STUDY CLOSEDOWN SOP

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Implementation plan

This Standard Operating Procedure (SOP) should be implemented as soon as possible after its implementation date for studies which are closing (as defined by protocol) or approaching the end date (in conjunction with the BTC-SOP-TM-002 Study Conduct SOP).

For studies that are being set up or ongoing, the BTC-SOP-TM-001 Study Start Up SOP and/or the BTC-SOP-TM-002 Study Conduct SOP should be implemented.

If unsure, the Trial Portfolio Leads and/or Quality Assurance Manager should advise.

Note to User:

It is your responsibility to ensure that you are using the latest approved version of this SOP. Please note that versions may be superseded before their initial review date.

THIS IS AN UNCONTROLLED VERSION WHEN PRINTED.

If you are reading this document in printed form, please check that the version number and date match the most recent SOP's details. Current versions of all Bristol Trials Centre (BTC) SOPs and accompanying documents are available on the BTC Teams.

Table of Contents

1. PURPOSE

This Standard Operating Procedure (SOP) describes the procedures to be followed in order to ensure that research studies undertaken at the Bristol Trials Centre (BTC) are closed according to the protocol, applicable SOPs, Good Clinical Practice (GCP) and regulatory and Sponsor requirements.

2. SCOPE

This SOP covers all research studies undertaken by BTC staff. It also applies to personnel involved in the close-down, termination, suspension or final reporting of research studies and any member of staff involved in the development or implementation of processes pertinent to such activities.

The Chief Investigator (CI) must be made aware of this SOP and, as a minimum, be signposted to the SOP by BTC.

“Research study” (or “study”) refers to health-related research projects (interventional trials or observational studies) involving people, samples and/or data, that are aimed at evaluating a medical, surgical, or behavioural intervention, or studying certain outcomes and certain groups of people. It includes clinical trials of investigational medicinal products, medical devices or advanced therapy medicinal products.

NB: Throughout this document the terms ‘research’, ‘study, ‘research project’, and ‘trial’ will be used interchangeably to denote those projects which fall under the remit of the UK Policy Framework for Health and Social Care Research 2017. The word “Trial” is accepted to be used when associated with established terms such as Trial Master File, Trial Management Group, etc., for research studies other than clinical trials.

3. DEFINITIONS, ACRONYMS AND ABBREVIATIONS

For definitions, acronyms and common abbreviations refer to the BTC-RES-TM-001 Definitions and Acronyms available on the BTC Teams.

4. RESPONSIBILITIES

Any delegation of responsibilities should be formally agreed by all parties and clearly documented.

4.1 Sponsor(s) or delegate

It is the responsibility of the Sponsor(s) or delegate to:

- Make the end of study declarations to the Research Ethics Committee (REC) within 90 days of the end of the study (as defined in the protocol) and to notify them if the study or a participating research site is terminated early or temporarily halted.

- Provide a summary of the final report on the research to the REC within 12 months of the end of the project.
- If applicable, notify the Confidentiality Advice Team as soon as possible in writing when the study is completed (for studies with CAG approval).
- Inform the local investigators and participating sites of the need for record retention and notify them in writing when documents are no longer needed and can be destroyed.
- Ensure that the completed study documentation is retained under environmental conditions that will preserve it for as long as necessary to comply with legal and regulatory requirements.
- Ensure sufficient archiving facilities are available and a suitable Nominated Archivist is identified.

In addition, for a Clinical Trial of an Investigational Product (CTIMP), it is the responsibility of the Sponsor(s) or delegate to:

- Maintain records documenting the disposition of unused Investigational Medicinal Product (IMP).
- Notify the Medicines & Healthcare products Regulatory Agency (MHRA) within 90 days of the end of the trial, or within 15 days if terminated early, via appropriate channels.
- Ensure that a summary of the final report on the research is prepared the relevant parties notified (see section 5.8).
- Where applicable, publish a summary of results in the public register(s) where the study is registered.

