Data Management

Division: Trust-Wide

Specific staff groups to whom this policy directly applies	Likely frequency of use	Other staff who may need to be familiar with policy
Staff employed by North Bristol Trust who directly or indirectly work on Clinical Research within the Trust	Role Dependant	Staff not employed by North Bristol NHS Trust who are working on Research studies sponsored or hosted by NBT

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Consultation:	R&D Sponsorship Team
Approval Authority (Committee/ Group/ Lead Clinician):	R&D Senior Team
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KEYWORDS:	Data management plan, Case report forms, Trial Master file, Investigator site file, Essential Documentation, computer systems validation
Summary of changes since the previous version	Changed format to align with NBT SOP template Changed R&I to R&D Added information in relation to responsibilities when working with Clinical Trials Units. Change the naming convention of R&D SOP's Editorial changes have been made to sentence construction to improve clarity, flow, and consistency across the R&D SOP suite.

1. Purpose	The purpose of this SOP is to describe the standards required for the collection, maintenance, verification, correction, transfer, and analysis of data generated by Clinical Trials of Investigational Medicinal Products (CTIMPs) sponsored by NBT. For CTIMPs, these standards are defined by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and by ICH Good Clinical Practice (E6 (R3)). Data generated through research may inform or influence changes in clinical practice; therefore, robust systems must be in place to ensure data integrity, traceability, and participant safety throughout the data lifecycle. This includes the ability to clearly demonstrate the origin of the data, how it has been processed and verified, and the systems through which it passes from collection through to analysis and publication, as well as to document the effects of investigational medicinal products on participants.
2. Key Messages	Research studies generate substantial documentation throughout their lifecycle, including before, during, and after study conduct. All documentation must be complete, accurate, legible, and readily accessible to support effective monitoring, audit, and regulatory inspection. NBT, as Sponsor, retains ultimate responsibility for ensuring that appropriately qualified and trained individuals are in place to oversee the conduct of the study, including data handling, verification, analysis, and reporting, in accordance with ICH Good Clinical Practice. For NBT-sponsored studies, data management activities may be delegated to the Chief Investigator (CI) and study team, however Sponsor oversight and accountability for data integrity, reliability, and compliance with regulatory requirements are retained. All study documentation for NBT-sponsored research must be developed, used, and maintained in accordance with NBT Research SOPs and the Trust's research governance framework. Patient-facing documentation and study protocols must be developed in line with Health Research Authority (HRA) guidance, ensuring appropriate ethical standards, transparency, and participant protection. Terminology: The term "participating site" is used throughout and should be read interchangeably with "trial location" where applicable for clinical trials of investigational medicinal products, in line with the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.

	Abbreviations **CI** Chief Investigator **CRF** Case Report Form **CTIMP** Clinical Trial of an Investigational Medicinal Product **CTU** Clinical Trials Unit **DMP** Data Management Plan **ICH GCP** International Conference on Harmonisation for Good Clinical Practice **IDMC** Independent Data Monitoring Committee **ISF** Investigator Site File **HRA** Health Research Authority **NBT** North Bristol Trust **PI** Principal Investigator **R&D** Research and Development **REC** Research Ethics Committee **RSI** Reference Safety Information **MHRA** Medicine Healthcare Regulatory Agency **SOP** Standard Operating Procedure **TMF** Trial Master File **TSC** Trial Steering Committee
3. Relevant Policies & Guidance	**Policies and Guidance:** Medicines for Human Use (Clinical Trials) Regulations 2004, as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 ICH Guideline for Good Clinical Practice E6 (R3) UK Policy Framework for Health and Social Care Research UK General Data Protection Regulation (UK GDPR) and Data Protection Act 2018

