DATA MANAGEMENT

DOCUMENT NO.:	POL012 v2.0
AUTHOR:	Lorn Mackenzie
ISSUE DATE:	05 MAY 2023
EFFECTIVE DATE:	19 MAY 2023

1 INTRODUCTION

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 Data management encompasses the design and production of the data capture tool(s), whether paper or electronic e.g. the case report form (CRF) or study database. Data management includes all aspects of data collection, data processing (entry/uploading, cleaning, and query management), and the production of the final dataset ready for analysis and/or archiving.

1.3 Appropriate quality control checks (QC) and computer system validation (CSV) applied during the data management process can provide assurance that the data and reported results are credible and accurate. How data is managed, and the level of validation required, will vary depending on the study design.

1.4 The Sponsor may delegate management of the trial data to the Chief Investigator (CI) or a specialist function group such as a Clinical Trials Unit. Any delegation of data management tasks will be clearly documented in appropriate agreements and/or the study protocol.

2 SCOPE

2.1 This Policy applies to all research staff involved in data management tasks for trials sponsored by the UoE and/or NHSL.

2.2 This Policy also applies to ACCORD personnel (e.g. UoE Research Governance, QA and Monitoring) with responsibilities for performing Sponsor activities relating to data management tasks on behalf of NHSL/UoE.

2.3 This Policy applies only to trials which have undergone a combined risk assessment (Standard Operating Procedure (SOP) GS002 Combined Risk Assessment).

3 POLICY

3.1 Data Management Plan

3.1.1 For studies subject to a combined risk assessment (GS002), the CI, or designee, will ensure that all data management activities are detailed in a

separate data management plan (DMP). Where data management tasks have been delegated to a specialist function group, the vendor DMP template can be used, if applicable. Otherwise the ACCORD DMP template (POL012-T01) will be used. Use of a vendor's DMP template can be used in place of POL012-T01 with prior agreement from the ACCORD QA Manager, or designee.

3.1.2 The DMP will include the following topics as a minimum;
- Case Report Form Design: Data collection procedures, including identification of key trial data
- Database Design and Validation
- Data Quality: Data entry, Quality Control (QC) checks and cleaning, including query management
- Reconciliation of Data: Pharmacovigilance and non-compliance reconciliation
- MedDRA Coding
- Database Lock & Release
- Archiving of Data

3.1.3 The DMP will be reviewed and signed by the Statistician and by Lead Clinical Trials Monitor, and filed in the Trial Master File (TMF).

3.1.4 The DMP will be signed prior to first Sponsor Authorisation to Open (SATO) (SOP CM001Site Initiation and SATO), unless risk adaption has been agreed with the Lead Clinical Trials Monitor, or designee. Where risk adaption is justified and agreed, this will be documented in the TMF and Sponsor File e.g. combined risk assessment report.

3.1.5 The DMP is a live document and will be updated regularly following any changes to data management activities. The frequency of review will be detailed in the DMP.

3.2   Case Report Form Design

3.2.1 The case report form (CRF) is a data collection tool used to capture the required data, as defined by the protocol, for each individual subject during their participation in the trial. The description of the data collection procedures (electronic or paper) will be detailed in DMP.

3.2.2 The CI or designee (e.g. Trial Manager) will ensure that the CRF is reviewed and approved by an ACCORD Clinical Trial Monitor before implementation at site. Any amendments required to the CRF during the trial will be sent to an ACCORD Clinical Trials Monitor for review. For a detailed description of the CRF design process see SOP CR013 (CRF Design and Implementation).

3.3   Database Design & Validation

3.3.1 The e-CRF and/or database will be set up and designed by an experienced database analyst/manager or delegated third party / collaborator (e.g. Clinical

Trials Unit). Where data management is contracted out to a third party / collaborator, an appropriate agreement must be put in place and vendor oversight maintained following SOP QA009 (Vendor Assessment).

3.3.2 The database will be designed to mirror the CRF.

3.3.3 To demonstrate that the database is 'fit for purpose' the Sponsor must confirm that the system is fully validated, ensuring integrity and security of the data to be collected. The process for establishing documented evidence that a database will consistently perform as intended is known as computer system validation (CSV).

3.3.4 When the need for a CSV review is identified during risk assessment, the QA Manager, or designee, will perform this task using the CSV Checklist (GS002-T02) in accordance with the CSV Policy (POL007). This review will include ensuring the CI, or designee (e.g. Trial Manager or member of the study team), carry out User Acceptance Testing (UAT) on the database. Any areas of non-compliance with the checklist noted during this review must be resolved, and the checklist signed as approved before the computer system can go live and be used by the trial team.

3.3.5 If any modifications are made to the database during its lifecycle, these must be tested, and the system re-validated and approved by the QA Manager, or designee, prior to implementation of the updated database.

3.3.6 Once all system testing has been carried out and documented, and the QA Manager, or designee, has confirmed Sponsor review/approval, the system can be released for use in the study by the Data Manager or Programmer/Analyst. Confirmation of this release notice will be sent to the QA Manager (QA@accord.scot) and retained in the TMF and Sponsor File.

