Standard Operating Procedure:

Project Closure

# Purpose

This standard operating procedure (SOP) describes the requirements relating to project closure. This includes notification for the end of project, early termination, and abandoned projects. It also outlines the requirements for the handling of clinical research samples at the end of the project and the final reports on research and publications, including reporting to public registries.

# Scope

This SOP is applicable to all clinical research sponsored by the University of Birmingham (UoB). Where clinical research is sponsored by another institution, this procedure should be followed as far as possible, and in line with the contractual agreement between the UoB and the other institution. This SOP may be used as a guidance document in all other cases.

Note: for clinical research approved by a UoB Research Ethics Committee (REC), there is no requirement for end of trial or study notifications or registration on a publicly accessible database.

# Implementation plan

This SOP will be implemented directly after its effective date for any clinical research that is in set-up phase and for existing clinical trials. For existing clinical studies this SOP will be implemented within three months of the effective date.

# Stakeholders

Note that where the UoB takes on the sponsor responsibility for project closure, the UoB will delegate the majority of these duties to the chief investigator (CI) and/or to a clinical trials unit (CTU), who may delegate these duties further to their trial team(s). All delegation of duties will be documented (e.g. using either the CI declaration and/or the Clinical Trials Task Delegation Log (UoB-SPO-QCD-001).

* CI: the CI may delegate activities to members of their research team, although evidence of CI oversight and approval is still expected and may not be delegated where ‘no delegation allowed’ is indicated. The SOP will state where delegation is possible. For clinical research approved by a UoB REC, the role of CI may be termed the principal investigator, or the supervisor for the postgraduate research student.
* Research Ethics Governance and Integrity Team (REGI)
* UKCRC-registered UoB CTUs

# Background and rationale

For the purposes of this SOP the terms ‘clinical research’ or ‘project’ will cover clinical trials of investigational medicinal products (CTIMPs), other interventional trials (e.g. surgical trials, device trials and non-CTIMP trials, and any other projects deemed to be ‘interventional’ by the sponsor), and clinical studies.

In accordance with the [Medicines for Human Use (Clinical Trial) Regulations (2004)](https://www.legislation.gov.uk/uksi/2004/1031/contents/made) and the [Health Research Authority SOPs](https://www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/), written notification for project closure is to be given for clinical research within 90 days of the global end of the project, or within 15 days if the project is terminated early.

Final analysis of the data and report writing is normally considered to occur after formal declaration of the project closure. A summary of the final research report must be sent to the REC and the competent authority (CA) (the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK for CTIMPs and clinical investigations of medical devices) within 12 months of the project closure and within 6 months for paediatric projects. Provision of a final report or summary report for early terminated projects is at the discretion of the sponsor. Further project specific actions to be performed at project closure may have been identified at project setup (e.g. whether information will be provided to participants at the end of the clinical research). For further details see the Project Set-up SOP (UoB-SET-SOP-001).

# Procedure

## Defining Project Closure

1. The CI (or delegate) will define the end of the clinical research project and document this in the protocol. It is expected to be defined in relation to the collection of all data required to answer the research questions in the protocol. Where a protocol requires follow-up monitoring and data collection to meet secondary or exploratory endpoints, it is expected the end of project is the final data capture rather than the last participant visit.
2. Where there is a change to this definition, after approval for the research has been given, the CI (or delegate) will notify the appropriate review body(ies) by the submission of a substantial amendment. For further details see the Project Set-up SOP (UoB-SET-SOP-001).
3. The CI (or delegate) will include in the protocol, if required, a description of the plan for the provision of any additional care for the participants once their participation in the project has ended, where it differs from what is normally expected according to the medical condition of the participant.

## Notifying End of Project

The protocol and any other documents approved by the REC (and the CA for CTIMPs) should be reviewed regarding the use of tissue and data collected during the project, the provision of information to participants and dissemination of results. If any changes to these approved arrangements are required, it is expected that consideration will be made as to whether a substantial amendment is required before submitting the end of project notification.