	The following NBT documents are available on the R&D website: www.nbt.nhs.uk/research **Associated SOP's and Templates:** RD QMS SOP 003 Research Study Modifications RD QMS SOP 007 Applying for North Bristol Trust Sponsorship RD SOP SOP 008 Writing a protocol for CTIMPs RD QMS SOP 015 Computer System Validation and Backup RD/QMS/SOP/012 Managing Breaches of Good Clinical Practice or the Protocol
4. Operational Areas Included	This SOP applies to all research studies sponsored by NBT, and to externally sponsored studies hosted by NBT, where NBT is responsible for the collection, management, processing, or oversight of research data.
5. Operational Areas Excluded	Trust-wide information governance, records management, or clinical data systems that are not used for research purposes and are governed by separate Trust policies and procedures.
6. Who should read this	This SOP should be used by Investigators and all members of the research team involved in research studies sponsored by NBT. This SOP may also be used as guidance by research team members involved in externally sponsored studies hosted by NBT, where NBT has responsibilities for the collection, management, or oversight of research data. Where NBT sponsors a study in collaboration with external stakeholders, such as Clinical Trials Units (CTUs), external SOPs or procedures may be utilised to support project delivery and governance, provided they meet the requirements of this SOP. The NBT Sponsorship Team must ensure that any external SOPs are reviewed and considered equivalent to, and aligned with, NBT procedures. In the event of any conflict between an external SOP and NBT procedures, this SOP will take precedence, unless an explicit exception has been reviewed and approved by the Research Operations Manager or the Deputy Director of Research.
7. Roles responsible for	**Chief Investigator (CI)**

carrying out this procedure	he Chief Investigator (CI) is responsible for the development and maintenance of the Data Management Plan (DMP) for NBT-sponsored studies, ensuring that it accurately reflects the approved protocol and planned data management processes. The CI must inform the Sponsor of any computerised systems used for the purpose of data collection, storage, processing, or analysis that require validation, in accordance with the SOP on Computer System Validation & Backup (RD/QMS/SOP/015). All study documentation for NBT-sponsored studies must be created, implemented, and maintained in accordance with NBT Research SOPs. The development of the Data Management Plan and the Protocol must be undertaken in line with Health Research Authority (HRA) guidance and applicable regulatory requirements. Any instances of data breaches, unauthorised data handling, or management of data outside the scope of the approved protocol will be considered breaches of Good Clinical Practice. Such incidents must be managed in accordance with the SOP on Managing Breaches of Good Clinical Practice or the Protocol (RD/QMS/SOP/012). **NBT Sponsorship Team** The NBT Sponsorship Team supports the Sponsor in providing oversight and assurance in relation to data management arrangements for sponsored studies. For CTIMPs and device trials, the Sponsorship Team will liaise regularly with the Chief Investigator and/or Trial Manager to review the Data Management Plan and determine whether updates or modifications are required during the lifecycle of the study. For CTIMPs, the NBT Sponsorship Team is responsible for the review and approval of Data Management Plans on behalf of the Sponsor. All approved Data Management Plans must be formally signed by both the Chief Investigator and the Sponsor prior to implementation and following any substantive updates. **Trial Manager / Study Manager:** Responsible for supporting the Chief Investigator in implementing and maintaining the Data Management Plan, coordinating data collection and data query resolution, and liaising with the NBT Sponsorship Team on data management issues, deviations, or required updates to the Data Management Plan.

8. Procedure:

8.1 Maintaining the Trial Master File (TMF) and Investigator Site File (ISF)

ICH Good Clinical Practice (GCP) defines documentation as “all records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, X-rays, and electrocardiograms) that describe or record the methods, conduct and/or results of a trial, the factors affecting a trial, and the actions taken.”

In accordance with ICH GCP E6(R3), essential records (previously referred to as “essential documents”) are those records which individually and collectively permit evaluation of the conduct of a trial, the compliance of the investigator and Sponsor with GCP and applicable regulatory requirements, and the reliability of the results produced. Essential records therefore represent the minimum records required to be maintained for a research project.

Essential records are generated and collected before, during, and after the conduct of a clinical trial. The specific essential records required will vary depending on the nature, complexity, and risk of the study and must be determined on a study-specific, risk-based basis, in collaboration with the Sponsor and the R&D Sponsorship Team.

