LinCTU
Lincoln Clinical Trials Unit

UNIVERSITY OF LINCOLN

STANDARD OPERATING PROCEDURE

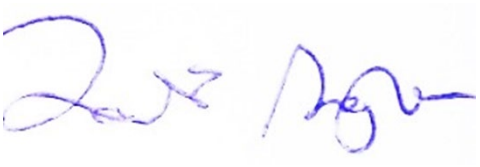
CASE REPORT FORMS (CRFs)

LinCTU SOP 01

Version Final 3.0. Date 08 August 2024

Effective Date: 01 September 2024

Next review: 2 years

Author:	Dr Elise Rowan Data Manager (Lincoln Clinical Trials Unit)
Approved in 2024 by:	 Dr Zahid Asghar (Lincoln Clinical Trials Unit Director)

Version History	Reason for change
1.0	First Clinical Governance version
2.0	First LinCTU version
3.0	Routine review of Version 2.0 was due in August 2024

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to date.

OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

The following have read, reviewed and advised on the SOP

Reviewer name	**Role**	**Date**
Elise Rowan	LinCTU Data Manager	13/08/2024
Tanja Kleinhappel	LinCTU Data Manager	19/08/2024

1. PURPOSE

This SOP applies to Case Report Forms (CRFs) in all types of clinical trials or studies sponsored or cosponsored by University of Lincoln, UK and developed, supported and managed by Lincoln Clinical Trials Unit (LinCTU). This includes Clinical Trials of Investigational Medicinal Products (CTIMPs) and medical devices. The term CRF for the purposes of this document, can mean a paper CRF or electronic CRF (eCRF).

2. SCOPE

This SOP is applicable to the Chief Investigator (CI) who should take overall responsibility for CRF design and completion on behalf of the sponsor. If needed, the CRF development task can be formally delegated to a LinCTU trial or data manager provided that the CI takes overall responsibility for final approval and sign off.

3. BACKGROUND

3.1. This SOP will ensure that clinical data is captured according to study/trial protocols and that the aims of the studies/trials are met as a result. The SOP will outline good CRF design practices and gives instruction for accurate and transparent CRF completion, maintenance, storage and archiving.

3.2. The CI may delegate the practical aspects of CRF design to a trial/data manager or researcher as appropriate but should take responsibility for providing overall supervision and final sign-off for this task.

3.3. All members of a trial/research study team who are involved with database design, data management, data collection and completion of CRFs should be familiar with this SOP particularly in relation to guidance for completing the CRFs.

3.4. The term CRF for the purposes of this document, can mean a paper CRF or electronic CRF (eCRF).

3.5. A CTIMP is a Clinical Trial of An Investigational Medicinal Product

4. CROSS REFERENCES AND RECOMMENDED RESOURCES

LinCTU SOP 02 Data Management

LinCTU SOP 03 Data Storage, Security and Backup

LinCTU SOP 04 Database Design

LinCTU SOP 12 Trial Master Site File

CG-QMS SOP CG15 Archiving (Clinical Data)

CG-QMS SOP CGD1 Data protection and confidentiality

RG-QMS RG03 Document Control – (Study documents)

Documents can be found on the LinCTU website under "Quality": https://linctu.lincoln.ac.uk/

5. PROCEDURE GENERAL REQUIREMENTS

5.1. All research study/trial data should be collected on study/trial specific case report forms (CRFs).

Note: In exceptional circumstances where source documents are to be used instead of CRFs then this must be stated in the protocol and approved by the sponsor. This may happen if for example, we are using raw data from interview recordings, scans or data downloaded automatically from sensors (such as step counters, heart rate, glucose monitors for example).

5.2. CRFs should only capture information essential to meet the aims of the study/trial and ensure the eligibility, safety, and well-being of the participants.

5.3. CRFs should be approved by the CI and (where appropriate) the trial/study statistician prior to use.

5.4. All current and previous CRF versions should be stored in the trial/site master file (TMF) as described in LinCTU SOP 12 Trial Master Site File.

