**JOINT RESEARCH AND DEVELOPMENT OFFICE**

**Somers Clinical Research Facility**

Designing a Case Report Form

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| GOSH ICH/07/S17/04 | |  | | --- | | Minor changes and review of SOP | | Emma Pendleton | 09/08/2016 |
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1. **Scope /Background**

This SOP is applicable to all the clinical trials sponsored, co-sponsored by Great Ormond Street Hospital. The SOP is applicable to Chief Investigators (CI), PIs, and delegated trial team members involved in Trust-sponsored CTIMPs and the Joint R&D Office Clinical Trials Team with responsibility for performing sponsor activities on behalf of the Trust.

1. **Legal basis**

The legal basis for this OP is Council Directive 2001/20/EC1 (Article 15). This Directive (published in 2001) is also known as the Clinical Trials Directive (CTD) and relates to the implementation of Good Clinical Practice in the conduct of clinical trials on medicinal products for human use. In the UK the CTD was transposed into law by the ‘The Medicines for Human use (Clinical Trials) Regulations 2004: SI 2004 No 10312. The UK Regulations took effect on 1 May 2004 and then further amendments.

**The following ICH GCP Principles apply to CRFs:**

Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s). (*ICH GCP 2.8*)

All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification. (*ICH GCP 2.10*)

The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s) ie DPA 1998 (*ICH GCP 2.11*).

1. **Purpose**

This SOP is intended to inform the investigator on how to design a CRF so that it contains all of the protocol required data.

1. **Definitions**

A **Case Report Form** **(CRF)** is 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. (ICH GCP 1.11)

**Source** **data:** 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. Source data are contained in source documents (original records or certified copies).

1. **Personnel responsible**

CRF design is the responsibility of the Chief Investigator. The development of CRF should be robust and demonstrate evidence of review by the appropriate personnel including the sponsor, pharmacovigilance, statistics and data management etc. Chief Investigator should send the Case Record Form to the Joint R&D Office Clinical Trials Team for review and approval before implementing it. It is the responsibility of the Chief Investigator and or the delegate to complete the change control form if there is any study amendment results in updating the CRF.

1. **Procedure**

A well designed CRF provides a powerful tool to monitor protocol compliance. Once the protocol has been finalised (or is close to completion) the Investigator will need to draft the CRF to ensure that all required data is recorded.

Source Data should subsequently be transferred to the CRF from the source. **If information is to be recorded directly into the CRF, this should be documented in the protocol and agreed in advance of a trial commencing.**

The designing of CRF should be based on the protocol requirements and the statistical analysis of the trial data. The CRF can be electronic or paper format.

* 1. **CRF Design**

There should be a space on each page of the CRF for the Subject Trial Code and visit date to be recorded. Please note there should **not** be any patient identifiable information recorded in a CRF.

* 1. **CRF Sections**

The CRF must contain **all** of the protocol required data, including each time point for each assay and clinical test.

The following sections have been included as a guide only and could be included depending on the type of trial and the information that is required:

* Patient Demographics
  + Gender
  + Date of Birth
  + Height
  + Weight
* Medical History / Physical Examination
* Inclusion and Exclusion Criteria with the evidence of review by the clinician
* Confirmation of consent
* Randomization
* Adverse Events
* Vital Signs
* Concomitant Medication
* Dispensation of IMP & Dose (if applicable).
* IMP administration with the time points if it is necessary
* Safety and Efficacy assessments
* Test Results with values e.g. Blood, ECG with the evidence for medical assessment
* Serious Adverse Events/Adverse Events
* Patient status
* Trial Completion
* Final Page with Chief Investigator sign off

In addition, there should be space to record the following:

* + Patient Non-Compliances related to IMP Administration & Trial Visits
  + Patient Withdrawals

Please note that Serious Adverse Event /Reactions must be documented using the appropriate reporting forms and always sent to the Sponsor.

The use of electronic CRFs is only allowed if these are validated according to the SOP GOSH/ICH/16/CT13/V1 for Computer System Validation

Each CRF will need to be signed by the person entering the data. This signature must be authorised by the Principal Investigator (PI) and will need to be on the Delegation of Responsibilities and Signature sheet.

