The University of Nottingham	**Sponsor Standard Operating Procedure**

Title: **Case Report Form (CRF) Design and Completion**

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1.	**1.**

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1. PURPOSE and SCOPE

PURPOSE:
To describe the procedure for developing Case Report Forms (CRFs), that allows the researcher to capture all the information that is required according to the study protocol.

SCOPE:
This SOP is applicable to all clinical research protocols.

2. NOTES

2.1 The definition of a CRF as given by ICH-Good Clinical Practice (ICH-GCP) guidelines (1996) is 'A printed, optical, or electronic document designed to record all of the protocol required information to be submitted to the [*Chief Investigator*] on each trial subject'.

2.1.1 An alternate definition for Case Report Form may be given in the protocol (e.g. Study Report Form, Data Collection Form, etc) however this SOP covers the design of all such means of data capture according to the protocol.

2.2 It is the responsibility of the Chief Investigator to ensure that CRFs are designed to ensure that they capture the information that is required according to the protocol. Data that is not specified in the protocol should not be captured.

2.3 Consideration should be given as to whether any data on a CRF can be validated through monitoring (SOP TA012, Monitoring) of the original source data or whether the CRF itself will be the source data. Source Data is defined by ICH-GCP as 'All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial'. The CRF should indicate if it has captured existing data or is a source data document itself.

2.4 Consideration should be given to the design of the CRF as to how the CRF will relate to the Clinical Trial Database; see SOP IT003, Clinical Trial Database Design.

2.5 Well designed CRFs will remind Principal Investigators at local sites to perform specific evaluations, collect the relevant data and allow research staff or monitors to ensure that the protocol is being followed and allow comparison with source documents.

2.6 It is the responsibility of the Principal Investigator at the local site for the accuracy of completion of the CRFs at that site. This may be monitored as per SOP TA012, Trial Monitoring.

2.7 Data collected on the CRF may be used directly as the basis for the study report and any publications, as well as supporting an application for marketing authority approval of a new or existing drug. All entries should be clear, validated and authorised (see 4.8)

2.8 CRFs should be stored in a secure location during the course of the study. CRFs should then be archived as per SOP QA005, Archiving.

2.9 For investigators that are involved in a sub-study and are therefore collecting additional data, a separate set of CRFs should be provided for the sub-study that are designed to capture this additional data.

3. CROSS REFERENCES

3.1	Trial Monitoring	SOP TA012
3.2	Clinical Trial Database Design	SOP IT003
3.3	Archiving	SOP QA005
3.4	Document Control	SOP QA004
3.5	Site Responsibility (Delegation) Log	RF2 TA008
3.6	SAE Reporting Form	RF1 TA014
3.7	Serious Adverse Event Reporting	SOP TA014

4. PROCEDURE

CRF Design

4.1 The CRF should contain the study title, unique study identifier (NRES Ref, Sponsor Protocol Ref, CTA Ref) participant unique study number and 2 other participant identifiers (e.g. Initials and date of birth). It must be version controlled (version number) and dated as per SOP QA004, Document Control.

4.2 Multiple pages should be indicated, e.g. Page 1 of 2 etc. Each page of the CRF should carry the participant's unique study number, and identifiers, the site/centre identifier and name (for multi-centre trials – if used).

Note: Personal data should be kept separate to the CRF.

4.3 Where the CRF is to be sent to the Chief Investigator or central coordinating site carbonless duplication paper can be used for the CRFs, otherwise photocopy the original completed document and send the original, retaining the copy at the local site.

4.4 The arrangement of the CRF should be clear, in logical sections and user friendly, and where possible the CRF should mirror the order in which the data becomes available. Only data required as part of the study protocol should be included in the CRF.

4.5 The date of each visit/date of data obtained (e.g. pathology report) should be recorded. Use a standard format throughout e.g. dd/mm/yyyy (this is especially important in international trials).

4.6 When possible, provide tick box options and keep free text and abbreviations to a minimum. Tick box options should be exhaustive e.g. provide an option for 'Other' or 'NA' if appropriate

4.7 The unit of measurement should be specified and the number of boxes should reflect the number of decimal places required. In the case of multi-centre trials consideration should be given that there may be a variation of reporting methods (for example in pathology reports) and an alternate option should be given (where appropriate).

Note: Where a conversion is required this should be done as a computerised action as part of the Clinical Trials Database (as per SOP IT003, Clinical Trial Database Design) and not by carried out by staff because of possible discrepancies in rounding.

4.8 Each page of the CRF should be signed and dated by the researcher entering the data to verify that all data is complete and provide an audit trail of completion. As far as possible the Principal Investigator or treating clinician should countersign to verify the accuracies of the completed CRF. There should be lines or boxes for completion to indicate this.

