SOP 350 Designing and Developing a Case Report Form

For Use in:	Research & Development
By:	All staff
For:	All staff involved in the conduct of research
Division responsible for document:	Research & Development
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SOP 350 v1.2

This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

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2. Definitions of Terms Used / Glossary

CRF	Case Report Form
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trial Unit
ICH GCP	International Conference on the Harmonisation of Good Clinical Practice
NCTU	Norwich Clinical Trial Unit
PI	Principal Investigator
QC	Quality Control
R&D	Research and Development
SI	Statutory Instrument
SOP	Standard Operating Procedure
TMF	Trial Master File

3. Scope

This SOP describes the procedure for development and design of Case Report Forms (CRFs) used in clinical trials

ICH GCP E6/SI 2004/1031

4. Introduction

A Case Report Form (CRF), according to the ICH GCP guidelines, is 'a printed, optical, or electronic document designed to record all the protocol required information to be reported to the sponsor on each trial subject.' ICH GCP section 1.11

In some cases, the CRF may be the source document, for example for a study where a participant is asked to perform a test and the score of the test is recorded directly in the CRF.

CRF's should collect **only** appropriate trial data, in an appropriate format, as set out in the protocol and for anticipated analyses. It is important that CRFs **do not** collect any additional data that is not to be analysed or outside the requirements of the study aims.

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. A CRF can either be paper or an electronic data capture system.

For guidance relating to completing a CRF refer to **SOP 351 Completing a Case Report Form.**

5. Rules

Quality Control (QC) of the CRF is required versus the protocol to ensure the CRF meets the protocol requirements

- QC must be undertaken prior to using the CRF for the participants on the trial

An electronic data capture system may require validation

- Refer to **SOP 730 Computer System Validation**

6. Responsibilities

The Chief Investigator (CI)

- Approve the first version of the CRF and any amendments prior to release
- May delegate the design to others, for example to the Trial Manager or a Clinical Trial Unit (CTU)
- Ensuring that copyright permissions are obtained for the replication of any licensed measures (for example EQ-5D™ and HADS), where applicable

The Principal Investigator (PI)

- Must ensure system users at their site are trained and confident to use the system.

The Database Manager

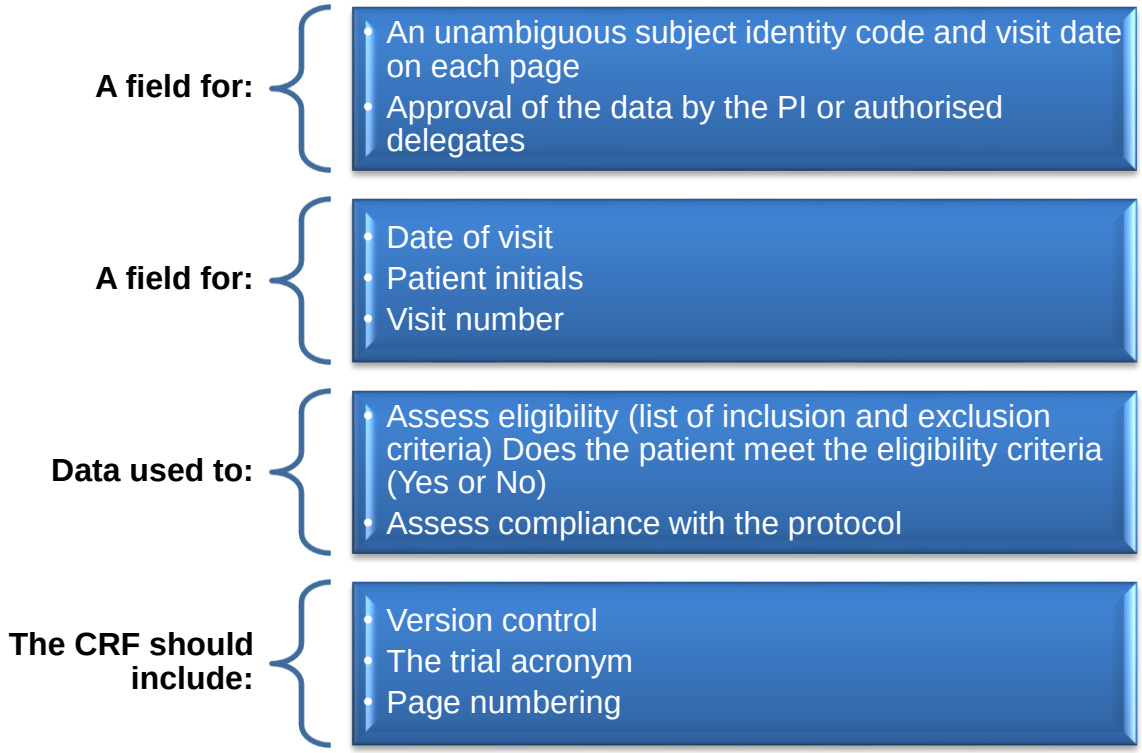
- Should sign off the CRF approval form to ensure that the data fields are consistent with the database