1. The CI (or delegate) will notify the appropriate review bodies of the conclusion of the project as defined in the protocol via a [‘Declaration of the end of a Clinical Trial’](https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial) (for CTIMPs) or [‘Declaration of the end of a study’](https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/) (for non-CTIMPs trials and studies). The appropriate review bodies will include those listed below.
* The REGI

The REC that gave a favourable opinion of the research. Notification to the REC will be in writing and within 90 days of project conclusion. Note: for non-CTIMPs, the REC reference number is required on the end of study declaration.

* Where applicable:
* The Confidentiality Advisory Group (CAG). If the project has an application with CAG, the CI (or delegate) will notify the Confidentiality Advice Team as soon as possible in writing and retain evidence of their written confirmation of receipt of the application closure notice in the study/trial master file (S/TMF).
* For international projects: where the UK arm of a project ends in advance of the global end of the project, the CI (or delegate) is expected to notify the relevant bodies as above. Note: the form for declaring the end of the project should not be used in this case.
1. For CTIMPs, the CI (or delegate) will also notify the CA within 90 days of the global end of the trial via a [‘Declaration of the end of a Clinical Trial’](https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial) form.
2. For projects that have received HRA approval but were not reviewed by an NHS REC, the CI (or delegate) will notify the HRA that the project has closed by email to approvals@hra.nhs.uk within 90 days and include the Integrated Research Application System (IRAS) ID and their contact information (phone and email) in the correspondence.
3. The CI (or delegate) will ensure other organisations are notified of the end of project including, NHS Research and Development (R&D) offices, funder, any participating sites and as defined in contractual agreements according to site local policies and procedures.
4. The CI (or delegate) will retain the end of project declaration, including confirmation of receipt from relevant bodies, e.g. the REC (and the CA for CTIMPs), with any related correspondence, and ensure it is filed in the S/TMF.
5. The CI (or delegate) will continue to submit the relevant safety updates and substantial amendments to the relevant review bodies, e.g. the REC (and the CA for CTIMPs) for the ongoing project, regardless of whether their country is still active or not, until the global end of project notification is submitted.

## Early Termination

1. If a project is terminated prior to the specified criteria being met, for reasons such as slow recruitment, the CI (or delegate) will notify the appropriate review bodies (the REC and REGI and the CA for CTIMPs) as described in ‘Notifying End of Project’ immediately and at least within 15 days.
2. The CI (or delegate) will clearly explain the reasons for early termination, including how the decision was made and by whom.
* Please note: if the project ends earlier than expected, not on the grounds of safety, but for other reasons, such as faster recruitment than anticipated, this is not considered as an ‘early termination’.
* A notice of substantial amendment can be submitted alongside a declaration of early termination where it is necessary to seek ethical review of related actions e.g. informing participants, continuity of care and follow-up outside the project.
1. Where follow-up actions must be taken for safety reasons, the CI (or delegate) will report these to the REC (and the CA for CTIMPs).
2. The CI (or delegate) will retain the end of project declaration, including confirmation of receipt from relevant bodies with any related correspondence, and ensure it is filed in the S/TMF.

## Abandoned Projects Prior to Commencement

The project is considered to have commenced when any of the procedures that are set out in the protocol, such as participant screening or consent, are initiated. For projects abandoned post-commencement for any reason the ‘Early Termination’ process described above will be followed.

Note: When a CTIMP with a clinical trial authorisation (CTA) is abandoned the ‘Early Termination’ process described above will be followed.

1. The CI (or delegate) will notify the appropriate bodies, giving reasons for abandoning the project, and copy the REGI into relevant correspondence. The appropriate bodies may include:
* the REC by letter; it is not necessary to submit the form for declaring the conclusion or early termination of the project. If a project is abandoned and it is later proposed to start it afresh, a new application is expected to be made
* local NHS R&D offices
* funders.
1. Where a project has HRA approval and was not reviewed by an NHS REC, the CI (or delegate) will inform the HRA when the project has ended via email to approvals@hra.nhs.uk including the IRAS ID and contact information (phone and email).

