The King's Health Partners Clinical Trials Office

Case Record Form Design

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Change History			
Date	Version Number	Change details	Approved by
28/Feb/2012	2.0	Administrative changes to formatting and change in the department name from JCTO to KHP-CTO	Jackie Powell
14/Oct/2014	3.0	Administrative changes to formatting.	Jackie Pullen

17/Jan/2018	4.0	Update to the glossary and minor amendments to the table in section 4.1	Jackie Pullen
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05/Feb/2021	5.0	Clarifications to sections 2.0, 4.1, 4.2, 4.7 and 4.8. Addition of section 4.9 - Archiving. Administrative changes to formatting.	Jackie Pullen
13/Jun/2024	5.1	Administrative changes to formatting.	Ann-Marie Murtagh

Table of Contents

1. 0 GLOSSARY

Case Record Form (CRF) – “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.

Chief Investigator (CI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the study.

Clinical Research Associates (CRAs) – Members of the KHP-CTO Quality Team who monitor trials to ensure GCP compliance.

Clinical Trial - Any investigation in human participants, other than a non-interventional trial intended to discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal product or to identify any adverse reactions to one or more such products and to study absorption, distribution metabolism and excretion in one of more such products with the object of ascertaining the safety or efficacy of those products.

Electronic Data Capture (EDC) - a computerised system designed for the collection of clinical data in electronic format for in clinical trials.

Good Clinical Practice (GCP) – As defined in Statutory Instrument 2006/1928.

Investigator Site File (ISF)- the storage system containing essential documents held at an individual site and maintained by the Principal Investigator for a clinical trial. These documents confirm compliance with protocol and GCP requirements during delivery of the study.

King’s Health Partners (KHP) – Kings Health Partners Academic Health Science Center is a pioneering collaboration between one of the King’s College London (University) and three of London’s most successful NHS Foundation Trusts - Guy’s & St Thomas’ NHS Foundation Trust, King’s College Hospital NHS Foundation Trust and South London & Maudsley NHS Foundation Trust

The King’s Health Partners Clinical Trials Office (KHP-CTO) Established in 2006 by Kings College London, Guy’s & St Thomas’ NHS Foundation Trust and King’s College Hospital NHS Foundation Trust to provide a streamlined approach for all aspects of trial administration.

KHP-CTO Standard Operating Procedure (SOP) – "detailed, written instructions to achieve uniformity of the performance of a specific function," SOPs are the base on which Quality Systems and Processes are conducted and monitored against.

The Medicines & Healthcare products Regulatory Agency (MHRA) - UK Competent Authority responsible for regulation of clinical trials.

The Regulations - Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004**.** An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928 *(as amended from time to time)*.

Remote Data Capture (RDC) - Remote data capture is the process of automatic collection of data.

Research Ethics Committee (REC) An independent body constituted of medical, scientific and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. (ICH GCP 1.31)

Trial Master File (TMF) - a standard filing system which allows the effective storage and location of essential documents, that is the large volume of regulatory documents and approvals needed for clinical research. The filing system can be in the form of a single project file or a number of files/filing cabinets, depending on what is deemed most appropriate for a particular clinical trial given its size and complexity. The regulatory documents and approvals within the TMF will be maintained alongside case report forms and source documentation

2.0 BACKGROUND AND PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the standard procedures to be followed when designing and developing CRFs for use within a Clinical Trial. The CRF is a data capturing tool used in all Clinical Trials to record eligibility of a participant and to capture the required data as defined by the trial protocol for each individual trial participant during the course of his/her participation in a trial. CRFs may be printed or electronic documents. The type of CRF used for the trial will vary according to the requirements of each individual study. The Chief Investigator and Quality Manager will decide what CRF is most suitable for each trial however the principles outlined in this document remain the same for both systems. The design of the CRF and its completion have a direct impact on the quality of the Clinical Trial data. It is subject to quality assurance and control during monitoring for GCP compliance on behalf of the Sponsor by the KHP-CTO (or other organisation from time to time), as well as during audits and inspections by the MHRA and REC.

