Writing a protocol for CTIMPs

Division: Strategy and Transformation

Specific staff groups to whom this policy directly applies	Likely frequency of use	Other staff who may need to be familiar with policy
This SOP should be used by investigators, trial managers and research team members involved in CTIMPs sponsored by NBT. However, it is also relevant for researchers preparing protocols for non-CTIMPs.	Role Dependant	Staff not employed by North Bristol NHS Trust who are requesting the Trust's sponsorship for a research study.

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Version:	Version 4.1
KEYWORDS:	Protocol, Protocol wording, CTIMPs, HRA templates.
Summary of changes since the previous version	SOP naming convention updated. R&I reference updated to R&D. Inclusion of wording to clarify the process of protocol writing. Regulatory and ICH references updated to align with the 2025 UK Clinical Trials Regulations and latest ICH GCP / ICH E3 (R6), effective from 28th April 2026.

	General editorial improvements have been applied throughout the SOP to enhance readability and improve the overall flow of content

1. Purpose	The purpose of this SOP is to set out the requirements for the development of study protocols that comply with ICH Good Clinical Practice (GCP) standards and the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended, including updates introduced in the 2025 Amendment Regulations. noting that amendments introduced by the 2025 Regulations come into force on 28 April 2026.
2. Key Messages	All NBT sponsored clinical trials of an investigational medicinal product must have a written study protocol prepared using the relevant Health Research Authority (HRA) templates and in accordance with the guidance set out in this SOP. A study protocol is a vital controlled document that describes how a research study will be conducted. It sets out, as a minimum, the background, objectives, rationale, study design, population to be studied, governance and oversight arrangements, data collection and management processes, statistical analysis, and archiving requirements. The protocol must clearly document the roles and responsibilities of all key stakeholders involved in the research, including (where applicable) the Sponsor, Chief Investigator, Statistician, Trial Coordinator, and Funder. **Abbreviations** **CTIMPS** Clinical Trials of Medicinal Investigational Products **HRA** Health Research Authority **MHRA** Medicine and Healthcare Products Regulatory Agency **ICH GCP** International Conference on Harmonisation guidelines for Good Clinical Practice **NBT** North Bristol NHS Trust **R&D** Research and Development **SOP** Standard Operating Procedure

	CI Chief Investigator
3. Relevant Policies & Guidance	**Policy and Guidance** • Health Research Authority ; https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/ • UK policy Framework for Health and Social Care Research • The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended. • ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 (R3) • https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/ The following R&D documents are available via LEARN or by contacting the R&D office on Research@nbt.nhs.uk **Associated SOPs** • RD/QMS/SOP/007 Applying for NBT Sponsorship • RD/QMS/SOP/010 Archiving • RD/QMS/SOP/013 Safety Reporting: Clinical Trials of Investigational Medicinal Products (CTIMPs) • RD/QMS/SOP/014 Monitoring
4. Operational Areas Included	This SOP is applicable to all research sponsored by the Trust.
5. Operational Areas Excluded	Research sponsored by other organisations.
6. Who should read this	This SOP should be used by investigators, trial managers, and research team members involved in CTIMPs sponsored by North Bristol NHS Trust (NBT). The principles outlined within this SOP are also applicable to researchers' developing protocols for non-CTIMP studies
7. Roles responsible for	A sponsor is an organisation which takes responsibility for the initiation, management, and quality assurance of a research study:

carrying out this procedure	The UK Policy Framework for Health and Social Care Research define a sponsor as: "The organisation taking primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting" [For Clinical Trials of Investigational Medicinal Products (CTIMPs), the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended, define the Sponsor as: *"The person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial."* Sponsor Responsibilities under the Clinical Trials Regulations Under the UK Clinical Trials Regulations, the Sponsor holds legal responsibility for ensuring that clinical trials are conducted in compliance with applicable regulatory and ethical requirements. These responsibilities include, but are not limited to: • Obtaining clinical trial authorisation and a favourable Research Ethics Committee opinion • Ensuring compliance with Good Clinical Practice (GCP) and oversight of the conduct of the clinical trial • Pharmacovigilance, including safety reporting and signal management • Arrangements for the manufacture, labelling, and supply of investigational medicinal products (IMPs) **Delegation of Sponsor Responsibilities** The Sponsor may delegate specific functions to third parties; however, any such delegation must be clearly documented and agreed in writing. Notwithstanding delegation, the Sponsor retains ultimate accountability and responsibility for all aspects of the study sponsorship.

