Closing, Suspending and Terminating Research

Division: Strategy and Transformation

Specific staff groups to whom this policy directly applies	Likely frequency of use	Other staff who may need to be familiar with policy
Staff employed by North Bristol NHS Trust who are directly or indirectly involved in Clinical Research in the trust	Role Dependant	Staff not employed by North Bristol NHS Trust who are working on research studies sponsored or hosted by NBT

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Date of Approval:	
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Version:	RD/QMS/SOP/011 Version 3
KEYWORDS:	End of study, Suspension, Termination, End of study declaration form, CTIMPs, REC and MHRA Reporting
Summary of changes since the previous version	Changed format to align with NBT SOP template Changed R&I to R&D Regulatory and ICH references updated to align with the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025/538) and latest ICH GCP E3 (R6)

	Updated reporting requirements to MHRA for studies submitted for combined review. Added information in relation to responsibilities when working with Clinical Trials Units. Change the naming convention of R&D SOP's Added Notification of end of study to Confidentiality Advisory Group (CAG) Added Guidance on disseminating information to participants

1. Purpose	The purpose of this SOP is to set out the matters to be considered upon the completion or early termination of a trial and the steps to be taken, including the notification of relevant bodies. This SOP is written in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, and applicable guidance issued by the MHRA and HRA, including the combined review process. It reflects the principles of proportionate, risk-based oversight as set out in ICH GCP E6(R3). There are a number of circumstances when it may be necessary for the regulatory authorities, the Sponsor, an NHS Trust or the CI/PI to suspend or terminate research trials. This SOP also explains the steps to be taken in such situations. The Sponsor is accountable for notifying the REC, MHRA, and other relevant bodies of the end of a clinical trial, CTIMPs and non CTIMPs. End of trial summary reports should also be submitted to REC. Where responsibilities under this SOP are delegated to a Chief Investigator or external Clinical Trials Unit, overall accountability remains with the Sponsor. Delegation of tasks does not constitute delegation of Sponsor responsibility. Suspension is a temporary cessation of some or all of the research activities by the CI, PI, Sponsor or NHS R&D Department(s) or the regulatory authorities, at a particular site or across all research sites. A decision not to restart a suspended trial amounts to termination of the trial. Termination is a permanent cessation of all research activities by the CI or PI, Sponsor or the regulatory authorities across all research sites.

	Transitional arrangements This SOP applies to all active clinical trials, including those approved prior to the implementation of the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025. For trials approved before these amendments, Where uncertainty exists, R&D will determine the appropriate regulatory route in liaison with the Sponsor and regulatory bodies. Terminology note: from 28 April 2026, the amended regulations use the term "modification" (including categories such as substantial modification). Where legacy documentation refers to "substantial amendments", this should be interpreted as the equivalent change control concept for the purpose of local documentation and filing
2. Key Messages	This SOP applies to all clinical trials sponsored by NBT and must be followed at study completion, suspension or early termination. When collaborating with external stakeholders, external SOPs may be used where appropriate however, these must align with NBT procedures, and in the event of any conflict, the NBT SOP will take precedence unless an exception is approved by the Sponsor. Where NBT is not the Sponsor, R&D retains the authority to suspend or terminate a clinical trial involving NBT patients if required. In such cases where the CI or a delegated research team member must suspend the trial due to safety concerns, the Sponsor must be notified promptly, who will then assume responsibility for informing the relevant regulatory bodies. Clear governance and appropriate delegation must be maintained throughout all collaborative and externally sponsored activities. The processes outlined in this SOP must be followed when ending a trial. **Abbreviations** **CI** Chief Investigator **CAG** Confidentiality Advisory Group **CTIMP** Clinical Trial of an Investigational Medicinal Product **CTU** Clinical Trials Unit **ICH GCP** International Conference on Harmonisation Guidelines for Good Clinical Practice **MHRA** Medicines and Healthcare Products Regulatory Agency **NBT** North Bristol NHS Trust **PI** Principal Investigator **REC** Research Ethics Committee **R&D** Research & Development

