute for Health Research Health Technology Assessment
NIMP	Non-Investigational Medicinal Product
PEAP	Process Evaluation Analysis Plan
PHR	Public Health Research
PI	Principal (local) Investigator
PIL	Patient Information Leaflet
PIP	Protecting Information Policy
PMG	Project Management Group
PPI	Patient and Public Involvement
PPIE	Patient and Public Involvement and Engagement
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
RS	Randomisation Specification
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
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 (IDEAGEN QUALITY MANAGEMENT (IQM) AND LOCAL SPONSOR SOPS)

Ideagen Quality Management (IQM)	Within this document there are a number of associated documents that are accessed via Ideagen Quality Management (IQM). The titles of these documents appear in the text coloured **red**. All CHaRT staff will have a specific login to IQM 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
[v10.0100.10]

LEAD AUTHOR
CHaRT director.

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.

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).

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 [v10.0101.09]
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, which reflect 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) (Amendment) Regulations 2025 (SI 2025 No. 538): www.legislation.gov.uk/uksi/2025/538/contents) which incorporates the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Harmonised Guideline on General Considerations for Clinical Studies E8(R1), and Good Clinical practice GCP E6 (R3) 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 16.4). 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 GCP as detailed in the ICH Harmonised Guideline on GCP

E6 (R3). Compliance with this standard provides public assurance that the rights, safety and well-being of trial participants 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 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 [v10.0102.01]

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 [v10.0103.04]

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.
- **Purpose:** Describe the procedure to be followed and the setting in which the SOP applies.
- **Background:** Briefly discuss the background to the SOP, referring to regulatory guidance, if applicable. Consider the driving forces or why the SOP is necessary.
- **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 [v10.0104.03]

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.ccss.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)
Version: <Version number> e.g. xx.ccss.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 [v10.0105.03]

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(s) (senior IT development manager, senior statistician, head of trial management/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 [v10.0106.05]

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 [v10.0107.04]

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 this SOP book (and relevant detail of the trial guidance (see section 5.5.1 for details) for all trials they have responsibilities for) and this is documented on Ideagen Quality Management

(IQM). 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 [v10.0108.03]

An electronic version of the currently approved **SOP book** is available on Ideagen Quality Management (IQM) and at www.abdn.ac.uk/hsru/what-we-do/trials-unit/chart-sops-556.php. The original signed copy of 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 [v10.0109.07]

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, head of trial management/senior trials managers, senior IT development manager, research manager(s), senior statistician, senior health economist, process evaluation leads and a 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 [v10.0110.02]

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 (IQM) 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	Aug 2015

	section 1.8 to amend the location of the SOP book from the Shared drive to Q-Pulse.	
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 1.7 to provide more clarity regarding training. Addition of deputy senior trials managers to the section 1.9.	Apr 2022
08	Updated the SOP review period from two to three years in sections 1.1, 1.6 and 1.9	Apr 2024
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. In section 1.5 and 1.9 the text has been updated to include the role of 'Head of trial management'.	Aug 2025
10	Section 1.1 updated to reference the new UK clinical trial regulations and ICH Guidelines on GCP E6 (R3) and General Considerations for Clinical Studies E8(R1). Minor updates to 1.3 regarding the ordering of the 'Background' and 'Purpose' bullets to reflect the order in each chapter, and 1.7 to document that staff acknowledgment of having read and understood the CHaRT SOP book is managed in IQM	Apr 2026

CHAPTER 2: CHaRT DETAILS
[v10.0200.08]

LEAD AUTHOR
CHaRT director.

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.

BACKGROUND
To describe the setting and environment in which CHaRT operates.

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 [v10.0201.02]

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.

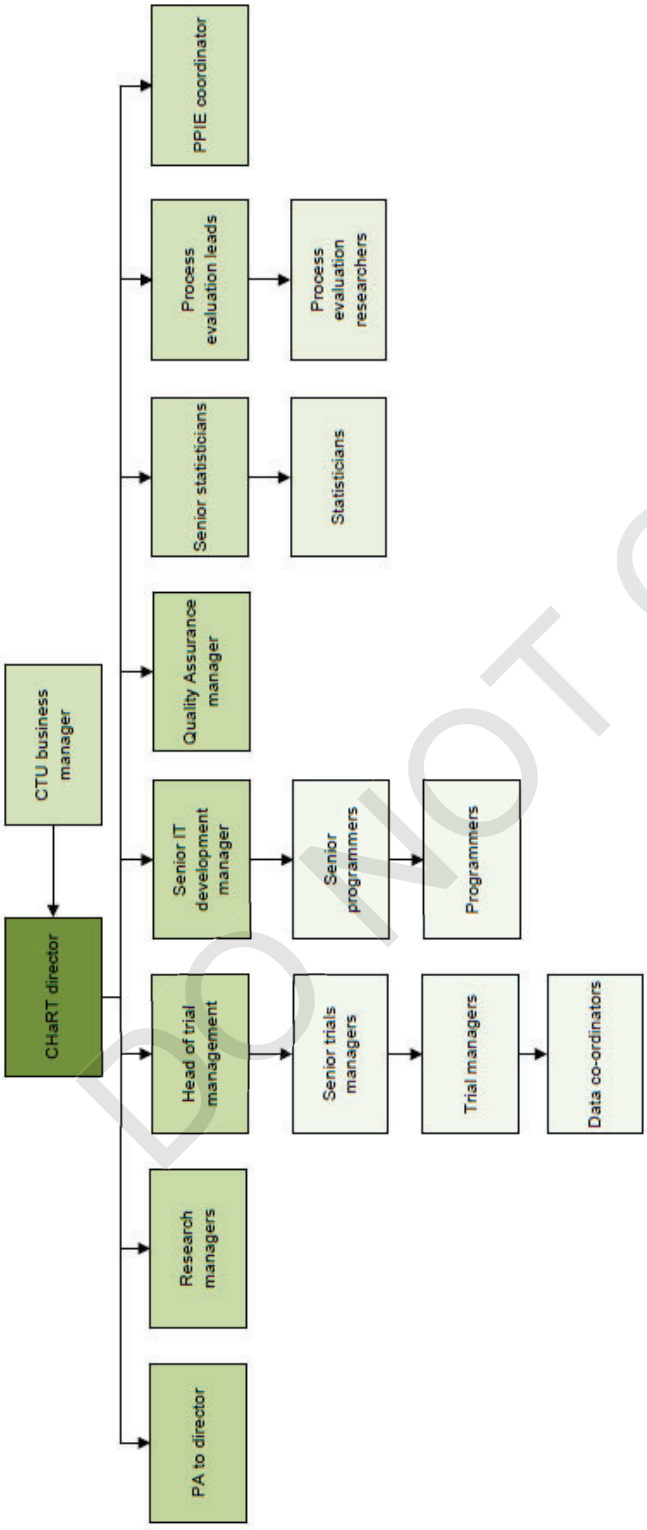
Members of CHaRT are therefore employed by the University of Aberdeen, and as such are subject to the rules and regulations of the University. CHaRT itself is likewise obliged to follow University policies and procedures. These policies include those governing:

- 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 [v10.0202.08]

Organogram of CHaRT



Organogram
CHaRT is part of ACE, and all its staff are members of ACE. A senior CHaRT management group comprises the head of trial management, senior IT development manager, senior statistician, research managers, QA manager and CHaRT PA, and the CHaRT director to whom they report. Other members of CHaRT (senior trials managers, 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 head of trial management (a senior trials manager) who reports to the CHaRT director, supported by the other senior trials managers. 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 senior statisticians. CHaRT is configured in such a way that, in principle, it could obtain statistical support from other academic units (see section 12.12: 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 13.10: 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 (operational, trial management, QA, information systems, statistics and monitoring). The input from these various sources 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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. In section 2.2, the organogram, and 'Trial management' text have been updated to include the role of 'Head of trial management' and the 'deputy senior trials manager' roles have now changed to 'senior trials managers'.	Aug 2025
10	Very minor changes to clarify the statistical input section and the examples of UKCRC subgroups updated to reflect current involvement.	Apr 2026

CHAPTER 3: QUALITY ASSURANCE (QA)
[v10.0300.10]

LEAD AUTHOR
Quality assurance manager.

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.

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.

APPLICABILITY
- Essential reading for all CHaRT staff.

QUALITY ASSURANCE (QA)

3.1 Overview of QA in CHaRT [v10.0301.04]
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 and 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 [v10.0302.08]
CHaRT's internal QA procedures operate at two levels (a) CHaRT generic procedures, and (b) trial specific procedures.

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 Ideagen Quality Management (IQM). 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 trials 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.

