Application & Maintenance of a Clinical Trial Authorisation

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1.0 BACKGROUND & PURPOSE

The purpose of this SOP is to describe the procedures for applying for and maintaining a Clinical Trial Authorisation for Trials sponsored, co-sponsored or managed by King's Health Partner Organisations in order to comply with UK Regulations.

2.0 SCOPE

All clinical trials of investigational medicinal products sponsored, co-sponsored or managed by one or more of King's Health Partners organisations and conducted in the United Kingdom.

The definition of CTIMP is as defined in the MHRA algorithm https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/949145/Algorithm_Clean__1_.pdf

3.0 PROCEDURE

3.1 Assessing whether a Clinical Trial is Notifiable

To enable a streamlined, risk-proportionate approach to its review of Clinical Trial applications, the MHRA is categorising certain Clinical Trials as 'notifiable'. Clinical Trial applications for notifiable Clinical Trials will receive automatic authorisation from the MHRA.

Information about assessing whether a Clinical Trial is notifiable can be found here:

https://www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials

Task	Responsibility	Activity
1	Chief Investigator	Assess if the Clinical Trial meets the criteria to be assessed as a notifiable trial: • Consult MHRA guidance for criteria (MHRA Guidance on Notifiable Clinical Trials eligibility: https://www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials) • Clinical Trials which meet notifiable trial criteria and are submitted for full review will be rejected at validation stage (Notifiable trials should not be submitted for full review, they should be submitted under the 'notification' pathway).
2	Chief Investigator	Ensure a record of the 'notifiable' assessment is placed in the TMF.
3	Chief Investigator	For Clinical Trials assessed as notifiable trials, document in a cover letter any additional criteria which apply to the Clinical Trial. • Consult MHRA guidance for details of additional criteria (MHRA Guidance on Notifiable Clinical Trials eligibility: https://www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials).

4	Chief Investigator	For Clinical Trials assessed as notifiable trials, ensure the necessary additional information is provided in the submission to meet MHRA requirements. • Consult MHRA guidance for details of necessary additional information (MHRA Requirements for Clinical Trial Authorisation Submission: https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk). **Note:** the required documents for a notifiable Clinical Trial are the same as for Clinical Trials submitted for full review.
5	Chief Investigator	Ensure the MHRA correspondence relating to the Clinical Trial being assessed as a notifiable trial is placed in the TMF. If the MHRA objects to the submission of the Clinical Trial as a notifiable Clinical Trial, or considers there are other reasons for a full review, the MHRA will inform the CI within 14 calendar days of validation.

3.2 Initial submission

Task	Responsibility	Activity
1	Chief Investigator	Identify the approvals that are necessary for the Clinical Trial. Per regulation 12 of the Regulations, favourable opinion from a REC and authorisation from the UK's licensing authority (the MHRA) are necessary. Additional approvals may also be required e.g. ARSAC and/or IRMER for Clinical Trials involving radiation. **Note:** preparation of submissions for additional approvals is not included in this SOP. Send the CRA a list of approvals that have been identified as necessary for the Clinical Trial.
2	CRA	Check the CI's list of approvals that have been identified as necessary for the Clinical Trial. Inform the CI if the list needs updating.
3	Chief Investigator	Update the list of approvals that have been identified as necessary for the Clinical Trial, if applicable.

		Prepare the CTA submission form, including all necessary supporting documents (the CTA Submission Package). Production of items may be delegated to members of the Clinical Trial Team, responsibility for the contents remains with the Chief Investigator. Include the Purchase Order PDF (for the applicable MHRA fees) in the CTA Submission Package. Note the Purchase Order number in the cover letter to be included in the CTA Submission Package. Send draft CTA Submission Package to the sole Sponsor/NHS Co-Sponsor R&D Dept. and CRA for review and approval.
4	CRA	Review draft CTA Submission Package for compliance with regulatory requirements. Provide feedback and comments to the Chief Investigator, to ensure all relevant regulatory requirements are met.
5	Sole Sponsor/NHS Co-Sponsor R&D Dept.	Review draft CTA Submission Package for compliance with REC requirements and NHS expectations. Provide feedback and comments to the Chief Investigator, to ensure all REC requirements and NHS expectations are met.
6	Pharmacy representative at the sole Sponsor/NHS Co-Sponsor	Review draft IMP label for compliance with regulatory requirements and the sole Sponsor's/NHS Co-Sponsor's SOP regarding the development and approval of labelling text for IMPs and NIMPs. Provide feedback and comments to the Chief Investigator. Approval of the final IMP label by the pharmacy representative by email to the Chief Investigator is required.
7	Chief Investigator or delegate	Ensure the draft CTA Submission Package is updated to address feedback from the CRA, Sole Sponsor/NHS Co-Sponsor R&D Dept., and the pharmacy representative.
8	Non-Commercial Trials Manager or delegate	Review the draft CTA Submission Package prior to submission. Ensure all necessary information is clear and consistent across all items. Ensure the correct protocol template has been used, and that the protocol is sufficiently detailed.

		Ensure the supporting documents provide sufficient information for the MHRA to review.
9	Chief Investigator	Sign (electronically) the CTA Submission Package to confirm it is complete and ready for submission.
10	Non-Commercial Trials Manager or delegate	Sign (electronically) the CTA Submission Package on behalf of the sole Sponsor/NHS Co-Sponsor: If KCL is sole or lead Co-Sponsor: The Non-Commercial Trials Manager or delegate is the appropriate signatory If KCH is sole or lead Co-Sponsor: The Non-Commercial Trials Manager or delegate is the appropriate signatory If GSTT is sole or lead Co-Sponsor: The Non-Commercial Trials Manager or delegate is the appropriate signatory If SLAM is sole or lead Co-Sponsor: The Non-Commercial Trials Manager or delegate is the appropriate signatory
11	Non-Commercial Trials Manager or delegate	Ensure email confirmation of submission from the HRA is saved in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
12	Chief Investigator or delegate	Ensure email confirmation of submission from the HRA is saved in TMF.
13	Non-Commercial Trials Manager or delegate	Ensure email confirmation of submission validation from the HRA is saved in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
14	Chief Investigator or delegate	Ensure email confirmation of submission validation from the HRA is saved in TMF.
15	Chief Investigator	If submission is not validated by the HRA, ensure issues are addressed. The MHRA may provide email notice of any deficiencies in the submission in the week following the submission; these deficiencies should be addressed within 7 calendar days of the original submission date. If a revised submission is required (the issues identified by the MHRA could not be addressed within the 7-calendar day deadline), or if the submission is rejected; the submission should be amended and the amended submission should follow the above process again from Step 3.