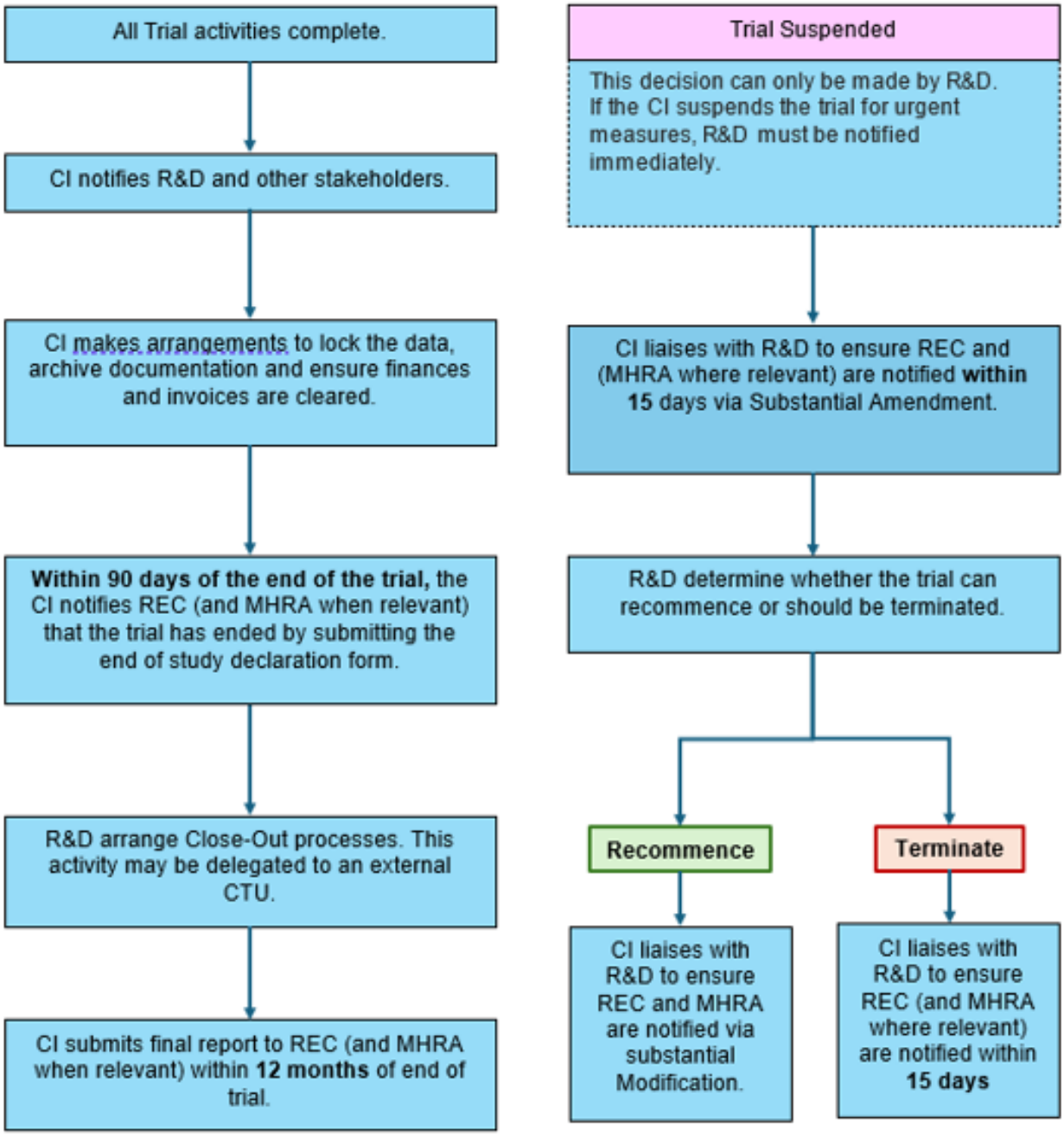
3. Relevant Policies & Guidance	**Policies and Guidance:** • Health Research Authority Notifying the end of study www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end- of-study • Medicines and Healthcare products Regulatory Agency Clinical trials for medicines: Manage your Authorisation, Report Safety Issues www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-eport-safety-issues • The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025/538). • ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 (R3) • Health Research Authority. UK Policy Framework for Health and Social Care Research (2017) **Associated SOPs:** RD/QMS/SOP/003 - Research Study Modifications RD/QMS/SOP/010 - Archiving
4. Operational Areas Included	This SOP is applicable to all research studies delivered at NBT
5. Operational Areas Excluded	Research Studies that are not sponsored by NBT - excluding situations where a PI or delegated member of staff must suspend a trial due to serious safety concerns such as Urgent Safety Measures.
6. Who should read this	This SOP should be used by Chief investigators, R&D staff and research team members involved in clinical trials sponsored by NBT. When collaborating with external stakeholders, such as Clinical Trials Units, on NBT- sponsored projects, it may be appropriate to utilise external SOPs to ensure proper project governance and the fulfillment of delegated roles and responsibilities. In such instances, both the external stakeholder and the NBT sponsorship team must ensure that the external SOP aligns with the