For trials that do not receive regular monitoring of the CHaRT trial master file (TMF) by the sponsor, consideration should be given to the level and frequency of internal monitoring. This will be detailed in the trial's **Trial Monitoring Plan** (TMP), available on IQM (see section 5.12).

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 TMP and any subsequent updates to the TMP thereafter. In addition, the QA manager or one of the senior trials managers, with an experienced trial manager (Grade 7) 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 IQM (see section 5.12). In addition, the QA and senior trials managers will perform a quarterly review of the trial specific deviation and breach logs, including those 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).

3.3 External audit and monitoring of QA procedures [v10.0303.05]

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. If required, changes may need to be made to specific CHaRT documentation and/or 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 [v10.0304.04]

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 16.4 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) 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 [v10.0305.03]

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).

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-proceedures-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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. In section 3.2.2, the text has been revised to reflect the change in QA process to allow an experienced trial manager (Gd7) to assist with the review of trial specific monitoring activities.	Aug 2025
10	Update to section 3.2.2 to include the process for reviewing the CHaRT TMF and the addition of breach logs to be part of the quarterly deviation review.	Mar 2026

CHAPTER 4: COLLABORATION
[v10.0400.05]

LEAD AUTHOR
Research managers.

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

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.

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 [v10.0401.05]

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. The Chief Investigator (CI), an appropriately qualified and trained professional (see also section 6.19), is responsible for assembling an appropriate team and developing the trial from initial concept through to securing funding with guidance from the CHaRT director and research manager (s). CHaRT 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.

4.2 CHaRT collaboration quality control [v10.0402.01]

CHaRT's quality-by-design approach is in line with ICH E6(R3) - GCP Principle 6 and ICH E8(R1) - Critical to quality (CTQ) factors. CHaRT expects that quality is built into the scientific and operational design of any trial it supports. When considering collaboration, CHaRT assesses whether the proposed study has:
- A design that is fit for purpose, with methods that support reliable, interpretable results

- Proportionate processes, focusing effort on aspects that protect participants and ensure data integrity
- Consideration to operational plans that minimise avoidable errors, particularly those that could compromise primary outcomes or participant safety
- A transparent rationale for methodological choices, enabling CHaRT to contribute meaningfully as an intellectual partner

In addition, CHaRT can support new investigators by advising on suitable mentoring and/or training e.g. the UKCRC 'How To Be A Good Chief Investigator' workshop.

RELATED REFERENCES AND RESOURCES

Chapter 2: CHaRT details

VERSION HISTORY

Version	Significant changes from previous version	Month reviewed
01	N/A	
02	N/A	
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs.	Aug 2025
10	Update to section 4.1 to define the role and responsibility of the CI in trial design. Addition of new section 4.2 CHaRT collaboration quality control to document the CHaRT's quality-by-design approach when designing a trial.	Mar 2026

CHAPTER 5: TRIAL INITIATION

[v10.0500.10]

LEAD AUTHORS

Senior trials managers.

PURPOSE

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

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 include 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.

APPLICABILITY

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

TRIAL INITIATION

5.1 Trial authorisations [v10.0501.10]

The trial manager must ensure copies of all appropriate trial authorisation approvals, as detailed in the sections below, together with any relevant correspondence are filed in the appropriate section of the Trial Master File (TMF; see section 5.10).

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 not based within Grampian, it is the trial manager's responsibility to check with the CI that sponsorship has been obtained. It is usual (obligatory, if the 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 trials managers. A CHaRT **risk assessment** template is available on Ideagen Quality Management (IQM). 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/ (or the new HRA 'Plan and Manage Health and Care Research' digital service) 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 nor 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. 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, third sector organisation 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 NHS 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/hsc-rd-approvals-service

Where the research is taking place outside the NHS, the relevant organisation will advise how management approval will be provided.

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. When considering whether or not a study falls within the regulations, consideration should also be given as to whether there any non-investigational medicinal products (NIMPs) within the study www.gov.uk/guidance/clinical-trials-non-investigational-medicinal-products.

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 combined review 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). It is usual for the CI to own this IRAS form, and for the trial manager to adopt the deputy role in IRAS.

For notifiable trials, as defined here: www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials, there is a risk proportionate approach to processing the CTA application and receive automatic authorisation from the MHRA. Applications are submitted via the combined review process using the IRAS. Please refer to www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials for further information.

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.

Following combined approval from the MHRA and REC, a CTIMP is expected to recruit their first participant in the UK within 2 years of that date. If a trial recruits no participants within 2 years, the approval for the trial will lapse, unless an extension is agreed. In this scenario, the sponsor will have to end the trial (see section 7.2 for details). Confirmation of first UK participant recruitment will be done using the modification tool to submit a 'modification of an important detail' (MOID) (see section 6.10). A request for an extension to this time period is possible if appropriate and justified. Further details are available at: www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/clinical-trial-regulations-reform/guidance-on-changes-to-the-clinical-trials-regulations/the-approvals-process-for-clinical-trials/approvals-lapsing-for-trials-with-no-recruitment/ https.

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 (PBPP) 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.

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 contracted 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 IQM. 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 [v10.0502.02]

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.

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 IQM. Further information about DPIAs, including details of the mandatory criteria, is available at www.abdn.ac.uk/staffnet/governance/legal-and-compliance/data-protection/#panel37263. You can also use the 'data protection checklist for researchers' to help guide you through your data protection obligations.

5.3 Trial registration [v10.0503.06]

All trials must be registered on a publicly available registry either by the date on which the first individual is recruited to be a participant in that trial, or within 90 days after the date of approval of the clinical trial, whichever is the earliest, except under special circumstances e.g. deferral. 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)

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 7.2).

In addition, most, if not all CHaRT trials will be eligible for National Institute for Health Research Development Network (NIHR RDN) portfolio support: https://www.nihr.ac.uk/support-and-services/support-for-delivering-research/rdn-portfolio

5.4 External relations [v10.0504.02]

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).

5.5 Trial protocol [v10.0505.08]

All CHaRT trials are required to have a trial protocol. **Protocol (CTIMP and non-CTIMP)** templates are available on IQM, and a HRA CTIMP protocol guidance and template is also available here: www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/. For device trials, the Clinical Investigation Plan (CIP) should follow the ISO guidance (ISO 14155). 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.

During protocol development, the sponsor is responsible for classifying all medicinal products as either an Investigational Medicinal Product (IMP) or a Non-Investigational Medicinal Product (NIMP) see www.gov.uk/guidance/clinical-trials-non-investigational-

medicinal-products for more information. The classification and justification should be documented within the protocol and Trial Master File (TMF; see sections 5.5 and 5.10 below).

The trial protocol is a statement of the scientific objectives of the trial, with clear detail on the methods and conduct (e.g. recruitment strategy, data collection, source data, pharmacovigilance etc as standard within the protocol template) and with input from all relevant disciplines. For CTIMPs, consideration should also be given to integrating critical to quality (CtQ) factors into the protocol embedded at the design stage (see section 4.2). These should be clearly documented within the protocol and/or trial Master file (TMF; see section 5.11). 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 checklist[1] 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.

5.5.3 Laboratory testing

Some clinical trials will require laboratory testing, for example to confirm eligibility or as outcome measures.

Where laboratory testing is part of standard of care and carried out in the NHS recruitment site's own laboratories, this should be clearly documented in the protocol and the patient information leaflet.

Where laboratory testing is NOT part of standard of care, a suitable laboratory (or laboratories) should be identified to carry out the testing. The contracts team will advise whether a laboratory services (or similar) agreement and/or an analytical protocol is required. For locally sponsored studies, please refer to **SOP-QA-13 Generation of contracts** and **SOP-QA-16 Selection and management of contracted third parties**; an analytical protocol template is also available. Consideration should be given to how samples are taken, labelled, stored and shipped to the laboratory, how results are returned to the trial

team and what happens to any residual sample. This should be detailed in the protocol and patient information leaflet.

5.6 Case report form (CRF) [v10.0506.06]

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, as well as a list of questionnaires regularly used by CHaRT trials, are available in the CHaRT resources repository on IQM. 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 modification processes for key documents, including questionnaires.

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

- investigators
- those responsible for the data collection e.g. trial nurses
- statisticians
- health economists (as appropriate)
- qualitative researchers (as appropriate)
- IT application programmers
- trial managers
- patient and public involvement (PPI) partners
- trial committees (Trial Steering Committee (TSC), Data Monitoring Committee (DMC))

Paper CRFs (excluding paper questionnaires) should record the signature of the person who completed the CRF. Where the CRF is electronic, the person's name will be recorded as part of the CRF, and the audit trail will link the record to their unique username. To comply with ICH GCP E6R3, the PI (or named delegate) should ensure the accuracy, completeness, legibility and timeliness of the data reported on the CRF for CTIMPs, by reviewing and endorsing the reported data. When designing the CRF, consideration should be given whether this endorsement is recorded either on a separate CRF sign off sheet or within the CRF. If the task is delegated, the endorsement of reported data should NOT be done by the person originally completing the CRF.

