DATA MANAGEMENT

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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.

3 Policy

3.1 Data Management Plan

3.1.1 Where applicable (for example where the management of study data has been delegated to a specialist function group or requested by the study funder) the CI, or designee, will ensure that all data management activities are detailed in a separate data management plan (DMP). This is a mandatory requirement for studies subject to a combined risk assessment (GS002). Where data management tasks have been delegated to a specialist function group, the vendor DMP template can be used. 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
- Database Lock & Release
- Archiving of Data

3.1.3 The DMP will be reviewed and signed by the Statistician. The Lead Clinical Trials Monitor will sign the DMP for those studies subject to a combined risk assessment (GS002). The DMP will be filed in the Trial Master File (TMF).

3.1.4 For studies subject to a combined risk assessment (GS002), the DMP will be signed prior to first Sponsor Authorisation to Open (SATO) (SOP CM001 Site 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 For studies subject to a combined risk assessment (GS002), 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) where applicable.

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 system must be 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 For studies subject to a combined risk assessment (GS002) the need for a CSV review will be identified during the 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, where applicable prior to implementation of the updated database.

3.3.6 Once all system testing has been carried out and documented, and where applicable 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. For studies subject to a combined risk assessment (GS002) confirmation of this release

notice will be sent to the QA Team (QA@accord.scot) and retained in the TMF and Sponsor File where this exists.

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. As a minimum, checks will be completed on all datapoints contributing to endpoint or safety data.

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. Data queries can be raised by delegated individuals performing QC checks, the Data Management Team and the Clinical Trials Monitor where applicable. 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 of individual cases of reported safety events 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 eCRF/database. the CI, or designee (e.g. Trial Manager), will request line listings of individual study non-compliances (i.e. deviations/violations) from the QA Coordinator. Any inconsistencies will be flagged and investigated with the QA Coordinator. The QA non-compliance reconciliation process, including who is responsible for this activity, will be documented in the DMP.

3.5.3 Reconciliation of safety and non-compliance events at the end of the trial will be undertaken by the Trial Manager or where applicable the Clinical Trial Monitor, or designee, in accordance with requirements of CM003. For studies subject to a combined risk assessment (GS002) the final line listing of reported safety events and non-compliances for statistical analysis will only be produced by the PV/QA team once they have confirmed with the Clinical Trial Monitor that all close out checks relating to safety reporting and non-compliance reconciliation (including final TMF review) have been completed.

3.5.4 The ACCORD risk assessment (GS002) will detail whether any additional 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. Reconciliation of data for planned interim analysis / provision of data to the DMC/TSC will follow section 3.5.1 and 3.5.2 where applicable.

3.6 MedDRA Coding of Data

3.6.1 MedDRA coding requirements should be considered as part of the planned statistical analysis. The requirement to use MedDRA coding to categorise adverse events 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 where applicable. A signed Statistical Analysis Plan (SAP) must also be in place where applicable. 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 where applicable. 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.
3.0	18 OCT 2024	Section 3.5 updated: Reconciliation of safety and non-compliance events at the end of the trial will only be produced by the PV/QA team (e.g. creation of a final line listing) once they have confirmed with the Clinical Trial Monitor that all close out checks relating to safety reporting and non-compliance reconciliation (including final TMF review) have been completed. POL012-T01 DMP Template. Section 9 updated: Clarification that query reports should be shared with the PI for oversight and prompt added to include a query escalation process.
4.0	13 JUN 2025	The scope of the policy has been widened to include non-risk assessed studies. Updates made throughout policy to reflect this. Clarification at section 3.4.2 that as a minimum, data validation checks should be completed on all datapoints contributing to endpoint or safety data. MedDRA coding section of the DMP is no longer a mandatory requirement however clarification added to section 3.6.1 that requirements should still be considered as part of the planned statistical analysis.

6 Approvals

Sign	Date

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 Gavin Robertson (30-May-2025 11:00 GMT+1) AUTHORISED: Gavin Robertson, QA Coordinator, NHSL, ACCORD	30-May-2025

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