University of Hertfordshire UH

University of Hertfordshire

DESIGNING A CASE REPORT FORM

Clinical Trial Support Network (CTSN)

Standard Operating Procedure for Designing a Case Report Form

SOP Number: gSOP-15-02	**Effective Date:** 28th July 2022
Version Number: v2.0	**Review Date:** Every 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure (SOP).

This document sets out the procedures to be followed by all staff for designing a case report form (CRF) either in paper (pCRF) or electronic format (eCRF).

Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

2.0 PURPOSE

- To provide guidance that will assist in the development of appropriate data collection tools e.g. CRFs.
- To define the review and approval process for data collection tools.
- To define the data collection process and define source documentation requirements for UH sponsored trials and/or CTSN adopted studies.

3.0 APPLICABLE TO

This applies to all staff involved in clinical research sponsored/co-sponsored by UH or adopted by the CTSN, including but not limited to: Chief Investigators (CIs), Principal Investigators (PIs), Research Fellows, Consultants, Statisticians, Clinical Trial Pharmacists, Research Managers, Research Nurses, Clinical Trial Practitioners, Allied Health Professionals, Trial Managers, Clinical Studies Officers, Data Managers, Research Assistants and students.

4.0 RESPONSIBILITIES

Case Report Forms and Data Collection Tools

The CI or delegate (DI) is responsible for the design and development of CRFs. The CI is also responsible for ensuring that there are adequate CRFs for use in the study in all participating sites. Instructions should be given to all participating sites on how to complete the CRFs to ensure data is collected in a standardised fashion. A CRF completion guide may be useful in a multicentre study.

The statistician and Sponsor, or CTSN if delegated, should review and approve the CRF of UH sponsored/co-sponsored clinical trials prior to study approval. Subsequent amendments to CRFs should also receive statistician and Sponsor/CTSN approval.

5.0 PROCEDURE

5.1 Design and Development of Case Report Forms

5.1.1 Case Report Forms (CRFs) are the usual data collection tool used in a clinical trial and are essential for quality assurance and control. The CRFs can be either in paper format (pCRF) or an electronic CRF (eCRF). The procedures outlined below apply to both CRF formats.

5.1.2 A CRF should be designed to ensure that it captures all the information which is required according to the protocol. **It should not capture additional information which is not specified in the protocol.** It is recommended that the study team also request review of the study CRF by an independent data manager.

5.1.3 The CRFs should be version controlled and a clear amendment history should be possible to follow/ view in the Trial Master File (TMF).

5.1.4 The CRF should follow the schedule of visits and should be consistent with the treatment schedule in the protocol. Preferably the CRF should be designed in such a way that it should act as a prompt to the investigators to perform the study specific investigations as laid out in the protocol's treatment schedule. This will help the Sponsor/CTSN to confirm that the protocol was followed and for the statistician to build in edit checks within the database to assist with the management and analysis of the data. As a minimum, the following should be taken into consideration during CRF design:

- The arrangement of the data fields should be clear, logical, and user friendly.
- When 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.
- For variables where the actual value is captured, the number of boxes required should be adequate and if appropriate reflect the number of decimal places desired.
- The unit of measurement should be specified.
- Consideration should be given as to how the CRF will relate to the database.
- Consideration should be given as to collection of data for unscheduled participant visits.

5.1.5 The design of the CRF should include some core data as minimum requirements to ensure data collected per study participant is Good Clinical Practice compliant, as follows:

- Inclusion/exclusion criteria checklist with tick boxes (with investigator's signature).
- Date informed consent taken (with investigator's signature).
- Participant demographics (e.g., age, gender, ethnicity).
- Relevant medical history.
- Results of physical exam.
- Baseline data.
- Primary and secondary endpoints (with investigator's signature).
- Laboratory data, ECG etc.
- Dosing and compliance data.
- Adverse events.
- Concomitant medications.
- Withdrawal/Off study form.
- Serious Adverse Event Reporting Form (with investigator's signature).

5.1.6 CRFs should have a study identification number (study number, study title, sponsor). All pages should have the participant ID and initials. The date of each participant visit should be captured. There should be a place, preferably at the end of the CRF for the PI's signature to verify that all data is complete and accurate. **To comply with the data protection laws, the CRF should not contain patient identifiable information unless this has received ethics approval and is stated within the protocol.**

5.2 CRF Approval Process

CRF design is a multidisciplinary process, involving collaboration with the research team, the trial statistician, data management (if applicable) and Sponsor or CTSN where relevant.

The final version of the CRF should be approved by the Sponsor, or member of the research team with delegated authority such as the Trial Manager. For UH sponsored clinical trials, draft CRFs should be sent to the CTSN for review prior to approval.

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.

5.3 Management of Amendments to CRFs and Statistical Database

5.3.1 Amendments to the CRF may be required from time to time due to, for example, a change of trial design or a change in data requirements as specified in an amendment to the protocol

and /or statistical analysis plan.

5.3.2 The CI or delegate submits the proposed change to the CRF to the Sponsor or CTSN for review and approval.

5.3.3 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.

5.3.4 Any amendments to the CRF should conform to requested amendments to study documents and/or revised protocol.

5.3.5 The CRF page numbering and version information should be updated to reflect the current status of the document.

5.3.6 Any changes to the statistical database should be controlled and a clear audit trail should be present.

6.0 RELATED SOPS & DOCUMENTS

- gSOP-09 Amendments
- gSOP-12 Monitoring
- gSOP-34 Statistical Input into Clinical Trials
- gSOP-041 Completing a CRF

7.0 APPENDIX

- Appendix 1: Definitions

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
2.0	28th July 2022	Review of content

9. AUTHORSHIP & APPROVAL

Author

Signature  **Date 16 June 2022**

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature **Date 16 June 2022**
Professor J M Senior

10. AGREEMENT (MOVE ON TO SEPARATE SHEET BEFORE PRINTING)

Please detach and retain within <u>your training files</u>

I have read and understood the contents and requirements of this SOP (ref gSOP-15-01) and accept to follow University policies implementing it.

Recipient

Signature: ……Date: ……..

Name & Position: ……

Please retain copy of the signed form for your reference in your training file

Appendix 1: Definitions

Adverse Event (AE)
Any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

Case Record Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject".

Chief Investigator (CI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial
A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Delegated Individual (DI)
An individual delegated by the PI to carry out their task(s).

Good Clinical Practice (GCP)
As defined in the Regulations.

International Conference on Harmonisation (ICH)
The ICH produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as (ICH-GCP).

Principal Investigator (PI)
A Registered Physician, Dentist, Pharmacist or Registered Nurse who has responsibility for the conduct of the trial at a host site.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)
Any untoward medical occurrence or effect that at any dose results in:
- Death
- Is life-threatening*
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly or birth defect
- Is an important medical event

* "life-threatening" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Site File
Site Files are held by the Principal Investigator at sites and contain copies of the essential documents, local approvals, signed consent forms and completed data forms.

The Regulations
Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Master File
The Trial Master File (TMF) will be held at the principal site by the sponsor, Chief Investigator or at the co-ordinating Centre. The TMF should contain all essential documents defined as documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. A Trial Master File should be set up at the beginning of a trial and maintained up-to-date throughout the trial until trial conclusion.

For trials currently running, it is recommended that Section 8 of the ICH-GCP Guideline is followed as guidance in order to meet statutory requirements. However, some of the documents listed may not be available or applicable in many non-commercial trials. The appropriate documentation will vary according to the trial and sponsor requirements.