## Clinical Research Samples

1. Upon project closure the CI (or delegate) will ensure that any remaining clinical research samples are handled in line with the ethical approval obtained, the protocol and with the consent obtained from the participant regarding the future use, storage (in a licensed tissue bank) or destruction of their samples.
* If the remaining samples constitute ‘relevant material’ as defined by the Human Tissue Act, they must also be handled in accordance with the [Human Tissue Act (2004)](https://www.legislation.gov.uk/ukpga/2004/30/contents). Where this is the case the samples (in line with the ethical approval, protocol and consent obtained) must be either:
* stored in a Human Tissue Authority (HTA) licensed tissue bank such as the [Human Biomaterials Resource Centre (HBRC)](https://www.birmingham.ac.uk/facilities/hbrc/index.aspx) or the Dentistry Research Tissue Bank.
* transferred to another project with favourable ethical opinion from an NHS REC. Note: an application/amendment must be submitted for ethical approval to transfer the samples to the other project before favourable opinion of the existing project expires.
* destroyed in accordance with the HTA Code of Practice and in line with local health and safety policies.
* For further details, see the Laboratory Set-up and Management SOP (UoB-CRL-SOP-001) and Sample Management SOP (UoB-CRL-SOP-003).

## Data Analysis

1. The CI (or delegate) will commence final analysis of the data (following “lock” of the project database) and report writing after formal declaration of the project closure and in accordance with the protocol, project- specific data management plan and statistical analysis plan. See also the Data Management SOP (UoB-DMA-SOP-001) *and* Statistics SOP (UoB-STA-SOP-001).

## Final Report on the Research Publications

1. The CI (or delegate) will follow the reporting and publication procedures as detailed in the protocol (see the Protocol Template for CTIMPS (UoB-CLN-PRO-QCD-002) and Protocol Development Tool for non-CTIMPs and Studies (UoB-ESD-QCD-003) for guidance).
* For CTIMPs, the funder reference number or unique public registry number will be added to reports and publications.
* For publications of randomised trials, the CI (or delegate) will also refer to the [CONSORT (Consolidated Standards of Reporting Trials) statement guidelines](http://www.consort-statement.org/), see the Statistics SOP (UoB-STA-SOP-001) for further details.
1. The CI (or delegate) will include details of research outputs in relevant University research publication databases. See [Pure](https://intranet.birmingham.ac.uk/collaboration/pure/index.aspx) (login required) for further information about the University’s research information management system.
2. In the case of early termination, the CI (or delegate) will discuss the provision of a final report with the REGI.

###  Summary Report and Public Registers

1. For reporting the summary of results, the CI (or delegate) will send a final report to the REC (and to the CA for CTIMPs where no public register is used; see point 22) within 12 months of the end of the project copying REGI into relevant correspondence. Where this is a global project, this is the end of the project in all participating countries, not just in the UK.
* Note: there is no standard format for final reports though, as a minimum, the CI (or delegate) is expected to supply the REC with information pertaining to whether the project achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants.
1. At the time of reporting to the REC, the CI (or delegate) will ensure that the clinical research summary results are posted in the relevant registries (see the [UoB Position Paper: Clinical Research Registration (PDF - 218 KB)](https://www.birmingham.ac.uk/documents/college-mds/crct/uob-position-papers/uob-position-paper-clinical-research-registration-v1.0-vd-14-jan-2021.pdf)) within 12 months following the project closure (or within 6 months for paediatric projects). Phase 1 trials may apply for exemption.
* For CTIMPs, the CI (or delegate) will send a confirmation email to CT.Submission@mhra.gov.uk once the result-related information has been uploaded to the public registry and will provide a link to the relevant site.
* Note: CTIMPs involving sites specifically in EU countries must be registered in the EU Clinical Trials Register. This will involve obtaining an authorisation letter from the REGI and submitting the results to the European Union Drug Regulating Authorities Clinical Trials Register (EudraCT).
1. The CI (or delegate) will retain all correspondence pertaining to the summary reports including acknowledgements of receipt, which will be documented in the S/TMF.
* If agreed, a copy of the summary report is expected to be sent to investigator sites.