8. Procedure:

8.1 Protocol template

All study protocols for Clinical Trials of Investigational Medicinal Products (CTIMPs) to be sponsored by North Bristol NHS Trust (NBT) must be prepared using the relevant templates and

guidance produced by the Health Research Authority (HRA), unless an alternative approach has been agreed in advance by NBT as Sponsor.

a) CTIMP Protocol Template and Guidance
The HRA CTIMP protocol template and associated guidance available via the Health Research Authority website (www.hra.nhs.uk).

b) Participant Information Sheet and Informed Consent Guidance
HRA guidance on the design and content of Participant Information Sheets and Informed Consent Forms, including applicable templates, available via the Health Research Authority website (www.hra.nhs.uk).

c) Inclusion Guidance
Research Studies, protocols, and study documentation should be developed with appropriate involvement of patient and public involvement with particular consideration of the relevant patient population ensuring under-served groups are enabled and empowered to participate. (Improving inclusion of under-served groups in clinical research: Guidance from INCLUDE project | NIHR

8.2 Protocol wording

Where NBT is the Sponsor of the CTIMP, the following wording should be incorporated into the relevant sections of the protocol:

Protocol Section	Standard Wording
Details of Sponsor	North Bristol NHS Trust, Research & Development, 3rd Floor, Learning & Research Building, Southmead Hospital, Westbury-on-Trym, Bristol, BS10 5NB
CI and Research Team Contact Details	Enter the Chief Investigator's contact details, including correspondence address and emergency contact details. Include contact details for relevant/key members of the research team such as trial manager, pharmacist and statistician.
Reference Numbers	Please ensure that you include all reference numbers including but not limited to the protocol version, IRAS number, trial registry number and Funder number
Study Medication	In addition to a description of study medication, doses, regimen, etc: Please refer to the pharmacy manual (version)… Study medication will be stored and dispensed by the trial site's pharmacy department in accordance with Good Clinical Practice, Good Manufacturing Practice and pharmacy department SOPs.

Safety Reporting	Adverse events will be recorded, assessed, and reported in accordance with North Bristol NHS Trust (NBT) Sponsor SOP for Safety Reporting and applicable regulatory requirements. The protocol may identify specific events that are excluded from expedited reporting, where these events are anticipated, well characterised, and commonly associated with the underlying condition or clinical procedures being undertaken. Any such exclusions must be justified, documented, and agreed with NBT as Sponsor prior to submission for regulatory and ethical approval. The justification for excluding events from expedited reporting must be supported by appropriate reference documentation, such as relevant product information, Investigator's Brochure, Summary of Product Characteristics (SmPC), published literature, and the justification captured within the study risk assessment. Further details regarding safety reporting requirements, including definitions, reporting timelines, and Sponsor oversight arrangements, are set out in NBT SOP: Safety Reporting – Clinical Trials of Investigational Medicinal Products (CTIMPs) (RD/QMS/SOP/013).
Reference Safety Information (RSI)	The following document will be used as the Reference Safety Information (RSI) for the duration of the trial: • Summary of Product Characteristics (SmPC) for XX [name of IMP], where the IMP is licensed and used in accordance with its marketing authorisation. OR • Investigator's Brochure (IB) for XX [name of IMP], where the IMP is unlicensed or used outside the terms of its marketing authorisation. And +/_ • Other documents (delete/amend as appropriate) The applicable RSI will be clearly identified prior to trial commencement and documented in the Trial Master File. If there are any updates made to the document described above, these will be reviewed by the Chief Investigator and Sponsor, and a joint decision is made to whether the updated

	document will be submitted to the MHRA as modification for use as the RSI in the trial. * Terminology note from 28 April 2026, the amended regulations use the term "modification" (including categories such as substantial modification). Where legacy documentation refers to "substantial amendments", this should be interpreted as the equivalent change control concept for the purpose of local documentation and filing
Data Management	The protocol should refer to the Data Management Plan (DMP) which will give specific information regarding the management of the data during and at the end of the trial. Please refer to SOP on Data Management (RD/QMS/SOP/017) for further information.
Monitoring, Audit and Inspection	The study will be monitored in accordance with North Bristol NHS Trust's Monitoring SOP. All trial related documents will be made available on request for monitoring and audit by North Bristol NHS Trust or a trial unit (if monitoring is delegated to them by sponsor), the HRA and for inspection by the Medicines and Healthcare Products Regulatory Authority or other licensed bodies. The monitoring plan will be developed and agreed by the sponsor.
Quality Control	Quality control activities will be undertaken in accordance with risk-based quality management principles, proportionate to the nature, complexity, and risk profile of the study, as determined during study setup. Where applicable, a representative sample of Case Report Forms (CRFs), normally at least 10%, will be reviewed to verify data accuracy, completeness, and consistency against the study database and relevant source documentation. The scope and frequency of these checks may be increased where a significant error rate, protocol non-compliance, or data integrity concerns are identified. For multicentre studies, data relating to the first participant recruited at a new site will undergo focused review. This review may include, but is not limited to, verification of informed consent documentation, key safety data, and primary endpoint data. NBT Sponsor Led Studies For studies in which North Bristol NHS Trust (NBT) acts as Sponsor and retains oversight and monitoring responsibilities, quality control and data review activities will be conducted by the trial coordinating unit and/or authorised R&D personnel in accordance with the approved monitoring and quality management arrangements.

