CASE REPORT FORM DESIGN AND IMPLEMENTATION

DOCUMENT NO.:	**CR013 v5.0**
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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 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.

1.3 Source data is defined as all information, in original records and certified copies of original records or clinical findings, observations, or other activities in a clinical trial, necessary for the reconstruction and evaluation of the trial. Source documents are original documents and records where source data are recorded for the first time.

1.4 The design of the CRF and its completion has a direct impact on the quality of the data collected during a clinical trial. A well designed CRF will ensure that; no essential data is missed, data queries are kept to a minimum, aid data management and assist with statistical analysis and reporting.

2 PURPOSE

2.1 The purpose of this SOP is to describe the procedure to be followed when designing and developing CRFs for use within a clinical trial sponsored by UoE and/or NHSL.

3 SCOPE

3.1 This SOP applies to all research staff involved in the development and implementation of CRFs in trials sponsored by the UoE and/or NHSL.

3.2 This SOP also applies to ACCORD Clinical Trials Monitors and any other member of staff involved in the development or review of CRFs.

3.3 Section 5.4 (CRF Review Process) and 5.5 (Amending the CRF) apply only to trials which have undergone combined risk assessment (GS002).

4 RESPONSIBILITIES

4.1 CRF design is the responsibility of the CI, or designee. Input should also be sought from other members of the research team including but not limited to the person responsible for the final statistical analysis (normally the trial statistician).

4.2 Review of the final CRF, and any subsequent updates, is the responsibility of the ACCORD Clinical Trials Monitor, or designee, for trials which have undergone combined risk assessment (GS002).

4.3 Implementation of the CRF and any subsequent updates is the responsibility of the CI, or designee.

5 PROCEDURE

5.1 General Principles

5.1.1 The CI, or designee, will design the CRF to ensure that only data defined in the protocol are captured.

5.1.2 The design of the CRF should ensure that;

- Data will be captured and entered into the CRF in a chronological order, reflective of the protocol.
- The order of trial visits and procedures will be taken into account, in order to make data entry as easy as possible for users and minimise the risk of missing data capture.
- Where data will be transcribed into the CRF from source documents, the layout and content of the CRF will be structured to minimise transcription errors e.g. terminology across source documents and the CRF should be consistent.
- Raw data will be collected, where this is practical, to minimise unnecessary calculations and reduce risk of error.

5.1.3 Free text is not easily analysed and therefore where possible should not be used to complete data fields.

5.1.4 Listing definitive options with check boxes will limit ambiguity.

5.1.5 Where appropriate, a combination of definitive answers and an option to enter ‘other’ and specify will allow for the collection of additional information.

5.1.6 If free text is essential, a comments box can be added. However, this should be used to collect relevant additional information only and not protocol defined outcomes, unless these are free text based e.g qualitative research.

5.1.7 Any data for which the CRF will act as the source document will be explicit in the study protocol and/or source data plan (CR004-T01).

5.1.8 Where an electronic database exists, the CI, or designee, will ensure the data captured in the CRF matches the data fields in the electronic database.

5.1.9 Any fields contained within the CRF which will not be entered into the database will be clearly identified. For example an annotated master copy of the CRF could be held highlighting any data points captured in the CRF only.

5.1.10 The site Principal Investigator (PI) must maintain a complete and independent copy of the data collected for their site participants. Where data will be collected centrally (e.g. patient reported outcomes sent directly to the trial management office/database by questionnaire or text message) a process must be in place to ensure PIs have access to this data for participants at their site during the course of the trial and a copy of this data is provided to the PI for archiving at the end of the trial. This is also the case where source data is entered directly into an eCRF and access to the eCRF is removed at the end of trial. A copy of the source data held only in the eCRF must be provided to the PI for archiving.

5.2 Format

5.2.1 The CRF can be one single form covering all aspects of the study or a collection of separate forms.

5.2.2 The CRF can be paper and/or electronic in format.

5.2.3 Example paper CRF templates are available (CR013-T03). These can be used as a guide for CRF design where required by research teams however, they are provided as an additional aid to CRF design and it is not a requirement to use them. Where used the templates will be made study specific to collect only the data required by the study protocol.