The Sponsor (Activities may be delegated to a CTU)

- Ensure training for all system users and effective access for support
- Restricted system access – individual ID / password log in for a database
- Secure database audit trail –users should not be able to access the audit trail.
- Database back-up procedures as determined by the Sponsor at appropriate intervals to minimise potential data loss

7. Design Procedure

The design of the CRF should be based on the requirements of the protocol and the statistical analysis of the trial data and should be appropriately structured, with each visit clearly defined. For example, a standard CRF would include:

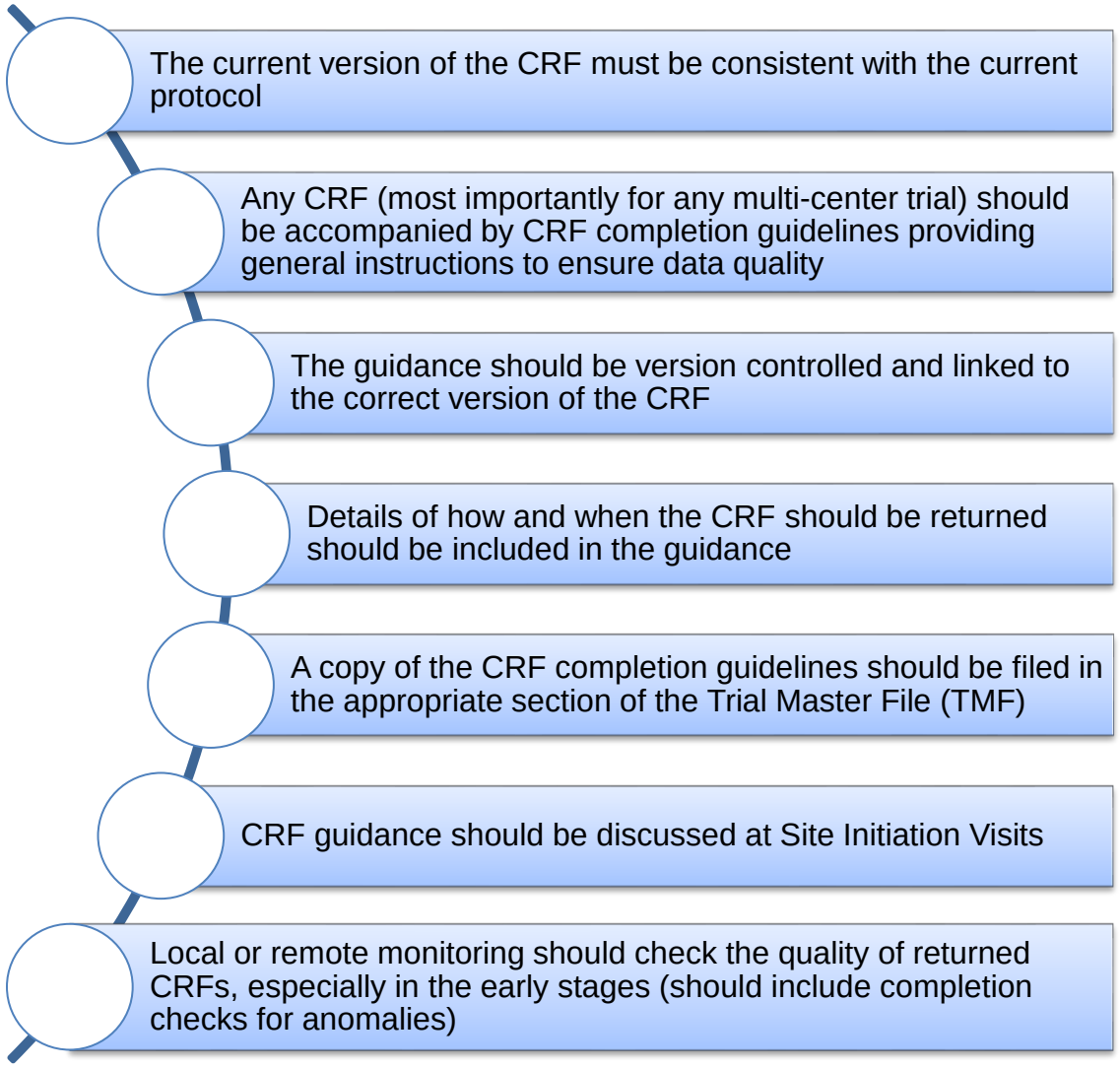


Further suggested specifics of the design of a CRF can be found in **Appendix 1 and 2**.

Unless explicit consent **and** ethical approval are granted, only non-identifiable patient data should be collected in the CRF

- The patient's hospital number or full name should not be collected in the CRF as it can be directly linked to the patient's medical records thereby compromising patient confidentiality

8. CRF Guidance



9. CRF Development

The CRF development process should demonstrate evidence of approval by the CI in collaboration with pertinent colleagues, for example PI, sponsor, clinical, operations, pharmacovigilance and statistics, health economics (if appropriate), data management and quality assurance experience.

