UNIVERSITY OF LEEDS / NHS The Leeds Teaching Hospitals NHS Trust Standard Operating Procedure	Title	Researchers Guide to Data Management				
	Scope	This SOP outlines the appropriate steps and considerations to be taken when constructing and implementing a data management plan				
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Distribution & Storage:

Distribution to:

Investigators and all members of research teams conducting or assisting with a CTIMP trial sponsored by the University of Leeds or Leeds Teaching Hospital NHS Trust.

Location of document:

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Electronic: http://www.leedsth.nhs.uk/research/information-for-researchers/key-documents
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Please note: *This SOP should be used and followed in conjunction with other UoL / LTHT SOPs developed for researchers to support study set up and management. These can be found on the LTHT website or by contacting R&I / QA directly. For clinical trials where Leeds is not the trial Sponsor, please refer to any Sponsor SOPs for further information.*

Section A: Introduction

1.1 A clear process for data management is critical to ensure that trial data is captured in accordance with the trial protocol and the Data Protection Act 1998.

1.2 Data management can be a complex process and inadequate planning from the outset can risk the overall integrity of the trial data.

1.3 Data Management encompasses a range of key aspects critical to a clinical trial such as data capture, data processing and the production of the final dataset for statistical analysis.

1.4 This SOP will outline the appropriate steps and considerations to be taken when planning and implementing the data management aspects of a clinical trial and must be read prior to completion of a data management plan and finalisation of the protocol.

1.5 All staff involved in data management must be appropriately trained in the relevant procedures they are expected to undertake prior to commencing the task.

1.6 The Sponsor delegates the overall responsibility for appropriate data management to the Chief Investigator (CI).

Section B: Applicability

1.1 This SOP is applicable to all members of staff working on non-CTU / Clinical Research Organisation managed CTIMPs sponsored by the University of Leeds (UoL) or Leeds Teaching Hospitals NHS Trust (LTHT).
(Note - A separate process is in place for CTU and CRO managed trials, please liaise directly with your point of contact for further information).

Section C: Researchers Guide to Data Management

1.0 Data Collection and Management

1.1 **The Chief Investigator and research team must decide on an appropriate method of data collection, documenting their decision within both the Data Management Plan (see section '2.0 Data Management Plans') and trial protocol prior to the commencement of the trial.**

1.2 Effective planning and implementation of data management procedures has many benefits for the research team including (but not restricted to):

- Ensuring data quality and integrity.
- Demonstrating compliance with ethical and regulatory requirements.
- Improved risk management by identifying any potential issues early.

- Ensuring that the data captured is easily understood and usable both now and in the future.

1.3 Consideration must be given to the appropriate capture of source data, the formal data capture tool (Case Report Form (CRF)) and any databases which will be used for data analysis.

1.4 Quality Control (QC) should be applied during each stage of the data collection and management process to ensure accurate and reliable reporting.

2.0 Data Management Plans

2.1 Data management plans are mandated for all trials submitted to Sponsor QA for approval from **1st October 2017.**

2.2 The purpose of a Data Management Plan (DMP) is to provide an overview of the data management processes that will be used for a particular trial, and provide assurance that trial data will be handled appropriately throughout the trial's duration.

2.3 A data management plan typically outlines the following key aspects:

- Source data location and capture (e.g. source data worksheets).
- Details regarding the Case Report Form (CRF) requirements.
- The planned validation and Quality Control (QC) checks.

2.4 The MHRA expect research teams to be able to demonstrate appropriate QC checks throughout the duration of the trial. A data management plan enables these checks / validation steps to be clearly defined and planned from the outset of the trial.

2.5 Sponsor QA must be provided with a complete data management plan using the ***CTT58 Data Management Plan*** template **before** Confirmation of Sponsorship can be issued. A copy of the template can be found on the R&I website or obtained directly from the Sponsor QA office.

2.6 **Please note, if an alternative data management plan has been completed as part of a grant application, this may instead be sent to QA. This will replace the need for a separate *CTT58 Data Management Plan*, however Sponsor QA may request further information to support their review.**

2.7 It is the responsibility of the Chief Investigator to ensure that the Data Management Plan is adhered to and updated as necessary for the duration of the clinical trial. Any changes to the plan **must be forwarded to QA for review in real time.**

3.0 Consolidation of Source Data

3.1 **Source data can be defined as all information in original records and certified copies of original records of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.** Please refer to ***LTU_QM23_A Researchers Guide to Source Documentation*** for further information.