The Trial Master File (TMF) and Investigator Site File (ISF) represent the standard filing systems for the storage of essential records. The Sponsor retains ultimate responsibility for ensuring that a complete and accurate TMF is maintained, with day-to-day maintenance delegated to the Chief Investigator (CI). For NBT-sponsored studies, the TMF and NBT’s ISF may be combined where appropriate. Each participating site must maintain a separate ISF under the responsibility of the site Principal Investigator (PI).

The Site File Template available on the NBT website must be used to determine the appropriate content and structure of the TMF and ISF. Standards for maintaining these files are outlined in Table 1 of this SOP.

The TMF and ISF may be maintained in paper, electronic, or hybrid format, provided that records are complete, secure, version-controlled, and readily accessible for monitoring, audit, or regulatory inspection.

The R&D Sponsorship Team will retain electronic records relating to research governance and sponsorship activities but is not required to retain Case Report Forms (CRFs) or other source documentation, which remain the responsibility of the research sites.

Storage	Documents and records contained within the Trial Master File (TMF) and Investigator Site File (ISF) may include original regulatory approvals and confidential or sensitive information. These files must therefore be stored securely with access restricted to authorised personnel only. Records may be maintained across separate folders, files, cabinets, or electronic systems; however, the TMF and ISF must clearly document where all records are held to ensure they can be readily identified and accessed when required. The TMF and ISF may be maintained in paper, electronic, or hybrid format, provided that systems used are secure, access-controlled, version-controlled, and include appropriate audit trails. Electronic systems used for the storage of trial records must comply with

	applicable regulatory requirements and NBT procedures, including validation, backup, and data security arrangements. Direct access to all trial-related data and records must be provided for the purposes of quality control, quality assurance, monitoring, audit, or regulatory inspection.
Quality	All records must be complete, accurate, legible, and contemporaneous, and must be maintained in a manner that allows monitors, auditors, and inspectors to readily access and understand the conduct of the study and the data generated.
Version Control	A system should be in place for version control of documents. It is recommended that a chronology of modifications is kept on file that records all the modifications submitted and the documents that they relate to. Old version of documents should be retained on file alongside the new versions and old versions clearly marked as no longer being used. Information on modifications can be found in SOP on Research Study modifications (RD/QMS/SOP/003).

Table 1: Standards that should be met when maintaining the TMF and ISF

8.2 Protocol

The protocol must clearly define which data will be collected and the timing of data collection in order to support the scientific objectives of the study and ensure data integrity. Further requirements for protocol design are outlined in the SOP on Writing a Protocol for CTIMPs (RD/QMS/SOP/008).

For NBT-sponsored studies, the protocol must be reviewed and formally approved by the Sponsor, through the R&D Sponsorship Team, prior to any regulatory submissions, including submissions relating to protocol modifications, in accordance with the SOPs on Applying for North Bristol NHS Trust Sponsorship (RD/QMS/SOP/007) and Research Study Modifications (RD/QMS/SOP/003).

The Chief Investigator must formally sign and approve the final protocol, either by wet-ink or electronic signature, following receipt of the relevant regulatory and HRA approvals and prior to study initiation.

8.3 Data Management Plan

A robust Data Management Plan (DMP) is required for all CTIMPs. The DMP must be approved by the Sponsor prior to study initiation and as required during the course of the trial.

Data management will be included as a standing agenda item at the trial management meetings between the Sponsor and Trial Manager and will be checked as part of monitoring. The DMP should be reviewed at least every 12 months.

In the case of non-CTIMPs, the Sponsor will take a proportionate risk-based decision regarding the need of a separate formal DMP, taking into consideration the complexity of the study and whether there is sufficient information in the Protocol.

