Department	Research & Development
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Authorized by		**Sign**	**Date**
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This page details the version history and the main changes for each new version.
The new changes are in red font.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, 16.10.12	J H Pacynko J Illingworth	First SOP approved by R&D Committee on 15.10.12
Version 2, 01.02.18	S Moffat J H Pacynko	Removal of what the CRF should record, replaced by instructions for investigators to use the current CRF template/guide. Addition of the following wording to Section 5: Any information that would routinely be expected to appear in a patient's casenotes should continue do so during the study to ensure the care of the patient is maintained. The casenotes should provide sufficient information to allow the investigator to enrol the patient in the trial in compliance with the protocol. Source documents should be: ➢ Accurate ➢ Legible ➢ Contemporaneous ➢ Original ➢ Attributable ➢ Enduring ➢ Available and accessible. Sponsor assessment of eCRF/database prior to greenlight.
Version 3, 18.02.21	S Moffat	3 yearly review carried out and the following changes made: Numbering of sections updated. Section 4, point 4.2 Addition of "All third party providers will be subject to a Sponsor vendor assessment in order to assess suitability prior to the signing of contracts. A fully signed contract with the vendor must in place prior to Sponsor Greenlight. Refer to R&D GCP SOP 19 – Vendor Selection, Assessment, Contracting and Oversight SOP."

Please note for definitions of acronyms refer to Appendix 1 of Management of SOPs. Refer to Appendix 2 of Management of SOPs for the standards to which clinical trials that investigate the safety and/or efficacy of a medicinal product are conducted.

All the HEY R&D GCP SOPs are available at:
https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

1 Purpose

1.1 CRF is an acronym for Case Report Form which is a pharmaceutical term referring to study subject data collection forms. There is usually one CRF per subject.

1.2 The CRF is used to gather and submit study data and must reflect the investigations described in the study protocol.

1.3 CRFs act like a checklist to ensure that the information collected from subjects' study visits is complete and standardized and adheres to the protocol. In effect the CRF is the 'working' protocol.

1.4 CRFs are part of the essential documents which make up the Trial Master File (ICH GCP 8.3.14). The TMF must at all times contain the essential documents relating to the clinical trial (UK CT reg 31A (3)).

1.5 This SOP covers the content, design and format of CRFs and the importance of documenting study visits in the casenotes and source data verification.

2 Who should use this SOP

2.1 This SOP should be used by:

- All research staff involved with HUTH-sponsored CTIMPs – Chief/Principal Investigator, co-investigators, research nurses, clinical trial assistants, project managers, clinical trial co-ordinators, data managers, administrators etc.
- Clinical trials pharmacy staff – technicians and pharmacists.
- All HUTH R&D staff who manage the sponsorship of HUTH-sponsored CTIMPs.
- Research staff involved with HUTH-sponsored non-CTIMPs may find this SOP a useful guide, although the SOP will need to be adapted for the non-CTIMP trial.
- Research staff involved with clinical trials sponsored by an external organisation where the sponsor has no SOP for the CRF. HUTH R&D SOPs are defaulted to in this case.

3 CRF content, design and format

3.1 The CRF must be designed by the Chief/Principal Investigator or delegated person as soon as the protocol has been finalised. The CRF must reflect exactly the inclusion and exclusion criteria, the investigations and the schedule of investigations described in the protocol.

3.2 Investigators should use the CRF template/guide produced by R&D. This is available from the R&D Monitor or QA Manager. There are clear instructions at the beginning of the template to help in the design of a CRF.

3.3 The template will need to be modified for each study to reflect the protocol.

3.4 The current template is available as Working Instruction 04 on the Y drive in Y:\Research\GCP SOPs & forms\Working instructions.