All collaborations should be recorded within the development documentation for each version of the CRF.

The CRF for an NNUH sponsored CTIMP must be developed in collaboration with NNUH Pharmacy.

The CRF and database (where applicable) should be developed in parallel.

10. CRF Review Procedure

As part of the data management processes, an annotated CRF may be produced

- The annotated CRF makes up part of the specification for the database and defines the type and format of data that the statistician will analyse
- The annotated CRF must provide all the information needed to complete the database specifications (**SOP 805 – Trial Data Management System – TDMS Set-Up**)
- Trial specific databases may be used as an alternative

As the CRF tool is the basis of obtaining the dataset for analysis:

- The CRF and the annotated CRF should be formally approved before use and this procedure documented

11. Amendment to a CRF post finalisation

Any changes to a CRF will require a new version of the specification documents (for example data management plan).

A risk assessment of the changes to the CRF must be undertaken prior to release of the new version.

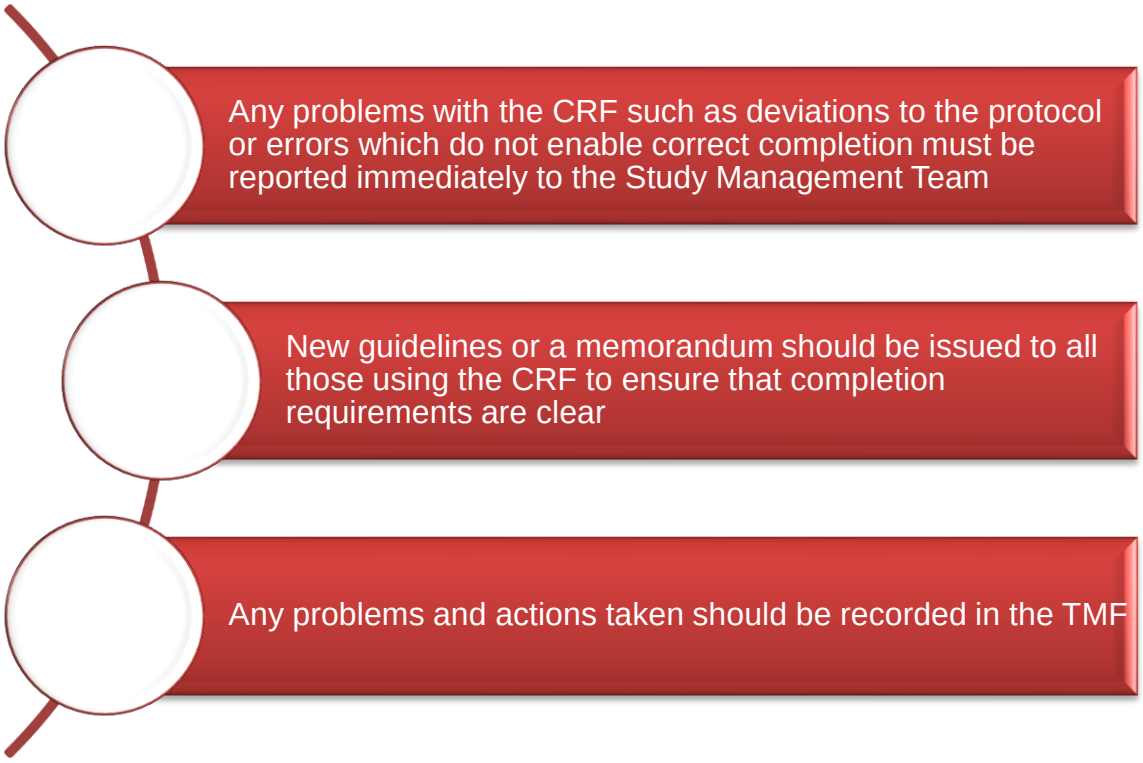
The risk assessment must include and changes which will have an impact on the functionality of the associated database.

