Sample Management in Clinical Trials

Policy Details	
Document Type	Standard Operating Procedure
Document name	KHP-CTO/CT/SOP20.0 Sample Management in Clinical Trials
Version	FINAL v2.1 19/May/2023
Effective from	19th May 2023
Review date	10th January 2026
Owner	King's Health Partners Clinical Trials Office
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Superseded documents	FINAL v2.0 05/01/2021
Relevant regulations/legislation/guidelines	Statutory Instrument 2004-1031 EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (2012) (EMA/INS/GCP/532137/2010) MHRA Good Clinical Practice Guidance Human Tissue Act

Change History			
Date	Version Number	Change details	Approved by
5th January 2021	2.0	Scheduled review, updated procedure for poorly labelled samples (4.2)	Jackie Pullen
19th May 2023	2.1	Scheduled review. Minor amendments	Jackie Pullen

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1.0 GLOSSARY

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

Clinical Research Associates (CRAs) – Part of the KHP-CTO Quality Team. Ensure compliance with the Regulations, GCP and SOPs, by monitoring clinical trials.

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 and/or to identify any adverse reactions to one or more such products and/or to study absorption, distribution metabolism and excretion in one of more such products with the object of ascertaining the safety and/or efficacy of those products.

Clinical Trial Samples - Any biological sample collected from a human participant of a clinical trial, as required by the protocol. Samples may include but are not limited to:

- blood, plasma, serum, urine, faeces, tissues and cells.

• This includes samples that are defined by the Human Tissue Act as Relevant or Non-relevant material.

• This includes newly acquired samples as well as those in archived and existing collections.

Co-Sponsors – Where two or more organisations take responsibility for the initiation, management and financing (or arranging the financing in relation to) a clinical trial. Co-Sponsors should decide which organisation will assume responsibility for carrying out the Sponsor functions of that trial and document this accordingly.

Computer Systems – For the purpose of this SOP, computerised systems are defined as systems (software) that collect data in electronic form and create, modify, maintain, archive, retrieve, or transmit that clinical data.

Curriculum Vitae (CV) - A summary of a person's education, professional history and job qualifications.

Good Clinical Practice (GCP) - as defined in the Regulations.

Investigational Medicinal Products (IMP) - means a pharmaceutical form of an active substance or placebo being tested, or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

(a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,

(b) used for an indication not included in the summary of product characteristics (or equivalent document) under the authorisation for that product, or

(c) used to gain further information about the form of that product as authorised under the authorisation

Investigator Site File (ISF) – A standard filing system which contains all essential documents held by Principal Investigator(s) conducting a trial which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.

King's Health Partners (KHP) - King's 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', King's College Hospital and the South London & Maudsley.

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

KHP-CTO Quality Team – Comprises the Clinical Quality Manager, Clinical Research Associate(s), Clinical Trial Administrator(s), Systems Executive, Training Executive(s) and Training Assistant.

KHP-CTO Standard Operating Procedures (SOPs) - "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.

Monitoring Plan (MP) – A document written by the CRA detailing how all the monitoring activities for the trial will be carried out based upon the trial risk assessment.

Principal Investigator (PI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse/midwife who has responsibility for the conduct of the trial at a site.

Quality Assurance (QA) - Systems and processes established to ensure that a trial is performed and the data are generated in compliance with GCP.

Quality Control (QC) - The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

Research & Development Dept. (R&D) – NHS department responsible for confirmation of capacity and capability for all clinical research.

Research Ethics Committee (REC) – The REC that undertakes the review of the research protocol, including the content of the patient information sheet and consent form rather than just site specific approval for each centre.

Serious Breach of GCP - a "serious breach" of the principles of GCP that is likely to affect to a significant degree, the safety or physical or mental integrity of the participants of the trial; or the scientific value of the trial.

Sponsor - The organisation who takes responsibility for the initiation, management and financing (or arranging the financing) in relation to a clinical trial. The Sponsor organisation has responsibility for carrying out the sponsor functions of that trial (as defined in the Regulations).

Standard Operating Procedures (SOPs) – "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 Regulations - The Medicines for Human Use (Clinical Trials) Regulations 2004, transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004

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.

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 SOP is to describe the management of laboratory samples taken for protocol endpoint analysis in clinical trials, is in accordance with the study protocol, GCP and applicable regulations and associated guidance.

3.0 SCOPE

All clinical trials sponsored by one or more of King's Health Partners Organisations, or clinical trials where the sponsor responsibilities are managed by the KHP-CTO, where laboratory samples are collected for the purpose of assessing protocol endpoints. These include:

- samples collected as routine clinical care, and also contribute to trial endpoint analysis.
- samples collected and managed for study objectives only.
- samples prepared and stored before shipping to a specialist laboratory.
- samples collected for use in an exploratory/experimental assay.

Samples managed by the local hospital or clinical laboratory as per routine standard of care, that do not contribute to protocol endpoint analysis, are outside the scope of this SOP. However, reference ranges and Clinical Pathology Accreditation (or equivalent) certificates will be filed within the trial TMF.

4.0 PROCEDURE

4.1 General Requirement for Sample Management

The trial sponsor is responsible for ensuring that laboratories managing sample analysis comply with the principles of GCP. It is the responsibility of the Laboratory Manager (or delegate) to ensure that samples are managed by an appropriately delegated, trained and qualified member of the trial team.