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 modifications).

Before the trial system can 'go live', user acceptance testing must be completed (see section 10.2.4).

5.7 Informed consent [v10.0507.08]

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 IQM). 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 IQM, 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 records of a trial.

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 (eConsent), or at least to have eConsent as an option for obtaining consent. The process for delivering eConsent, 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 refer to the **eConsent process** (which is available on IQM) for all the email and web message templates to be used in a trial using eConsent. 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.

The new clinical trials regulations offer sponsors of clinical trials that meet certain conditions, the option to use simplified arrangements for seeking and evidencing informed consent, see www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/clinical-trial-regulations-reform/guidance-on-changes-to-the-clinical-trials-regulations/simplified-arrangements-for-consent-in-clinical-trials/ for details of these conditions, together with guidance to support the simplified arrangements for seeking and evidencing informed consent .

5.8 Other documentation [v10.0508.01]

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 [v10.0509.01]

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 (PWI) 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 (TSD) document which specifies the functionality (see section 10.2.2).

5.10 Essential records [v10.0510.08]

5.10.1 Trial master file index (TMF)

The trial master file index (TMF) must include all essential records 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. The full TMF is normally composed of the following:

- a sponsor TMF, held by the sponsor organisation,
- a trial TMF, managed and held by the CHaRT trial manager. The latter is referred to as the CHaRT TMF. A CHaRT **TMF index** template is available on IQM. The index should be very clear about what essential records are held as hard copy (and their location) and what essential records 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 IQM) or within the **TMF index**.
- a Programming TMF, managed and held by the CHaRT programming team.
- a Statistics TMF, managed and held by the trial statistician.

In addition, aspects of the TMF may be held by the process evaluation team and health economics team. The TMF also comprises the Investigator site files (see section 5.10.2) and, where relevant, pharmacy and laboratory files.

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 IQM. The ISF index, should be very clear about what essential records are held as hard copy (and their location) and what essential records are held electronically (and their location). The ISF must include all essential records 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.

In addition, there may also be pharmacy files (held by investigator site clinical trial pharmacies; a pharmacy site file index template is available on IQM) and laboratory file(s) (held by the laboratory providing analysis).

5.11 Site selection and initiation [v10.0511.07]

Sites (defined as trial locations in the new regulations) are identified in a variety of ways, such as those listed in the grant application, sites CHaRT or the CI have 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. An investigator site **expression of interest form** template, which may include recruitment target, is available on IQM 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 IQM, 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 IQM). 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 CHaRT 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 investigator sites** is available on IQM.

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 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. In addition, database training will be provided to the site staff who will be using the trial database (see section 16.3). 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.

It is the responsibility of the trial manager to understand and comply with the sponsor requirements in relation to green-lighting individual recruitment sites. Where the sponsor delegates this activity to CHaRT, a **site set-up green light form** template is available on IQM. The trial lead STM should consider whether they (or one of the other STMs) should review and countersign the greenlight forms for a specific trial. If there is a change to the green-lighting process as the trial progresses, this should be documented. Accordingly.

5.12 Trial monitoring [v10.0512.07]

The sponsor usually conducts a risk assessment for randomised controlled trials, though on occasion, this may be delegated to CHaRT (see section 5.1.1). 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 IQM. For studies sponsored elsewhere, the sponsor may provide a template. The CHaRT TMP should be reviewed by the 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 records 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 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 managers and the QA manager that a CHaRT TMP is not required and if so, this will be documented in the CHaRT 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 IQM. 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.
- 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 IQM, 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 IQM. 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) [v10.0513.03]

One key consideration in the design of CHaRT trials is that the question being investigated is important 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 IQM)

CHaRT list of validated questionnaires available on IQM

[1]www.consort-spirit.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	Mar 2020

	around role of the DMC and timing of agreeing terms of reference for TSC and DMC (5.10.1).	
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 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).	Apr 2024
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Inclusion on a new sentence at the start of section 5.1 to provide guidance on the filing of all appropriate approvals in the TMF. Addition of a link to CHaRT's new eConsent process. Update to wording in sections 5.10 (essential documents to essential records) and 5.11 (trial site to investigator site) as per ICH-E6R3, and addition of text in section 5.10 to highlight that some trials may also include Pharmacy and/or Laboratory file(s).	Aug 2025
10	Major update to text (section): to include information on the regulatory approval process with regard to NIMPs & notifiable trials and the time frame for recruiting first participant and the process thereafter (5.1.4), to provide further details on trial registration (5.3), to provide links to protocol templates and consideration given to CtQ factors within protocol for CTIMPs (5.5), inclusion of new subsection on lab testing (5.5.3), details of process for PI sign off on CRFs for CTIMPs (5.6), reference to guidance and arrangements for simplified consent (5.7), reference to all aspects of essential records making up the full TMF (5.10), details on the greenlighting process (5.11). Minor update to section 5.12 to note that a trial risk assessment may be delegated to CHaRT on occasion	Apr 2026

CHAPTER 6: TRIAL CONDUCT AND MANAGEMENT
[v10.0600.10]

LEAD AUTHOR
Senior trials managers.

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.

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.

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 [v10.0601.04]
Good Clinical Practice (GCP) is an ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve participation of human participants. Compliance with the principles of this standard, as outlined in the ICH Harmonised Guideline for Good Clinical Practice E6 (R3)[1], provides public assurance that the rights, safety and well-being of trial participants 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/2025/538/contents for further information on GCP in clinical trials relating to the UK Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025 No. 538). 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 [v10.0602.05]
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).

6.3 Governance arrangements [v10.0603.04]

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/support/research-support/research-governance/#panel32566.

6.4 Finance [v10.0604.01]

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 [v10.0605.03]

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/legal-and-compliance/data-protection/#panel37241.

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.

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.

6.5.4 Complaints

Complaints may be received from participants, their families or friends, from people working on the trial or elsewhere. If a complaint is received, please consult with a member of the senior CHaRT team for advice on how to deal with the complaint.

6.6 Progress reporting [v10.0606.08]

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) within 60 calendar days from the day after the end of the reporting year. 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 IRAS for trials approved through the combined review process. For all other CTIMPs, submit your DSUR using the MHRA submissions 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). There is a fee payable to the MHRA for submission of a DSUR (mhrainspectorate.blog.gov.uk/2024/04/04/dsur-submissions-and-fees-are-changing-from-1-june-2024/). The MHRA submission details should be used as evidence of the DSUR submissions and should be retained in the CHaRT TMF and forwarded to the sponsor. Please refer to the **SOP-QA-21: DSURs** for details on preparing and submitting DSURs for locally sponsored studies; examples of recent **DSUR reports** are available on Ideagen Quality Management (IQM).

The DSUR preparation may highlight if there is a requirement for a modification to update the reference safety information (RSI) within the Summary of Product Characteristics (SmPC) or Investigator's Brochure 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 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 [v10.0607.08]

The level of safety reporting can vary between studies. For all interventional studies (including both CTIMPs and non-CTIMPs) safety reporting procedures (including who is responsible for recording and reporting) must be detailed within the trial protocol. The local PIs, CI or their medically qualified deputies are usually responsible for assessing seriousness, relatedness (causality), severity and expectedness. See the HRA 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 Serious Adverse Events (SAEs), including Serious Adverse Reactions (SARs), Serious Adverse Device Effects (SADEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs), that require to be recorded and reported as part of the trial protocol should be recorded on the appropriate SAE form. CHaRT **SAE form** templates are available on IQM, 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** and **SOP-QA-39: Adverse Events in Medical Device Clinical Investigations** for further details on identifying, recording and reporting SAEs.

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.

6.7.1 Suspected unexpected serious adverse reactions (SUSARs)

Suspected Unexpected Serious Adverse Reactions (SUSARs) must be reported to the MHRA through ICSR Submissions (for submitting single SUSARs) or the MHRA Gateway (for submitting single or bulk reports) as detailed here: www.gov.uk/guidance/register-to-make-submissions-to-the-mhra#registering-to-use-the-vigilance-systems-mhra-gateway-and-icsr-submissions. SUSARs do not need to be reported to the REC, the MHRA will liaise with the REC if deemed appropriate.

Fatal or life-threatening SUSARs must be reported as soon as possible, but no later than 7 days after you first became aware of the reaction. Additional relevant information needs to be sent within 8 days of the initial report.

Non-fatal or non-life-threatening SUSARs must be reported as soon as possible but no later than 15 days after you first became aware of the reaction.