3.3 Registration of the Clinical Trial

It is a condition of REC approval that the Clinical Trial is registered with a publicly accessible registry. Clinical Trials submitted through combined review after the 1st of January 2022 will automatically be registered on the ISRCTN Registry when given full approval.

Task	Responsibility	Activity
1	Chief Investigator	Before making the CTA submission, if full registration on a registry must be delayed due to commercial sensitivity, the Chief Investigator must include a rationale for the delay in a cover letter to go into the CTA Submission package. HRA guidance on registration deferral can be found here: Research registration and research project identifiers - Health Research Authority (hra.nhs.uk)
2	Chief Investigator	The Chief Investigator has overall responsibility for maintaining an accurate entry for the Clinical Trial on the ISRCTN Registry. When making updates to the registry entry, ensure email confirmation from the registry (with respect to each update made) is placed in the TMF.
3	CRA	When making updates to the registry entry, ensure email confirmation from the registry (with respect to each update made) is placed in the TMF.

3.4 MHRA Responses

Requests for Further Information (RFIs) from the MHRA

Task	Responsibility	Activity
1	Non-Commercial Trials Manager or delegate	Upon receiving an RFI, send to the CI. Ensure the RFI is saved in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
2	Chief Investigator or delegate	Draft response to the RFI as a letter in preparation for sending to the MHRA. In addition to drafting the response letter, changes to Clinical Trial documents may be necessary. Send the draft response letter (and amended Clinical Trial documents if applicable) to the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. for their review.

3	Sole Sponsor/NHS Co-Sponsor R&D Dept.	Review draft response letter (and amended Clinical Trial documents if applicable) to check that all aspects of the RFI have been addressed, and that the Clinical Trial remains compliant with Sole Sponsor/NHS Co-Sponsor R&D Dept. expectations. Inform the CI if the draft response letter (and amended Clinical Trial documents if applicable) are acceptable or if further changes are required.
4	CRA	Review draft response letter (and amended Clinical Trial documents if applicable) to check that all aspects of the RFI have been addressed, and that the Clinical Trial remains compliant with KHP-CTO Non-Commercial Team expectations. Inform the CI if the draft response letter (and amended Clinical Trial documents if applicable) are acceptable or if further changes are required.
5	Chief Investigator or delegate	Update the draft response letter (and amended Clinical Trial documents if applicable) to address the feedback from the Sole Sponsor/NHS Co-Sponsor R&D Dept. and KHP-CTO Non-Commercial Team, so the Clinical Trial remains compliant with Sole Sponsor/NHS Co-Sponsor R&D Dept. and KHP-CTO Non-Commercial Team expectations.
6	CRA	Save the draft response letter (and amended Clinical Trial documents if applicable) in the TMF, and upload it to EDGE and the KHP-CTO SharePoint.
7	Chief Investigator	If any Clinical Trial documents have been amended, list these documents in the draft response letter. If any Clinical Trial documents have been amended, prepare clean versions and versions with tracked changes to send with the response letter. Send the response letter (and amended Clinical Trial documents if applicable, both clean versions and versions with tracked changes) to the MHRA, taking care to ensure they're sent to the MHRA within 60 calendar days of the RFI.
8	Chief Investigator	If the CI believes the response letter (and amended Clinical Trial documents if applicable) will not be ready in time to meet the 60-calendar day deadline, the CI must request an extension from the MHRA. Save correspondence relating to the extension request in the TMF.

9	Chief Investigator	Ensure a copy of the response letter (and amended Clinical Trial documents if applicable) that were sent to the MHRA, are saved in the TMF.
10	CRA	Update the Sponsor Oversight Tracker to confirm the date upon which the response to the RFI was sent to the MHRA.

3.5 Conditional approval from the MHRA

Task	Responsibility	Activity
1	Non-Commercial Trials Manager or delegate	On receipt of a letter of conditional approval from the MHRA, ensure the CI is informed. Ensure the letter is saved in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
2	Chief Investigator	Ensure the necessary actions to meet the conditions of approval are taken. Send written confirmation to the Sole Sponsor/NHS Co-Sponsor R&D Dept. and the CRA that the conditions have been met. Save a copy of the written confirmation in the TMF.
3	CRA	Update the Sponsor Oversight Tracker to confirm the date upon which the conditions of approval were met.

3.6 Approval from the MHRA

Task	Responsibility	Activity
1	Non-Commercial Trials Manager or delegate	Upon receipt of written confirmation of approval from the MHRA, forward it to the CRA.
2	CRA	Upon receipt of written confirmation of approval from the Non-Commercial Trials Manager or delegate, forward it to the CI and: 1. Remind them that participant recruitment cannot commence until the CRA has issued 'sponsor greenlight' on a 'research site by research site' basis (including the research site that the CI is PI for, if applicable); and

		2. Inform them about the next steps. Upon receipt of written confirmation of approval from the Non-Commercial Trials Manager or delegate, forward it to the Sole Sponsor/NHS Co-Sponsor R&D Dept. Save written confirmation in the TMF, and upload it to EDGE and the KHP-CTO SharePoint. Update the Sponsor Oversight Tracker to record the date upon which approval was granted.

3.7 Rejection by the MHRA

Task	Responsibility	Activity
1	Non-Commercial Trials Manager or delegate	Upon receipt of written confirmation of rejection from the MHRA, forward it to the CRA.
2	CRA	Upon receipt of written confirmation of rejection from the Non-Commercial Trials Manager or delegate, forward it to the CI Upon receipt of written confirmation of rejection from the Non-Commercial Trials Manager or delegate, forward it to the Sole Sponsor/NHS Co-Sponsor R&D Dept. Save written confirmation in the TMF, and upload it to EDGE and the KHP-CTO SharePoint. Update the Sponsor Oversight Tracker to record the date upon which application was rejected.
3	Chief Investigator or delegate	Upon receipt of written confirmation of rejection from the CRA, forward it to the CI Inform other necessary parties of rejection.