Clinical Trial Samples will be collected and processed in accordance with the approved trial documents – i.e. protocol, Participant Information Sheet & Consent form and in accordance with documented consent given by the participant.

Instructions and processes for key activities relating to the management of samples may be detailed in the protocol or separate laboratory manual, work instruction, analytical protocol or analytical plan. If a document other than the protocol is utilised it must be written in accordance with the protocol (and any subsequent amendments), be reviewed by the KHP-CTO CRA (or delegate) and approved by the Laboratory Manager (or delegate). The agreed sample management document must be in place prior to any sample management being undertaken for a trial.

Where samples are to be sent to an external organisation for storage or analysis, a contract must be in place prior to any sample shipment.

In order to fully reconstruct laboratory work, records must be maintained, including records for the preparation of buffers, standards and reagents required by the analytical method. This is to ensure that the quality of the reagents are traceable and that they were fit for purpose. In addition, the equipment to be used must be fit for purpose and there must be records to demonstrate the calibration and maintenance of equipment used to measure trial parameters.

4.2 Samples Labelling

Clinical Trial Samples should be labelled clearly with information regarding trial identification, participant ID, date and time of collection and the type of specimen. Steps should be taken to ensure that label information remains intact during sample storage. If samples are poorly labelled or missing the CI and Sponsor must be informed. Any poorly labelled samples should not be analysed until it has been identified (unless delay in processing would lead to degradation of the sample in which case analyse sample and quarantine results until identity established). If the identity of the sample cannot be established the result should not be reported and the sample must be destroyed.

4.3 Sample Storage

A system for recording the storage conditions within the fridge/freezer or other containment method must be in place to ensure storage conditions are kept within defined limits and meet protocol requirements. Temperature logs for sample storage will be reviewed by the KHP-CTO CRA as described in the monitoring plan.

A copy of all temperature logs will be filed in the Laboratory File at the end of the study.

In the event of a temperature excursion, a system must be in place to report and record any temperature excursions and corrective actions taken such as moving samples to a backup location. Temperature excursions in storage / transit should be recorded and retained in the TMF / ISF to be reviewed by the KHP-CTO CRA at intervals specified in the monitoring plan.

4.4 Sample Tracking

It is a requirement to provide a chain of custody and audit trail of samples from collection to disposal by way of sample tracking.

Automated systems or manual sample tracking logs can be used to track samples (see 5.3 template Sample Tracking Log).

Sample tracking logs must be retained in the TMF / ISF to be reviewed by the KHP-CTO CRA at intervals specified in the monitoring plan.

4.5 Sample Transport and Receipt

If samples are transported for storage or analysis, documentation detailing the date of shipment, the number of samples being shipped and the nature of the samples will be maintained and filed within the ISF or TMF as appropriate

Details for shipment conditions and packing materials will be described in the protocol or agreed sample processing document.

The laboratory receiving the samples will provide a signed receipt confirming that the correct number of samples have been received in an appropriate condition.

Details of all shipments and receipts will be filed in the TMF/ISF and reviewed by the KHP-CTO CRA as detailed in the study specific monitoring plan. The sponsor and the CI will be notified of any issues identified during sample shipment. A template sample transfer log is available (See related documents).

4.6 Sample Processing

An approved and validated sample handling and analysis process must be in place at the laboratory prior to the conduct of sample handling or analysis.

Data from analysis must be recorded accurately, legibly and promptly. A QC check will be conducted and documented to confirm the accuracy of the data.

4.6.1 Repeat Analysis

There may be instances where repeat analysis of specific samples or batches is required e.g. in the case of equipment failure. Repeat analysis must only be undertaken in accordance with a written procedure which will include reasons for the repeat analysis, authorisation decisions for repeat analysis and how the repeat analysis will be conducted. Appropriate documentation for the rationale behind the decision, the original and results, along with the reason why one result is accepted over the other must be maintained in the TMF and must be reflected in the final study report.

4.6.2 Unblinding and Blinding

The KHP-CTO CRA or delegate must ensure that measures are taken to protect the integrity of the blind with respect to sample analysis. This will include ensuring that laboratory data are only communicated to appropriate members of the trial team.

4.7 Sample Disposal or Long Term Storage

Once an End of Study notification has been submitted. All remaining samples will be disposed of or transferred for long term storage, in an appropriate HTA licensed area, in accordance with the trial protocol, ethical approval and each participant's consent status.

Samples must be either disposed of or transferred to long term storage within twelve (12) months of the End of Study notification or the time specified in ethics application.

If consent has been given for storage for future research or biobanking, relevant samples must be transferred to suitable storage within a Human Tissue Authority (HTA) licensed premises. Consent forms must be retained for the duration of sample storage. Sample disposal must be documented and retained by the laboratory. A disposal log template is available (see related documents).

All documents pertaining to sample management must be retained by the laboratory.

5.0 RELATED TEMPLATES

5.1 Template Temperature Log

5.2 Template Nitrogen Vessel Storage Log

5.3 Template Sample Tracking Log

5.4 Template Sample Transfer Log

5.5 Template Sample Disposal Form

6.0 RELATED DOCUMENTS

6.1 EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (2012) (EMA/INS/GCP/532137/2010)

6.2 MHRA Good Clinical Practice Guide, Chapter 13 (2012)

7.0 APPROVAL and SIGNATURE

19 May 2023

Jackie Pullen
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King's Health Partners Clinical Trials Office

Date