The DMP should specify the following information:

- Where the Reference Safety Information (RSI) is located, i.e. Investigational Brochure or SmPC.
- How data will be collected, clarified, stored and analysed with reference to the database lock process and audit trails.
- How eligibility of participants is assessed and documented.
- How trial related information is provided to participants and documented.
- The requirements for baseline data to be obtained and documented, and the implications if this is not adhered to.
- Registration of studies on appropriate public registries
- Publication of research data and study outcomes
- Communication of research findings and data to participants following study completion

An R&D recommended DMP template is available on the NBT website (www.nbt.nhs.uk/research). If an alternative DMP template is to be used, approval by the Sponsor is required.

8.4 Case Report Forms (CRFs)

A CRF is "a printed, optical or electronic document designed to record all of the protocol-required information to be reported to the Sponsor on each [research] subject." The CRF is the primary document enabling collection of data. The case report form (CRF) may be maintained in either electronic or paper format. Standards that should be met in relation to the design, completion, review and storage and corrections to CRFs are outlined in Table 2.

Design	The CRF must be designed by the CI before the research begins. It should be designed to only collect data as required in the protocol and nothing more, to comply with data protection requirements. CRFs may be paper or electronic. Original paper CRFs form part of the trial master file, as an essential records. Any electronic CRF collection systems must be validated in and managed in accordance with the Computer System Validation & Backup SOP (RD/QMS/SOP/015). Any verification of data which must be done by particular members of the research team (e.g. inclusion/exclusion criteria and safety data by medically qualified staff) must be evidenced. For paper CRFs, this would usually take the form of a signature and date; for electronic CRFs, this may be carried out by means of audit software incorporating particular logins or documented separately within the source data. The CRF and any amended versions must be signed off by R&D prior to implementation.
Validation	The CRF must be reviewed by an appropriate range of staff prior to use to ensure that it supports efficient and accurate data collection, is user-friendly, and captures all data required to meet the aims and objectives of the study as defined in the approved protocol. Any changes to the CRF must be clearly documented, version-controlled, and retained within the Trial Master File (TMF). Revised versions of the CRF must be reviewed and

	approved by both the Sponsor, through the R&D Sponsorship Team, and the Chief Investigator before implementation.
Completion	The recording of data on the CRF should be performed by the PI at each trial site, however this responsibility may be delegated to other members of the team if appropriately trained. Paper CRFs should be completed in ink and data fields should not be left blank. Where there is no data to record in certain fields, they should be marked Not Applicable (N/A) or No Data (N/D). The precise completion of CRFs is vital to preserving confidence in the findings of the project and therefore any discrepancies between the data required and the data collected or the source data should be minimised and explained. Any changes or corrections to a CRF or entries within them should be dated, initialled and explained (where necessary) and should not obscure the original entry. There should be an agreed system and process in place for authorising changes to data. The CI should agree with the research team what changes are acceptable, and document this. For example, the CI may agree that any member of the research team can amend clear transcription errors where the source data have not been transcribed correctly into the paper CRF. Other items, such as medical assessments and safety data changes should be authorised by the CI. The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data recorded in the CRFs. CRFs should be completed at the earliest opportunity, contemporaneously with collection of source data wherever possible.
Review	The PI should regularly review the CRFs and source documents to identify any discrepancies, errors or deviations from the approved protocol. Protocol deviations should be documented and managed in accordance with the SOP on Managing Breaches of Good Clinical Practice or the Protocol (RD/QMS/SOP/012). The review of each CRF and source documents should be documented by the PI.
Storage	The CI must ensure provision is made for trial sites to retain a copy of the CRF at site, in accordance with this SOP and applicable regulatory requirements Direct access to CRF data must be provided for quality control and quality assurance reviews (e.g. monitoring and audit) or regulatory inspection.

Table 2: Standards that should be met with regards to CRFs

8.5 Source Data

Source data are defined as all information contained in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial that are

necessary for the reconstruction and evaluation of the trial. Source data represent the first recording of an item of information.