4.9 The CRFs and the entries required should be arranged in the order of participant visits and the treatment regimen given. This may include the following (but not exhaustive) list:

4.9.1 Inclusion/exclusion criteria checklist with tick boxes
4.9.2 Date of Informed Consent and trial enrolment
4.9.3 Subject demographics – as applicable (e.g. age, gender, ethnicity)
4.9.4 Relevant medical history
4.9.5 Physical examination / pre-trial tests and baseline data (part of the eligibility criteria)
4.9.6 Randomisation form (when not part of the trial enrolment)
4.9.7 Laboratory data, ECG etc
4.9.8 Dosing and compliance data
4.9.9 Adverse Events - There should be clear reporting for adverse events especially where safety is an end-point of the study
4.9.10 Concomitant medications and treatments
4.9.11 Withdrawal/End of Study form
4.9.12 Serious Adverse Event Reporting Form – use RF1 TA014 SAE Reporting Form for SUSARs use CIOMS form (SAE's /SUSARs should be reported as per SOP TA014, SAE Reporting)
4.9.13 Relapse/Recurrence Form
4.9.14 Follow-up Form(s)
4.9.15 Death Form

Note: Consideration should be given when grouping together procedures and investigation(s) data on the CRF as results may not be available for a period of time. This may leave room for error and non-completion of the CRF. It is essential that CRFs are completed in a timely manner and that at any one time the full status of the trial can be known from the collected data thus far. Therefore it is better to design CRFs such that data is collected in real time and not retrospectively as far as possible.

4.10 Once designed the CRF should be reviewed and signed off by the Chief Investigator and Trial Statistician to ensure that the data collected will be applicable to the final analysis, before it is implemented in the trial.

CRF Completion

4.11 CRFs should be completed in black ball point pen and in English.

4.12 CRFs should only be completed and countersigned by individuals authorised by the Principal Investigator and named on the Site Responsibility (Delegation) Log, RF2 TA008,

4.13 No fields should be left blank. ND (Not Done) should be used if data is unavailable either because a measure was not taken or a test was not performed. NA (Not Applicable) should be used if a measure was not required for that participant. NK (Not Known) should be used if the data is unknown, and every effort has been made to find the data.

4.14 Any corrections to a CRF should be handled at the local site and verified by the Principal Investigator. A full audit trail of the decision making should be retained in the local Trial Site File.

4.15 Corrections should be made by drawing a single line through the incorrect item, with the correction being initialled and dated. Only individuals identified on the Site Responsibility (Delegation) Log, RF2 TA008, are authorised to correct the CRF.

Note: Correction fluid should not be used, nor should the entry be obliterated.

4.16 Submit the completed CRF as per the protocol. Original CRFs should to be sent to the Chief Investigator or coordinating site with a copy being retained at the local site.

Data Queries

4.17 Data Queries should be dealt with in a timely manner in order to maintain data integrity.

4.18 Where a data query has results in records being corrected, there must be an audit trail so that the correction can be verified. It is essential that records are not deleted or erased (see 4.15).

4.19 Any corrections to a CRF arising from a data query should be handled at the local site and verified by Principal Investigator (see 4.16).

Note: Where data queries are identified by the Chief Investigator corrections should be made by the local site in conjunction with the PI. The amended CRF should then be sent to the CI or coordinating site with a copy retained at the site. If the original CRF already had been sent to the CI then the local site should amend their copy as per 4.16 and forward this to the CI or coordinating site and make a duplicate for their records.

Transferring data from the CRF to a clinical trial database

4.20 A clinical trial database should be setup as per SOP IT003, Clinical Trial Database Design, collecting the same information as the CRFs.

4.21 Consideration should be given to ensure that any data transferred electronically is done in a safe and secure manner in order to maintain data integrity and participant anonymity. Password access and encryption should be utilised to maintain confidentiality.

4.22 The clinical trial database should have inbuilt checks to verify data. Any data queries thus identified should be resolved on the CRF **before** being finally entered onto the database.

Note: Where a data query is identified after the data has been entered onto the clinical trial database the CRF should first be corrected as 4.17 - 4.19 and then corrected on the database.

4.23 Only complete CRFs should be entered onto the database and a facility should be built in to the database to ensure that part completed CRFs are not accepted.

4.24 Data (and corrections) should only be entered onto the clinical trial database by authorised individuals as identified on the Site Responsibility (Delegation) Log, RF2 TA008.

4.25 Consideration needs to be given whether the input of data is carried out centrally or by the local site, this needs to be clear in the protocol.

Note: Where data is to be directly entered locally consideration should be given as to how the data will be verified and validated.

Direct Electronic Data Capture

4.26 Direct Electronic Data Capture (EDC) refers to data being directly inputted onto a clinical trials database and not pre-recorded in a paper format. The database entries could therefore be source data themselves. Consideration should therefore be given to the ability to reconstruct the trial at any participating sites, the local requirements for recording and retention of treatment data and to the robustness of the inbuilt checks on the database (as there may be no documents as such with which to verify entries).

4.27 There must be a means of electronically verifying the entries from a participating site and this must be carried out by the Principal Investigator or treating clinician as authorised on the Trial Delegation Log, RF2 TA008.

5. FLOW CHART

Not applicable.