STANDARD OPERATING PROCEDURE FOR PREPARING AND MAINTAINING CASE REPORT FORMS (CRF) FOR USE IN CLINICAL RESEARCH

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1. PURPOSE

A Case Report Form (CRF) is defined in ICH GCP as "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".

2. SCOPE

This document applies to studies sponsored or co-sponsored by the University of Dundee (UoD) and/or NHS Tayside (NHST).

This Standard Operating Procedure (SOP) is intended for use by data managers, researchers, trial co-ordinators, research nurses and any other UoD or NHS Tayside staff who design and/or complete CRFs.

3. RESPONSIBILITIES

Chief Investigator (CI):	Design CRFs to comply with Good Clinical Practice (GCP) and the protocol. Ensure validation of any electronic CRF (eCRF) prior to use. Review and approve eCRF/CRF for use. Provide Sponsor with copy of approved and all amended versions. Ensure CRFs are available at sites prior to first consent. Ensure documented training is provided to study team in CRF completion to ensure data is collected in a consistent manner.
CI/ medically qualified delegate:	Confirm eligibility prior to participant being randomised into study or receiving study treatment. For a Clinical Trial of an Investigational Medicinal Product (CTIMP), eligibility must be confirmed by a medically trained doctor, dentist or pharmacist, as appropriate.

4. PROCEDURE

4.1 Policy

The use of a CRF is mandatory for a CTIMP and is highly recommended for all other studies.

A CRF for any project falling within the scope of the Medicines and Healthcare Products Regulatory Agency (MHRA) cannot be used as source data without prior approval of the Sponsor and included in source data identification list provided to the Monitors.

Where this is agreed, it is mandatory that data relevant to a participant's medical history be recorded in the medical records and be available to those responsible for the patient's ongoing care. This may include but not be limited to, copies of safety investigations e.g., blood results, ECGs.

4.2 General

- Clinical research data must be collected using CRFs.
- The CRF must be designed to collect only the information required to meet the aims of the study and to ensure the eligibility and safety of the participant.
- Where possible in electronic CRFs/Electronic Data Capture (EDC), upper and lower limits for variables must be imposed to minimise the risk of data entry error.
- CRFs must be version controlled in accordance with TASC SOP on version control.
- Each page of paper CRFs must be numbered and include the version number and date.
- Each CRF must include the Study reference number, protocol title (or acronym).
- CRFs must not include personal identifiable information.
- A unique ID must be provided for each participant.
- CIs may include other identifiers on each page, such as site (for multicentre studies), participant initials, or visit numbers as in accordance with data protection.
- There must be clear evidence that the CI or a statistician has approved the CRF prior to use.
- Paper CRFs must be stored in a secure location and available for monitoring purposes whilst the study is active.
- eCRFs must be on secure servers with limited access as per sponsorship risk assessment.
- Read only access to eCRFs must be available to the monitors/auditors.
- CRF completion must be a delegated task from the CI or Site Principal Investigator (PI) and documented in the Delegation Log (Doc Ref 057).

- All versions of paper CRFs must be filed in the Trial Master File (TMF) and/or link provided to direct to electronically held data.
- CRFs must be archived in accordance with the TASC SOP on Archiving.

4.3 Standard CRF Design

- The CRF must be consistent with the protocol.
- The Inclusion/Exclusion criterion must be clear and unambiguous and include confirmation of eligibility.
- The arrangement of the data fields must be clear, logical, and user friendly. It must not be open to misinterpretation.
- There must be no unnecessary duplication.
- Consideration must be given to layout of paper CRFs in relation to database entry.
- Space for free text is discouraged unless a specific requirement of protocol.
- For variables where the actual value is captured, the number of boxes provided must be adequate and, if appropriate, reflect the number of decimal places.
- The unit of measurement must be specified.
- Laboratory values must be entered without conversion from printed reports. If conversions are necessary, e.g. in multicentre studies where units of measurement differ, space must be made available on the CRF for the original figure, the conversion factor (this may be pre-printed) and the converted result.