5.5. Principles of Good Clinical Practice (GCP) should be followed when completing CRFs. Further guidance is available for CTIMPS at the following link:

Joint Statement on the Application of Good Clinical Practice to Training for Researchers (HRA, MHRA, Devolved Administrations for Northern Ireland, Scotland and Wales)

5.6. CRFs should be archived as advised by the sponsor in accordance with CG-QMS SOP CG15 Archiving (Clinical Data)

5.7. CRFs should be stored securely. Electronic CRFs should be maintained and stored in accordance with LinCTU SOP 03 Data Storage, Security and Backup.

5.8. CRFs should be made available for inspection/audit by Sponsor representatives and regulators.

5.9. Data captured in CRFs should accurately match any source of origin documents (i.e. it should be copied carefully if it is sourced from medical records, scans, blood test result print outs etc).

GENERAL CRF DESIGN REQUIREMENTS

5.10. CRFs should capture all data and procedures to be carried out on each participant at each visit as defined by the study protocol and in line with the statistical analysis plan. CRFs can include a check list for inclusion/exclusion criteria if appropriate. No additional information should be collected above and beyond this.

5.11. Participants should only be identified in CRFs using a unique participant identification code.

Note: The Participant Screening Enrolment log and any other documents/electronic records/data sheets storing the link between participant identification codes and any other personal participant identifiers (e.g. participant name, address, email) should either be encrypted with restricted access or stored securely with restricted access.

Personal participant identifiers should only be accessible by those members of a research team who need access to that information for the purposes of running the project. Guidance on protection of personal identifiers is given in LinCTU SOP 02 Data Management.

5.12. Consideration should be given to CRF layout to facilitate the correct sequence of data collection and easy data recording (or data entry in the case of electronic CRFs).

5.13. CRFs should capture participant demographics as defined in the protocol but should not capture any other personally identifiable information above and beyond what is necessary for the conduct of the study and relevant statistical analyses of results.

5.14. Data fields should be unequivocal, logical, indicate units of measurement and give space for decimal places where appropriate.

5.15. Free-text fields should be kept to a minimum unless there is a good reason for this as described in the protocol or due to the nature of the data to be captured.

5.16. Prior to release of the CRFs as either paper CRFs or eCRFs (via a database/data management system), there should be a validation/testing phase whereby members of the research team and CI critically review the CRFs and where dummy data is captured on any paper CRFs/entered directly into the study database. CRFs should be checked to establish that the CRF is easy to use, free of errors and facilitates collection of data in the correct format (e.g. uses the correct units, decimal places, date formats etc.) Some guidance on this is given in the LinCTU SOP 04 Database Design.

5.17. CRFs can be revised during an on-going study and revised versions must be formally tested, approved and documented. CRF changes may be required under (but not limited to) the following circumstances for example:

- Protocol changes (note these will need formal ethics approval)
- To correct errors in the CRF design

- To add new category responses to existing questions e.g. adding an “if other, please specify option” or similar.
- Closing recruitment to a comparison group

5.18. Records of CRF validation and release should be retained in the TMF.

ADDITIONAL DESIGN REQUIREMENTS FOR PAPER CRFS

5.19. Paper CRFs shall be version controlled, paginated and dated in accordance with RG03 Document Control – (Study documents). Finalised electronic versions of paper CRFs should be stored as read only files so that there is no risk of inadvertent changes being made prior to printing the pro-forma(s).

5.20. The unique participant identification code shall be documented at the top of each page.

5.21. Study ID (e.g. IRAS ref) and short study name shall be documented in the header/footer of each CRF page.

5.22. Paper CRFs should be designed to avoid the need for free-hand text as much as possible. This will facilitate more accurate data transfer into the study/trial database and coding prior to analysis.

DATA TO BE CAPTURED

5.23. CRFs can include, but not be limited to, capturing the following categories of information:

- Unique Participant identification code (this is always essential and should be recorded on every page if paper CRFs are used)
- Date of birth (consider if the full date of birth is needed for any statistical analyses or protocol time-related calculations using dates, if not, age is a less personally identifying alternative)
- Date/indication of consent.
- Confirmation of any inclusion criteria being met (eligibility confirmation)
- Gender/sex
- Information about drug and alcohol use
- Demographics (as described in protocol)
- Geolocation or partial post-code information (only collect this if it is necessary for analysis for the study/trial primary and secondary outcomes)
- Medical history
- Primary and secondary outcome measures (including standardized and validated test scales) *.
- Record of any dosing and compliance issues
- Randomisation
- Trial treatment
- Adverse events
- Concomitant medications
- Withdrawal from the study/trial
- End of treatment form

*Where standardized and validated test scales are used, it is the responsibility of the CI to obtain/pay for any approvals and licence agreements for using and or reproducing these in either paper or electronic format. This information should be forwarded to the trial and data managers for storage in the TMF and to assist with database design.