SUSARs specified in the protocol as not requiring immediate reporting should be reported in accordance with the requirements detailed in the protocol.

In trials that involve blinding of participants, when an event may be a SUSAR, the blind should be broken for that specific participant only for safety evaluation and regulatory reporting purposes as per the trial specific RSI. The unblinded information should only be accessible to those who need to be involved in the safety reporting, or persons performing ongoing safety evaluations during the trial, for example the DMC. See section 11.6 on unblinding for further information.

Following submission of a SUSAR, an acknowledgement of the submission should be received within 48 hours and filed in the CHaRT TMF. If not, then contact E2B.support@mhra.gov.uk to determine next steps, including whether resubmission is required.

6.8 Deviation and breach reporting [v10.0608.07]

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 IQM. Possible breaches should be discussed with the trial CI and 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 participants of the trial or the scientific value of the trial. The CHaRT **guidance on deviations and breaches** can be found on IQM.

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.

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/legal-and-compliance/data-protection/#panel37251.

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 participant'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 [v10.0609.03]

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 7 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 7 days, or via IRAS for CTIMPs submitted via combined review. If the USM requires a modification to study documentation, a substantial modification covering the changes should be submitted as soon as possible and marked as being in response to the USM.

Where a USM requires modification to trial documentation, this should be submitted as a modification to REC (and MHRA if applicable) as soon as possible and marked as being in response to a USM and should include a copy of the USM notification.

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 Modifications [v10.0610.09]

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 proposed modifications prior to submission. SOP-QA-19: Modifications provides further details on how to process and submit modifications for locally sponsored studies.

The modification tool and full guidance, which can be found at www.myresearchproject.org.uk/help/hlpamendments.aspx, should be used for all modifications for project-based research submitted through the standard IRAS only. The tool categorises the modification and provides tailored guidance on which review bodies the modification needs to be sent to, based on the changes that are being made to the trial. A **modification**

checklist is available on IQM, providing prompts of the potential tasks to be actioned when submitting a modification.

The locked version of the modification tool can then be submitted to the appropriate review bodies. It also provides detailed information about the modification to participating sites. The modification tool, together with a cover letter (for CTIMPs) and all the supporting documents, should be submitted using the online IRAS modifications submission platform: www.myresearchproject.org.uk/help/hlpamendments.aspx.

In a CTIMP, modifications can be categorised into substantial modifications (route A and route B), modifications of an important detail (MOID) or a minor modification, see www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval#types-of-modification for definitions.

Substantial modifications and MOIDs require submission of an application to the MHRA for approval.

- For CTIMPs submitted through combined review this will be via the new part of IRAS
- For CTIMPs NOT submitted through combined review this will be via IRAS portal described above and the MHRA Portal which can be found at mhrabpm.appiancloud.com/suite/sites/MHRA_Submissions. Further guidance on submitting a modification using the MHRA portal, is available on IQM: **guidance for submitting a modification using the MHRA portal**.
- For device trials, the modification 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).

Minor modifications may be implemented at any time without informing the MHRA or REC at the point of implementation and you should outline any minor changes in the cover letter that accompanies the next substantial modification application.

For CTIMPs, once a substantial modification (route A or route B) has been submitted, the application initially undergoes validation checks: Valid applications for route A substantial modifications are then reviewed and assessed by MHRA and/or REC, depending on the nature of the modification, before a decision is made as to whether the application is approved, approved subject to conditions or not approved. Valid applications for route B substantial modifications will be automatically approved by MHRA but may require review by REC before approval. See www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval#documents-that-should-accompany-an-application-to-make-a-substantial-modification for full details of the process.

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

If a substantial modification is made to the protocol, the Trial Monitoring Plan (TMP) must be reviewed and, if required, updated accordingly (see section 5.12). If CHaRT is responsible for

the risk assessment (see section 5.1.1), the risk assessment must also be reviewed, and if required, updated accordingly.

For CTIMPs, if a substantial modification 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 modification. 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/, mhrainspectorate.blog.gov.uk/2017/01/18/reference-safety-information-ii/) and https://mhrainspectorate.blog.gov.uk/2021/02/05/reference-safety-information-rsi-for-clinical-trials-part-iii/.

A **modification log** (available on IQM) should be maintained in the CHaRT 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. 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 IQM, is required for any changes to the data collection tools built on the trial website. In addition, if planned changes to the protocol have implications for the programming and/or statistics teams these should be discussed so that the trial database, DMP (see section 10.1) and SAP (see section 12.3) can be updated as required. 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 Modification 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). Modifications 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 IQM, should be used to record changes made to key documents and can be made available to sites.

6.11 Error correction [v10.0611.04]

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/initialling 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 IQM. 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 [v10.0612.03]

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 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 IQM for information on how to do this.

6.13 Filing [v10.0613.04]

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 is 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 [v10.0614.04]

Project Management Group (PMG), Trial Steering Committee (TSC) or Data Monitoring Committee (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 the management of recording meetings in MS Teams** is available on IQM. 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 [v10.0615.01]

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 IQM 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.

6.16 Participant contact [v10.0616.04]

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 [v10.0617.07]

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 IQM. 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. For CTIMPs, the summary of results must be provided within 12 months of the end of the trial. The sponsor and / or the REC should be consulted as to whether such correspondence requires approval before distribution.

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). See section 10.3.2 for further information on data linkage. 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 IQM.

6.18 The role of the Chief Investigator (CI) [v10.0618.04]

The Chief Investigator has overall responsibility for the trial. For CTIMPs, the CI must be a health care professional. 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 modification will be required.

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 modification.

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) [v10.0619.03]

The Principal Investigator (PI) has overall responsibility for the trial at site. For CTIMPs, the PI must be a health care professional. 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, a modification will be required.

RELATED REFERENCES AND RESOURCES.

[1] https://ich.org/page/efficacy-guidelines (E6(R3))

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 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).	Mar 2020
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	Apr 2022

	'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.	
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 CHaRT's 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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs Update to section 6.10 to provide guidance on reviewing & updating (if appropriate) the Trial Monitoring Plan (TMP) if an amendment is made to the protocol.	Aug 2025
10	Major update to text (section): to include a new subsection 6.5.4 on complaints (6.5), to revise text and provide clarification on level of safety reporting and include a new subsection 6.7.1 on SUSARs and the process for reporting as per new regulations (6.7), to update the title from 'Amendments' to 'Modifications' and clarify the submission and approval process as per the new regulations (6.10). Minor update to text (section): to reference ICH GCPE6(R3) (6.1); to include timelines and update links regarding DSUR reporting (6.6), to update timelines and process for notification for USMs (6.9), to include timeline for reporting summary results to participants for CTIMPs and x-reference to data linkage (10.3.2) for information (6.17.1), and to clarify the role of the CI and PI (6.19 & 6.20)	Apr 2026

CHAPTER 7: TRIAL CLOSE-OUT
[v10.0700.10]

LEAD AUTHOR
Senior trials managers.

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

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, which is defined and documented in the protocol, must be anticipated and planned for accordingly from its start. This will either be the date of the last visit of the last participant, or it may be the completion of any follow-up monitoring and data collection.

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

TRIAL CLOSE-OUT

7.1 Close-out procedures [v10.0701.08]
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 an investigator site**, are available on Ideagen Quality Management (IQM). 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 CHaRT 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.
- 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 [v10.0702.06]

- **For *CTIMPs*** submitted through combined review, complete and submit the end of trial form in the new part of IRAS within 90 days of the trial ending, as defined by the protocol. This automatically submits the notification to the REC and MHRA. A copy of this form should also be sent to sponsor.

- ***For CTIMPs*** NOT submitted through combined review, the MHRA, REC and sponsor(s) should be notified of the end of trial within 90 days of the end of trial 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.

- ***For CTIMPs*** that have not recruited within 2 years, the approval for the trial will lapse (see section 5.1.4) unless an application for an extension is made, otherwise the trial will be terminated and will be required to follow the process detailed below (see section 7.3 below).

- ***For non-CTIMP trials***: the end of study notification form is sent 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.

A final trial report should then be submitted to the REC by completing and submitting the following www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/ within 12 months of end of the trial. Receipt of submission should be

received within 30 calendar days of submission and filed within the TMF accordingly, together with the end of study declaration form.

7.3 Early termination of a trial [v10.0703.06]

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 to ensure that no further participants are recruited or randomised to the trial

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 IQM to consider what actions might need to be addressed.

Once this is achieved, the plan for the scheduled close-out should then be exacted (see section 7.2 above).

- ***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 above 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 above for details of the process for non-CTIMPs. Local R&D office(s) should also be informed.

