Quality Control Document:

Guide to Case Report Form Development

# Purpose

This document can be used as a guide and training tool when developing a case report form (CRF) for use in a clinical research project. It provides guidance on the format and design of the CRF to ensure accurate data capturing, advice on procedures for implementing and amending CRFs, and factors to consider for CRF completion. This document is designed to be used in conjunction with the CRF Development SOP (UoB-CRF-SOP-001).

# Background

A CRF can be a printed, optical or electronic document designed to record all the protocol-required information on each participant. A CRF can be the source data or used to transcribe from the source data. The purpose of a CRF is to provide a standard, consistent, timely and structured way of capturing data in accordance with the protocol, which will allow for efficient and complete data processing, analysis and reporting. In addition, the CRF allows the chief investigator (CI) to verify that the protocol is being followed.

# Related documents

* UoB-ARC-SOP-001 Archiving
* UoB-CRF-SOP-001 CRF Development
* UoB-DMA-SOP-001 Data Management
* UoB-ESD-SOP-001 Essential Documents Development & Maintenance
* UoB-PEI-SOP-001 Participant Engagement & Informed Consent

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# References and frameworks

* Data Protection Act 2018: <https://www.legislation.gov.uk/ukpga/2018/12/contents/enacted>

# Guidelines

## Format

1. Choose the most appropriate format for the CRF based on the design of the project and resources available. Examples of the type of format the CRFs can take are as follows:

* fully electronic
* no carbon required paper (also known as carbonless copy paper)
* electronically distributed forms that are to be printed locally
* fully paper.

The format of the CRF needs to take into consideration the facilities of the participating investigator sites and any additional costs that may be incurred. For instance, if deciding on electronic CRFs (eCRFs) ensure that all sites will have access to the appropriate software and hardware to complete the eCRFs; whilst paper CRFs would require sites to send the completed paper CRFs to the coordinating centre (e.g. via post).

1. It is expected that the CRF will be user-friendly, following a clear, logical and consistent format that is set out in chronological order. The options below may help with the useability of the CRF.

* Arrows, to indicate question flow.
* Illustrated skip patterns.
* Required data fields are in the same position when repeated in the CRF.
* Consistent fonts/colour scheme.
* Size of text boxes is sufficient to allow for required data capture.
* Visual indicators e.g. shaded boxes to indicate ineligibility.
* Questions of a certain theme are grouped together.

1. It is expected that the CRF has a header and footer on all pages, following a consistent format and to include the following:

* Header: project’s identifier/name, participant’s unique identifier and site’s identifier/name
* Footer: page number (e.g. page x of y), visit time point, CRF (section) version number and date. Where a CRF is considered to be confidential on its completion, this will also need to be indicated accordingly (e.g. confidential on completion).

1. It is strongly recommended that the CRF includes instructions/prompts informing the user on how to complete the CRF to reduce misinterpretations/variability. The list of prompts below may be used.

* Always complete the CRF with ink – clarifying the colour of ink if necessary.
* Complete the CRF in a timely manner.
* Initial and date any corrections.
* Initial and date any extra data that is added to the CRF, e.g. a site’s explanatory notes.
* Only authorised members of the team (as documented on the signature & delegation log) can enter data on the CRF.
* All entries need to be complete and legible.
* All fields need to be completed on each page where indicated. Where the required information cannot be obtained, this will need to be appropriately recorded. For example:
* N/A for not applicable
* UNK for unknown
* N/D for not done.
* Insert units and data in the format specified.

## Data collection

1. When creating the questions for the CRF, the factors listed below should be incorporated.

* Effective communication style.
* The questions are clear and concise.
* The questions are not unnecessarily repeated.
* The terminology used in the CRF matches that used in other key documents, particularly with regards to the categorisation of adverse events.
* The answer options are flexible enough to accommodate all potential answers to the questions.
* Protocol compliance is promoted by including questions to document that tests/procedures have been completed at the correct times
* Effective questions.
* Questions are about one item only.

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| --- | --- | --- |
| **Bad example**  1. Has the patient been admitted to hospital or taken any additional medication since the last visit? | Yes | No |
| **Good example**  1. Has the patient been admitted to hospital since the last visit?  2. Has the patient taken any additional medication since the last visit? | Yes | No |

* Complicated multi-part questions are avoided.

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| **Bad example**  1. Has the patient taken the trial drug, and if yes have they had anything to eat within the last 24 hours and consumed any alcohol within the last 48 hours? | Yes | No |
| **Good example**  1. Has the patient taken the trial drug?   * If yes, please answer Q1a and Q1b * If no, please go to Q2   1a. Has the patient had anything to eat within the last 24 hours?  1b. Has the patient drunk any alcohol within the last 48 hours? | Yes  Yes | No  No |

* Vague questions are avoided.