5.2.4 Regardless of the format, the CRF will be version controlled and dated (QA008 Document Version Control) and will also include page numbers in sequential order.

5.2.5 Sufficient information will be included in the header of the CRF to attribute every page to a participant e.g. study identifier and participant number.

5.2.6 Hospital/Community Health Index (CHI) numbers are not suitable as participant identifiers. Where collection of CHI number is required in the CRF this must be done in accordance with ACCORD policy (POL003, Data Protection and Confidentiality).

5.2.7 Personal data/Information (e.g. name, CHI number, date of birth, initials or other characteristics relating to the physical or social identify of a participant) will not be captured in the CRF unless considered absolutely necessary, by the Chief Investigator/Trial Manager for study conduct or, by the Trial Statistician, for analysis. If necessary, the Clinical Trials Monitor can consult the eResearch Lead to determine if a combination of characteristics can be considered

potentially identifiable. Where potentially identifiable personal data/information is considered absolutely necessary and will be included within the CRF, consent documents (e.g. PIS) must inform participants that potentially identifiable data/information will be available to the relevant parties.

5.2.8 It will also be clear in the header which time point during the study each page belongs to, clearly identifying the visit or data collection time point as defined in the protocol and the date this data was collected.

5.2.9 For multi-centre studies the site at which the CRF was completed will also be identifiable.

5.2.10 The format of data entry will be specified in the CRF e.g. dates (DD-MMM-YYYY, DD-MM-YY) and times (12 hour, 24 hour).

5.2.11 Units will be specified in the CRF where appropriate, ensuring that these match those described in the protocol and source documents.

5.2.12 The CRF should include, unless otherwise agreed and justified with the clinical trials monitor, appropriate sign off areas for:

- Confirmation of eligibility by the PI or designee
- Oversight of test results by the PI or designee
- Completion of each section of CRF
- Overall sign off of the CRF by the PI or designee

5.3 CRF Completion Guidelines

5.3.1 Trial specific CRF completion guidelines may be generated by the CI, or designee, if required. These are recommended where the study is multicentre to facilitate consistency of data entry across sites or where the data collected is particularly complex.

5.4 CRF Review Process

5.4.1 CRF design is a multidisciplinary process. The person responsible for final statistical analysis should be consulted early in the design process, should have input to the final design and be provided with the final agreed version of the CRF to be implemented at site.

5.4.2 CRFs do not require approval from the Research Ethics Committee (REC) or local R&D office. However, where forms are self-completed by the participant

(for example questionnaires or diary cards) and form part of the CRF, the relevant approvals for these documents should be sought.

5.4.3 The ACCORD member of staff conducting the Sponsor review (GS003 Sponsorship Approval) should be alerted by the CI, or designee, to any parts of the CRF completed by the participant at the time of Sponsor review.

5.4.4 For trials subject to combined risk assessment (GS002 Combined Risk Assessment) the CI, or designee, will ensure that the CRF is reviewed and approved by an ACCORD Clinical Trials Monitor, or designee before implementation at site. This review will be conducted using the CRF Review template (CR013-T01), unless otherwise agreed with the Senior Clinical Trials Monitor for review to be documented elsewhere.

5.4.5 Initial review of the CRF by the ACCORD Clinical Trials Monitor, or designee, is the completion of section 1-3 of CR013-T01 or equivalent. This must be completed prior to first Site Initiation Visit (SIV) according to CM001 (Site Initiation and Sponsor Authorisation).

5.4.6 Any issues identified during the review process will be fed back to the CI, or designee, by the ACCORD monitoring team. Input will be sought from the person responsible for final statistical analysis of the trial for issues which affect data collected.

5.4.7 Review of the CRF will be completed prior to final database validation.

5.4.8 Once the final version of the CRF has been agreed it will be approved by the CI, or designee, and ACCORD Clinical Trials Monitor or designee. This approval will be documented using the CRF Version Tracker (CR013-T02) unless otherwise agreed by the ACCORD Senior Clinical Trials Monitor, in which case the approval will be documented elsewhere.