4.4 Example data to be included in CRFs

- Study identification.
- Unique participant ID number.
- Date of Informed Consent.
- Age at consent (to confirm all participants are fully eligible prior to any study related activity). Full date of birth shall not be recorded.
- Demographic data as per protocol requirements.
- Confirmation of eligibility by the CI or an individual delegated the task – for CTIMPs eligibility must be confirmed by a medically trained doctor, dentist or pharmacist, as appropriate.
- Medical history.
- Concomitant medications.
- Date of Randomisation.
- Primary and secondary outcomes.
- Dosing and compliance.
- Study visit data – including baseline/screening.
- Adverse events (AEs) and Serious Adverse Events (SAEs).

- Discontinuation of trial medication.
- End of treatment form (withdrawal/completed) including CI or PI signature to verify that all data are complete and accurate.

4.5 Training in CRF completion

- Clear instructions or training must be given on how to complete the CRFs to ensure that data are collected in a standardised fashion.
- CRF training must be documented in a training log and/or meeting minutes.
- A CRF user guide is recommended for use in a multicentre study.

4.6 Completing the CRF

- CRFs must be completed only by those authorised to do so in the Delegation Log (Doc Ref 057).
- The CRF must be completed as soon as possible after each participant assessment/visit.
- Data shall be complete without omissions. Any missing data must be explained e.g. “no information”, “not applicable”, “not done” or “unknown” and not left blank.
- Entries must be accurate, legible and verifiable.
- Laboratory values that lie out with reference ranges, must be highlighted/noted in the CRF along with a record of action taken e.g. AE reported.

4.7 Verifying against source data

- CRFs must at all times match with source data; discrepancies shall be clearly noted, and the reason explained.
- Data with personal identifiers within, such as copies of ECGs and Biochemistry Reports must be clearly identified with the following information:
    - Study code
    - Participant ID
    - Visit Number.

All personal identifiers must be redacted within the CRF as required by Protocol and/or DPIA.

4.8 Corrections

4.8.1 Paper CRFs:

- Incorrect entries in paper CRFs and Source Data must be crossed out with a single line so that the incorrect entry is still legible.
- The correct data must be entered.
- The correction must be Initialled and dated.

- An explanation of the correction must be documented if not obvious why the change was made.
- Correction fluid must not be used.

4.8.2 Electronic CRFs:

The Sponsor must be provided with the following information for any electronic CRF:

- Software supplier
- Version number as approved for use by CI
- Installation date
- Validation status
- Confirmation of who validated the system
- Server host and location.

Corrections must be subject to an audit trail to enable the following to be tracked:

- The data point
- Who entered the original data
- When this occurred
- Who changed the data
- What data was changed
- When this occurred
- Why this occurred.

4.9 Storing and accessing CRFs

- Completed paper CRFs must be stored when not in use in a locked secure storage area with limited access.
- Electronic CRFs must be on a secure server with limited access and automatically backed-up.
- Access to CRFs must be restricted to delegated study staff, monitors, relevant UoD or NHST staff and regulatory authorities.
- At the end of a study, archiving must be conducted in compliance with the TASC SOP on archiving.

5. ABBREVIATIONS & DEFINITIONS

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Forms
CTIMP	Clinical Trial of Investigational Medicinal Product
eCRF	Electronic CRF
EDC	Electronic Data Capture
GCP	Good Clinical Practice
MHRA	Medicines and Healthcare Products Regulatory Agency
NHST	NHS Tayside
PI	Principal Investigator

SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TASC	Tayside Medical Science Centre
TMF	Trial Master File
UoD	University of Dundee

6. ASSOCIATED DOCUMENTS & REFERENCES

Doc Ref 057: Delegation Log

7. DOCUMENT HISTORY

History prior to 2021 is in the archived SOPs available from TASC Quality Assurance Dept.

Version Number:	Reviewed By (Job Title):	Effective Date:	Details of editions made:
10	Patricia Burns (Senior Research Governance Manager)	10/09/2021	Section 4.4 updated to comply with GDPR with regards to Date of Birth.
11	Patricia Burns (Senior Research Governance Manager)	15/08/2023	Updated section 4.2, regarding eCRF, to align with sponsorship risk assessment. Minor clarifications throughout.
12	Patricia Burns (Senior Research Governance Manager)	12/01/2024	Updated section 4.7 with regards to redacting personal identifiers in CRFs.

8. APPROVALS

Approved by:	Date:
Dr Valerie Godfrey, TASC Quality Assurance Manager, on behalf of TASC Clinical Research Guidelines Committee	12 Jan 2024