The CRF will be designed in an appropriate format in order to collect only trial data as set out in the protocol for planned analyses. A well-designed CRF will ensure that no essential data is missed and that data queries are kept to a minimum as well as aiding data management, statistical analysis and reporting.

This SOP will ensure that CRF design enables trials sponsored or co-sponsored by the Partner Organisations comply with the regulations encompassed in the UK Law.

SI 2006/1928 Part 2 Conditions and Principles which apply to all Clinical Trials:

"9. All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected"

3.0 SCOPE

All Clinical Trials sponsored by one or more of King's Health Partner Organisations, or clinical trials where the sponsor responsibilities are managed by the KHP-CTO. An exception being when a Clinical Trial is co-sponsored with organisations other than the Partner Organisations and the task of CRF design is delegated to the other organisation. However, this SOP can be referred to if the other party does not have a CRF design SOP in place.

When Electronic Data Capture (EDC) or Remote Data Capture (RDC) is planned to be used for capturing Clinical Trial data, the principles defined in this SOP are applicable.

4.0 PROCEDURE

CRF design is the responsibility of the CI or delegate, but should involve other members of the Research Team, including but not limited to: researchers, trial coordinators or managers, research nurses, data managers and statisticians. The final CRF should be available before the first patient is enrolled into the Clinical Trial.

4.1 General Forms

The CRF will be designed to ensure that all data required by the protocol and statistical analysis are captured in an appropriate format; only data defined in the protocol will be entered into the CRF.

The following forms are normally found in a standard CRF (see related template for examples in section 5.1). However, this list is not exhaustive – mandatory forms are highlighted as bold. Depending on individual trial requirements additional forms may/will be added:-

	Case Record Form
	Unambiguous participant identity code and visit dates
Screening	Baseline data including: **Confirmation of consent & Demographics** Medical History, and if applicable, prior treatment History of diagnosis studied (if applicable)

	Physical Examination **Inclusion / Exclusion criteria review** **Initial Primary and Secondary Endpoint Data (if applicable)**
Randomisation / Registration	**Participant Eligibility Review** Confirmation of randomisation (if applicable)
Data during treatment period	**Administration of Trial Medication** Safety and/or Efficacy Assessments **Participant Status** **Primary and Secondary Endpoint Data**
Adverse Events	**Adverse Events Log**
Concomitant Medication Form	Concomitant Medication data on protocol-defined period of recording
Trial Completion	**Trial Completion form**
Follow-up	Concomitant Medications, if applicable
Unscheduled Form (if applicable)	Data for visits that are not protocol scheduled visits
CRF Final page	**Principal Investigator sign off**

4.2 General Principles

When designing a CRF, the following general principles should be applied:

- Adopt a standardised format to achieve consistency in data recording.
- Ensure that the data to be captured is entered into the CRF in a logical order – take into account, for example, the order of trial procedures during a trial visit, order of entry in medical notes and laboratory reports.
- Collect raw data to minimise calculations and conversions.
- Structure the layout in an organised manner to minimise transcription error where data will be transcribed from source documents to CRF.
- A Comments Form can be included in the CRF where comments can be recorded centrally. However free-text entry cannot be analysed and hence should be kept to a minimum.
- Separate the CRF into sections by visit to ease organisation and include a checklist at the front of each section as reminder of assessments required per visit.

- Provide a CRF trial schedule, to indicate which CRF pages are applicable to particular visits.
- Use questions, prompts and provide instructions, which must be clear and concise and must not contradict other CRF pages or the protocol.
- Ensure that copyright permissions are obtained for the replication of any licensed measures (i.e. questionnaires), where applicable.