For paper CRF, the below sections should be added

**Title Page**

The title page should include the following information:

* Sponsor Name and Address
* Sponsor Protocol Number
* EudraCT number
* Title of Project
* Investigator Name and Address
* Site Name

**Header**

The header of each CRF should include the following information:

* Subject trial identification number
* Study title and R&D number
* Date
* Subject Initials
* Site/centre name/number (for multi-centre trials only)
  1. **General Principles of CRF**

1. Accurately and completely reflect the protocol and allow for collection of all data required by the protocol.
2. Collect the data in a logical order according to the trial procedures
3. Allow accurate and complete data capture
4. Encourage data entry in a precise, clear and unambiguous way
5. Allow data entry as far as possible to be intuitive (where necessary it should also include instructions for its completion)
6. Separate CRF into sections by visit and completion of each visit needs to be authorised by the Principal Investigator or authorised clinicians
7. Be completed in a timely manner.
8. Be signed by the person who is entering the data and who is also an authorised person by the investigator. For eCRF should have audit trail to ensure the data entry and verification has been done by the appropriate personnel.
9. CRF **must be** version controlled, page controlled and dated. This information will need to be in the footer of the document for paper CRF. For eCRF, there should be audit trail for each version.
10. The CRF must be updated (and version controlled) if there are protocol amendments that affect the information required in the CRF.
    1. **CRF Release Process**

The CRF should be designed and reviewed according to the protocol. Appropriate personnel, including the person who will be analysing the data, should review the CRF to ensure appropriate data are being collected.

The CRF release process should be documented by the Chief Investigator in the Trial Master File. The template CRF in the TMF should be signed by the CI to confirm the release. For eCRF, there should be audit trail for each version of the CRF. A change control form should be completed and signed by the sponsor and the CI if a substantial amendment results in updating the CRF.

**6.5 Training and User Manual**

It is the responsibility of the Principal Investigator to ensure the data management staff is appropriately trained to enter the data according to the protocol and training should be documented in the training log. For eCRF user manual should be made available to all the staff.

**6.6 Retention of CRF**

The original copies of the completed paper CRF should be kept at the site file and then archived according to the local policy. For eCRF, the sites should have a copy of the contemporaneous certified copy of the CRF. In order to meet the requirements a contemporaneous certified copy of the data, in addition to the record maintained on a central server, a certified copy of the data with the audit trail should be created before the transfer to the sponsor and retained at the investigator site.

1. **Associated documents and SOPs\***

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| **Document Name** | **File Path** | **Author** |
| Change Control Form: Appendix 2 SOP 21 Amendments to a GOSH sponsored Clinical Trial of Investigational Medicinal Product (CTIMP) | <http://www.gosh.nhs.uk/research-and-innovation/information-researchers/joint-rd-office/clinical-trials/standard-operating-procedures-sops-and-forms> | Praseeda Thaikalloor |

1. **Recommendations**

A standardised format for the CRF should be perfect to ensure the data consistency. Please also read the SOP GOSH/ICH/16/CT13/V1 for Computer System Validation if you are using electronic CRF.

1. **References**

Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products. Official Journal of the European Communities, 9 April 2005; L91/13-19

Directive 2001/20/EC of the European Parliament and of The Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Official Journal of the European Communities*,* 1 May 2001; L121/34-44

ICH Harmonised Tripartite Guideline for GCP: adopted in Europe by CPMP in 1996 and published as CPMP/ICH/135/95/Step 5 in Eudralex: The Rules Governing Medicinal Products in the European Union: Volume 3-Guidelines (3CC1A).

Statutory Instrument 2004 No. 1031. The Medicines for Human Use (Clinical Trials) Regulations 2004, The Stationary Office Limited ISBN 0110490487

Statutory Instrument 2006 No. 1928. The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 The Stationary Office Limited. ISBN 0110748611

1. **Appendices**

\*all these documents are available electronically