# Laboratory Procedures and Sample Analysis in Clinical Trials

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| Originally Prepared by | Helen Critchley KHP-CTO Quality Manager |
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| CHANGE HISTORY | | | |
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| Date | Version Number | Change details | Approved by |
| 5th January 2021 | 1.1 | Update to documentation of oversight (4.3) | Jackie Pullen |
| 17th March 2023 | 1.1 | Scheduled review no changes to SOP content. | Jackie Pullen |

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# 1.0 GLOSSARY

**Chief Investigator (CI) -** A Registered Physician, Dentist, Pharmacist or Registered Nurse 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.

**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

**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.

**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.

**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 oversight of samples taken for protocol endpoint analysis in clinical trials to ensure collection, handling and analysis of samples is conducted 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 sample analysis is conducted for the purpose of assessing protocol endpoints. These include:

- samples collected and analysed as part of routine clinical care, that may also contribute to the study dataset.
- samples collected and analysed for study objectives only.
- samples prepared and stored before shipping to a specialist laboratory.
- samples analysed using a standard clinical assay in laboratory with a functional, audited quality system.
- samples analysed using an exploratory/experimental assay.

Samples processed by the local hospital or clinical laboratory as per routine standard of care 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 Responsibility

The trial Sponsor is responsible for ensuring that any laboratory conducting sample analysis comply with the principles of GCP. The task of assessing the compliance of a laboratory is delegated to the KHP-CTO CRA or delegate. During the study set up the CRA will ensure each laboratory conducting protocol endpoint analysis completes the Laboratory Self-Assessment Checklist. The checklist may not need to be completed for laboratories used previously to conduct sample analysis where no previous concerns have been raised. This will be subject to the risk assessment conducted by the KHP-CTO Quality Manager or delegate.

## 4.2 Laboratory Assessment

The risks associated with the selection of laboratories conducting sample analysis for a trial will be documented in the study specific risk assessment.

### 4.2.1 Research Samples for Primary and Secondary Endpoints

The KHP-CTO CRA or delegate will review (and document the review) the documentation describing the sample processing. The documentation and checks will include: -

- Laboratory agreements or lab manuals detailing the assays being conducted.
- The availability within the laboratory of an individual suitably trained to conduct Quality Control checks of sample analysis reports.
- Written procedures in place for all processes specific to the sample handling including labelling, receipt, storage, analysis, reporting and QC control.
- Evidence of appropriate GCP training for the laboratory staff.
- Ensuring that the processing laboratory has a quality system in place for document control, training, data handling, computer system validation (if applicable) and equipment maintenance.
- The KHP-CTO may recommend to the Sponsor the commissioning of an audit of a new laboratory or a laboratory where issues have been identified. The responsibility for the commissioning of such an audit remains with the Sponsor organisation.
- Ensuring that appropriate, documented validation of the assay(s) and associated key items of equipment are in place or will be prior to sample analysis.
- Where available, the assay should be subject to internal or external QC and/or QA processes.
- There should be robust processes for the acquisition, review and transfer of analytical data and associated metadata (audit trails, supporting data and documentation).

### 4.2.2 Sample Analysis for Exploratory Endpoints

The study protocol may include the processing of research samples for exploratory objectives that do not have a clear definition. It may not be possible to ensure that these objectives receive specific oversight. However, the samples should be stored and analysed in accordance with the study protocol, the patient's informed consent and the criteria listed in sections 4.2.1.

The sponsor or co-sponsor is responsible for ensuring that all samples are processed within the timeframe of the ethical approval for the trial or moved to a HTA licensed tissue bank for storage, if the patients have consented to further storage of their samples. The KHP-CTO CRA will ensure that the sponsor, co-sponsor and/or Chief Investigator is aware of this requirement at the time of the lead site close out visit.

## 4.3 Oversight During the Conduct of the Trial

The KHP-CTO CRA will conduct laboratory visits for a trial as detailed in the trial specific monitoring plan. Each visit will be documented via a written Laboratory Visit report (see Section 5) and promptly submitted to the KHP-CTO (acting on behalf of the Sponsor). Any other communication with the laboratory which requires documentation will be recorded on a Contact Comment Form or email (see Section 5)

## 4.4 Laboratory Staff Training

All laboratory staff processing research samples must have a level of understanding of the research process sufficient to allow them to process the sample according to the protocol.

All laboratory staff processing research samples should have study specific training proportionate to their role. Evidence that all staff processing research samples are qualified and trained to do so should be maintained as required by the laboratory SOP.

## 4.5 Other Considerations

The laboratory and trial team must ensure that procedures are in place for notifying the laboratory if a participant withdraws consent for trial samples to be analysed.

The laboratory should have procedures in place for reporting suspected serious breaches of GCP to the Sponsor.

The laboratory should have procedures in place to ensure that trial staff are not inadvertently unblinded to treatment when they receive the results of the sample analysis. The laboratory should have procedures in place to ensure expedited reporting of any laboratory result which could be potentially life-threatening to the participant.

# 5.0 RELATED TEMPLATES

5.1 Laboratory Self-Assessment Checklist

5.2 Laboratory Visit Report Form template

## 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

31 March 2023

Jackie Pullen, Director
King's Health Partners Clinical Trials Office

Date