UNIVERSITY OF LINCOLN

CLINICAL GOVERNANCE - STANDARD OPERATING PROCEDURE

CASE REPORT FORMS

CG-QMS SOP CGD5

Version Final 1.0 Date 01 May 2021

Effective Date: 01 August 2021

Next review: 2 years

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Version History	**Reason for change**

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OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

1. PURPOSE

This SOP applies to Case Report Forms (CRFs) in all types of clinical trials or studies sponsored or co-sponsored by University of Lincoln, UK. 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.

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, 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 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

4.1 CG-QMS SOP CG07 Trial Master / Site File

4.2 CG-QMS SOP CG15 Archiving (Clinical Data)

4.3 CG-QMS SOP CGD1 Data protection and confidentiality

4.4 CG-QMS SOP CGD2 Data Management

4.5 CG-QMS SOP CGD3 Data Storage, Security and Backup

4.6 CG-QMS SOP CGD4 Database Design

4.7 RG-QMS RG03 Document Control – (Study documents)

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 or 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).

5.5 NHS Principles of Good Clinical Practice (GCP) should be followed when completing CRFs for CTIMPs. Further guidance available:

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/good-clinical-practice/joint-statement-application-good-clinical-practice-training-researchers-hra-mhra-devolved-administrations-northern-ireland-scotland-and-wales/

5.6 CRFs should be archived as advised by the sponsor in accordance with SOP CG15Archiving (Clinical Data)

5.7 CRFs should be stored securely. Electronic CRFs should be maintained and stored in accordance with SOP CGD3 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 (this 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.

5.12 Note: The Participant Screening Enrolment log and any other documents/electronic records/data sheets storing the link between participant identification codes and personal participant identifiers (e.g. participant name, address, email) should either be encrypted with restricted access (if within the main study database) or stored securely with restricted access (if stored separately). 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 SOP CGD2 Data Management, CGD1 Data Protection and Confidentiality and CG07 Trial Master / Site File.

5.13 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).

5.14 CRFs should capture participant demographics as defined in the protocol but should not capture any other personally identifiable information.

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

5.16 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.

5.17 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/entered and 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 SOP CGD4Database Design.

5.18 Records of CRF validation 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
- Date of consent
- Confirmation of any inclusion criteria being met (eligibility confirmation)
- Demographics (as described in protocol)
- Medical history
- Primary and secondary outcome measures
- Record of any dosing and compliance issues
- Randomisation
- Trial treatment
- Adverse events
- Concomitant medications
- Withdrawal from the study/trial
- End of treatment form

5.5 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 Database Design SOP (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 trial master file. 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.

5.38 Correction fluid should never be used in CRFs.

5.39 All required fields should be completed. If a procedure is not carried out, then this should be noted.

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

STORAGE AND ARCHIVING

5.41 During the course of 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.

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

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

6. FLOW CHART