



| | | |
|--------------------------|--|-------------------------|
| Document category | | Core SOP |
| Index number | | Core SOP 015 |
| Title | | Data Management |
| Version number | | 2.0 |
| Author(s) | | Clare Riddle (Inactive) |
| Authorised by | | Heather House |
| Authorised date | | 02-Sep-2020 |
| Effective Date | | 28-Oct-2020 |
| Next Review Date | | 27-Oct-2023 |

Agreed by the QA Focus Group

SOP Number **015**
SOP Title **Data Management**

| | Name | Title | Signature | Date |
|---|---------------|--|------------------|-------------|
| Author on behalf of the QA Focus Group | Clare Riddle | Senior QA and Compliance Manager, Clinical Trials and Research Governance | | |
| Reviewer on behalf of the QA Focus Group | Elaine Chick | Deputy Head of Clinical Trials and Research Governance | | |
| Authoriser | Heather House | Head of Clinical Research Support (University Lead of the Joint Research Office) | | |

| | |
|---------------------------------|-----------------------|
| Agreed by QA Focus Group | 07 August 2020 |
| Effective Date | |
| Review Date | |

1. PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to outline the procedures for managing trial data on paper and in electronic format, to ensure all data are collected, verified, validated, reconciled, analysed and stored in a manner that preserves the scientific integrity of the clinical research generated by the University of Oxford.

2. INTRODUCTION

In the course of a trial, all data required by the clinical trial protocol needs to be recorded. The process for this is described below with emphasis on the main tasks for trial set up, conduct and close. As per Good Clinical Practice (GCP) all clinical trial information must be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification. Clinical Data Management is concerned with the collection, validation, and presentation of clinical data according to the principles of GCP in order to support statistical analysis and subsequent reporting.

3. SCOPE

The scope of this procedure is for all Clinical Trials of an Investigational Medicinal Product (CTIMPs) sponsored by the University of Oxford, but may also be used for other clinical research studies at the discretion of the unit.

4. DEFINITIONS

Data Management Plan (DMP) or equivalent documentation

A data management plan is an essential document that outlines how data are to be handled both during a research project, and after the project is completed.

Case Report Form (CRFs)

A printed, or electronic (eCRF) document designed to record the protocol-required information about trial participants.

Non CRF data

Non CRF data is the data collected or transferred from other sources which may or may not be designed for use in clinical trials e.g. diary cards, imaging. This data is entered into the clinical research data repositories without entering the data onto a CRF.

Data point / field validation rules

List of criteria against which data entered into the CRF is checked.

Database Lock

To ensure integrity of the trial database after data validation, the database must be locked. The process declares a database to be closed to additional modifications by removal of all user access rights.

Clinical Database Management System (CDMS)

A software tool used to collect and manage data associated with a clinical trial.

5. RESPONSIBILITIES

Sponsor (these responsibilities may be delegated in a written agreement)

- Ensure investigators have control of, and continuous access to data
- Oversee data management activities
- Ensure a DMP is produced

Chief Investigator (CI) or delegate

The CI is responsible for the overall data management of the trial including reviewing and approving the CRF and DMP, identifying and/or authorising who receives trial data.

Individual with data management responsibilities

The Individual with data management responsibilities is responsible for the design and review of the CRFs and DMP, construction and maintenance of the trial database, including where appropriate the creation of the trial specific data point / field validation rules, testing and documentation of all testing material.

Statistician

The statistician responsibilities may include, but not be limited to, analysing data, spotting trends within datasets, and undertaking final data analysis. They may also be the individual with the data management responsibilities described above.

6. SPECIFIC PROCEDURE

6.1 Data Management Plan (DMP)

The DMP details all aspects of data management as applied to that particular trial and as such it can be considered as an essential document. The extent of the data management activities described in the DMP will be dependent on the complexity of the trial and the associated risks. The DMP should be created by the Individual with data management responsibilities and should be thoroughly reviewed and authorised by the CI and appropriate members of the trial team. This could include but should not be limited to the trial statistician. The content of the DMP may include:

- Data flow by CRF and visit
- CDMS(s) to be used for handling trial data, including requirements for access control, security and audit trail.
- Data validation (details of data validation and cleaning, discrepancy and query management, and edit specifications)
- Non-CRF data considerations (ECG, Blood test results, Laboratory and subsequent reconciliation of data)
- Data coding conventions
- Details of serious adverse events (SAE) collection and reconciliation
- Trial specific data transfer requirements
- Type and schedule of data management status reports / tracking metrics
- Time point and procedure for database lock(s)
- Data entry guidelines
- Data correction rules
- Details of the procedure for unresolved queries, protocol deviations, non-compliance with procedure, file notes which will be presented to the Statistician

The DMP should be approved prior to enrolment of the first participant into the trial but may need to be updated as and when additional information becomes available. All amendments to the DMP should be detailed and explained within the version history in line with University of Oxford Core SOP 014 Version Control and re-distribution and authorisation where appropriate.

