



University of Leicester Research Governance Office Standard Operating Procedures

SOP S-1039 UoL

Case Report Form Development for Research Studies Sponsored by the University of Leicester

Version 4.0 May 2024

Effective Date: July 2024

This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used.

1.0 Introduction and Scope

The purpose of this standard operating procedure (SOP) is to describe the processes to be followed when designing and developing a Case Report Form (CRF) for research Sponsored by the University of Leicester (UoL).

The CRF is a data collection tool and should be used to record the eligibility of a participant and the research data as defined by the study protocol for each individual participant during the course of their participation in a study.

The complexity and design of a CRF will vary depending on the nature and type of research (i.e., qualitative study vs. interventional study vs. complex highly regulated Clinical Trials of Investigational Medicinal Products (CTIMPs)). Regardless of the type, size or complexity of the study, the principles of CRF design are the same:

- Data must be captured in accordance with the approved protocol (no more and no less than what is specified)
- Data must be collected in a format that supports the anticipated analysis.
- Data must be collected in a way that supports the accurate reconstruction of the research.
- Where a participant receives a blood test and the results of the test are obtained from electronic medical records, the medical records would be considered the source data.

2.0 CRF Design

CRFs are a type of data collection tool. They can be printed or electronic documents. The CRF will be designed to ensure that all data required by the protocol and statistical analysis are captured in an appropriate format; only data defined in the protocol must be entered into the CRF. A well-designed CRF will ensure that no essential data is missed and that data queries are kept to a minimum as well as aiding data management, statistical analysis and reporting.

The Chief Investigator in collaboration with the Sponsor/Statistician will need to decide which system is most suitable for each particular study (e.g., paper or electronic data capture). More information on the specifications for electronic data capture systems can be found in the Data Management SOP, SOP S-1036 UoL.

It is important that CRFs do not capture information that is not specified in the protocol. Collaboration with a trial statistician is recommended early in the design of a CRF in conjunction with the Data Management Plan/Data Manager, if involved.

The CRF needs to be appropriately structured with each study visit clearly defined. A CRF developmental tool is available for use and includes examples of potentially required fields (Appendix 1).

3.0 General Principles

When designing a CRF, the following general principles should be considered, the CRF should;

- Adopt a standardised format to achieve consistency in data recording

- Ensure that the data to be captured is entered into the CRF in a logical order – take in to account, for example, the order of trial procedures during a trial visit, order of entry in medical notes and laboratory reports
- Collect raw data to minimise unnecessary calculations and conversions
- Be laid out in an organised manner to minimise transcription error where data will be transcribed from source documents
- Where possible, provide tick box options and keep ‘free text’ to a minimum. (Tick box options should be exhaustive (e.g., provide an option for “other” or “NA” if appropriate)).
- Be separated into sections (e.g., by visit) to ease organisation, and include a checklist at the front of each section as a reminder of assessments required at each visit
- Use questions, prompts and provide instructions, which must be clear and concise and must not contradict other CRF pages or the protocol
- Have consideration for the study database and how data will be entered

3.1 General Format

The CRF will;

- Be clearly version controlled
- Have sufficient information in the header/footer, to identify every CRF page (e.g., be paginated in the page X of Y format), the Sponsor reference number, study name and participant ID of the CRF
- Have the appropriate number of boxes for the information required and if appropriate reflect the number of decimal places desired.
- Specify the unit of measurement ensuring they are the same as that listed in the protocol and source documents.
- Have a designated area for sign-off at eligibility review and at the end of the CRF by the investigator.

3.2 General content

The following content is typically found in a standard CRF (refer to Appendix 1). Please note this list is not exhaustive, nor is it all mandatory. The content will depend on the individual requirements of the study. Typically, the CRF will

- *List the visit name/number and date*
- *Provide confirmation of consent to the study or continued consent for each visit*
- *Screening and baseline data*
 - *Inclusion/exclusion criteria checklists with tick boxes*
 - *Confirmation of eligibility with a space for CI / PI signature to confirm eligibility (or medically qualified delegate)**
 - *If informed consent has been taken, date this occurred*
 - *Subject demographics (e.g. age, gender, ethnicity)*
 - *Disease characteristics of the subject*
 - *Relevant medical and medication history*
 - *Results of physical examination*
 - *Baseline data for the primary and secondary endpoints*
- *Subject randomisation*
- *Trial visits*
 - *During and post-treatment data for the primary and secondary endpoints*
 - *Data to assess compliance with the protocol and the (IMP) treatment regimen*

- *Exploratory or health outcome data not related to the main end-points*
- *Safety data*
- *Final visit (trial completion/withdrawal)*
- *Adverse events*
 - *A log of the adverse events which the participant has experienced during the trial*
- *Concomitant medications and other interventions*
- *Unscheduled form*
 - *To capture data from visits that were unscheduled as per protocol*
- *A place, preferably at the end of the CRF for the Principal Investigator (or delegates) signature to verify that the data is complete and accurate.*

*For CTIMPs where any eligibility are confirmed there must be evidence of who performed this confirmation to verify that the final decision to enter a subject into a trial was made by a medically qualified doctor. This must be reflected on the Delegation of Authority and Signature Log.