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| --- | --- | --- |
| **Bad example**  1. Has the patient had anything to eat? | Yes | No |
| **Good example**  1. Has the patient had anything to eat within the last 24 hours? | Yes | No |

* Technical questions are simplified.

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| --- | --- | --- |
| **Bad example**  1. Has the patient had treatment with >1 IV dose of cyclophosphamide and/or >14 days of oral cyclophosphamide and/or >14 days of prednisone/prednisolone (>30 mg/day) and/or treatment with >1 dose of rituximab within the last 28 days and /or treatment with plasma exchange in the 6 months prior to trial entry? | Yes | No |
| **Good example**  1. Has the patient had:   * Treatment with >1 IV dose of cyclophosphamide * >14 days of oral cyclophosphamide * >14 days of prednisone/prednisolone (>30 mg/day) * Treatment with >1 dose of rituximab within the last 28 days * Treatment with plasma exchange 6 months prior to trial entry | Yes | No |

* Questions are positively worded.

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| **Bad example**  1. No prior surgery for Pelvic Inflammatory Disease? | Yes | No |
| **Good example**  1. Prior surgery for Pelvic Inflammatory Disease? | Yes | No |

* Open questions that require free text responses are avoided.

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| --- | --- | --- |
| **Bad example**  1. Has the patient suffered from any side effects? Please list. | | |
| **Good example**  1. Has the patient suffered from any side effects? Please select from the below.   * Headache * Nausea * Dizziness * Other (if yes, please specify \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_) | Yes | No |

* Units are provided to ensure comparable values.

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| **Bad example**  1. Potassium: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| **Good example**  1. Potassium: 🞎🞎.🞎 mmol/L |

1. Consider collecting/including the items listed below. Note this is dependent on the project design and the data needed for endpoint analyses, therefore not all items listed below will be applicable or required.

* Participant’s demographics.
* Participant’s medical history.
* Inclusion/exclusion criteria checklist.
* Confirmation of eligibility.
* Details on participant randomisation.
* Concomitant medications.
* Adverse events.
* Serious adverse event forms.
* Exploratory data as identified in the protocol.
* Participant’s decision to withdraw.
* Principal investigator (PI) (or delegate) signatory page.

1. Consider the appropriateness of any participant identifiable data to be collected. In line with the [Data Protection Act 2018](https://www.legislation.gov.uk/ukpga/2018/12/contents/enacted), the personal data collected must be adequate, relevant and not excessive in relation to the purpose for which it is processed. Refer also to the Essential Documents Development & Maintenance SOP (UoB-ESD-SOP-001) and Participant Engagement & Informed Consent SOP (UoB-PEI-SOP-001) to ensure the participant is appropriately informed about the processing and storage of their data.
2. It is strongly recommended to engage with staff involved in completing the CRFs at the sites (e.g. research nurses) or involved in reviewing the CRFs (e.g. monitors and/or data managers) to ensure the CRFs are designed in a user-friendly way, and are easy to understand.

## Implementation

1. Consider piloting the CRFs with site staff before the CRFs are rolled out to all sites to minimise the potential of any required changes in the future.
2. Develop a plan for rolling out the CRFs and providing appropriate training (if required) in completing the CRFs to the sites. Consider whether this can be done remotely or whether this would require a site visit.

## Amendments

1. Where amendments are required to be made to the CRF template, engage with the different site staff who will be using the CRFs to gain an understanding of the best approach to incorporate the amendment.
2. Develop a plan for rolling out the amended CRFs to the sites. This is to include the provision of training on using the amended CRFs (if required) and a timeframe from which the new CRF templates are to be used. Additionally, remind sites to remove any remaining blank copies of the superseded CRFs (only keeping one copy in the Investigator Site File (ISF)), once the amended CRFs are ready to be used.

## Completion

1. The PI (or delegate) is to review the completed CRF to confirm whether the observations recorded within it are accurate; confirmation is typically represented by the PI (or delegate) signing off the CRF. Where the CRF is electronic, the PI (or delegate) is expected to have their own user account and password to allow them to review the CRFs which will be able to be evidenced by the audit trail and electronic signature.
2. Once the CRF has been completed for the participant, the CRF is to be submitted to the coordinating centre. As this needs to be done throughout the project, the costs attributed to this will need to be factored in (e.g. posting paper CRFs). See also Data Management SOP (UoB-DMA-SOP-001).
3. The archiving requirements for the CRFs also need to be considered by both the site and the coordinating centre. See also Archiving SOP (UoB-ARC-SOP-001).