7.4 Temporary suspension of a trial [v10.0704.05]

Possible reasons for a temporary suspension may include safety issues (e.g. an urgent safety measure (USM), to investigate a Suspected Unexpected Serious Adverse Reaction (SUSAR); see sections 6.7.1 and 6.9 respectively), 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 must be informed immediately, if suspended on safety grounds, and 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 IQM.

- ***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 modification (see

section 6.10 for further details), using the notification of modification 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.

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 modification using the modification tool 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 [v10.0705.02]

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 CTIMPs, the summary of results must be published on the public registry, and offered to participants, within 12 months after the conclusion of the trial. For CTIMPs that were previously registered on EudraCT, the clinical trial summary results will also need to be reported to EudraCT within six or 12 months depending on the type of trial.

For locally sponsored studies, please refer to **SOP-QA-31: Research Project Closure**.

7.6 Finance [v10.0706.01]

The trial manager should work with the sponsor's finance team, together with a member of the senior CHaRT team and the UoA colleagues 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 [v10.0707.07]

The CI is responsible for liaising with the sponsor's named archivist to ensure the CHaRT TMF, together with other parts of the full TMF that are maintained by CHaRT (e.g. programming TMF, statistics TMF etc, as detailed in section 5.10), and all other trial data are archived appropriately. The named archivist is then responsible for ensuring this data is stored securely, retrieved, destroyed and recorded appropriately (see **SOP-QA-32: Archiving** for details relating to archiving for locally sponsored studies).

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

from participants). To archive electronic data, including the CHaRT eTMF, the trial manager will complete the **ACE: e-folder and study website archive form** (available on IQM) and send to aceqa@abdn.ac.uk for the ACE QA team to arrange for the trial data and documentation to be moved to a secure archive area. The trial manager should then file the completed signed form in the TMF accordingly. For hard-copy trial data and essential documentation, the trial manager will follow the sponsor's archiving SOP to agree where it will be stored. The completed sponsor archive approval form, or equivalent, will be filed in the TMF.

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 (please refer to section 10.2.10). See CHaRT's **guidance on archiving and top tips**, which is available on IQM, for details and guidance on various archiving requirements.

The sponsor and/or funder will advise on the retention period for the entire TMF which includes the CHaRT TMF and trial data at the outset of the trial. This is usually documented in the protocol, the IRAS application and site agreements. For CTIMPs, all essential documents contained in the TMF (both electronic and hard copy) will be retained for a period of at least 25 years beginning the day after conclusion of the trial and that during that period are a) readily available to the licensing authority on request; and (b) complete and legible. 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 CHaRT TMF.

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

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 CHaRT 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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Update to section 7.7 to provide clarification on the retention of the TMF, which includes the CHaRT TMF and trial data.	Aug 2025
10	Update to background to provide the definition of end of trial. Major updates to text (section): to provide additional information on the process and timelines for trial termination for CTIMPs (7.2), the trial reporting process for CTIMPs (7.5), and the addition of information on e-archiving processes, and the archive time period for CTIMPs (7.7). Minor updates to section 7.3 to include the following sentence 'to ensure that no further participants are recruited or randomised to the trial' and 7.4 to include USMs as an example of a safety measure.	Apr 2026

CHAPTER 8: TRIAL PUBLICATION(S) AND DISSEMINATION
[v10.0800.10]

LEAD AUTHOR
CHaRT director and head of trial management.

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

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.

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 [v10.0801.05]
The CI, in conjunction with the CHaRT lead where appropriate, is responsible for understanding the requirements of the stakeholders in the trial (the funder, the sponsor, ethics, regulatory, consumer groups, and so on) and reporting guidelines[1], 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 and 7.5 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 [v10.0802.05]
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 and should be done within 12 months of the end of study for CTIMPs. For the majority of CHaRT trials, it is anticipated that there will be a results paper published through an open-access mechanism in a peer-reviewed medical/scientific journal. Particular attention should be paid to ensuring this requirement is met for trials that fail 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 and 7.5 for full details of the trial reporting 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).

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)[2]. Where possible the **CHaRT authorship policy**, which can be found on Ideagen Quality Management (IQM), 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 IQM.

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 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 a clear and accessible 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 IQM for use. For CTIMPs, a summary of the trial results must be provided to participants and/or any other relevant people within 12 months of the end of the trial.

8.3 Patient and public involvement in dissemination [v10.0803.02]

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 authorship[1] should be offered a co-authorship of scientific outputs, recognising them as equal partners in the study. Otherwise, an acknowledgment should be given.

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 [v10.0804.02]

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 [v10.0805.01]

Requests for clinical trial data 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 trials managers, QA manager or senior IT development manager. Please refer to the **data sharing policy** available on IQM for information about CHaRT's data sharing process. Further information can also be found at www.abdn.ac.uk/ace/what-we-do/chart/data-sharing/.

RELATED REFERENCES AND RESOURCES

Guidance to authors: Study outputs

Publication preparation timetable and checklist

RefWorks ProQuest - guidance on sharing documents

(all the above documents can be accessed via IQM)

[1]Reporting Guidelines (Equator Network: www.equator-network.org/reporting-guidelines/)

[2]Recommendations 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
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Reference to reporting guidelines added to section 8.1, and the appropriate weblink added to the 'Related references and resources' section.	Aug 2025
10	Update to section 8.2.1 and 8.2.4 to provide information on the timelines and method for the publication and dissemination of trial results to participants for CTIMPs.	Mar 2026

CHAPTER 9: IT INFRASTRUCTURE
[v10.0900.05]

LEAD AUTHOR
Senior IT development manager.

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

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.

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 [v10.0901.04]
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 allow them to install some software without getting permissions from IT services.

9.2 Modification to existing hardware and software [v10.0902.02]
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 implement 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 10.2.7).

9.3 Description of redundancy features [v10.0903.01]
Redundancy features for the CHaRT's critical systems are managed by IT Services.

9.4 System decommissioning [v10.0904.01]
Hardware and software decommissioning will be handled by IT Services.

9.5 System and data back-up [v10.0905.02]
Routine server and individual PC backup are managed by IT Services.

For CTIMPs, back-up arrangements for clinical trial systems must support restoration of essential records for a minimum of 25 years following trial completion in line with the current clinical trial regulations, (see section 7.7 for details).

9.6 Preventative maintenance [v10.0906.01]
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 [v10.0907.02]
Notification of new patches will be received from IT Services. New patches will be installed remotely if considered necessary.

For systems supporting regulated clinical trials, the impact of patches and updates on data integrity, audit trails, and system functionality will be assessed by the CHaRT programming team prior to, or following deployment, and documented where appropriate by IT services.

9.8 Servers: start up and shut down [v10.0908.01]
All server start-ups and close-downs will be managed by IT Services.

9.9 System monitoring: capacity management [v10.0909.01]
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 [v10.0910.02]
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 [v10.0911.03]
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.

Records of system failures affecting regulated trial systems will be recorded in the Error Log and retained in the CHaRT project management portal in accordance with essential records retention requirements.

9.12 Third party networks: interfacing of local networks to wide area networks [v10.0912.01]

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 Ideagen Quality Management (IQM).

9.13 Distribution of software upgrades [v10.0913.01]

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 [v10.0914.01]

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 [v10.0915.04]

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 investigator site staff) leaves, all access to the trial website will be removed accordingly.

In cases of extended sick leave, planned leave, or prolonged unavailability, user access will be reviewed and may be temporarily suspended or restricted in accordance with the **Management of system access in case of sick leave or unavailability** working practice document (available on IQM), to ensure data security and continuity of operations. Any such changes to access rights will be formally documented and approved in line with organisational governance procedures.

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 IQM).

Logging of user authentication and access for trial systems will be retained and made available for audit and inspection purposes in line with regulatory requirements

9.16 Network security [v10.0916.01]

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

9.17 Server environmental monitoring [v10.0917.01]

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

RELATED REFERENCES AND RESOURCES

None.

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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs.	Aug 2025
10	Updates to text (section): clarification of the length of time backups must be kept for (9.5), clarification of the review of what patches can be applied and when (9.7), addition of system failure monitoring (9.11) and addition of access control procedure for absent staff (and clarification of log on/authentication logging (9.15).	Feb 2026

CHAPTER 10: DATA MANAGEMENT
[v10.1000.10]

LEAD AUTHOR
Senior IT development manager.

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

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.

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 [v10.1001.05]
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.
  - 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.
- Data retention and long-term archiving arrangements

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 electronic folder used by the CHaRT programming team. A **DMP** template is available on IQM.

The DMP must reflect applicable regulatory transparency, reporting, and retention requirements introduced under the UK clinical trials regulatory framework.