3.8 Lapses in Trial Approval

For trials submitted for approval on or after 28th April 2026 only:
If no participants have been recruited within 2 years from the date the trial was approved, Clinical Trial approval will lapse. The MHRA will contact the Sponsor to confirm, and request to submission of an end of trial declaration (see section 3.15).

3.9 Modification Assessment

Task	Responsibility	Activity
1	Chief Investigator or delegate	Categorise the proposed modification. Categorisation should follow this decision tree: Fig1. Modification types.pdf There are four types of modification: • Route A substantial modifications, • Route B substantial modifications, • Modifications of an Important Detail (MOIDs), • Minor modifications. These are defined in the glossary. There are three types of Route B modification: 1. Approvals from other authorities 2. Changes to the protocol 3. Changes to the Investigator's Brochure (IB) or Summary of Product Characteristics (SmPC) Here are examples of Route B modifications: Tab1. Route B substantial modifications in Modifying a Clinical Trial Approval Ensure a record of the categorisation decision and rationale is placed in the TMF.
2	Chief Investigator or delegate	If the modification requires submission, ensure the categorisation decision and rationale is available to submission reviewers. These can be provided in a cover letter to be sent with the submission.

3.10 Urgent Safety Measures (USMs)

USMs relating to a Clinical Trial should be communicated to the MHRA immediately.

Task	Responsibility	Activity
1	Chief Investigator	Decide that a USM is appropriate to protect the participants of the Clinical Trial against an immediate hazard to their health or safety. Record the decision in the TMF.
2	Chief Investigator or delegate	Inform the Non-Commercial Trials Manager of the USM and: • Share the rationale for applying the USM • Explain what the USM is

3	Chief Investigator or delegate	Inform all members of the Clinical Trial Team and Host Site Teams of the USM. Provide written instructions to the Clinical Trial Team and Host Site Teams for how to apply the USM, to ensure consistent implementation of the USM. **The CI or delegate should set expedient and realistic deadlines for USM application for all Host Site Teams.** Ensure a record of the USM announcement and any subsequent USM communications with the Clinical Trial Team and Host Site Teams is placed in the TMF.
4	Non-Commercial Trials Manager or delegate	On the day the Non-Commercial Trials Manager is notified of the USM, they should (ideally within 24 hours but no later than 3 days after the measure has been taken): 1. Call the MHRA to inform them of the implementation of a USM (Reporting USMs to the MHRA: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures); or *(if unable to contact via telephone*) 2. Email the MHRA to inform them of the implementation of a USM (Reporting USMs to the MHRA: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures) In either case, a record of the interaction with the MHRA should be placed in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
5	Non-Commercial Trials Manager or delegate	Inform the CI that the MHRA have been informed. A record of this interaction with the Chief Investigator should be placed in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint.
6	Non-Commercial Trials Manager or delegate	If any other Clinical Trials, sponsored or co-sponsored by King's Health Partner Organisations, may be impacted by the same hazard to participant health or safety (e.g. a Clinical Trial using the same IMP); inform the respective Chief Investigators or the respective Clinical Trials. Provide the respective Chief Investigators with: • Details of the hazard identified • Details of the USM that was implemented. A record of these interactions with the respective Chief Investigators should be placed in the respective Clinical Trials'

		TMFs, and uploaded to the respective Clinical Trials' EDGE and KHP-CTO SharePoint folders.
7	Chief Investigator	Ensure submission of a written notification of the USM within 7 calendar days of the USM. For studies submitted via IRAS combined review this notification must be via IRAS. For studies which did not submit through combined review this notification should be sent via email to the MHRA & REC.
8	Chief Investigator	If the MHRA confirm the measure is an USM, ensure submission of a substantial modification (using same process as detailed in 3.11) within **2 weeks** of the date on which the MHRA was first informed (via telephone or email -see step 4 section 3.10) of the USM.

3.11 Modifications Proposed by the Chief Investigator

Task	Responsibility	Activity
1	Chief Investigator	The CI has overall responsibility for modifications and should follow current MHRA guidance with respect to the threshold for modifications (MHRA Modification guidance: https://www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval). **Note:** the actual recruitment date of the first participant must be submitted as a MOID.

2	Chief Investigator or delegate	Prepare the submission package.
		
		At this point it will not be known if the submission package will need to be submitted or not, but the submission package should still be prepared.
		
		Preparation of the submission package should include:
		• Completing the modification tool
		• Update the existing Clinical Trial documents as necessary (save clean versions and versions with tracked changes)
		• Draft the new Clinical Trial documents as necessary
		• If the modification is substantial or a MOID, draft a cover letter to go into the submission package:
		  ○ For substantial modifications, state whether it's a Route A substantial modification or a Route B substantial modification, and provide the rationale for the decision, and list any minor modifications made since the last substantial modification was submitted.
		  ○ For MOIDs, provide the information that the modification tool indicates is necessary.

3	Chief Investigator or delegate	If the modification tool indicates that Patient and Public Involvement (PPI) is required with respect to the modification, arrange for the required involvement to take place. Record the PPI review and outcome in the TMF if applicable. Update the modification tool to include details of the PPI review and outcome if applicable.
4	Chief Investigator or delegate	Send the draft submission package to the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. for review.
5	CRA	Review the draft submission package. Complete the KHP-CTO modification assessment form. Provide feedback to the Chief Investigator or delegate. Detail any aspects requiring clarification or changes in order to demonstrate adherence to legal requirements and MHRA guidance (MHRA Modification guidance: https://www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval), so the CRA can approve the submission package.
6	Sole Sponsor/NHS Co-Sponsor R&D Dept.	Review the draft submission package. Provide feedback to the Chief Investigator or delegate. Detail any aspects requiring clarification or changes in order to demonstrate that NHS expectations are met, so the Sole Sponsor/NHS Co-Sponsor R&D Dept. can approve the submission package
7	Chief Investigator or delegate	Ensure the feedback on the draft submission package from the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. is addressed. Send the draft submission package (now the feedback has been addressed) to the CRA and Sole Sponsor/NHS Co-Sponsor R&D Dept. for approval.
8	Sole Sponsor/NHS Co-Sponsor R&D Dept.	Inform the Chief Investigator or delegate that the draft submission package has been approved.
9	CRA	Inform the Chief Investigator or delegate that the draft submission package has been approved. Lock and sign the modification tool.