	procedures outlined in this SOP. If there is a conflict between the external SOP and NBT's procedures, the NBT SOP will take precedence, except in exceptional cases where approval is obtained from the Research Operations Manager or the Deputy Director of Research
7. Roles responsible for carrying out this procedure	Chief Investigators (CI) • Use this SOP for all NBT-sponsored clinical trials, including at study completion or when suspending/terminating a CTIMP early. • Make decisions regarding early suspension or termination of CTIMPs sponsored by NBT. • Notify the Sponsor if an NBT-hosted but externally sponsored trial is suspended or terminated (may be delegated to a research team member). Sponsor • Confirm that any external SOPs used in collaborative projects are aligned with NBT procedures. • Ensure that when conflicts arise between external SOPs and NBT SOPs, the NBT SOP takes precedence unless an exception is formally approved. Research Operations Manager or Deputy Director of Research • Review and approve exceptional cases where an external SOP may take precedence over the NBT SOP. R&D / R&D Staff • Use this SOP when involved in NBT-sponsored clinical trials. • Support the CI in decisions relating to suspension or termination of NBT-sponsored CTIMPs. • Reserve the right to suspend or terminate the conduct of any clinical trial involving NBT patients when NBT is *not* the Sponsor, if necessary. • Ensure that external SOPs used in collaborations align with NBT SOPs. Research Team Members • Follow this SOP when working on NBT-sponsored clinical trials. • Notify the Sponsor promptly if an externally sponsored trial is suspended or terminated (when delegated by the PI/CI). External Stakeholders (e.g., Clinical Trials Units) • Ensure their external SOPs are appropriate for use and align with NBT procedures when collaborating on NBT-sponsored projects.

	• Participate in ensuring proper project governance and fulfilment of delegated responsibilities.

8. Procedure:

8.1 Flow Chart of procedure: Closing, Suspending and Terminating Research



8.2
Trial completion

The definition of the end of a trial should be documented clearly in the protocol (and any subsequent modifications). In the majority of trials, completion will be the date of the last patient's last visit (LPLV) or the completion of any follow-up, monitoring and data collection as described in the protocol. This route of study closure is classified as planned closure.

As soon as the Sponsor confirms that a study has ended, there are a number of actions that need to be completed. **For NBT sponsored trials, responsibility for undertaking these actions is delegated to the CI.**

(a) For non-CTIMP studies, REC (which originally issued favourable opinion of the study) must be notified of the trial ending within **90 days** of it ending. Notification should be submitted using the 'Declaration of the end of a Clinical Trial' forms, and copies of these forms sent to R&D:

i. The REC form is available via: Declaration-end-study-form-v1-6_YiR7Sfb.odt. The completed form should be emailed to the REC. For trials submitted through combined review you should complete and submit the end of trial form in the new part of Integrated Research Application System (IRAS). This automatically submits the notification to the REC and MHRA.