10.2 Development standards [v10.1002.10]

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 Computerised system assurance (risk-proportionate)

Systems supporting clinical trials will be developed, configured, and maintained proportionate to the level of trial risk. Documentation will be maintained in the trial specific programming TMF to demonstrate system suitability, including configuration records, testing evidence, audit trail verification, and data restoration testing where appropriate.

10.2.2 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).

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 Ideagen Quality Management (IQM).

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 10.2.7.

A **trial service definition (TSD)** document available on IQM 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 **randomisation specification (RS)** document available on IQM will be completed by the trial statistician and trial manager. This document will be used as reference during development and through to testing.

A **project website initiation (PWI)** document available on IQM 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.

10.2.3 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 IQM.

Software and the underlying databases are developed in line with the **coding standards** document on IQM.

10.2.4 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 including verification of audit trails, access controls, and data export functionality. See the **form generator – testing** document available on IQM.

Internal testing is performed against the 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 IQM.

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.

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

In addition, a User Acceptance Testing (UAT) re-check process is in place. A defined percentage of completed UATs are selected at random for independent review. The process for conducting re-checks is documented, including selection methodology, acceptable error thresholds, escalation procedures where thresholds are exceeded, and responsibility for conducting the checks. Records of each re-check are maintained, detailing the UATs reviewed, dates of review, personnel involved, findings, and any corrective or preventive actions taken. See the **User acceptance and All site testing** working practice document (available on IQM) for further details.

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 10.2.7 for more details.

Testing documentation will demonstrate that system outputs used for regulatory reporting and public disclosure are complete, accurate, and traceable to source data and will be retained in the respective trial programming TMF.

10.2.5 Computerised system validation status

CHaRT will maintain controlled documentation describing the computerised systems used to support the conduct and management of clinical trials; Validation summary of systems.
This documentation will include, as a minimum:

- the name of each system,
- a description of its purpose and functionality,
- its validation status,
- details of system interfaces,
- system ownership and management responsibility,
- a description of access controls, and
- internal and external security measures implemented to protect the system and its data.

The overarching validation framework for CHaRT-developed systems is described in the **system validation summary** document, available on IQM, which outlines the governance, lifecycle processes, and validation approach applied to in-house systems, including randomisation and IMP/pack management systems.

Trial-specific validation activities, including UAT, simulation testing, and 'go live' authorisation, are documented separately for each trial.

Records of system validation status and associated documentation will be maintained by the CHaRT programming team and retained as essential records and filed in the trial specific CHaRT TMF. These records will be available for audit and regulatory inspection.

CHaRT ensures that computerised systems are appropriately validated prior to release for use in clinical trials and are maintained in a controlled and validated state throughout their operational lifecycle. Validation activities are proportionate to the system's intended use and associated risks and provide documented evidence that the systems are fit for purpose.

10.2.6 Go live

Before a trial system can go live, all required system readiness checks must be completed and documented. These checks are recorded within the **Database Authorisation to Go Live Form** (available on IQM), which incorporates the required website green light verification activities. The 'Database Authorisation to Go Live Form' provides a record of:

- the required readiness checks,
- the individual responsible for completing each check, and
- the date each check was completed.

Completion of these checks provides documented evidence that the trial system has been appropriately developed, configured, and tested, and is suitable for use in a live clinical trial. Following completion of all required checks, the 'Database Authorisation to Go Live Form' must be formally reviewed and approved.

Formal approval is documented by electronic signature using Adobe Acrobat Sign. The signed 'Database Authorisation to Go Live Form' provides formal authorisation for the system to go live and records:

- the name and role of each signatory, and
- the date and time of approval.

The minimum required signatories will include:

- a senior member of the CHaRT programming team (typically the Senior IT Development Manager or Senior Programmer), and
- the Trial Manager, or an appropriately delegated trial team representative.

The fully executed 'Database Authorisation to Go Live Form' will be retained as an essential trial record within the trial programming folder and referenced in the programming Trial Master File (TMF). This documentation will be available for audit and regulatory inspection.

The go live date will be agreed between the programming team and the trial team following completion and approval of the Go Live Form.

Prior to go live, all test data within the system must be deleted. This includes, but is not limited to:

- participant records,
- case report form data,
- questionnaire data

No live participant data may be entered into the system until the Database Authorisation to Go Live Form has been fully approved.

10.2.7 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 a modification (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 IQM.

Modifications to trial systems will be classified as substantial modifications, of a minor detail (MOID), or minor modifications to align with the clinical trial regulations for CTIMPs. The classification and rationale will be documented prior to implementation.

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. Where a modification requires regulatory or ethics approval (see section 6.10), implementation will not proceed until the relevant authorisations have been obtained and 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.
All modifications will be supported by a documented assessment of potential impact on participant safety, data integrity, and trial outcomes.

10.2.8 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.

The data dictionary and associated metadata are considered essential records and will be maintained and archived in accordance with retention requirements.

10.2.9 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.

10.2.10 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 will be documented in the statistics TMF and the trial team will be informed where necessary to update 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 ends, essential electronic records, including databases, audit trails, metadata, and associated documentation, must be archived. For CTIMPs this will be for a minimum of 25 years, in line with the current clinical trial regulations.

The trial manager will complete the **ACE: e-folder and study website archive form** (available on IQM). Upon receipt of the completed form, the project website and study e-folder will be archived in line with the approved procedures. 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.

10.2.11 Retention and restorability

Archived databases and records must be maintained in formats that allow restoration, inspection, and review throughout the retention period. Periodic testing of restoration procedures will be undertaken and documented.

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.

Responsibility for long-term storage, access control, and restorability will be agreed between CHaRT and IT Services and documented for each trial.

10.3 Data transfer [v10.1003.08]

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 sharing request (DSR) form** found on IQM. 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 IQM.

Please refer to the NHS Information Governance Toolkit (www.dsptoolkit.nhs.uk/) for further information regarding the handling of information.

10.3.2 Data received from the NHS

Strict guidelines apply to the receipt, storage, access, and management of data obtained from NHS England (NHSE), Secure EDRIS, and other restricted or secure data providers.

Researchers must comply with all relevant University of Aberdeen (UoA) policies and standard operating procedures, including the **UoA NHS England Data Management SOP** and any equivalent guidance relating to other secure data sources. These documents provide instructions on access control, secure storage, and appropriate handling to ensure compliance with data sharing agreements and governance frameworks.

All secure data must only be accessed and processed within the approved secure environment. Secure files must not be downloaded, copied, transferred, or stored outside the

designated secure system. Access permissions are provided solely to enable authorised work within these environments and must not be used to facilitate local or external storage.

Any downloaded or locally stored copies of secure data are strictly prohibited and must be deleted immediately if identified.

NHSE data must be kept secure and tightly controlled to ensure that access management and deletion requests can be implemented appropriately. Access to NHSE data, and requests for deletion, are managed by the NHSE Gateway Manager and Deputy via nhsgateway@abdn.ac.uk.

Equivalent access control and deletion procedures must also be followed for other secure datasets, including those accessed through Secure EDRIS or similar platforms.

These processes are essential to prevent misuse of sensitive data and to maintain compliance with contractual, legal, and ethical obligations. All staff must adhere to the relevant data access, storage, and management SOPs whenever personal or sensitive patient-related data is used for research purposes.

Any queries regarding secure data access, handling, or governance should be directed to the appropriate data custodian or, where applicable, the NHS Gateway Manager.

10.4 Information security [v10.1004.03]

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:

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 investigator 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 [v10.1005.03]

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 IQM.

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 [v10.1006.01]

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 [v10.1007.03]

The University of Aberdeen maintains an overarching Resilience Plan, supported by Emergency Response Plans and Business Continuity Plans, which provide guidance for responding to and recovering from major incidents affecting staff, infrastructure, IT systems, data, and critical services. Further information is available via the University's Business Continuity webpages (www.abdn.ac.uk/staffnet/governance/business-continuity-352.php#panel5528).

CHaRT operates within this institutional framework and is covered by University-level and School-level business continuity arrangements, including procedures for loss of buildings, utilities, IT systems, data, suppliers, or key personnel.

Central IT recovery and resilience measures are in place to support the restoration of critical systems and services in line with University policies and priorities.
Recovery arrangements and timescales are defined, maintained, and subject to regular testing and review within the University's Resilience and Business Continuity framework, providing assurance of compliance with ICH GCP requirements for the security, integrity, and availability of clinical trial data.

Since most trial data entry systems are web-based, access to these systems may be temporarily disrupted following a critical incident. During such events, priority is given to restoring essential communications between the trial office, sites, and participants in line with University resilience arrangements.

CHaRT maintains documented procedures to support the continuity of randomisation and essential trial functions in the event of system disruption (see section 11.9). These arrangements are aligned with University IT recovery processes and include contingency measures to ensure participant safety and data integrity.