		Add the locked modification tool to the submission package. Submit the submission package if applicable Send the finalised submission package to the Chief Investigator or delegate
10	Chief Investigator or delegate	Save the finalised submission package to the TMF
11	Non-Commercial Trials Manager or delegate	If the submission package is submitted, the outcome will be sent to the Non-Commercial Trials Manager. Share the outcome with the Chief Investigator or delegate. Ensure the outcome is recorded in the TMF, and uploaded to EDGE and the KHP-CTO SharePoint. **Note:** • If the MHRA identify that a submission of a MOID should actually be a submission of a substantial modification, the MHRA will review the submission as a substantial modification, no resubmission is required. • If the MHRA identify that a submission of a substantial modification should actually be a submission of a MOID, the MHRA will reject the submission, and resubmission will be required.

3.12 Modifications requested by the MHRA or the REC

Both the MHRA and the REC can propose modifications to a Clinical Trial.

Task	Responsibility	Activity
1	Non-Commercial Trials Manager or delegate	On receipt of the modification request, inform the CI. The modification request is sent out by the MHRA or the REC at least 7 calendar days before the modification is set to take effect.
2	Chief Investigator	Decide if the proposed modification is acceptable, if so, go to step 3 below, if not, go to step 11 below.
3	Chief Investigator or delegate	Prepare the submission package. At this point it will not be known if the submission package will need to be submitted or not, but the submission package should still be prepared.

		Preparation of the submission package should include:
		• Completing the modification tool
		• Update the existing Clinical Trial documents as necessary (save clean versions and versions with tracked changes)
		• Draft the new Clinical Trial documents as necessary
		• If the modification is substantial or a MOID, draft a cover letter to go into the submission package:
		  ○ For substantial modifications, state whether it's a Route A substantial modification or a Route B substantial modification, and provide the rationale for the decision, and list any minor modifications made since the last substantial modification was submitted.
		  ○ For MOIDs, provide the information that the modification tool indicates is necessary

4	Chief Investigator or delegate	If the modification tool indicates that Patient and Public Involvement (PPI) is required with respect to the modification, arrange for the required involvement to take place. Record the PPI review and outcome in the TMF if applicable. Update the modification tool to include details of the PPI review and outcome if applicable.
5	Chief Investigator or delegate	Send the draft submission package to the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. for review, **making it clear that a response is urgently required as the modification will take effect within 7 calendar days of the date of the MHRA's or REC's modification request**.
6	CRA	**Review the draft submission package urgently.** Complete the KHP-CTO modification assessment form. Provide feedback to the Chief Investigator or delegate. Detail any aspects requiring clarification or changes in order to demonstrate adherence to legal requirements and MHRA guidance (MHRA Modification guidance: https://www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval), so the CRA can approve the submission package.
7	Sole Sponsor/NHS Co-Sponsor R&D Dept.	**Review the draft submission package urgently.** Provide feedback to the Chief Investigator or delegate. Detail any aspects requiring clarification or changes in order to demonstrate that NHS expectations are met, so the Sole Sponsor/NHS Co-Sponsor R&D Dept. can approve the submission package.

8	Chief Investigator or delegate	Ensure the feedback on the draft submission package from the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. is addressed. Send the draft submission package (now the feedback has been addressed) to the CRA for submission.
9	CRA	Lock and sign the modification tool. Add the locked modification tool to the submission package. Submit the submission package if applicable Send the finalised submission package to the Chief Investigator or delegate
10	Chief Investigator or delegate	Send a response letter to the MHRA or the REC within 7 calendar days of the MHRA's or REC's modification request. The letter should confirm that the modification will take effect within 7 calendar days of the MHRA's or REC's modification request, and that the corresponding submission package has been prepared/submitted as applicable. Save the response letter and the finalised submission package to the TMF
11	Chief Investigator	Draft response letter appealing the modification request. Draft supporting documents to be sent with the response letter if applicable. Send the draft response letter and draft supporting documents to the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. for review, **making it clear that a response is urgently required, so the response letter can be sent to the MHRA or REC within 7 calendar days of the date of the MHRA's or REC's modification request**.
12	CRA	**Review the draft response letter and draft supporting documents urgently.** Provide feedback to the Chief Investigator.
13	Sole Sponsor/NHS Co-Sponsor R&D Dept.	**Review the draft response letter and draft supporting documents urgently.** Provide feedback to the Chief Investigator.
14	Chief Investigator	Ensure the feedback on the draft response letter and draft supporting documents from the CRA and the Sole Sponsor/NHS Co-Sponsor R&D Dept. is addressed.

		Send the response letter and supporting documents to the MHRA or REC within 7 calendar days of the date of the MHRA's or REC's modification request. Save the response letter and supporting documents to the TMF

3.13 Modification log

A modification log is a mandatory, centralised record that tracks every modification made to a Clinical Trial, whether they're modifications made during the Clinical Trial application process, or modifications made after the Clinical Trial is open.

Task	Responsibility	Activity
1	CRA	Train the CI and Clinical Trial Team on the modification log (see **KHP CTO SOP 13: Study Set-Up and Initiation of an Investigator Site**).
2	Chief Investigator or delegate	Maintain the modification log during the Clinical Trial. Keep the modification log in the TMF.
3	CRA	Review the modification log as part of routine TMF monitoring activity. Record any issues with the modification log in the monitoring report (see **SOP 3 Clinical Trial Monitoring**).
4	Chief Investigator or delegate	During the Clinical Trial, provide the modification log to the Host Site Teams on request, or per protocol requirements.
5	Chief Investigator	At EoT, confirm all modifications have been accurately recorded in the modification log. Save a copy of the signed confirmation with the modification log in the TMF.