ii. For CTIMP and IMP/Device trials that were not submitted through combined review, you will need to complete the form available on the MHRA website using this link: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial. The completed form should then be emailed to the MHRA and REC.

iii. For studies that have HRA and HCRW approval, but did not require REC review, you will need to notify the HRA directly when the study has ended. You should email us at approvals@hra.nhs.uk including your IRAS ID and your contact information (phone and email).

iv. Notification of end of study to Confidentiality Advisory Group (CAG): for studies that have applied to the CAG, the HRA provides guidance on how and when to notify the CAG of study completion: https://www.myresearchproject.org.uk/help/hlpconfidentiality581.aspxParticipants following the end of study Any commitments made to participants should be fulfilled, including providing information about the outcome of the study, and any care available following the end of the research. This could be in the form of a summary sheet of the findings or advising participants on where they can access the results of the study. Any end of study information sheets that are provided to participants should also be submitted with the final study report to the relevant REC.

v. The HRA provides guidance on disseminating information to participants following the end of the study: https://www.hra.nhs.uk/planning-and-improving-research/bestpractice/publication-and-dissemination-research-findings/

(b) A final research report must be submitted to the following bodies within **12 months** of the date of the end of the trial:

i. REC. This can be submitted via email. The form can be found through this link: Ending your project - Health Research Authority

ii. For studies submitted through the combined review, the final report form should be completed and submitted in the new part of Integrated Research Application System (IRAS).

iii. A copy should also be sent to NBT sponsor. R&D will send a reminder to the CI.

iv. Plain-language summaries must be offered to be shared with participants, ensuring they understand the outcomes of the research they contributed to. This includes clear communication about treatment assignments and results, tailored to participants' preferences and literacy levels.

(c) The CI should notify other stakeholders of trial completion, including R&D departments of other NHS Trusts where the trial took place and any other bodies, as required under separate agreements (such as funding bodies, universities or specialist committees).

(d) At the end of trial, the CI must contact R&D in order to arrange close-out monitoring visits. Support departments (e.g. pharmacy) should also be notified in order that they can prepare for close-out. Close-out activities will be conducted by the sponsor or delegated to a CTU. Close activities include:

i. Checking that the Trial Master File (TMF) and/or Investigator Site file is organised and ensuring all necessary documents are present.

ii. Ensuring that archiving procedures have been initiated by the CI in line with the SOP on Archiving (RD/QMS/SOP/010).

iii. Ensuring pharmacy close-out has been undertaken in accordance with Pharmacy SOPs.

(e) The CI should also ensure arrangements are made for the following:

i. Data-lock of the database prior to analysis.

ii. Resolving any outstanding financial obligations including ensuring and outstanding invoices payable or to be raised.

iii. Documents should be archived in accordance with the SOP on Archiving (RD/QMS/SOP/010).

8.3 Suspending and/or terminating trials

Suspension is a temporary cessation of some or all of the research activities at a particular site or across all research sites. A decision not to restart a suspended trial amounts to termination of the trial. Termination is a permanent cessation of all research activities across all research sites.

Suspension of a trial often follows an Urgent Safety Measure but may also have the potential to occur following an MHRA Inspection, external or internal Audit, Substantial Modifications or Serious Breach.

i. Trial suspended or terminated by R&D:

Where NBT is the Sponsor for a trial, all the rights, powers and duties of a Sponsor will be exercised in relation to the suspension and termination of any trial where necessary. Decisions to suspend or terminate a trial may only be taken by the Director or Deputy Director of Research (or delegated authority in their absence).

ii. Trial suspended or terminated by the CI/PI:

While the Medicines for Human Use (Clinical Trials) Regulations 2004 do not expressly provide a CI/PI with the power to suspend or terminate a clinical trial, ICH-GCP paragraph 4.12 sets out the process for doing so. If a trial is prematurely terminated or suspended for any reason by the CI/PI, then the trial subjects must be promptly notified, and appropriate therapy and follow-up must be arranged for the subjects.