3.4 Data Quality

3.4.1 The procedure for assessing data quality (e.g. Quality Control (QC), data validation and data cleaning) will be conducted prior to data analysis and will be documented in the DMP or a specific QC plan. Where QC checks are carried out by a third party / collaborator, the DMP or QC Plan will specify the types of QC checks required and specify the details of what will be included in the check, and who is responsible for performing these checks.

3.4.2 Data validation is the process of checking the data for elements such as logical consistency, missing, incorrect or implausible data. Checks should be built into the database where possible. The data validation plan should either be detailed in the DMP or a separate document. It should list all computerised and manual data checks that will be carried out for the study and at what point.

3.4.3 Data cleaning is the process for identifying and correcting inaccuracies in the dataset before analysis. Data queries are raised and sent to site for all

discrepancies identified during monitoring visits and/or from QC and data validation processes. Data queries can be raised by delegated individuals performing QC checks, the Data Management Team and the Clinical Trials Monitor. Queries should not be leading. All queries raised and subsequent changes made to the data must be documented via an audit trail. All inaccuracies identified, should be corrected in a timely manner by the investigator or designee.

3.4.4   Data cleaning is an ongoing process throughout the lifecycle of the trial and must be complete prior to final database lock at the end of the study, or prior to any planned interim analyses. The DMP will detail specific query management instructions for generating and handling study specific queries (e.g. specify the scope, frequency and proposed schedule of data quality checks for the duration of the study).

3.4.5   In order to ensure the accuracy, completeness, legibility and timeliness of the data reported in the CRFs, the study team should ensure that data entry guidelines and/or training is provided to site staff. A record will be kept of the training.

3.5   Reconciliation of Data

3.5.1   Pharmacovigilance (PV) reconciliation is the process of ensuring that reported events e.g. serious adverse events (SAEs), serious adverse reactions (SARs),pregnancy forms and medical device events/ deficiencies are reconciled with the data held in the trial database. The CI, or designee (e.g. Trial Manager) will request a line listing from the Pharmacovigilance (PV) Manager and reconcile this against the eCRF/database (SOP PV002 Pharmacovigilance: Sponsor Oversight and Trend Analysis). Any inconsistencies will be flagged and investigated with the PV Manager. The PV reconciliation process, including who is responsible for this activity, will be documented in the DMP.

3.5.2   Trial non-compliances are reported to the Sponsor in accordance with SOP CR010 Management of Protocol and GCP Deviations and Violations. Non-compliance reconciliation is the process of ensuring that reported deviations and violations are reconciled with the data held in the trial database. The CI, or designee (e.g. Trial Manager), will request line listings of study non-compliances (i.e. deviations/violations) from the QA Coordinator for reconciliation and inclusion in final analysis. Any inconsistencies will be flagged and investigated with the QA Coordinator. This process will be detailed in the DMP.

3.5.3   The ACCORD risk assessment (GS002) will detail whether any reconciliation of safety data and / or non-compliances will occur prior to any planned interim analysis or provision of data to the Data Monitoring Committee (DMC)/Trial Steering Committee (TSC), and prior to database lock.

3.6 MedDRA Coding of Data

3.6.1 MedDRA coding requirements will be detailed in the study protocol and DMP in accordance with SOP PV004 Pharmacovigilance: MedDRA Coding Serious Adverse Events.

3.7 Database Lock & Release

3.7.1 Database lock is the process of locking the data and restricting access to it once it is deemed final and ready for analysis. Database lock will only occur once all site close out visits are conducted, all data is entered into the database, data checks (e.g. QC checks, data cleaning) are complete, all data queries are addressed and closed, and reconciliation of PV data and non-compliances has occurred. A signed Statistical Analysis Plan (SAP) must also be in place. The CI, or designee (e.g. Trial Manager / Statistician), will confirm when the study database/eCRF is ready to be locked, ensuring the Lead Clinical Trial Monitor is copied into any correspondence. The Data Manager, or designee (e.g. Data Programmer) will ensure the date and time of study database/eCRF lock is documented.

3.7.2 The database lock process, including who is responsible for each activity leading to database lock, will be documented in the DMP.

3.7.3 At the point of database lock the Statistician, or designee, will request a final line listing of PV events and non-compliances from the Sponsor in accordance with SOP PV002 and CR012, respectively.

3.7.4 Where interim analysis is planned, the process and responsibilities for a temporary database freeze (or equivalent), to allow data extraction for a limited time, will be detailed in the DMP. Data QC/cleaning requirements, prior to the temporary database freeze, will be documented in the DMP and must be complete prior to the temporary freeze.

3.7.5 After the database/eCRF has been locked, under exceptional circumstances it may be necessary to unlock the database e.g. important data corrections that will have a significant impact on the reliability of the results. Where there is a requirement to unlock the database, the CI, or designee (e.g. Trial Manager), will provide written justification for the request to the Sponsor Representative and Statistician, including consideration of impact on statistical outcome. A documented review of the audit trail will be conducted at re-locking. This task will be performed by a separate member of the trial team who has not performed the data entry task. When re-locked, the database should not overwrite any analysis of datasets that were created at the original database lock. All details of any changes made to the database, and the justification for making the changes, will be documented in the TMF.