	Externally Managed Studies Where monitoring or data management activities are delegated to an external organisation, including a Clinical Research Organisation (CRO) or collaborating partner, the extent of quality control, source data verification, and monitoring activities will be defined within the relevant agreements. NBT, as Sponsor, will retain oversight responsibility and will ensure that appropriate assurance mechanisms are in place to confirm that delegated activities are conducted in compliance with regulatory and GCP requirements. **Link to Risk Assessment** The extent and intensity of quality control activities will be informed by the documented risk assessment conducted at study set-up and reviewed throughout the lifecycle of the study, with adjustments made as necessary in response to emerging risks or issues.
Data Handling & Protection	Data handling arrangements for all studies will be designed to ensure the confidentiality, integrity, and security of participant information and to comply with applicable data protection legislation, including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. Study databases and, where applicable, randomisation systems must be configured to restrict access to authorised personnel only and to protect personal data against unauthorised access, loss, or disclosure. Trial staff are responsible for ensuring that participant confidentiality is maintained at all times through secure handling, processing, and storage of study data at trial sites and coordinating centres, as appropriate. Participant data will be anonymised or pseudonymised wherever possible, in accordance with the study protocol and data protection requirements. All essential documents and source data will be stored securely, whether in electronic or paper format, and will be accessible only to authorised study personnel, the Sponsor, and regulatory authorities, as required. Data will be collected, processed, retained, and archived in accordance with the study protocol, Sponsor requirements, and relevant data protection legislation.

Storage of Records	Study documents (paper and electronic) will be retained in a secure location during and after the trial has finished. All essential documents, including patient records and other source documents, will be retained in accordance with North Bristol NHS Trust's Archiving SOP following the end of a study. Where electronic records are in use, Trust policy will be followed.
Indemnity	"**North Bristol NHS Trust (NBT)**, as the Sponsor of this study, provides indemnity for negligent harm to participants through the NHS indemnity schemes. This covers negligent acts or omissions by NBT or by NHS staff conducting the research as part of their NHS duties. NBT is unable to offer compensation for non-negligent harm, as NHS indemnity does not provide no-fault cover. Participants retain the right to pursue a negligence claim through normal legal channels. Where any part of the study is conducted by non-NHS organisations or individuals, those parties will have their own appropriate insurance or indemnity arrangements in place."
Authorisations	The study will be conducted subject to the receipt of all required regulatory approvals, favourable opinions, and permissions, as applicable. This includes approvals from relevant bodies such as the Medicines and Healthcare products Regulatory Agency (MHRA), Health Research Authority (HRA), Research Ethics Committee (REC), and participating NHS organisations, where required.
Research Governance Statement	This study will be conducted in accordance with: The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended, including amendments introduced by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 International Council for Harmonisation (ICH) Guideline for Good Clinical Practice (GCP) E6 (R3) UK Policy Framework for Health and Social Care Research

8.3 DISSEMINATION AND TRAINING

SOPs will be distributed in accordance with the SOP on Preparation of Research SOPs (RD/QMS/SOP/001).

This SOP and any associated templates and forms will be uploaded to the Trust website (www.nbt.nhs.uk/research) and to LEARN on the Trust intranet shortly after having been released.

All staff whose activities are subject to this SOP should ensure that they read and understand the content of this SOP.

The training log within the Investigator Site File/Trial Master File should be completed to document that members of staff have read and understood the content of this SOP.

9. References (if applicable):

- Health Research Authority
  - *UK Policy Framework for Health and Social Care Research*
  - www.hra.nhs.uk

- ICH Secretariat
  Guidelines for Good Clinical Practice (GCP) (E6 R3 Step 4, 2025)
  https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

- The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025/538).
- https://www.legislation.gov.uk/uksi/2004/1031/contents
  https://www.legislation.gov.uk/uksi/2025/538/contents

- Health Research Authority
  Protocol guidance and template for use in a CTIMP
  www.hra.nhs.uk