3.2 Data is most frequently captured using a source data worksheet or recorded directly into the patients' medical records; however source data may also be located in patient diary cards, pharmacy records or captured directly at source electronically (e.g. laboratory results, imagining scans etc.).

3.3 All source data must be retained and be readily accessible throughout the trial's duration.

3.4 It is the responsibility of the Chief Investigator to ensure all CRF data points have a corresponding source, allowing monitors and GCP inspectors to perform Source Data Verification (SDV) checks.

3.5 Internal SDV checks must also be conducted in house, with the research team checking CRF and database entries for accuracy and completeness. **Such checks should be documented and referenced within your Data Management Plan.**

3.6 When source data is spread across multiple locations or formats (e.g. paper notes, electronic notes, scan images) **a source data location sheet is required**. Please see ***Appendix A*** for an example source data location sheet.

3.7 Source data location sheets allow staff to easily identify where specific data may be located at source. More than one location may be appropriate for different data (e.g. Adverse Events may be recorded in the medical notes, source data worksheets, clinic letters etc.) and the source data location sheet should be reviewed and updated as necessary throughout the trial's duration.

3.8 The source data location sheet should be submitted to QA alongside the ***CTT58 LTHT UoL CTIMP Data Management Plan***. Please forward any updated versions of this document to QA **in real time**.

4.0 Case Report Forms (CRFs)

4.1 A case report form (CRF) is a printed or electronic document used to record all information required by the protocol for each trial subject that is reported to the Sponsor (GCP E6 1.11). **The CRF must capture all protocol defined visits.**

4.2 The template CRF must be sent to QA for review during the trial setup process and finalised prior to the trial commencing.

4.3 The CRF may either be paper (see section 4.8) or electronic (see section 4.9). **On no occasion should both be used.** It is the responsibility of the CI to decide what format will be used for the CRF based on the needs of the trial and the decision must be clearly documented.

4.4 If the data is to be recorded directly in the CRF rather than being transcribed from source, it **must be clearly stated in both the trial protocol and DMP**.

4.5 The team should have an agreed process for QC checking of the CRF prior to the trial commencing. This process should include frequency of QC checks and the percentage of data to be checked (e.g. 10% data check, full data check etc.). This detail should be included on the DMP.

4.6 CRFs must be readily accessible both during and after the trial has completed.

4.7 Please refer to '***LTU_QM23 A Researchers Guide to Source Documentation***' for guidance on populating a CRF from source data.

4.8 Paper CRFs (pCRFs):

4.8.1 Paper CRFs are a flexible tool that are easily accessible by members of the research team. These are often used for simple, single site clinical trials which do not require remote data entry by sites.

4.8.2 The following guidelines apply when using a paper CRF:

- Each visit should have its own, clearly identifiable form.
- Each visit should include a signature and date field to document that the data was entered by an authorised member of staff on an appropriate date.
- Each trial participant must have an individual CRF pack with the CRF pages filed in date order.
- Consideration must be given to the filing and storage of pCRFs ensuring they are held securely and are not easily accessible by unauthorised individuals.
- In instances where additional paper work such as data query forms are to be held in the CRF, consideration needs to be given to how these will be filed safely and securely.
- Any changes made to a pCRF should be documented and the version updated accordingly.

4.9 Electronic CRFs (eCRFs)

4.9.1 eCRFs allow the trial data to be entered into a specific computer programme or website portal and are usually adopted for complex trials or those with the budget to "buy in" additional I.T resource.

4.9.2 The following guidelines apply when using an electronic CRF:

- The eCRF must be validated prior to use to ensure it is working as expected. Evidence of this validation must be included in the Trial Master File (TMF).
- All eCRF users must receive their own user account and password to maintain a full audit trail in the absence of wet ink signatures. **Passwords must never be shared between users.**
- Any pre-programmed calculations must be appropriately checked and validated for accuracy. Evidence of such checks must be recorded in the TMF.
- Any changes made to the eCRF must be documented and version control implemented accordingly.
- Consideration must be given to eCRF access after the trial has ended and to how frequently data will be backed up.
- The team must consider how any technical issues that may arise will be handled and who will be the point of contact if IT advice is required. **eCRFs should not be used if there is not considered to be adequate technical support in place.**

5.0 Databases

5.1 Database systems may be commercially bought or designed and developed in-house. For small trials, Microsoft Excel may be appropriate for use as a database, providing appropriate quality control steps can be evidenced.