3.3 Timing

CRF design can be performed simultaneously with the development of the protocol or following finalisation of the protocol. The CRF should be finalised prior to the study Site Initiation Visit.

3.4 Review, approval and amendments to the CRF

Typically, CRFs do not require regulatory/competent authority approval however it should be reviewed by multiple personnel such as statisticians, data managers, research nurses and where necessary the Sponsor. Each draft should be version controlled and it is recommended that there is documented evidence of approval of the final version. Amendments to the CRF may be required from time to time due to, for example, a change to the trial design or data which is to be collected following an amendment to the protocol. Any amendments should be appropriately version controlled and reviewed.

For CTIMP studies, Sponsor Green Light will not be given until the CRF is finalised.

4.0 CRF Completion Guidelines

For large, complex or multi-centre trials it may be useful to compile a CRF completion guideline which would typically include advice on:

- Date format and partial dates
- Time format and unknown times
- Rounding conventions
- Trial – specific interpretation of data fields
- Definitions and guidance for completion of trial-specific activities/ procedures
- Entry requirements for concomitant medications (generic or branded names)
- Which forms to complete when
- What to do in certain scenarios, for example when a subject withdraws from the trial
- Missing/incomplete data
- Completing SAEs and reporting SAEs
- Repeat laboratory tests
- Protocol and GCP non-compliances/deviations.

5.0 Source Data

All study data should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification and applies to all types of records, irrespective of the type of media used.

While the CRF is normally used for transcribing data from the source data, there may be circumstances where the CRF has data directly recorded onto it, meaning that at least part of the CRF is a source document. In these circumstances, such data should be listed as source data in the study protocol and/or Source Data Agreement (see Appendix 4 to SOP S-1007 UoL).

Source Data is where the data are first captured (either written or electronically)
For example,

- Where a participant is asked to perform a test and the score of the test is recorded directly in the CRF, the CRF would be considered the source data.

Where a copy of an original record is provided (irrespective of the type of media used) it should be certified to have the same information as the original.

6.0 Data Recording Tools for Study Subjects

Occasionally data are entered by the study subjects themselves (or their carers) into paper or electronic diaries/self-assessment questionnaires. Where this is the case, it is recommended that diaries are designed to facilitate data collection by taking into account possible infirmities of the subjects, such as difficulty in writing or eyesight problems. The recorded data may have a high level of importance – for example, they may be an end-point for a study recording pain or asthma symptoms. This should be identified at the risk assessment stage. Consideration must be given to the importance of the subject recorded data and appropriate control processes implemented to ensure the robustness of the data.

If paper diary data are to be entered into a database by a separate data management facility, the diaries must be checked to ensure there are no subject identifiers present prior to removal from the investigator site and a copy should be retained by the investigator.

7.0 Worksheets and CRFs


There are situations where study-specific observations or tests are not performed routinely on site and therefore to avoid missing data use of a worksheet may be warranted. This may be particularly important for studies with high throughput and/or time-dependent data requirements such as vital signs in an intensive therapy unit setting. In these instances, the worksheets should be version controlled to ensure they are updated in line with any amendments to the protocol (e.g. eligibility criteria, additional data points). When worksheets are used as source data they must be retained and filed with patient notes.

8.0 Responsibilities

Responsibility	Undertaken by	Activity
Sponsor/CI	Head of Research Governance or delegate & CI	Decide and document what type of CRF will be appropriate during the Sponsor Risk Assessment/ Sponsor Review.
CI or delegate	CI or delegate	Design the CRF in accordance with the protocol specifications.
Statistician (or other person analysing the data) and other relevant personnel	Statistician (or other person analysing the data) and other relevant personnel	Review the CRF to verify the appropriate data are being recorded and to ensure consistency with the protocol. Document and retain evidence of this review.
Chief Investigator	Chief Investigator or delegate	Ensure the accuracy, completeness, legibility and timeliness of the data recorded in the CRF.
Chief Investigator	Chief Investigator or delegate	In the event of a protocol amendment perform a review of the CRF and ensure appropriate changes are made and version controlled.

9.0 Development and approval Record for this document

This table is used to track the development and approval of the document

Author	Job title	Reviewed by	Approved by	Date approved
Cat Taylor	Head of Research Governance	UoL Research Management and Operations Group (RSMOG)	Professor Nigel Brunskill 	14/06/2024

10.0 Review Record

This table is used to track any changes made on revised / reviewed versions:

Date	Version number	Reviewed by	Description of changes (If any)
June 2015	2	Diane Delahooke	Introduction of CRF template.
Oct 2016	3	Diane Delahooke	Change of logo and RGO address. Addition of need for CRF to be finalised before Sponsor green light given for CTIMP studies.
Sept 2021	3.1	Cat Taylor	Administrative changes
May 2024	4.0	Cat Taylor	<ul style="list-style-type: none"> • Minor update to SOP name • Removal of distribution record • Removal of office address. • Clarification as to the content and format of the CRF. • Major revisions to Appendix 1 – CRF development tool (previously template). Renamed appendix from 1 to 1a. • Concomitant medications log and adverse events table drawn out of previous appendix 1 to form appendix 1b and c respectively. • Removal of appendix 2 – guide to designing a CRF – information now contained within SOP and Appendix 1.