# Investigator Site Close-out Procedure (non-commercial)

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| Owner | King's Health Partners Clinical Trials Office |
| Original Prepared by | Hannah Mason, Senior Clinical Research Associate |
| Reviewed by | Sophie Espinoza, Quality Manager KHP-CTO |
| Approved by | Ann-Marie Murtagh, Director KHP-CTO |
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| CHANGE HISTORY | | | |
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| Date | Version Number | Change details | Approved by |
| 24th January 2012 | 2.0 | Change to section 4.1.5 - Deletion of requirement to notify Competent Authority if a site closes prematurely | Jackie Powell |
| 26th January 2016 | 3.0 | Scheduled review and minor adjustment to reflect revised practice | Jackie Pullen |
| 31st August 2017 | 4.0 | Addition of requirement for Investigator to sign the delegation log, update to glossary, addition of HRA requirements for end of trial notification and minor formatting changes | Jackie Pullen |
| 1st October 2018 | 4.1 | Minor amendment to include trials managed by KHP-CTO | Jackie Pullen |

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| 25th January 2019 | 5.0 | Scheduled review and minor amendments to section 4.1.3 and 4.2 to reflect current practice | |
| 5th January 2021 | 5.1 | Minor amendment to include registering on a publicly accessible database | Jackie Pullen |
| 22 September 2022 | 5.2 | Scheduled review and minor adjustment to reflect revised practice | Jackie Pullen |
| 21 October 2025 | 5.3 | Scheduled review | Ann-Marie Murtagh |

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## 1.0 BACKGROUND AND PURPOSE

The purpose of this SOP is to describe close-out procedures for CTIMPs monitored by the KHP-CTO in order that CTIMPs sponsored by one or more King's Health Partners Organisations, or CTIMPs where the sponsor responsibilities are managed by the KHP-CTO, comply with UK Regulations.

Close-out is the act of ensuring that all clinical trial related activities are appropriately reconciled, recorded and reported at the end of a trial in accordance with the protocol, SOPs, GCP, and the applicable regulatory requirement(s).

Close-out is integral to the quality assurance of a clinical trial and GCP compliance of the study according to Sponsor requirements and to ensure that all necessary documents are in place should it be necessary for the trial information to be retrieved or inspected in the future.

## 2.0 SCOPE

All CTIMP trials sponsored by one or more King's Health Partners Organisations, or CTIMP trials where the sponsor responsibilities are managed by the KHP-CTO, will be closed out as described in this SOP.

The close-out process will be conducted by the KHP-CTO CRAs and overseen by the Quality Manager or delegate. From time to time as required, the close-out process may be contracted out to external organisations/CRAs, but oversight will be retained by the KHP-CTO.

## 3.0 PROCEDURE

The KHP-CTO ensures that the Investigator site conducts the clinical study in compliance with the final protocol and subsequent protocol amendments, if any, as well as GCP and applicable safety reporting and regulatory requirements.

The trial close-out procedures will be performed as soon as practicable after the end of the trial as defined in the protocol or premature termination and after KHP-CTO monitoring activities have been completed. However, site close-out activities may be performed earlier, for example, if a site fails to recruit or requests early closure.

The procedures may span several days; however, one final Close-out Report or Remote Study Site Close-out Checklist should be completed for each site. Once close-out has been completed all further contact with the site(s) should be documented appropriately.

## 3.1 CRA Responsibilities

### 3.1.1 Study Status

The CRA will act as the main line of communication between the KHP-CTO (on behalf of the Sponsor) and the Investigator. The specific timelines and scheduling for study close-out will be defined in the Monitoring Plan.

1. The CRA will ensure that all documents needed to conduct close-out of the trial/site, and to comply with the applicable regulatory requirements, are available.
2. The CRA will confirm recruitment status at the end or premature end of the trial. If the site is to be closed prior to the end of the trial a reason for early closure should be clearly documented in the notification to HRA and any other bodies as required by regulations.
3. The CRA will ensure that all Serious Adverse Events (SAEs) have been reported by the Investigator to the Sponsor and that the Investigator is aware of any ongoing reporting requirements and follow-up of any ongoing SAEs. A line listing of all SAE/SUSARs that occurred at the site must be filed in the ISF. In a multicentre trial a line listing for all SAEs/SUSARS at each site must be filed in the TMF.
4. The CRA will ensure that all outstanding data queries at the time of site close-out are resolved and that there are clear systems in place for continuing data entry and query resolution after the close-out procedures have been completed. All outstanding issues from previous monitoring visits will be resolved or appropriately documented.
5. The CRA will ensure that the Delegation of Duties and Authorised Signature log has been fully completed and signed by the Principal Investigator. A copy of the final delegation log should be provided for filing in the TMF and Sponsor File.
6. The CRA will ensure that a provisional timeline for database lock has been determined by the Chief Investigator.