If the trial is suspended or terminated without the prior agreement of the Sponsor, then the CI/PI must inform R&D **immediately** with a detailed written explanation of the reasons for termination or suspension. The CI/PI would not be expected to terminate or suspend a trial without prior discussion with R&D unless in an emergency, where there are immediate safety concerns.

(a) **Suspending trials**

If a trial is suspended temporarily, the MHRA and REC must be notified immediately or at least within **15 days** from when the trial is temporarily halted. R&D will liaise with the CI regarding submission of notification.

The notification must be made in the form of a substantial modification using the modification tool and explain what has been suspended (such as patient recruitment or interruption in treatment) and the reasons for the suspension. For further information on substantial modifications see SOP on Research Study Modifications (RD/QMS/SOP/003).

Substantial modifications relating to temporary suspension must be submitted using MHRA Submissions by emailing CI-applications@mhra.gov.uk
For applications that have gone through the combined review process, refer to the HRA website. Step by step guide to using IRAS for combined review - Health Research Authority

(b) **Restarting trials**

If R&D are satisfied that any concerns or issues have been appropriately addressed, then permission may be given to restart suspended trials. Trials must not recommence without this permission.

A substantial modification will need to be sent to the MHRA and REC to recommence activity. R&D will liaise with the CI regarding submission of these.

(c) **Terminating trials**

If R&D decide not to recommence a suspended trial, the MHRA and REC should be notified within **15 days of** the decision, following the procedure in section 8.3 of this SOP. In particular, the following information must be provided:

i. Justification of the premature ending of the trial and the number of patients still receiving treatment at the time of termination
ii. Proposed management of patients receiving treatment at the time of trial termination
iii. Consequences for the evaluation of results.

The end of trial declaration form must be completed if the trial is terminated prematurely. The CI should include a brief explanation of the reasons for ending the trial.

(d) Lapsing Approvals

If a clinical trial recruits no participants within two years of the date of regulatory approval, the approval for the trial will lapse. In this circumstance, the Sponsor must terminate the trial and submit written notification to the relevant regulatory bodies by the date the approval lapses. Continuing to conduct a CTIMP after the approval has lapsed constitutes an offence under the Medicines for Human Use (Clinical Trials) Regulations.

The Sponsor is responsible for confirming the date of recruitment of the first UK participant. This confirmation must be submitted using the appropriate modification process to notify the MHRA that recruitment has commenced.

Where the Sponsor anticipates that the first UK participant will not be recruited within the initial two-year period, an extension to the recruitment window may be requested.

An extension may be requested by either:

- requesting an extension as part of the initial clinical trial application (if agreed, this will be confirmed in the approval outcome); or
- submitting a written request to the MHRA (via *clintrialhelpline@mhra.gov.uk*) if the trial has already received approval.

Requests for extension must be submitted no later than 31 calendar days before the end of the two-year recruitment period. Once considered, the MHRA will notify the Sponsor of its decision within 30 calendar days.

The extension request must include:

- the reason an extension is required; and
- the duration of the extension being sought.

If the MHRA agrees that an extension is appropriate and justified, the recruitment window may be extended by up to a maximum of three additional years. Where a three-year

extension is granted, the trial will therefore have up to five years from the original approval date to recruit its first UK participant.

If a trial approaches the end of an agreed extension period and further extension is required, the Sponsor may submit a subsequent written request to the MHRA via *clintrialhelpline@mhra.gov.uk*. Such requests must be made at least 31 calendar days before the end of the current extension period. Any further extensions granted will be for a period of up to two additional years, starting from the end date of the previously agreed extension.

If the Sponsor does not submit an extension request within the required timeframe, or if an extension is not granted, the approval will be considered to have lapsed automatically at the end of the two-year period (or agreed extension period). In these circumstances, the Sponsor must formally end the trial and ensure that all required notifications are completed.

9. References (if applicable):

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