5.2 Database systems are used to develop a database specific to a trial and include a data entry system with fields and tables that reflect those in the CRF.

5.3 The finalised CRF should be used to aid database design to ensure simple and accurate population.

5.4 Database Validation

5.4.1 All databases must be validated prior to trial data being entered to ensure that the database is fit for purpose.

5.4.2 All steps taken to validate and test the database must be documented and filed in the TMF.

5.4.3 The MHRA recommend that database testing and validation considers at least the following points:

- The database system flows correctly and the presentation is consistent with the CRF.
- All links function correctly.
- Fields accept the correct type of data (e.g. numerical fields should reject characters/symbols).

- Field lengths are appropriate (e.g. comment fields are designed to allow entry of a large number of characters).
- On-entry validation edit checks are functioning (e.g. fields designed to accept values within a specific range will flag the answer if it is unexpected).
- All data fields required for any calculations are present.
- How to handle any ambiguous values (e.g. poor handwriting in the CRF) or missing CRF data.
- There is a fully functioning audit trail.
- Any import / export functions work correctly.

5.4.4 Any problems identified during the validation process must be resolved prior to the database being made 'live' for the trial. Any changes made must be well documented.

5.5 Once all trial data has been collated in the database and the appropriate QC checks have been implemented, the database should be locked to prevent any future alterations. How the database is locked is dependent upon the system used and advice should be sought from the appropriate IT personnel.

5.6 There may occasionally be circumstances whereby corrections are required to be made to the database after it has been locked. As such, it is important that there is a process to unlock the database to allow corrections to be made however, access to this function should be restricted for major changes only (e.g. if the change will significantly impact the reliability of the results). Any changes made must be recorded for audit trail purposes.

6.0 Data Security

6.1 Appropriate restrictions and precautions must be taken to ensure that all trial data is held securely and is not accessed by unauthorised personnel.

6.2 Trial documentation must be retained in accordance with the agreed timelines to prevent premature destruction of data.

6.3 Where electronic systems are to be used, the backup of data must be considered prior to the trial commencing. No electronic system should be used until the team can demonstrate that appropriate backup systems are in place.

6.4 Advice should be sought from the relevant personnel regarding appropriate security measures for trial data prior to the trial commencing and as required for the duration of the trial.

7.0 Data Analysis

7.1 Data analysis must be carried out in accordance with the protocol and Statistical Analysis Plan (SAP).

7.2 The trial statistician(s) should be involved in all aspects of data analysis and any proposed changes to the SAP must be documented and agreed in collaboration with the statistician.

7.3 Please consult with the trial statistician prior to the trial commencing and before initiating any data analysis. Regular communication with the statistician throughout the trial is recommended.

Section D: References

MHRA Good Clinical Practice Guide 2012
LTU_QM23_A Researchers Guide to Source Documentation

Section E: Acronyms

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTU	Clinical Trials Unit
CTIMP	Clinical Trial of an Investigational Medicinal Product
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
LTHT	Leeds Teaching Hospitals NHS Trust
MHRA	Medicines and Healthcare products Regulatory Agency
pCRF	Paper Case Report Form
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SOP	Standard Operation Procedure
TMF	Trial Master File
UoL	University of Leeds

Section F: Previous versions of Document

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Appendix A - Example Source Data Location Sheet

Please note: the table below is an example of a source data location sheet only and is to be used as a guide only. The items and locations listed will vary between trials and as such a trial specific version must be developed.

Data Item	Location of Source
Informed Consent	Consent form and medical notes
Confirmation of eligibility	Medical notes and Case Report Form
Vital signs	Medical notes and source data worksheets
Blood results	Results server
Urinalysis	Source data worksheet
Pregnancy test	Medical notes and source data worksheet
Adverse Events	Medical notes
Serious Adverse Events	SAE form and medical notes
Concomitant medications	
Withdrawal	

Points to remember when developing a source data location sheet:

- All data points to be collected for the trial should be listed.
- For some data points there may be more than one potential source.
- The source data location sheet may require updating during the trial and should be reviewed regularly, particularly when the protocol has been amended.
- The document should be version controlled and easily accessible to all trial staff.