3.14 Temporary Halt of a Clinical Trial

A temporary halt is any halt to protect participant safety or avoid potential harm to participants which is not pre-defined or envisaged in the protocol where the intent is to resume the trial. The halt can include:

- a halt of the trial as a whole
- a halt to part of a trial
- stoppage at one or more trial locations

Note: A notification of temporary halt is **not** expected:

- when a trial is 'paused' due to logistical reasons (see MHRA Clinical Trials Hub for examples: Clinical trials for medicines: collection, verification, & reporting of safety events - GOV.UK)
- when a trial is 'paused' to determine if a temporary halt is warranted
- for halts based on predefined rules in the protocol (stopping rules)

Failure to notify the MHRA of the implementation of a temporary halt for safety reasons may be considered a serious breach see **KHP CTO SOP 6: Notification of a Serious Breach**.

Task	Responsibility	Activity
1	Chief Investigator or delegate	In the event of a decision to temporarily halt the trial, document the decision fully in the TMF and inform the Non-Commercial Trials Manager immediately. **Note:** in addition to halting the Clinical Trial, if actions must be taken to address a hazard to the health or safety of the participants (e.g. additional follow-up visits must be incorporated into the Clinical Trial), also follow the **USM process in section 3.10.** Ensure a copy of the correspondence with the Non-Commercial Trials Manager is placed in the TMF.
2	Chief Investigator or delegate	Inform Host Site Teams that the Clinical Trial will be temporarily halted. Provide the Host Site Teams with instructions explaining how the Clinical Trial will be halted (e.g. explain how participant recruitment will be suspended, how administration of the IMP will be interrupted). This will ensure the Clinical Trial is halted consistently across all research sites. Ensure a copy of the correspondence with each of the Host Site Teams is placed in the TMF.
3	Chief Investigator or delegate	The temporary halt to the Clinical Trial must be submitted to the MHRA and the REC as a substantial modification within 15 calendar days of the date the Clinical Trial is halted. Follow the procedure described in 3.11 Modifications.
4	Chief Investigator or delegate	To restart the Clinical Trial a second substantial modification must be submitted to the MHRA and the REC. Follow the procedure described in 3.11 Modifications.
5	Chief Investigator or delegate	If the temporary halt to the Clinical Trial is made permanent, and no further follow up of participants will occur the EoT

		notification should be submitted to the MHRA and the REC within 15 calendar days of the decision to terminate the Clinical Trial. Follow the procedure described below: 3.15 End of Trial Notifications. If recruitment will not restart but participants will continue to be followed up on the trial, update protocol (e.g. to amend target recruitment numbers and/or end of trial definition) and submit modification per 3.11 Modifications.

3.15 End of Trial (EoT) Notifications

Task	Responsibility	Activity

1	Chief Investigator or delegate	Ensure the following have been completed before preparing EOT notification:
		
		• All modifications to the Clinical Trial, including revisions to the statistical analysis plan and the publication plan, have been documented in locked modification tools.
		• Any modification submissions have received the necessary approvals.
		• Confirm the REC approved arrangements (i.e. those submitted in the initial IRAS application or subsequent amendments/modifications) are as planned for:
		  ○ dissemination of trial results to participants (see section 3.16).
		  ○ future use of human tissue/biological samples and data.
		
		Submit a modification (see section 3.11) if the plan for either of the above has changed, this includes changing the EOT definition to complete the analysis of human tissue/biological samples.
		
		Note: In the UK all human tissue/biological sample movement and analysis **covered by REC approval** for a trial must be completed before the EOT is declared. Continued storage after the EOT is declared must be in a HTA licensed premises or under a new REC approval. For further guidance refer to HRA Use of Human Tissue in research: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/use-tissue-research/ also refer **to KHP CTO SOP 16 Clinical Trial Close Out Procedure.**

2	Chief Investigator or delegate	Complete the EoT notification form following the conclusion of the trial (as defined in the protocol) or early termination of the trial, allow time for CRA review to meet regulatory timelines details in 4. Save the draft EoT notification form in the TMF. Send the draft EoT notification form to the CRA for approval.
3	CRA	Review and approve the draft EoT notification form. Share approval or feedback with the CI.
4	Chief Investigator or delegate	Action the CRA's feedback if applicable. If the Clinical Trial is being terminated early, the EoT notification should be submitted to the MHRA and the REC within 15 calendar days of the decision to terminate the Clinical Trial. If the Clinical Trial is ending per the protocol, the EoT notification should be submitted to the MHRA and the REC within 90 calendar days of EoT. Submit the EoT notification form: • For Clinical Trials submitted via Combined Review, the EoT notification form should also be submitted via Combined Review. • For older Clinical Trials, submit the EoT notification form separately to the MHRA (How to Submit EoT Notifications to the MHRA for Clinical Trials not Submitted via Combined Review: https://www.gov.uk/guidance/register-to-make-submissions-to-the-mhra#gaining-access-to-mhra-submissions) and the REC (Submit your Final Report to the HRA: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/). You will also need to submit a cover letter with the EoT notification form. Save a copy of the EoT notification form you submitted, along with the cover letter if applicable, in the TMF. Inform the following parties that the EoT notification form has been submitted: • The CRA • The Non-Commercial Trials Manager • The Sole Sponsor/NHS Co-Sponsor R&D Dept. Send a copy of the EoT notification form to the CRA.

5	CRA	Upload a copy of the EoT notification form that was submitted to EDGE and the KHP-CTO SharePoint.

3.16 Summary of trial results

From the 28th April 2026 for all trials *which have not declared EOT before this date* it is a legislative requirement that within 12 months of the end of the trial a summary of trial results is published in the same public registry* that the trial was registered in (e.g. ISRCTN). In addition, include a plain language summary of results where feasible. The only exception will be if sponsors have a deferral or waivers see *https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/clinical-trial-regulations-reform/guidance-on-changes-to-the-clinical-trials-regulations/research-transparency-requirements-for-clinical-trials/deferrals*,

*If a trial is registered in more than one public registry results must be published in each registry.