5.4.9 Where applicable, Sponsor Authorisation to Open (SATO) (CM001 Site Initiation and Sponsor Authorisation) cannot be given until this review and sign off process has been completed.

5.4.10 Once the CRF has been approved for use by both the monitor, or designee, and CI, or designee, the CRF can be implemented at site. The implementation date should be recorded on the CRF Version Tracker or equivalent document.

5.4.5 Some electronic CRF systems may have their own version tracking facility. This can be used in place of CR013-T02 with prior agreement from the Senior Clinical Trials Monitor, or designee. However, approval by the CI, or designee, and ACCORD Clinical Trials Monitor, or designee, must be documented for each version.

5.4.11 The version of the protocol the CRF is based on, and the date each version became live, must also be documented in the CRF Version Tracker (CR013-T02), or equivalent document.

5.5 Amending the CRF

5.5.1 For trials subjected to combined risk assessment (GS002), unapproved versions of the CRF must not be implemented at site. Any amendments required to the CRF after approval will be sent to an ACCORD Clinical Trials Monitor or designee, for review.

5.5.2 A review of changes to the CRF will be completed using CR013-T01 (CRF Review), unless otherwise agreed with the Senior Clinical Trials Monitor for review to be documented elsewhere.

5.5.3 Any amendment which affects the data collected will be communicated to the person responsible for final statistical analysis by the CI, or designee, and feedback sought where required. Any issues identified during review will be fed back to the CI, or designee, by the ACCORD monitoring team, or designee.

5.5.4 Once agreed, the amended version will be added to the CRF Version Tracker (CR013-T02) and approved by the ACCORD Clinical Trials Monitor and CI, or designee. Once CR013-T02 (or agreed equivalent) has been completed, the amended CRF can be implemented at site. The implementation date will be documented in CR013-T02 (or agreed equivalent).

6 REFERENCES AND RELATED DOCUMENTS

- CR013 -T01 – CRF Review
- CR013 -T02 – CRF Version Tracker
- CR013-T03 – CRF template
- CR004 Recording and Reporting Study Data
- CM001 Site Initiation and Sponsor Authorisation
- GS002 Combined Risk Assessment
- GS003 Sponsorship Approval
- QA008 Document Version Control
- POL003 Data Protection and Confidentiality

7 DOCUMENT HISTORY

Version Number	Effective Date	Reason for Change
1.0	08 NOV 2016	New SOP.
2.0	31 OCT 2018	Scheduled review. Minor updates to 5.1.7 and 5.2.10

3.0	07 NOV 2019	Process for inclusion of personal data/information in the CRF added to 5.2.6. CR013-T01 updated to include a check for personal data/information.
4.0	30 JUN 2020	Addition of 5.4.5 defining initial review in relation to Site Initiation. Minor administrative update to add Section 4 to CR013-T01.
5.0	24 FEB 2022	Addition of 5.1.10 clarifying requirement for PI to hold complete and independent copy of site data. Reference to example paper CRF templates (5.2.3) and addition of templates (CR013-T03). Minor updates to 5.1.7 and 5.2.5.
/	/	Periodic Review 15-Mar-24: No changes were deemed necessary to the SOP following review by the author. New review date of 24-Feb-26 has been assigned. Minor changes made to CR013-T02 (CRF version tracker)

8 APPROVALS

Sign	Date
Elizabeth Craig Elizabeth Craig (Apr 8, 2024 16:16 GMT+1) AUTHOR: Elizabeth Craig, Senior Clinical Trials Monitor, NHSL, ACCORD	Apr 8, 2024
L. Mackenzie APPROVED: Lorn Mackenzie, QA Manager, NHSL, ACCORD	Apr 8, 2024
Gavin Robertson (Apr 10, 2024 09:10 GMT+1) AUTHORISED: Gavin Robertson, QA Coordinator, NHSL, ACCORD	Apr 10, 2024

CR013 CRF Design and Implementation v5.0 (no changes necessary following 2024 author review)

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