Alternative operational procedures are communicated to trial teams and sites as required during incident response and recovery.

10.8 Encryption [v10.1008.03]

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)

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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. New paragraph added to section 10.2.1 to reference the new randomisation specification document and associated process.	Aug 2025
10	Major update to text (section): inclusion of new subsection on Computerised system assurance (risk-proportionate) (10.2.1), to include details on UAT re-check process (10.2.4), inclusion of new subsection on computerised system validation status (10.2.5), to provide more details on the go-live process (10.2.6), to include details of modification classification in respect to change management (10.2.7), further details on the timelines for archiving and reference to the new archive form (10.2.10), inclusion of new subsection on retention & restorability (10.2.11), re-write of the process regarding receipt, storage, access, and management of data received from NHS (10.3.2), re-write of the business continuity / disaster recovery process (10.7). Minor update to section 10.1 to include link to DMP template, 10.2 to provide details on document management related to validation, archiving and retention, where appropriate	Apr 2026

CHAPTER 11: RANDOMISATION
[v10.1100.06]

LEAD AUTHOR
Senior IT development manager.

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

BACKGROUND
Randomisation is the process used for assigning participants 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.

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 [v10.1101.02]
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). This will be documented in the protocol and the **randomisation specification (RS)** document (available on IQM).

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 [v10.1102.03]
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 RS document.

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 Ideagen Quality Management (IQM).

11.3 Implementation [v10.1103.01]

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

11.4 Testing and simulations [v10.1104.05]

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

A CHaRT statistician for the trial will then check the RSV against the randomisation design, as detailed in the RS document, and sign off the RSV after checking the simulation results are correct.

Supporting documentation and datasets for all simulations for each trial will be managed in the appropriate programming Trial Master File (TMF).

11.5 Non-CHaRT trials [v10.1105.02]

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 [v10.1106.03]

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. All other members of the trial team will only have access to unblinded data after the end of the trial when final analyses have been completed (also refer to section 12.6: Unblinding).

If unblinding of an individual participant due to safety concerns is likely to be required (e.g. because of a medical emergency where knowledge of the allocation is required to inform treatment, or a potential SUSAR, or to plan future treatment), then a trial specific 'Unblinding Procedure' will be created and kept in the CHaRT TMF. Unblinding in these instances 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). Consideration should be given as to whether a fail-safe mechanism for unblinding is required. Please see **SOP-QA-35: Unblinding** for further details on unblinding procedures for locally sponsored studies.

11.7 Quality Assurance [v10.1107.04]

- 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 least once during trial recruitment, 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.
- Quality assurance activities will be proportionate to trial risk and aligned with the principles of GCP as outlined in the ICH E6(R3).

11.8 Training [v10.1108.01]

Randomisation applications will be used routinely by non-CHaRT personnel, usually trial co-ordinators, 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 [v10.1109.02]

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 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 and unauthorised use [v10.1110.01]

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
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Updates made to sections 11.1, 11.2 and 11.4 to reference the new randomisation specification document and associated process.	Aug 2025
10	Updates to sections 11.4 to refer to the programming TMF, 11.6 to provide examples of when unblinding is likely to be required and, 11.7 to refer to regulatory requirement for quality assurance.	Feb 2026

CHAPTER 12: STATISTICS
[v10.1200.10]

LEAD AUTHOR
Senior statisticians.

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

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.

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 [v10.1201.02]
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 Ideagen Quality Management (IQM).

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 [v10.1202.01]
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).

12.3 Statistical analysis plans [v10.1203.06]

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 IQM. This document will specify the statistical analyses for the trial and filed in the statistics TMF. 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.

Modifications to a trial protocol and/or the associated trial-specific CRFs or questionnaires (see section 6.10), may require the SAP to be updated. Any changes to statistical analysis will be detailed in the version history.

12.4 Pilot / feasibility studies [v10.1204.01]

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) [v10.1205.04]

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 provide the details of the randomisation method, as specified in the protocol, within the **randomisation specification (RS)** document (see section 11.2; available on IQM). 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 [v10.1206.05]

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). 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. **Guidance on dealing with statistician blinding and unblinding** is available on IQM.

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 [v10.1207.03]

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 [v10.1208.03]

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.

Outputs should be traceable to the statistical software programs used, dated and time stamped, protected against any changes, and have access controls implemented to avoid inappropriate viewing of information that may introduce bias.

12.9 Handling of Secure External Data for Statistical Analysis [v09.1209.01]

Where CHaRT statisticians are required to access and analyse data from secure external providers (e.g. NHS England, Secure EDRIS, or other restricted-access data sources), all access, handling, storage, and processing of such data must be conducted in accordance with the requirements described in section 10.3.2. **Guidance on the handling of secure external statistical data** is available on IQM.

The trial statistician is responsible for ensuring that statistical analyses using these data are conducted only within the approved secure environment and in compliance with the relevant data governance requirements, data sharing agreements, and University of Aberdeen policies.

Statistical code, outputs, and associated documentation must be managed and archived in accordance with CHaRT statistical procedures (see section 12.13), whilst continuing to comply with the restrictions defined in section 10.3.2.

All statisticians must adhere to these requirements when working with secure external data to ensure compliance with legal, contractual, and ethical obligations.

12.10 Statistical quality control [v10.1210.04]

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 as detailed in **guidance on primary outcome analysis validation** available on IQM. 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.

All CHaRT statisticians must undergo appropriate Good Clinical Practice (GCP) training (see section 6.1)

12.11 International Conference on Harmonisation (ICH) statistical principles [v10.1211.02]

All statisticians working on CHaRT trials are expected to read the ICH Tripartite Guideline: Statistical Principles for Clinical Trials together with the ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials (see: www.ema.europa.eu/en/ich-e9-statistical-principles-clinical-trials-scientific-guideline). 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.

12.12 Partnerships with external statisticians [v10.1212.01]

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.

12.13 Interaction with Data Monitoring Committee [v10.1213.03]

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.

12.14 Statistical archiving [v10.1214.01]

At the end of 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 within the statistics TMF 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	
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Updates made to sections 12.5 to reference the new randomisation specification document and associated process, 12.9 to provide information on the Good Statistical Practice (GSP) training and 12.10 to update ICH weblink to include the ICH E9 (R1) addendum.	Aug 2025
10	Updates to text (section): to include information on changes to the SAP if a trial protocol, CRFs and questionnaires are amended, and filing of SAP in the statistics TMF (12.3), to reference guidance on dealing with statistician blinding and unblinding (12.6), to include detail on the traceability of outputs from statistical software programs (12.8), to reference guidance on primary outcome analysis validation and remove text specifically referring to the Good Statistical practice (GSP) training (12.10). Addition of a new section: 12.9 Handling of Secure External Data for Statistical Analysis.	Apr 2026

CHAPTER 13: HEALTH ECONOMICS
[v10.1300.07]

LEAD AUTHOR
Senior health economist.

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

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.

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 [v10.1301.03]
CHaRT is committed to designing and delivering trials that are methodologically sound.

The economic evaluations conducted as part of such trials should, at a minimum, conform to guidelines for the design, conduct and reporting of economic evaluations.[1-5] The conduct and reporting of all economic evaluations are expected to conform to the Consolidated Health Economic Evaluation Reporting Standards.[1]

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 [v10.1302.01]
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.

Table 13.1 Constructing a care pathway for an economic evaluation

Care pathway	Example
Clinical event ↓ Clinical event management + subsequent clinical events ↓ Resources used to manage events and outcomes of events ↓	Stroke ↓ Acute care and rehabilitation + sequelae and complications of treatment ↓ 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 [v10.1303.05]

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 Ideagen Quality Management (IQM). 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 IQM. 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.

Modifications to a trial protocol (see section 6.10) may require the HEAP to be updated. Any changes to the HEAP will be detailed in the version history.

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.

13.4 Pilot studies and pre-trial modelling [v10.1304.02]

Data collection tools should always be piloted before use within trials. Where relevant, preference should be given to published validated instruments for collection of resource use and quality of life outcome data.[6-8] 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[3,5].

13.5 Economic reports [v10.1305.01]

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 [v10.1306.03]

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 [v10.1307.02]

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 Handling of Secure External Data for Economic Analysis [v10.1308.01]

Where the health economists are required to access and analyse data from secure external providers (e.g. NHS England, Secure EDRIS, or other restricted-access data sources), all access, handling, storage, and processing of such data must be conducted in accordance with the requirements described in section 10.3.2.

The trial health economists are responsible for ensuring that economic analyses using these data are conducted only within the approved secure environment and in compliance with the relevant data governance requirements, data sharing agreements, and University of Aberdeen policies.