4.3 Format

The CRF will:

- Be clearly version controlled; by version number and date (see section 6 of the Document Version Control Guidelines).
- Be page numbered in sequential order. In cases where multiple page insertions are required, e.g., Adverse Event Form and Concomitant Medication Form, the use of sub-numbering may be appropriate. *(The following numbering pattern can be followed: the initial page as XXX.0, the suffix will increase sequentially with each inserted page as XXX.1, XXX.2, XXX.3).*
- Be in chronological order, clearly identifying the visit or data collection point, as defined in the protocol.
- Have sufficient information in the header, to identify EVERY CRF page - for example, trial name, protocol number, patient trial number and initials. *Hospital numbers are not acceptable as patient identifiers.*
- Have an appropriate number of boxes for the digits required, for example, date, laboratory results, and vital signs readings.
- Have pre-printed decimal points where applicable.
- Specify units if appropriate, ensuring units are the same as that in the protocol and source documents.
- Have a designated area for sign-off at eligibility review and at the end of the CRF by the investigator.

4.4 Layout

The layout of the CRF will:

- Be consistent throughout the entire CRF including alignment, page margins, spacing and fonts.
- Have sufficient space in the page margin to accommodate hole punching/binding.
- Have text aligned with associating boxes where applicable.
- Not be overly cramped.

4.5 Data Collection

By specifying a required format for data entry, the responses received will be supplied in a uniform manner.

- Data collected as “free text” should be limited as far as possible, as this complicates data analysis, wherever possible use boxes to ensure consistency.

e.g.

i) |_|_|-|_|_|_|-|_|_|_|_| DD - MMM - YYYY	ii) Date:_____

- Listing definitive options with checkboxes will demand defined responses to minimise ambiguity.

e.g.

Has the patient had any Adverse Events? ☐ **No** ☐ **Yes**

- Using a combination of definitive options, and option to enter “other” or “specify” will allow for the collection of additional information if applicable.

e.g.

Ethnicity:	☐ White / Caucasian ☐ Black or African ☐ Asian ☐ Other, specify: _____

- When assessing subjective variables e.g. pain, only use validated instruments.

4.6 Trial Specific CRF Completion Guidelines:

Trial specific CRF completion guidelines may be generated if required and can be a useful training tool for accurate data entry and CRF completion.

4.7 CRF approval process:

CRF design is a multidisciplinary process, involving collaboration with the research team, the trial statistician, data management *(if applicable)* and KHP-CTO CRA. An independent review will ensure quality control is maintained (e.g. by Statistician, KHP-CTO CRA). Documented approval of the CRF by the Chief Investigator is mandatory *(see section 5 for CRF approval form template)* and evidence of review must be retained in the Trial Master File. The CRF should be finalised prior to the first patient being enrolled into the trial.

4.8 CRF amendment

Amendments to the CRF may be required from time to time due to, for example, a change of trial design or a change in data requirements as specified in an amendment to the protocol and/or statistical analysis plan. Amendments to the CRF should be made during the amendment approval process. All CRF amendments will be tracked by the version number and date and approval documented in the Trial Master File. Where paper CRFs are being used updated versions should be provided to all sites and filed in the ISF. Superseded versions should be marked as such and retained in the TMF/ISF. eCRFs should be updated and finalised before the amendment is implemented.

4.9 Archiving

CRFs shall be archived according to the requirements outlined in the Sponsor's protocol.

5.0 RELATED TEMPLATES

5.1 CRF templates

5.2 CRF Approval Form

6.0 RELATED DOCUMENTS

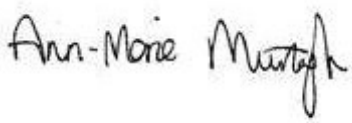
6.1 CRF Design Manual

6.2 Document Version Control Guidelines

6.3 CRF Completion Guidelines

6.4 Data Management Plan Template (see SOP 18 Data Management in Clinical Trials)

7.0 APPROVAL and SIGNATURE



_____ _____12/06/2024_____

Ann-Marie Murtagh
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Date