3.5 CRFs for HUTH-sponsored trials are frequently in paper format. If CRFs are to be in electronic format, investigators must ensure that there will be an audit trail in place to record any changes made to the data so that there is a clear record of who made the change, when, what the new value is and what the old value was. The eCRF will also need to be validated prior to use. The EMA eCRF reflection paper on expectations for electronic source documents used in clinical trials should be adhered to which is available on the EMA website:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004385.pdf

4 CRF review, confidentiality and security

4.1 As part of quality assurance checks prior to Sponsor Greenlight, the QA Manager or R&D monitor will review the CRF and send any comments back to the investigator. This prevents modifications to the CRF after the study has started.

4.2 Any eCRF/database being used from a third party vendor should be assessed for suitability by the Sponsor prior to any commitment to use it. All third party providers will be subject to a Sponsor vendor assessment in order to assess suitability prior to the signing of contracts. A fully signed contract with the vendor must in place prior to Sponsor Greenlight. Refer to R&D GCP SOP 19 – Vendor Selection, Assessment, Contracting and Oversight SOP.

4.3 When creating the CRF it is important to respect patient confidentiality by keeping the CRF anonymous and only referring to patient's initials and study number on each form.

4.4 The only place in the Investigator Site File that there should be patient identifiable data is on the signed informed consent forms and on the Patient Identification List (ICH GCP 8.3.21), and in the Pharmacy Site File on prescription forms.

4.5 Once the CRF has been created, the database/spreadsheet should be designed to store the information collected in the CRFs. For details on the database/spreadsheet requirements, data entry, data validation, data protection, database lock etc refer to the R&D GCP SOP 13 - Data Management SOP.

4.6 CRFs must be stored during the study in a secure but accessible location. An ideal location is a lockable filing cabinet or cupboard in an office kept locked when not in use.

4.7 At the end of the study, CRFs must be archived along with the Investigator Site File for at least 5 years after the end of the trial (UK CT reg 31A (7)).

4.8 If the study is multi-centre, Principal Investigators should keep original or certified copies of CRFs in the Investigator Site File (or with the file) for the duration of the study and archiving.

5 Documenting study visits in casenotes and source data verification

5.1A study participant may see a variety of clinicians, GPs and other health care professionals over the course of the study. It is important that the data from a patient study visit is written clearly into casenotes so that other clinicians and health care professionals are informed of any relevant results or information that may affect the patient's ongoing medical care.

5.2 Any information that would routinely be expected to appear in a patient's casenotes should continue to do so during the study to ensure the care of the patient is maintained.

5.3 The casenotes should provide sufficient information to allow the investigator to enrol the patient in the trial in compliance with the protocol.

5.4 The minimum information required in casenotes is:

- Clearly written date, brief study title and visit number to confirm the subject is in the study.
- Date patient given patient information sheet
- Version number of Patient Information Sheet
- Date of consent
- Version number of Informed Consent Form
- Date of screening
- Medical history, concomitant diseases and medication including study medication, and
- any changes in concomitant diseases and medication at subsequent visits.
- Anything which is relevant to the ongoing care of the subject;
    a. Relevant results and study medic's assessment of these results.
    b. Brief description of any AEs with start & stop times/dates and any significant test results or a medical summary of events if more appropriate.
- Any other relevant details.

5.5 At the site initiation visit, the study monitor may prepare a study casenotes sheet with the investigator to make it easier and quicker for investigators to complete the required and relevant information in the casenotes.

5.6 It is usual practice for study data to be recorded in the patients' casenotes before transferring the data to the CRF. Patients' casenotes are referred to as source documents and include X-rays, MRI scans, ECG printouts, lab reports, coroner's reports etc. Source is the original entry.

5.7 The purpose of source documents in clinical research is to document the existence of the subject and substantiate the integrity of the trial data collected (ICH GCP 8.3.13).

- Source documents should be:
- Accurate
- Legible
- Contemporaneous
- Original
- Attributable
- Enduring
- Available and accessible.

5.8 During a monitoring visit, the R&D monitor will check the CRF against the source data in patients' casenotes. This is known as source data verification (SDV).

6 Implementation

6.1 Implementation of this SOP will conform to the process outlined in R&D SOP 01 Management of SOPs.