Where dates of birth and other personally identifying items such as postcode, partial postcode, geolocation are collected in e-surveys and eCRFs, consider whether electronic database encryption features can be utilized to add further security to these items.

TRAINING STAFF TO COMPLETE CRFS

5.24. Study staff should be trained to complete CRFs before the study begins.

5.25. This training should take place at all study sites and should be delivered in a consistent manner.

5.26. Training should include an explanation of the CRF contents and how they relate to the study/trial protocol.

5.27. Training can be provided by the CI/Trial manager and/or data manager as appropriate.

5.28. Attention should be given to the number, periodicity, and sequence of study assessments / visits / treatments; study staff should be clear about what data should be collected and recorded at each interval.

5.29. Where data is transferred into a database (either transcribed retrospectively from paper CRFs or directly via electronic CRFs (eCRFs)), then training should be provided for this also. Study staff should be given instruction as to how to log into and out of the database and enter the data.

5.30. If any regular data transfer is required during the course of the study (for example database replicas/updates being sent from individual sites to a central data manager) then training and on-going support for this should be provided. Guidance for database training and user support is given in the LinCTU SOP 04 Database Design (see section 4 above).

5.31. Any CRF/database training should be documented in a training log for each study which is stored within the TMF. It is at the discretion of the CI to decide whether the CRF training forms part of the site initiation visit or whether it is provided separately.

RECORDING OF DATA IN CRFs

5.32. CRFs should only be completed by those who have been trained and delegated to do so.

5.33. CRFs should be completed as soon as possible either during or after each participant treatment/assessment.

5.34. No personally identifiable information (e.g. participant name, phone, email and address) shall be recorded on the CRFs (unless there is a specially encrypted section of the study database for this particular information).

5.35. Paper CRFs should be completed in permanent ink only (i.e., <u>not</u> pencil).

5.36. CRF entries should be precise, readable and it should be possible to cross-reference them back to source data where this exists. (N.B. Source data can be medical records or other agreed documentation that serves as a source of information for the study).

5.37. Any errors on paper CRFs should be crossed through once, corrected then initialled and dated by the researcher. The original value/errors should still be visible for reasons of audit/transparency. If necessary, file notes can be appended to the CRF to further explain edits/corrections. Audit features of online database systems should be used to track changes to data in eCRFs.

5.38. Correction fluid should <u>never</u> be used in paper CRFs.

5.39. All required fields should be completed. If a procedure is not carried out, then this should be noted. In eCRFs audit features should be used to indicate when data items are missing and record reasons for this.

5.40. CRF completeness and data quality will be monitored on an on-going basis during trials (usually by the trial manager, data manager, researchers -as agreed during trial set-up). This will maximise the amount of data collected and minimise errors and breaches of protocol.

5.41. Any data queries/concerns/recommendations for change arising from CRF data monitoring will be circulated to relevant members of trial teams. Within eCRFs it should be possible to raise queries within the database itself.

5.42. Data queries shall be addressed quickly, and an audit trail should detail the outcome. (N.B. This could take the form of file notes, emails, or be captured electronically in the case of more sophisticated electronic data capture systems).

STORAGE AND ARCHIVING

5.43. During an on-going study/trial, paper CRFs should be stored securely in the relevant study site/ trials unit/ research office space - inside filing cabinets which are accessible only to members of the specific study/trial team.

5.44. At the end of the study paper CRFs should be archived along with other study documents as described in the CG-QMS SOP CG15 Archiving (Clinical Data)

5.45. At the end of the study all electronic data shall also be archived as described in the CG-QMS SOP CG15 Archiving (Clinical Data).

6. FLOW CHART