Economic code, outputs, and associated documentation must be managed and archived in accordance with health economic procedures (see section 13.9, below), whilst continuing to comply with the restrictions defined in section 10.3.2.

All health economists must adhere to these requirements when working with secure external data to ensure compliance with legal, contractual, and ethical obligations.

13.9 Economics archiving [v10.1309.01]

At the end of the trial, all code used to process and analyse the data for the health economic evaluation will be preserved so that the results in the report may be re-produced if required at a future date. Once the final analyses are completed and the results published, all economic analysis code and data will be securely archived by the trial health economists(s).

13.10 Partnerships with external economists [v10.1310.01]

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).

RELATED REFERENCES AND RESOURCES

[1] Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value in Health 2022; 25(1): 3-9

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

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

[4]Ramsay SD, et al. Cost-Effectiveness Analysis Alongside Clinical Trials II—An ISPOR Good Research Practices Task Force Report - Value in Health 2015; 18(2): 161-172

[5]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.

[6] ModRUM - Modular Resource-Use Measure - Bristol

[7] EuroQol Group - EuroQol Five Dimension Five Level Descriptive System

[8] Reilly Associates – Work Productivity and Impairment Questionnaire

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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs.	Aug 2025
10	Updates to text (section): to add references to the updated CHEERS reporting standards and ISPOR good research practices for Cost-Effectiveness Analysis Alongside Clinical Trials II (13.1) and validated health economic data collection instruments that are typically to be used where relevant (13.4). Minor changes to section 13.3 to detail the process following protocol modifications. Addition of two new sections: 13.8 on Handling of Secure External Data for Economic Analysis and 13.9 on Economic evaluation archiving.	Feb 2026

CHAPTER 14: EMBEDDED PROCESS EVALUATIONS
[v10.1400.05]

LEAD AUTHORS
Process evaluation leads.

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

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.

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 [v10.1401.03]
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 [v10.1402.03]
Analysis of process evaluation work within CHaRT trials will be specified in the trial protocol, and supported, where appropriate, by a process evaluation analysis plan (PEAP). A **PEAP** template is available on Ideagen Quality Management (IQM) to support trial delivery.

The PEAP sets out a pre-specified analysis plan for the analysis of process evaluation data, aligned with the evaluation's aims and objectives and the methodological approaches to be used. Consistent with the purpose of process evaluations, the analysis may also be responsive to emerging and pertinent issues identified during the course of the trial.

The PEAP will be developed iteratively as the trial progresses, in accordance with the plans outlined in the trial protocol and in collaboration with the wider research team. It will be finalised before any data analysis commences. Where appropriate, the PEAP is expected to include a set of *dummy tables* (*a priori*–agreed tables illustrating how the final process evaluation results will be reported).

Modifications to a trial protocol (see section 6.10) may require the PEAP to be updated. Any changes to the PEAP will be detailed in the version history.

It is expected that the PEAP should be available to interested researchers (for example, on the trial website). It is authored by the trial process evaluation lead and approved by the (CI) on behalf of the TSC (and grant holders).

14.3 Process evaluation reports [v10.1403.02]

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.

14.4 Process evaluation quality control [v10.1404.02]

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 essential records relating to process evaluation can be held as a hard copy, electronic or a hybrid system, and form part of the wider trial master file (TMF; see section 5.10). The process evaluation aspects of the TMF, which is referred to as a Study Master File (SMF), will be created and maintained by the trial specific process evaluation researcher(s).

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

14.5 Process evaluation archiving [v10.1405.01]

At the end of the trial, once the final analyses are completed and the results published, all process evaluation documentation and data will be securely archived by the process evaluation researcher(s). In addition, the SMF (described above), should be checked for completeness to ensure documents are filed and/or stored correctly before archiving.

14.6 Partnerships with external researchers [v10.1406.03]

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** available on IQM.

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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs	Aug 2025
10	Updates made to sections 14.2 to provide more detail on the development and use of the PEAP, and 14.4 to provide information regarding the filing of process evaluation essential records and maintaining a process evaluation master file. Addition of a new section: 14.5 on Process evaluation archiving.	Mar 2026

CHAPTER 15: PATIENT AND PUBLIC INVOLVEMENT
[v10.1500.09]

LEAD AUTHOR
PPIE coordinator.

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

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**' them[1]. 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 a 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 instance[2].

APPLICABILITY
Essential reading for all CHaRT staff

PATIENT AND PUBLIC INVOLVEMENT (PPI)

An 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 a 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 standards to promote best practice in the involvement of patients and the public for better health and social care research, for example:

- sites.google.com/nihr.ac.uk/pi-standards/home
- 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

15.1 Who should I involve? [v10.1501.03]

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 [v10.1502.05]

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/).

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 Ideagen Quality Management (IQM)) and a role descriptor (please see the **role descriptor for PPI partner co-applicant** document available on IQM) 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 IQM, 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 [v10.1503.06]

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

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 5.12).
- 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 IQM.

15.4 Remuneration of PPI partners [v10.1504.04]

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 IQM. 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 [v10.1505.02]

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

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 IQM) 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 IQM 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, 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 a 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 [v10.1506.02]

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[4] 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)[5].

15.7 ACE Public Involvement Partnership Group [v10.1507.02]

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

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.

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

[1]www.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).

[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

[4]Staniszewska S, Brett J, Simera I, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. Res Involv Engagem 2017;3:13.

[5]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.

Additional references:

ACE PPI Handbook available on IQM

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.

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 of two new sections to provide information on Supporting PPI partners and the best methods for documenting PPI (15.5 and 15.6).	Feb 2020
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs. Reference to the ACE PPI Handbook added to the 'Related references and resources' section.	Aug 2025
10	Addition of the weblink to the UK Standards for Public Involvement in Research website in text before section 15.1. Deletion of the sentence 'The PPIE coordinator can be contacted to identify individuals in the group with the relevant experience' at the end of the first paragraph in section 15.7. Reference to the GRIPP2 reporting checklists added to the 'Related references and resources' section.	Mar 2026

CHAPTER 16: CHaRT STAFF TRAINING
[v10.1600.08]

LEAD AUTHOR
Head of trial management and quality assurance manager.

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.

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.

APPLICABILITY
- Essential reading for all CHaRT staff.

CHaRT STAFF TRAINING

16.1 General [v10.1601.05]
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 [v10.1602.01]
It is a minimal requirement that **all** CHaRT staff – including trialists, trial managers, statisticians, IT programmers, data co-ordinators, research managers, health economists, qualitative researchers, clinicians– have appropriate up to date Good Clinical Practice ((GCP) or Good Research Practice (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.

16.3 Trial system training [v10.1603.01]

Prior to the CHaRT trial system going live, the CHaRT trial team will receive training in the use of the trial-specific system as detailed in the **User acceptance and All site testing** working practice document available on IQM. The trial system is a single integrated web-based application which supports trial activities such as participant registration, eligibility, randomisation, electronic consent (eConsent), electronic patient-reported outcomes (ePRO), participant follow-up, and Investigational Medicinal Product (IMP) management, where applicable.

The purpose of this training is to ensure that the trial team are familiar with all aspects of the trial system and can support participating sites and deliver site training. Training will be coordinated by the CHaRT programming team, in liaison with the trial manager, and will include demonstration and explanation of all relevant functionality.

The trial team, who will be provided with access to the trial system test environment, will be required to complete documented end-to-end testing prior to go live, including user acceptance testing (UAT; see section 10.2.4). This will include undertaking the full participant journey and relevant trial management functions within the trial system, as applicable to the trial, including:

- Participant registration/eligibility
- Completion of baseline data
- Electronic consent processes, where applicable
- Randomisation, where applicable
- IMP management, including ordering, accountability, and reconciliation, where applicable
- Completion of participant questionnaires (ePRO), where applicable
- Follow-up and participant management functions

The trial team, together with the programming team, is responsible for confirming that the trial system is functioning as expected from a user perspective.

Following completion of this training and testing, the trial team will use the trial system and supporting guidance to train and support site staff. Access to the live trial will only be provided once trial team training and testing has been completed. Documentation of the completion of trial team training and testing will be recorded on the **database authorisation to go-live form** (see section 10.2.6).

16.4 Training records [v10.1604.06]

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. A **training log** template can be found on Ideagen Quality Management (IQM) (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 CHaRT 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 CHaRT TMF for the trial they worked on.

16.5 Training feedback [v10.1605.03]

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 on relevant Sponsor SOPs, and section 16.4 includes more detailed information about the new training feedback process.	Nov 2021
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
09	Swapping the order of the 'Background' and 'Purpose' paragraphs.	Aug 2025

10	Addition of a new section: 16.3 Trial system training to document the purpose and process for training on the local trial-specific system managed by the CHaRT programming team.	Mar 2026