3.7.6 Data release happens after database lock and is the process of providing the dataset(s) to the statistician for analysis. The CI, or designee, will ensure that

the process for data release following database lock is documented in the DMP. This will include who is responsible for each task and any unblinding considerations, if applicable.

3.7.7   Where there are plans to share datasets and/or results with another institution or third-party, or data sharing requests are received by the CI, this may require a contractual agreement and guidance should be sought from the Sponsor Representative.

3.8   Archiving of Data (paper and electronic)

3.8.1   Archiving arrangements of trial data (paper and electronic) will be defined in the study protocol and DMP in accordance with SOP GS005 Archiving Essential Study Documents.

3.8.2   The requirements for providing Principal Investigator(s) with a complete and independent copy of the data collected for their site participants for archiving at the end of the trial, will be considered at the CRF Design process (see SOP CR013 CRF Design and Implementation) and documented in the DMP template.

4   REFERENCES AND RELATED DOCUMENTS

- POL012-T01 Data Management Plan Template
- CR013 CRF Design and Implementation
- GS002 Combined Risk Assessment
- GS003 Sponsorship Approval
- GS005 Archiving Guidance for Researchers
- POL007 Computer System Validation
- QA009 Vendor Assessment
- CM004 Developing Monitoring and SDV Plans
- PV002 Pharmacovigilance: Sponsor Overview and Trend Analysis
- PV004 Pharmacovigilance: MedDRA coding SAEs for DSURs
- MHRA Grey Guide

5   DOCUMENT HISTORY

Version Number	Effective Date	Reason for Change
1.0	21 MAR 2022	New Policy
2.0	19 MAY 2023	Section 3.1.4 updated: the Data Management Plan will be signed prior to first Sponsors Authorisation To Open. Section 3.7.1 updated: Database lock will only occur once all site close out visits are conducted,

		all data is entered into the database, data checks (e.g. QC checks, data cleaning) are complete, all data queries are addressed and closed, and reconciliation of PV data and non-compliances has occurred. A signed Statistical Analysis Plan (SAP) must also be in place.

6   APPROVALS

Sign	Date
AUTHOR: Lorn Mackenzie, QA Manager, NHSL, ACCORD	May 4, 2023
Elizabeth Craig Elizabeth Craig (May 4, 2023 16:05 GMT+1) APPROVED: Elizabeth Craig, Senior Clinical Trial Monitor, NHSL, ACCORD	May 4, 2023
Gavin Robertson (May 5, 2023 08:11 GMT+1) AUTHORISED: Gavin Robertson, QA Coordinator, NHSL, ACCORD	May 5, 2023

POL012 Data Management Policy v2.0

Final Audit Report   2023-05-05

Created:	2023-05-04
By:	Roisin Ellis (v1relli8@exseed.ed.ac.uk)
Status:	Signed
Transaction ID:	CBJCHBCAABAAnRThdN48N6Vqlf_FjwG4CW4LBxETJchw

"POL012 Data Management Policy v2.0" History

📄 Document created by Roisin Ellis (v1relli8@exseed.ed.ac.uk)
2023-05-04 - 1:50:37 PM GMT

✉ Document emailed to Lorn Mackenzie (lorn.mackenzie@nhslothian.scot.nhs.uk) for signature
2023-05-04 - 1:52:03 PM GMT

✉ Document emailed to elizabeth.a.craig@nhslothian.scot.nhs.uk for signature
2023-05-04 - 1:52:03 PM GMT

✉ Document emailed to Gavin Robertson (gavin.robertson@nhslothian.scot.nhs.uk) for signature
2023-05-04 - 1:52:04 PM GMT

📄 Email viewed by Lorn Mackenzie (lorn.mackenzie@nhslothian.scot.nhs.uk)
2023-05-04 - 1:57:50 PM GMT

✍ Document e-signed by Lorn Mackenzie (lorn.mackenzie@nhslothian.scot.nhs.uk)
Signature Date: 2023-05-04 - 1:58:00 PM GMT - Time Source: server

📄 Email viewed by elizabeth.a.craig@nhslothian.scot.nhs.uk
2023-05-04 - 3:02:04 PM GMT

✍ Signer elizabeth.a.craig@nhslothian.scot.nhs.uk entered name at signing as Elizabeth Craig
2023-05-04 - 3:05:45 PM GMT

✍ Document e-signed by Elizabeth Craig (elizabeth.a.craig@nhslothian.scot.nhs.uk)
Signature Date: 2023-05-04 - 3:05:47 PM GMT - Time Source: server

📄 Email viewed by Gavin Robertson (gavin.robertson@nhslothian.scot.nhs.uk)
2023-05-05 - 7:11:15 AM GMT

✍ Document e-signed by Gavin Robertson (gavin.robertson@nhslothian.scot.nhs.uk)
Signature Date: 2023-05-05 - 7:11:48 AM GMT - Time Source: server

 Adobe Acrobat Sign

✅ Agreement completed.
2023-05-05 - 7:11:48 AM GMT