Source data are contained within source documents, which may be original records or certified copies. Source documents are considered essential records and serve to demonstrate compliance with ICH Good Clinical Practice (GCP) and applicable regulatory requirements.

The standards that must be met in relation to the identification, verification, retention, and accessibility of source data are outlined in Table 3 of this SOP.

Identifying source documentation	Prior to a trial commencing at a participating site, the PI at that site should identify what constitutes source documents at that site, and must record this on a Source Data Form. Source documentation may include (but is not limited to): hospital records, clinical and office charts, laboratory notes, memoranda, participant diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial. In certain circumstances, the Case Report Form (CRF) may act as the source document, where this is prospectively defined and documented. Source data may be captured initially within a permanent electronic record. In this context, permanent means that the system maintains a secure audit trail, capturing all data changes, including, as a minimum, the identity of the individual making the change and the date and time the change was made.
Source documentation verification	It must be possible to demonstrate that the source information supporting data recorded in the Case Report Form (CRF) existed at the appropriate point in time. Electronic systems used to capture source data must incorporate appropriate audit trail functionality or version control mechanisms that record, as a minimum, the date and time of data entry or amendment and the identity of the individual making the change. Paper source records must be contemporaneously completed and include a date and signature (or initials) to confirm when the data were recorded.
Source data retention	Source data must remain at the location at which it was generated. The location of all source data records should be documented to allow quick access. Direct access to data must be provided for quality control and quality assurance reviews (e.g. monitoring and audit) or regulatory inspection.

Table 3: Standards that should be met with regards to source data

8.6 Databases

A database is a repository for electronic data. Databases vary widely, depending on the size, type and complexity of the research being carried out. For a simple, small study, an excel spreadsheet can be used. At the other end of the spectrum are complex databases which have automated audit software and consistency checking capability, as well as the ability to generate data queries.

Standards that should be met with regards to databases are outlined in Table 4. The CI is delegated responsibility for setting up and managing databases for recording trial data. These must meet the standards described in the SOP on Computer System Validation & Backup (RD/QMS/SOP/015).

Design	A database must accurately reflect the CRF so that the data required by the protocol can be collected. The chief investigator must check that the database meets the needs of the study by reviewing and testing it and documenting that the database meets the required specifications (user acceptance testing). The database must have suitable audit trail functionality to ensure that all data entry and subsequent changes are fully traceable. All electronic database systems must be validated and managed in accordance with the SOP on Computer System Validation & Backup (RD/QMS/SOP/015). Points to consider when designing the database are: ease of setting up and maintaining data entry screens; the ability for more than one user to use the system at the same time; and the ability to store and retrieve all data required for the study efficiently. Where a trial includes blinded elements, the database must be designed to maintain blinding in accordance with the approved protocol and study procedures.
Data entry	CRF data queries should be raised, reviewed and resolved before entering data in the database. The process for managing data queries should be specified in the DMP. Data entry must be undertaken by appropriately trained members of the research team who have been formally delegated to perform these activities. Data should be entered in a format that allows for analysis, e.g. coded. Clinical data also needs to be coded for recording of all adverse events. Plans for coding must be incorporated into the DMP. To reduce errors, data should be checked. This may involve double entry checking (if sophisticated systems that allow for this are in use) or visual checking the database against CRFs. Records of checks and audit trails must be retained as part of the essential documents. Expected timelines for inputting the data across all participating sites should be included in the DMP, with a contingency plan should these timelines not be met. The Sponsor should be informed if the contingency plan is drawn upon, with regular reviews of the action.
Validation	Post-entry validation checks must be performed to verify the completeness, accuracy, and consistency of data entered into the study database. These checks