## Information to Participants at the End of a Project

1. At the closure of the research project, the CI (or delegate) will be expected to fulfil commitments made to participants; see the Participant Engagement and Informed Consent SOP (UoB-PEI-SOP-001) for further details.
* Examples of commitments to participants include:
* direction to published or summary results
* for CTIMPs, and other interventional trials, continued access by the participants to the IMP/intervention.

## Sponsor Oversight

1. The CI (or delegate) will ensure that where external CTUs are involved in the management of the project, any formal communications (e.g. ‘Declaration of the end of a study’ form) is sent to the REGI for review prior to submitting to the REC/HRA (and the CA for CTIMPs).
2. When informed of a project’s closure, either through an annual report, a project closure report or otherwise, the REGI will monitor that relevant documentation is submitted to the REC (and CA for CTIMPs) in a timely fashion, and that the summary report is submitted within a year following submission to the REC (and the CA for CTIMPs). The REGI will liaise with the CI (or delegate) where timelines are not met, and report to the CTOC where delays have been observed, and the actions taken by the REGI.

## Archiving

1. Following the development of the summary report and subsequent distribution, the CI (or delegate) will archive the project. See also the Archiving SOP (UoB-ARC-SOP-001).

# List of expected outputs

* Definition of the end of the project documented in the protocol and evidence of a substantial amendment notification to the REC (and the CA for CTIMPs) of any changes made regarding the end of the project.
* A description in the protocol of the plan for the provision of additional care to participants after the research has ended, should it differ from standard care.
* Reporting and publication policy documented in the protocol.
* For projects with an application with the CAG, evidence that the Confidentiality Advice Team has been notified and that their confirmation receipt for the application closure notice is filed in the S/TMF.
* Documented evidence in the S/TMF of notification to the REGI, REC (and the CA for CTIMPs), as applicable, of the conclusion of the project or for early terminated projects within the specified timescales which are 90 days and 15 days respectively from the defined end of project date. This will include one of the items of evidence listed below.
* For non-CTIMPs and studies, a ‘Declaration of the end of a study’ form.
* For project with HRA approval only (no NHS REC review), an email to approvals@hra.nhs.uk.
* For CTIMPs, a ‘Declaration of the end of a Clinical Trial’ form.
* Relevant organisations (i.e. NHS R&D offices and funders) have been notified of the end of the project as defined in contractual agreements.
* Evidence that the REC (and the CA for CTIMPs) have been informed in cases where a project has been abandoned prior to commencement and HRA where appropriate.
* For projects that have been terminated early, evidence of a documented explanation of the rationale.
* Continued submission of relevant safety updates and substantial amendments to the relevant review bodies for ongoing projects, regardless of whether their country is still active, until the global end of the project notification is submitted.
* Any follow-up actions taken for safety reasons have been notified to the REC (and the CA for CTIMPs) with proposed actions.
* Evidence that the REC (and the CA for CTIMPs) have been informed in cases where a project has been abandoned prior to commencement and HRA where appropriate.
* Evidence that remaining clinical research samples are handled in line with the ethical approval obtained, the protocol and participant consent in relation to future use or destruction.
* Reporting and publication procedures outlined in the protocol are followed.
* Following analysis, evidence of a project report, for example, in the form of a publication.
* Details of research outputs included in the relevant UoB research publication (i.e. Pure).
* Where external CTUs are involved, evidence of formal communication (e.g. ‘Declaration of the end of a study’ form) sent to the REGI prior to submission to the appropriate review bodies.
* Evidence that a summary report has been provided to the REC (and to the CA for CTIMPs) within 12 months of the end of project date and within 6 months following the end of project for paediatric trials, and that this has been posted on the relevant public registries.
* Evidence of the REGI reporting to the CTOC where delays have been observed regarding the notification of the end of project and submission of summary reports.