### 3.1.2 Investigational Medicinal Product and Pharmacy

1. The CRA will verify that final drug accountability is complete.
2. The CRA will give authorisation for IMP destruction in accordance with the Monitoring Plan and ensure that the destruction or return of unused, partially used or returned Investigational Medicinal Product is appropriately completed and documented in the Pharmacy File.
3. If applicable, the CRA will verify that Code Break Documentation is still intact and any code that has been broken or lost during the study has been appropriately documented. Details and remaining documentation will be filed in the Pharmacy File.
4. The CRA or appropriate delegate will review Pharmacy File for completeness to ensure that it has been maintained throughout the trial. Documentation will be filed ensuring a clear audit trail of study conduct at the site. If applicable, the CRA will oversee reconciliation of the Pharmacy File with the ISF according to local requirements.

### 3.1.3 Laboratory, Biological Samples other study supplies

1. The CRA will ensure that all unused trial supplies and equipment are returned or destroyed according to trial requirements.
2. If applicable, the CRA will ensure that the Sponsor(s) and CI are aware 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 and use of their samples.
3. If applicable, the CRA will ensure that arrangements are in place for the destruction of retained biological samples and diagnostic material.

### 3.1.4 Ethics, Regulatory and Research and Development

For single centre trials both "End of Trial" and "Closure of a Site" activities listed below should be completed. For multicentre trials, if a participating site is to be closed then only "Closure of Site" activities need to be completed. If all sites are to be closed due to study end/premature termination, then "Closure of a Site" activities should be completed for each participating site and "End of Trial" and "Closure of Site" activities should be completed at the lead site.

### 3.1.5 Closure of Site

Close-out processes will be defined in the trial monitoring plan and will be conducted either on site or remotely according to the risk assessment for the trial.

1. In the case of closure of a participating site prior to end of the study, the CRA will ensure that the Chief Investigator is aware of their responsibility to notify the REC of the closure of the participating site.
2. The CRA will ensure that the Investigator at the participating site is aware of their responsibility to notify the local R&D Department of the closure of the site and provide copies of required documentation to their R&D department and to the CRA as confirmation of notification, for filing in the TMF and Sponsor File.

### 3.1.6 End of the Trial

1. The CRA or delegate will be responsible for submitting the End of Trial Notification to the Competent Authority within required timelines from the "end of trial" as defined in the protocol or clinical trial authorisation application or at premature trial end. For trials submitted pre-combined review, the CRA or delegate will ensure that the Chief Investigator is aware of their responsibility to notify the REC, and their local R&D Department. Where a project has HRA Approval and has been reviewed by a REC there is no requirement to notify the HRA of the end of trial.

2. The CRA will remind the Chief Investigator of their regulatory obligation to submit a Clinical Study Report to the KHP-CTO within 12 months of the End of Trial Notification. The KHP-CTO will upload the Clinical Study Report or lay summary to the publicly accessible database where the trial was originally registered on behalf of the Sponsor and notify the Competent Authority by email that this has been done. For CTIMPs registered on EudraCT which began after 01 January 2021, the KHP-CTO are not required to upload the Clinical Study Report to EudraCT.

3. The CRA will remind the Chief Investigator of their obligation to submit a Final Report to the REC within 12 months of the End of Trial. For combined review studies, this should be done by completing the final report form on IRAS. For pre-combined review studies, the final report form should be completed on the HRA website. There is no need to submit a CSR to the REC.

4. The CRA will ensure that the Chief Investigator is aware of their responsibility to notify their Organisational Research and Development Department of the end of the study.

### 3.1.7 Sponsor File, Trial Master File and Investigator Site File

1. The CRA or appropriate delegate will review all Sponsor, Trial Master File and Investigator Site File (as applicable) documentation for completeness. Documentation will be filed according to the filing scheme, ensuring a clear audit trail of study conduct.

### 3.1.8 General Considerations

1. If commercial / external funding was obtained for the study, the CRA will ensure that the Investigator is aware that all contractual reporting obligations must be fulfilled.

2. All Investigators will be reminded that all essential documentation must be retained for the required length of time according to the protocol and current regulations. This must also ensure traceability, secure archiving, and proportionate oversight of retained records. Trial Master File documentation will be archived according to the KHP-CTO Archiving SOP. If necessary, the CRA may assist in the archiving of the TMF in collaboration with the KHP-CTO Archivist.

3. The CRA will remind the Investigator of their obligation to inform the Sponsor and the KHP-CTO if they are notified of a regulatory inspection.

4. The CRA will inform the Investigator of their obligation to immediately inform the Sponsor/KHP-CTO (on behalf of the Sponsor) of any change in circumstances that may affect their ability to retain study material.

The CRA will immediately notify the Quality Manager or KHP-CTO Director in the event of any suspicion of scientific misconduct, fraud or breach of GCP. This will be dealt with according to appropriate local organisational policy and the KHP-CTO Notification of a Serious Breach SOP.

### 3.2 Close-out Documentation

Following close-out activities, the CRA will promptly submit a written report to the KHP-CTO. This will be done using the either the Close-out Visit Report template (see Section 5.1) or the Remote Study Site Close out Checklist template (see Section 5.4) (as applicable). Any other communication with the site after the close-out which requires documentation will be recorded appropriately e.g. on a contact comment form (see Section 5.2).