Where study results have been published in a peer-reviewed journal, within 12 months of the end of the trial, it is sufficient to simply upload a link to the publication to the registry (this could be a PubMed link or its DOI link starting https://doi.org/). If the study is complete but results will not be published in a peer-reviewed journal within 12 months of the end of the trial, the summary of trial results must be uploaded to the public registry per the registry's requirements within 12 months of the end of the trial. **Note:** uploading a summary of trial results to a public registry per the registry's requirements is not considered prior publication and should not prevent publishing in a peer-reviewed journal.

Task	Responsibility	Activity
1	CRA	At Clinical Trial initiation, inform the CI of the legislative requirements for publishing a summary of trial results. Save a copy of the correspondence to the TMF, and upload to EDGE and the KHP-CTO SharePoint.
2	CRA	Six months before planned EoT, remind the CI of the requirement to produce a summary of trial results or link to a peer-reviewed publication that can be submitted to a publicly accessible registry within 12 months of EoT. Save a copy of the correspondence to the TMF, and upload to EDGE and the KHP-CTO SharePoint.
3	CRA	At EoT, remind the CI that they're required to send a summary of trial results or link to a peer-reviewed publication to the CRA within 8 months of EoT, so the study results can be reviewed and submitted to a publicly accessible registry within 12 months of EoT. Offer practical support to the CI to help them draft the trial results (e.g. clarify content expectations, confirm data cut-off and database lock status).

		Save a copy of the correspondence to the TMF, and upload to EDGE and the KHP-CTO SharePoint.
4	Chief Investigator	If the CI believes they'll be unable to provide a link to a peer-reviewed publication to the CRA within 8 months of EoT, they should draft the summary of trial results and: • Ask members of the Clinical Trial Team (e.g. the statistician) for support as necessary. • Include (serious) adverse event line listings or tables in the summary results. The CI is ultimately responsible for the summary of trial results and publication. Send the draft summary of trial results or link to a peer-reviewed publication to the CRA within 10 months of EoT. Save a copy of the draft summary results in the TMF.
5	CRA	If the CI provided a summary of trial results, review the summary of trial results to confirm that all safety data corresponds with KHP CTO records for the trial and send feedback to the CI if applicable. If applicable, save a copy of the feedback to the TMF, and upload it to EDGE and the KHP-CTO SharePoint. **Note:** The CRA review is not an additional scientific review. It is to ensure the study safety data presented corresponds with KHP CTO records, including the final DSUR and eCRF data at the time of database lock.
6	Chief Investigator	If the CI provided a summary of trial results update the draft summary results or draft publication to address the CRA's feedback if applicable. Send the updated draft summary of trial results to the CRA if applicable. Save a copy of the updated draft summary of trial results in the TMF if applicable
7	CRA	If the CI provided a link to a peer-reviewed publication, send this link to the Operations Manager. If the CI provided a summary of trial results, save the reviewed summary of trial results to the SharePoint in the Clinical-Trial specific folder, and inform the Operations Manager that the summary of trial results is ready for upload to a public registry.

8	Operations Manager or delegate	Upload the summary of trial results or link to a peer-reviewed publication to the publicly accessible registry the Clinical Trial was registered with. For trials that were approved through separate applications to the MHRA and REC (i.e prior to IRAS combine review) notify the MHRA via that a summary of the trial results haves been submitted to a publicly accessible registry. For trials approved via IRAS combined review there is no requirement to notify the MHRA, notification is via the final report to the REC in IRAS combined review, also see section 3.18.

3.17 Lay summary of results for participants

For all trials submitted for Clinical Trial approval and an ethics committee approval on or after 28th April 2026 is it a legislative requirement to offer trial participants (and where applicable other relevant people e.g. parents and those with parental responsibility, legal representatives see HRA guidance) a lay summary of trial results. For trials submitted for approval prior to this date it is good practice to provide trial results to participants unless there is a good reason not to.

Task	Responsibility	Activity
1	Chief Investigator or delegate	Detail the arrangements for dissemination of trial results to participants in the initial application for REC approval (see section 3.2).
2	Chief Investigator or delegate	Check the REC approved arrangements (i.e. those submitted in the initial IRAS application or subsequent amendments/modifications) are correct. Any changes to these plans must be submitted as a modification (see section 3.11) prior to declaring the end of the trial.
3	Chief Investigator or delegate	Write a lay summary of Clinical Trial results and ensure it is distributed in accordance with the REC approved arrangements. Save a copy of the draft lay summary in the TMF.

3.18 Final Report to the REC

Task	Responsibility	Activity
1	Chief Investigator or delegate	Submit the Final Report to the REC within 12 months of EoT:

		• For trials that were approved through separate applications to the MHRA and REC (i.e prior to IRAS combine review submit via the https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/ For trials approved via IRAS combined review, the final report should be completed in IRAS combined review. Save any correspondence and the final report to the TMF and provide a copy to the CRA.

3.19 Other activities

The following activities also contribute to the maintenance of the CTA but are outside the scope of this SOP:

- Reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) to the MHRA and the REC within the required timeframes (See the Pharmacovigilance and Safety Reporting Policy).
- Providing the MHRA and the REC with Development Safety Update Reports (See SOP 17 Development Safety Update Reports (DSURs))
- Permit inspection of any Clinical Trial premises by MHRA inspectors as appropriate.

3.20 MHRA Clinical Trial Application Fees

Task	Responsibility	Activity
1	Chief Investigator or delegate	Generate a Purchase Order PDF for the applicable MHRA fees for making the Clinical Trial application. Details of the current fees can be found on the MHRA website: https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees#clinical-trials-application-fees Include the Purchase Order PDF (for the applicable MHRA fees) in the draft CTA Submission Package. Note the Purchase Order number in the cover letter to be included in the draft CTA Submission Package.
2	CRA	Upon receipt of the draft CTA Submission Package for review, check the Purchase Order PDF (for the applicable MHRA fees) is included, and check the Purchase Order number is included in the cover letter. If applicable, inform the CI if the Purchase Order PDF (for the applicable MHRA fees) has been omitted from the

		draft CTA Submission Package, and/or if the Purchase Order number has been omitted from the cover letter.
3	Chief Investigator or delegate	If applicable, include the Purchase Order PDF (for the applicable MHRA fees) in the draft CTA Submission Package, and/or note the Purchase Order number in the cover letter to be included in the draft CTA Submission Package.
4	Sole Sponsor/NHS Co-Sponsor representative	The Sole Sponsor/NHS Co-Sponsor representative (the party who signed (electronically) the CTA Submission Package on behalf of the sole Sponsor/NHS Co-Sponsor) will be informed by the MHRA if there are problems with the Purchase Order. Contact the CI to resolve any problems with the Purchase Order.