# Related documents

* UoB-ARC-SOP-001 Archiving
* UoB-CLN-PRO-QCD-002 Protocol Template for CTIMPs
* UoB-CRL-SOP-001 Laboratory Set-up and Management
* UoB-CRL-SOP-003 Sample Management
* UoB-DMA-SOP-001 Data Management
* UoB-ESD-QCD-003 Protocol Development Tool for non-CTIMPs and Studies
* UoB-PEI-SOP-001 Participant Engagement and Informed Consent
* UoB-SET-SOP-001 Project Set-up
* UoB-SPO-QCD-001 Clinical Trials Task Delegation Log
* UoB-STA-SOP-001 Statistics

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# References and frameworks

* Clinical Trials Toolkit: <https://www.ct-toolkit.ac.uk/>
* Confidentiality Advice Team: <https://www.hra.nhs.uk/about-us/contact-us/>
* CONSORT (Consolidated Standards of Reporting Trials) statement guidelines: <https://www.consort-statement.org/>
* EU Clinical Trials Register: <https://www.clinicaltrialsregister.eu/>
* European Commission ‘Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency (EMEA), in accordance with Article 41 of Regulation (EC) No 1901/2006’: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52009XC0204%2801%29>
* European Commission: ‘Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1)’: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:082:0001:0019:en:PDF>
* European Commission “Commission Guideline – Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52012XC1006(01)&from=EN>
* European Medicines Agency: ‘Posting of clinical trial summary results in European Clinical Trials Database (EudraCT) to become mandatory for sponsors as of 21 July 2014’: <https://www.ema.europa.eu/en/news/posting-clinical-trial-summary-results-european-clinical-trials-database-eudract-become-mandatory>
* Human Biomaterials Resource Centre (HBRC): <https://www.birmingham.ac.uk/facilities/hbrc/index.aspx>
* Human Tissue Act (2004): <http://www.legislation.gov.uk/ukpga/2004/30/contents>
* HRA guidance on ending your project: <http://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project>
* HRA guidance on participant information at the end of a study: <http://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/#informingparticipants>
* HRA guidance on phase 1 clinical trials: <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/phase-1-clinical-trials/>
* ICH E3 guideline: Structure and Content of Clinical Study Reports: <https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-3-structure-content-clinical-study-reports-step-5_en.pdf>
* The Medicines for Human Use (Clinical Trials) Regulations (2004): <http://www.legislation.gov.uk/uksi/2004/1031/contents/made>
* MHRA Guidance: Clinical trials for medicines: apply for authorisation in the UK: <https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk>
* MHRA Guidance: Clinical trials for medicines: manage your authorisation, report safety issues: <https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues>
* Pure Research Information System: <https://intranet.birmingham.ac.uk/collaboration/pure/index.aspx>
* MHRA Guidance: Registration of clinical trials for investigational medicinal products and publication of summary results: <https://www.gov.uk/guidance/registration-of-clinical-trials-for-investigational-medicinal-products-and-publication-of-summary-results>
* UoB Position Paper: Clinical Research Registration: <https://www.birmingham.ac.uk/documents/college-mds/crct/uob-position-papers/uob-position-paper-clinical-research-registration-v1.0-vd-14-jan-2021.pdf>

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| CA | Competent authority |
| CAG | Confidentiality Advisory Group |
| CI | Chief investigator |
| CTA | Clinical trial authorisation |
| CTIMP | Clinical trial of an investigational medicinal product(s) |
| CTOC | Clinical Trials Oversight Committee |
| CTU | Clinical trials unit |
| EudraCT | European Union Drug Regulating Authorities Clinical Trials Register |
| HRA | Health Research Authority |
| HTA | Human Tissue Authority |
| IRAS | Integrated Research Application System |
| MHRA | Medicine and Healthcare products Regulatory Agency |
| REC | Research ethics committee |
| REGI | Research Ethics, Governance and Integrity Team |
| SOP | Standard operating procedure |
| S/TMF | Study/trial master file |
| UoB | University of Birmingham |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).