	may include the generation and review of listings identifying missing values, values outside predefined ranges, and other predefined validation criteria. Logical checks must also be undertaken to identify implausible or inconsistent data. All post-entry validation checks to be applied must be prospectively defined within the Data Management Plan (DMP) prior to study commencement. Records of all validation checks performed, together with associated outputs, resolutions, and audit trails, must be retained as part of the essential records.
Change control	As more data are entered, or changes are made it is important that an audit trail of the changes is available, so that previous versions of the datasets can be accessed if necessary. For validated database systems, audit trails should be generated automatically by the database software and must record all changes to data fields, including the previous value, the updated value, the date and time of change, and the identity of the individual making the change. For simpler database systems where automated audit trails are not available, change control must be managed through the controlled saving of successive dataset versions, with each version clearly labelled using a version number and date, and identifying the individual responsible for the modification (e.g. initials and surname). All records relating to data changes and version control must be retained as part of the essential records for the study.
Management	The CI should ensure there is a specific SOP for managing the study database. Adequate data backup arrangements must be in place to protect against data loss. Backup procedures must ensure that study data can be restored accurately and in a timely manner and must be implemented in accordance with Trust requirements and the SOP on Computer System Validation and Backup (RD/QMS/SOP/015), where applicable.
Access	Access to the study database must be appropriately restricted to prevent unauthorised access to data. The database must be secured through password-protected, role-based access controls, ensuring that users are granted access only to the functions necessary to perform their delegated duties. A current and auditable list of individuals authorised to access and make changes to the database must be maintained and reviewed periodically. Access rights must be updated promptly to reflect changes in roles, responsibilities, or study involvement.
Data Lock	Database locking is the formal process by which a study database is declared final and no further routine changes to the data are permitted. Once the database has been locked, no data must be amended, and appropriate technical and organisational controls must be in place to prevent unauthorised editing or deletion of data.

	Arrangements to protect locked data must be proportionate to the complexity and risk of the study and may include restricting user access, applying read-only permissions, and securing dataset versions in controlled storage locations. Unlocking a locked database must occur only in exceptional circumstances and requires prior agreement from the Sponsor, through the R&D Sponsorship Team, and the trial statistician(s). Written approval must be obtained before unlocking and must document the justification for unlocking, the specific changes to be made, and any potential impact on data integrity or statistical analysis. This documentation must be retained in the Trial Master File (TMF).
Data Release	Data should be extracted from the locked database to carry out the final analysis. The process to do this should be adequately described. Test extracts may be made, and these must be stored in a separate location to the extracted datasets on which the analysis will be performed.

Table 4: Standards that should be met with regards to databases

8.7 Publication Plan

A publication plan should be created as a standalone document or included within the DMP to ensure suitable dissemination of the results. This should include the publication of non-significant results and lessons which have been learnt from any errors during the development or delivery of the study.

8.8 Independent Data monitoring Committee (IDMC)

For large complex trials, the CI should establish an Independent Data Monitoring Committee (IDMC) to carry out reviews of trial data at staged intervals during the study.

The role of the IDMC is to review interim trial data and assess participant safety, study conduct, and, where applicable, emerging efficacy data, in order to determine whether there are any safety concerns or other reasons why the study should be modified, paused, or discontinued

The data reviewed by the monitoring committee should be as up to date as possible and should be validated up to the point of the interim analysis to ensure it is of sufficient quality.

The membership of the IDMC should include individuals with relevant expertise, such as experienced trial investigators, statisticians, and clinicians, all of whom must be independent of the study team. IDMC reviews should be conducted at intervals appropriate to the nature, complexity, and risk of the trial, as data accrue.

If there is a Trial Steering Committee (TSC) for the study, the IDMC would normally make their recommendations for action through them.

8.9 Data Protection

During all stages of data collection, management, validation, storage, analysis, and retention, study data must be processed in accordance with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018, as well as applicable Trust information governance policies and procedures.

Appropriate technical and organisational measures must be in place to ensure the confidentiality, integrity, and security of personal data, and to protect the rights and privacy of research participants.

9. Dissemination and Training

SOPS will be distributed in accordance with the SOP on Preparation of R&D Research SOPs (RD/QMS/SOP/001). This SOP and any associated templates and forms will be uploaded to the NBT website (www.nbt.nhs.uk/research) 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.