4.0 RELATED TEMPLATES

KHP-CTO Modification Assessment form
KHP CTO Modification Log

5.0 RELATED SOPs

KHP CTO SOP 13: Study Set-Up and Initiation of an Investigator Site
KHP CTO SOP 6: Notification of a Serious Breach
KHP CTO SOP 16 Clinical Trial Close Out Procedure.

6.0 REFERENCES

Applying for a Clinical Trials Authorisation

https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk
Guidance for managing your CTA and for reporting safety issues

https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues

MHRA fees

https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees#clinical-trials-application-fees

The MHRA's 'Is it a Clinical Trial of a Medicinal Product?' algorithm

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/949145/Algorithm_Clean__1_.pdf

MHRA Guidance on Notifiable Clinical Trials eligibility

https://www.gov.uk/guidance/clinical-trials-for-medicines-notifiable-trials

Decision Tree for Determining the Correct Category for a Modification

https://assets.publishing.service.gov.uk/media/69e63b638c9f882ae5997f86/Fig1._Modification_types.pdf

Examples of Route B Modifications

https://assets.publishing.service.gov.uk/media/69e6413059ffffb9ecfcf964/Tab1._Route_B_substantial_modifications_in_Modifying_a_Clinical_Trial_Approval.pdf

MHRA Modification guidance

https://www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval

Deferral of Clinical Trial Registration with a Publicly Accessible Registry

https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/#deferral

Submit your Final Report to the HRA

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/

MHRA Requirements for Clinical Trial Authorisation Submission

https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-approval-in-the-uk

Reporting USMs to the MHRA

Clinical trials for medicines: collection, verification and reporting of safety events - GOV.UK

How to Submit EoT Notifications to the MHRA for Clinical Trials not Submitted via Combined Review

https://www.gov.uk/guidance/register-to-make-submissions-to-the-mhra#gaining-access-to-mhra-submissions

Change History			
Date	Version Number	Change details	Approved by
15 Jun 2011	2.0	Addition of Type A trials and correction of typographical and formatting errors	Jackie Powell
14 Sept 2011	3.0	Amendment of ASR to DSUR as per ICH E2 guidance	Jackie Powell
11 Nov 2013	4.0	Change of branding from JCTO to KHP-CTO and changes to MHRA fee structure	Jackie Powell
01 Dec 2016	5.0	Scheduled review, update of glossary, addition of the HRA and other clarifications	Jackie Pullen
12 May 2017	5.1	Minor amendment to remove web links, correction to references to section 7 which should have referred to section 6, removal of pre-payment requirements to MHRA as no longer applicable. Update to section 4.9 as pre-payment of fees is no longer applicable. Fees will be paid on receipt of invoice.	Jackie Pullen
09 May 2018	6.0	Section 4.1 updated regarding pharmacy review and approval of IMP labels. Section 4.1.4.2 numbering corrected in Table of Contents and in section heading.	Jackie Pullen
01 Oct 2018	6.1	Minor amendment to include trials managed by KHP-CTO	Jackie Pullen
05 Jan 2021	7.0	Updated to incorporate BREXIT changes to UK Clinical Trial Authorisations	Jackie Pullen
28 May 2021	7.1	Minor updates to reflect HRA practices and website links updated	Jackie Pullen
16 Jun 2021	7.2	Minor update to 4.3	Jackie Pullen
20 Sep 2023	8.0	Updated to include process for combined review and clarify KHP-CTO responsibilities	Kirsty Hough
31 Aug 2025	9.0	Update to include process for final clinical study report at End of Trial	Ann-Marie Murtagh
22 Apr 2026	10.0	Updated to incorporate Clinical Trial Regulations 2025 and R3 changes to UK Clinical Trial Authorisations and move to new SOP template • Addition of the 'notifiable trial' process • Change of 'amendments' to modifications' • Addition of 'New Rules Trials' transparency requirements • Updates to glossary definitions • Clarifications throughout	Ann-Marie Murtagh
28 Apr 2026	10.1	Signatures of SOP replaced for administrative reasons Updated links to MHRA website No changes to SOP content	Ann-Marie Murtagh

7.0 CHANGE HISTORY

8.0 GLOSSARY

Chief Investigator (CI) – The overall lead researcher for a research project (Outside the UK the term 'Coordinating Investigator', 'Principal Investigator' or 'Investigator' may be used for the overall lead researcher for a research project). Chief Investigators are responsible for the overall conduct of a research project.

Clinical Research Associate (CRA) – The staff member(s) employed by the KHP-CTO who are responsible for the initiation phase, routine phase, and close down phase of a Clinical Trial.

Clinical Study Report (CSR) – A Clinical Study Report is a comprehensive, regulatory-standard document that provides a complete and structured account of a Clinical Trial's methods, conduct, results, and conclusions. It includes all analyses — efficacy, safety, and protocol deviations — and is used by regulators, Sponsors, and auditors to verify the integrity and outcomes of the Clinical Trial. Academic publication cannot double as a Clinical Study Report, a journal article does not meet the regulatory requirements for a Clinical Study Report. A funder report cannot double as the Clinical Study Report, a funder report does not meet the regulatory requirements for a Clinical Study Report.
Clinical Trial of an Investigational Medicinal Product (CTIMP) - Any investigation in human participants (other than a non-interventional trial) intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products and/or to identify any adverse reactions to one or more such products and to study absorption, distribution, metabolism and excretion of one or more such products with the object of ascertaining the safety and/or efficacy of those products.

Clinical Trial Authorisation (CTA) – Authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) to conduct a Clinical Trial. No Clinical Trial can commence in the UK without both a CTA and a favourable ethical opinion. Applications to the MHRA and the Research Ethics Committee (REC) may be made in parallel.