6.2 Trial Data Initiation Activities

6.2.1 CRF Creation

The CRFs and other non CRF data documents should be designed or obtained by the Individual with data management responsibilities to accurately capture the required data, based on the approved trial protocol and trial specific requirements. After documented discussions amongst the trial team, the final versions should be authorised by the CI or delegate and where applicable the trial statistician.

6.2.2 Database Build

Following the 4 stages of computer system validation, the Individual with data management responsibilities should proceed to risk assess (stage 1), build, test (stage 2 - validation master plan), and document testing of the trial specific database. Any testing activities should be captured and documented (stage 3 – validation tests). This could include, for example, the use of a specification document. Once the database build and testing has been fully validated within the testing instance, the release to the live/production instance/server should be initiated upon authorisation (stage 4 – validation summary report).

N.B. The trial database audit trail must be sufficient to ensure traceability of the data.

6.2.3 Data Protection and Storage

Data needs to be maintained in a way that preserves their accuracy, integrity and legibility with user access restrictions and data retrievable by designated personnel only. This applies to electronic and paper records.

6.2.4 Data Backup Systems

The CDMS must have appropriate verified back-up processes in place to guard against loss of data due to software or environmental disasters.

6.3 Trial Data Maintenance Activities

6.3.1 Data Entry

The process of data entry is dependent upon the trial design (i.e. paper CRFs or electronic data capture). For multicentre clinical trials and/or those using electronic data capture, a CRF completion guideline would assist with this. All staff completing CRFs should be sufficiently trained in CRF completion to achieve accuracy at this stage prior to being granted access.

6.3.2 Data Queries

An essential part of the data management process is validation to ensure the most accurate 'clean' set of data is provided for statistical analysis. Query management should be tracked within the CDMS. Any missing data, incomplete responses, or data outside of normal ranges should be queried. A record or log should be maintained of all data queries sent out from the CDMS.

6.3.3 Database Queries

Database queries/escalations should be sent to the nominated individual to review; discuss and document in a timely manner with the CI and the statistician if required.

Required updates to the database should be documented, updated in the required data management plan or equivalent documents and implemented for testing.

Testing of the updated database should be validated and the updated release should be communicated upon authorisation with updated training if required.

6.4 Trial Data Finalisation Activities

6.4.1 Trial Close Out

The final database must be “locked” to ensure access to the final dataset is permanently restricted for final analysis. The Individual with data management responsibilities should ensure the following activities are completed prior to database lock:

- All participants must have completed their final visit and any follow-up visits prior to database lock.
- All CRFs, questionnaires, etc. received and data entry completed.
- All outstanding queries have been resolved, source data verified, and the database updated.
- All the CRFs have been signed where applicable.
- If applicable, data transfer is complete and reconciliation performed.
- All members of the trial team have been notified of the proposed date of lock.

Database lock is completed prior to un-blinding and prior to final data analysis by the Trial Statistician.

6.4.2 Data Transfer

A documented procedure should be followed in relation to data transfer (electronic, paper, internal, and external) and any such activity should be captured.

6.5 Archiving

See University of Oxford Core SOP 005 Archiving of Essential Documents

7. RELATED DOCUMENTS

University of Oxford Core SOP 005 - Archiving of Essential Documents

8. REFERENCES

Example of a summary Data Management Plan for grant submissions (requires expansion for operational use) <https://mrc.ukri.org/documents/doc/data-management-plan-template/>

9. CHANGE HISTORY

| Version No. | Effective Date | Significant Changes | Previous Version No. |
|-------------|----------------|---|----------------------|
| 1.0 | 28 Sept 2018 | This is the first version of this SOP. | n/a |
| 2.0 | See page 1 | Correction to Statistician’s responsibilities | 1.0 |