Changes to the database must undergo a change control procedure and must be tested before the database release, see (**SOP 810 - Trial Data Management System – Specification, Development, Test and Deployment**).

Amendments to the CRF must be made in collaboration with relevant colleagues (see section 9 for guidance).

Any amendments made to the CRF must be documented and approved on a controlled document change log before any changes to the database can be made.

12. Reporting of Problems with the CRF



13. Appendix 1 Guidance for CRF design

All CRF pages must:

- Be the same format to provide consistency
- Have a standard header and footer
- Allow adequate amounts of free space on the CRF page to aid readability
- Be designed with consistent and linear format to ease completion

The header should include:

- Short title or number of the trial and logo (if applicable)
- Title or unique ID number of the CRF
- Site reference (name or number / this may be a component of the patient's trial ID)
- Participants Trial ID
- Participants Initials
- Participants date of birth

The footer should include:

- CRF name, version number and date
- Page number and total page number

CRF Main Page Content:

- The layout should have a logical ordering that follows with the schedule of visits as defined in the clinical trial protocol
- The layout should allow for ease and clarity of data entry in order to limit the number of data queries
- Questions should be grouped into sections with headings indicating their content
- Question instructions should be clear, succinct, appropriately located and presented in the same manner and position throughout
- Format of questions must provide standardised answers that aid completion
- Questions should be constructed in the yes/no format or with a set list of options wherever possible, to limit errors and collection of unnecessary or ambiguous data
- Where a list is not exhaustive an 'other' option should be included with space for free-text comments

Design format should:

- Avoid collecting free text, where possible
- Ask explicit unambiguous questions with only one clause
- Avoid double negatives in the questions
- Provide pre-coded answer options to ease the analysis
- Indicate if a question can have one answer or multiple answers
- Use absolute, rather than comparative, questions
- Collect raw data rather than calculated data, e.g. for age, collect birth date. If a measure has a computed value, please do not compute the value unless this is needed for decision making at that time
- Collect dates in a uniform fashion (DD/MMM/YYYY) and provide guidance on the expected format
- Pre-specify the choice of units wherever possible e.g. mg, ml, cm
- Avoid requesting unnecessary calculations
- Avoid duplication of data
- If missing data is anticipated for key questions (e.g. primary endpoint) then provide additional questions that allow the reason why the data is missing to be pre-coded wherever possible rather than leaving the field or box blank
- The additional questions will depend on the study and visit, but may include participant did not attend, equipment malfunction, participant withdrew consent, sample unobtainable, range of test unknown

Visit Schedule:

- Must be produced to:
- Document which forms will be used at which visits
- Inline with **SOP 810 – Trial Data Management System – Specification, Development, Test and Deployment.**

14. Appendix 2 Guidance for CRF Content

Depending on the data required by the protocol, a standard CRF document might include, but is not limited to, the following pages:

- Front cover sheet
- Eligibility form
- Demographic information
- Medical and medication history and physical examination (including relapse/recurrence form)
- Screening visit
- Randomisation/registration form
- Confirmation of eligibility
- Primary and secondary end-points
- Treatment form (treatment, doses, administration routes, reductions, reconciliation, expiry date and batch numbers)
- Participant Completion (documenting the date, reason and circumstances for the cessation of visits or data collection due to withdrawal, death, progression or other)
- Concomitant Medication
- Adverse Event
- Serious Adverse Event
- Follow-up forms
- Patient Withdrawal
- End of Trial/Withdrawal form
- Investigator sign-off

15. Approval

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16. Reason for Update and Training Implication

This replaces SOP 350 v1.1

Update	Reason	Training Implication	Action
Updated throughout Updated to new template	To reflect current practice	Yes	Review SOP and update training matrix