Clinical Trial Team – The team selected by the CI to undertake the sponsorship functions of the Clinical Trial.

Co-Sponsors – Two organisations that take responsibility for the initiation, management and financing (or arranging of the financing) in relation to a Clinical Trial. The Co-Sponsors agree how the sponsor functions for the Clinical Trial are divided between themselves and document this accordingly.

Combined Review - The UK system under which a Sponsor submits a single Clinical Trial application that is reviewed jointly by the MHRA and REC, and results in one combined regulatory decision.

CTA Submission Package - The CTA submission form and all necessary supporting documents for the CTA submission.

Data Lock Point – Day prior to the anniversary of the DIBD. The Sponsor can designate this as the last day of the month.

Development International Birth Date (DIBD) – Date of the first authorisation to conduct a Clinical Trial of a specific Investigational Medicinal Product in any country worldwide.

Development Safety Update Report (DSUR) - A common standard for periodic reporting on drugs under development (including marketed drugs that are under further study).

End of Trial (EoT) – The end of the trial as defined in the protocol. The end of the trial is typically expressed as a condition-based event, not a predetermined date.

Final Report - This is a UK-wide final report for all project-based research studies that have been reviewed by a REC within the UK Health Departments' Research Ethics Service. The information contained in the final report helps the Research Ethics Service monitor whether the research was conducted in accordance with the REC favourable opinion and applicable transparency requirements.

Good Clinical Practice (GCP) - An international ethical and scientific quality standard for designing, conducting, recording, and reporting Clinical Trials that involve human participants. 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) – The national body in England responsible for protecting and promoting the interests of patients and the public in health and social care research.

Host Site Teams – The team selected by the PI (and including the PI) who undertake the hosting functions of the Clinical Trial at a research site.

Investigational Medicinal Product (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.

Integrated Research Application System (IRAS) - The online application system used to apply for most permissions and approvals for research in health and social care in the UK.

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' NHS Foundation Trust, King's College Hospital NHS Foundation Trust and South London and Maudsley NHS Foundation Trust - and a world-leading university, King's College London

King's Health Partners Clinical Trials Office (KHP-CTO) – The department established by King's College London, Guy's and St Thomas' NHS Foundation Trust, King' College Hospital NHS Foundation Trust, and South London and Maudsley NHS Foundation Trust to 1) undertake the set up and financial Management of commercial research hosted by one or more of the KHP Partners, and 2) undertake the regulatory submissions and oversight, as well as monitoring activity for non-commercial research studies sponsored by one of the KHP Partners

KHP-CTO Non-Commercial Team - Comprises the Non-Commercial Trials Manager, CRA(s), Clinical Trial Administrator(s), and Training Executive(s).

Lead Co-Sponsor – Where the Clinical Trial is co-sponsored, the Lead Co-Sponsor is the entity who substantively employs the Chief Investigator.

Licensing Authority - The licensing authority is responsible for the grant, renewal, variation, suspension and revocation of licences, authorisations, certificates and registrations under the regulations. The MHRA is the UK's licensing authority.

Medicines & Healthcare products Regulatory Agency (MHRA) – The UK government agency responsible for regulating medicines, medical devices, and Clinical Trials. In the context of Clinical Trials, the MHRA i) acts as the licensing authority for Clinical Trials, ii) reviews the scientific, quality, and safety aspects of a Clinical Trial application, iii) issues CTAs, iv) oversees GCP and GMP inspections, v) monitors pharmacovigilance and safety reporting, and vi) enforces compliance with UK medicines legislation.

Minor modification – A change to a Clinical Trial that has no significant impact on the safety or rights of participants, the conduct of the Clinical Trial, or the scientific value of the data.

Modification of an Important Detail (MOID) - A type of change made to a Clinical Trial that does not substantially affect participant safety, rights, or the reliability of the study's data, but which regulatory authorities need to be informed about for administrative or oversight purposes.

New Rules Trial - A Clinical Trial where the application to approve it is submitted on or after 28 April 2026, per schedule 14 of the Medicine for Human Use (Clinical Trials) (Amendment) Regulations 2025.

Non-Commercial Trials Manager – The most senior member of the KHP-CTO Non-Commercial Team.

Non-Investigational Medicinal Product (NIMP) - Any medicinal product (licensed or unlicensed) used in a Clinical Trial for reasons other than testing its safety or efficacy.

Old Rules Trial – A Clinical Trial where the application to approve it is submitted before 28 April 2026, per schedule 14 of the Medicine for Human Use (Clinical Trials) (Amendment) Regulations 2025.

Principal Investigator (PI) – The individual at a research site who has primary responsibility for the conduct of the Clinical Trial at that research site.

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

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

Route A substantial modifications - Changes to a Clinical Trial that are likely to have a significant impact on participant safety, rights, or data integrity, requiring full assessment by both the licensing authority and the ethics committee.

Route B substantial modifications - Changes to a Clinical Trial that are considered substantial but that don't introduce significant new safety concerns and are subject to a risk-proportionate review instead of a full assessment.

Setup CRA – The CRA who's responsible for Clinical Trial setup activities on behalf of the KHP-CTO.

Sponsor - The person or body who takes on ultimate responsibility for the initiation, management and financing (or arranging of the financing) of a Clinical Trial. Note: The Regulations allow for two or more persons or bodies to take on responsibility for Sponsor functions.

Sponsor Oversight Tracker – A shared Microsoft Excel document used by the KHP-CTO Non-Commercial Team to manage the necessary actions that must be taken by the KHP-CTO Non-Commercial Team with respect to Clinical Trials.

Standard Operating Procedures (SOPs) - Detailed, written instructions to achieve uniformity of the performance of a specific function. SOPs are the basis upon which Quality Systems and Processes are conducted and monitored against.

Regulations – The Medicines for Human Use (Clinical Trials) Regulations 2004 as amended including the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, UK Statutory Instrument: 2025 No. 538

Trial Master File (TMF) - A standard filing system which contains all essential documents which individually and collectively permits the evaluation of the conduct of a trial and the quality of the data produced. 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.

Urgent Safety Measure (USM) - An urgent safety measure that must be taken to protect Clinical Trial participants against an immediate hazard to their health or safety.