The protocol deviation log (see section 5.5), and if applicable a Note to File (see Section 5.3), will be used to document any deviations from the protocol or other issues and these should be filed in the ISF and/or TMF with copies submitted to the KHP-CTO for inclusion in the sponsor file. All deviations generated on the trial will be collated by the CRA and sent to the trial statistician to be reviewed for impact on the trial results.

The close-out process documents will be reviewed by an authorised KHP-CTO individual promptly after the visit or communication. Documentation of the close-out process will be filed in the Trial Master File.

The Investigator will be informed in writing of discussions that took place during the close out procedures and of any follow-up items that were identified. These items will be followed up until completion. If there is evidence of systematic failure to comply with GCP the Sponsor will be informed.

Once all outstanding actions and data queries are resolved and the Clinical Study Report is complete the trial may be archived (SOP 4 Archiving Clinical Trial Data).

## 4.0 RELATED TEMPLATES

### 4.1 Close-out Visit Report Form template

### 4.2 Remote Close Out Checklist

## 5.0 APPROVAL AND SIGNATURE

Ann-Marie Murtagh

_____ _____ ___31/08/2025_____

Ann-Marie Murtagh
Director
King's Health Partners Clinical Trials Office

Date

# Appendix 1

## GLOSSARY

**Adverse Event (AE) -** Any untoward medical occurrence in a patient or clinical trial trial participant administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

**Chief Investigator (CI) -** The chief investigator is the overall lead researcher for a research project (Outside the UK the term Coordinating Investigator or Investigator may be used). In addition to their responsibilities if they are members of a research team, chief investigators are responsible for the overall conduct of a research project

**Clinical Trial of an Investigational Medicinal Product (CTIMP) -** a type of clinical trial that investigates the safety and efficacy of a drug or other medicinal product that is not yet authorised for general use. It can also involve studying how the drug is absorbed, distributed, metabolised, and excreted, or identifying any adverse reactions.

**Clinical Research Associate (CRA) –** A professional who organises and monitors clinical trials to assess the safety and effectiveness of new or existing drugs, medical devices, or treatments. CRAs play a vital role in ensuring that clinical trials are conducted ethically, safely, and in accordance with established protocols and regulations. CTO CRA's monitor compliance, for clinical trials where regulatory oversight has been delegated to the KHP CTO

**Close Out Visit Report (COVR)** – A report written by the CRA to the Sponsor (or representative) after a site close out visit.

**Contact** Comment Form **(CCF) –** Used to record communication with a trial site that requires documentation.

**Good Clinical Practice (GCP)** – an international ethical and scientific quality standard for designing, conducting, recording, and reporting clinical trials. It ensures the safety, well-being, and rights of participants are protected while maintaining the credibility and accuracy of trial data. GCP is crucial for safeguarding participants and ensuring clinical trials produce reliable, scientifically valid results

**Health Research Authority (HRA)** – An authority in England established in 2011. The authority exercises functions in connection with the facilitation and promotion of research and the establishment of research ethics committees.

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

**Investigational Medicinal Products (IMP) -** a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with marketing authorisation when used in a way different from the approved form, for an unapproved indication, or to gain further information about an approved use.

**King's Health Partners – (KHP) -** King's Health Partners brings together research, education and clinical practice across three NHS Foundation Trusts - Guy's and St Thomas', King's College Hospital and South London and Maudsley - and a world-leading university, King's College London

**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 NHS Foundation Trust to provide a streamlined approach for all aspects of trial administration. The King's Health Partners CTO has two sections: the Commercial Team which provides a single interface for those wishing to conduct trials sponsored by the pharmaceutical industries and the Quality Team that supports investigators at King's Health Partners institutions who undertake CTIMP trials where King's Health Partners are the sponsor or co-sponsor

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

**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.

**Licensing Authority** The licensing authority is responsible for the grant, renewal, variation, suspension and revocation of licences, authorisations, certificates and registrations under the Clinical Trial Regulations. The MHRA is the UK licensing authority.

**Principal Investigator (PI)** - the individual primarily responsible for the conduct of a research study at a specific research site

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

**Remote Study Site Close-Out Checklist (RSSCC)** – A report written by the CRA to the Sponsor (or representative) after each remote site close-out contact.

**Research Ethics Committee (REC) –** An independent body consisting of healthcare professionals and non-medical members, whose responsibility is to protect the rights, safety and well-being of human trial participants involved in a trial and to provide public assurance of that protection by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to inform trialparticipants and obtain their informed consent.

**Research & Development Dept (R&D) –** Department in an NHS Trust responsible for confirmation of capacity and capability for all clinical research.

**Serious Adverse Event (SAE) -** A serious adverse event is defined as an adverse experience that results in any of the following outcomes:

- death
- a life-threatening adverse experience (any adverse experience that places the patient or trial participant, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death)
- inpatient hospitalisation or prolongation of existing hospitalisation
- a persistent or significant disability/incapacity (a substantial disruption of a person's ability to conduct normal life functions)
- a congenital anomaly/birth defect.

**Trial Master File (TMF) -** a standard filing system which allows the effective storage and location of essential documents. 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 record forms and source documentation.

**The Regulations -** The Medicines for Human Use (Clinical Trial) Regulations 2004 which transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031**.** 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.