4.2 Chief Investigator (CI) or delegate

It is the responsibility of the CI or delegate to:

- Ensure that site closures are carried out adequately.
- Ensure that the local Research and Development (R&D) offices at participating sites receive copies of all correspondence regarding study closure.
- Fulfil all contractual reporting obligations e.g. to Funder.
- Ensure that after the end of study declarations have been communicated to the REC and MHRA, the change in study status is also communicated, as applicable, to:
    - For studies adopted on the National Institute for Health Research (NIHR) Portfolio, the Clinical Research Network (CRN);
    - The International Standard Randomised Controlled Trial Number (ISRCTN);
    - Any other applicable registry;
    - Research and Enterprise Development (RED) at University of Bristol.
- Inform the study participants if the study terminates early.
- Ensure participants' appropriate care and follow-up and provide information about the outcomes of the research project, as detailed in the protocol and Participant Information Leaflets.
- Ensure that all participating sites follow the process for retrieval of any investigational medical devices or other device or equipment and accessories from participants and the return of such devices/equipment to the Sponsor, or alternative arrangements as authorised by the Sponsor.
- Agree with the Sponsor the exact requirements for local archiving and make or assist the necessary arrangements. Whilst the Trial Master File (TMF) management may be delegated to the research team, the CI retains overall responsibility for archiving.

- Ensure that the research data is archived in a way that permits accurate reconstruction of the research and is not destroyed before the agreed date, nor retained longer than stated in the REC application, Funder's obligation or Sponsor's policy.
- Ensure research data is available for audit and inspection as appropriate.

In addition, for CTIMPs, it is the CI or delegates responsibility to:

- Ensure that all participating sites follow the process for retrieval of unused IMP from the participants and return of any unused IMP to the to the Sponsor, or alternative arrangements as authorised by the Sponsor. Once all supplies have been accounted for, they should be destroyed as per pharmacy SOPs and/or contractual arrangements.

4.3 Principal Investigator (PI) or delegate

It is the responsibility of the PI or delegate to:

- If applicable, arrange for return or disposal of any devices, equipment and/or unused consumables in accordance with the relevant contractual arrangements.
- Archive the essential documents and data generated at the respective site appropriately/in accordance with contractual arrangements and applicable legislation.

In addition, for CTIMPs, it is the PIs responsibility to:

- Follow the process for the return of any unused IMP, which must be in accordance with local policies. Once all supplies have been accounted for, they should be destroyed as per pharmacy SOPs and/or applicable contractual arrangements.

4.4 Trial Pharmacist (CTIMPs only)

It is the responsibility of the trial pharmacist or equivalent (where applicable) to:

- Oversee drug accountability and follow the process for the return of any unused IMP and/or destruction of IMP in accordance with local policies and any contractual arrangements.
- Ensure that the study pharmacy file is archived appropriately.

4.5 Bristol Trials Centre, University of Bristol

It is the responsibility of the BTC to:

- Facilitate the notification of end of study to the Funder, REC and MHRA.
- Ensure the study teams have completed all relevant tasks associated with study closedown.
- Ensure the essential documents kept in the central files are complete and adequately prepared for archiving, and ensure archiving, in accordance with applicable arrangements.

The trial specific responsibilities of the BTC should be clearly documented in any contractual agreements.

4.6 SOP Authors or delegate

It is the responsibility of the SOP author or an appropriately qualified/trained delegate to:

- Generate, finalise, and release the SOP in accordance with the BTC-SOP-QM-001.
- Ensure that the SOP remains fit for purpose.
- Ensure that the SOP is reviewed and amended as required.
- Provide relevant training and education materials to ensure that staff are aware of their responsibilities in relation to SOP content and management.

4.7 SOP user

It is the responsibility of the SOP user to:

- Ensure compliance with this document.
- Review procedures during use of the SOP and inform the author of any changes required.
- Undertake training on all aspects of this SOP and record training on the BTC Teams.

5. SPECIFIC PROCEDURES

5.1 End of study activities and planning

The definition of the end of the study should be documented in the protocol. Any change to this definition after approval has been given for the research should be notified to the appropriate review bodies as an amendment.

Closedown is defined as the act of ensuring that all study related activities are reconciled, recorded and reported at the end of the study in accordance with the protocol, applicable SOPs, GCP and applicable regulatory requirements.

Plans for closedown should have been discussed during the set-up of the study and close down processes should be considered in the risk assessment and quality management/monitoring plan.

The actions to be performed as part of the study closedown may vary according to the type of study and the requirements of the Sponsor and Funder. There may be several different organisations who require a formal end of study notification procedure to be followed when a study ends. Requirements for such reporting should be identified and discussed so that submissions are coordinated, in a timely fashion and as required.

The CI or delegate shall inform and, if required, seek approval from the relevant project oversight committees, as appropriate (Trial Steering Committee (TSC), Data Safety and Monitoring Committee (DSMC)), prior to initiation of end of study activities.

Study specific TSC and/or DSMC charters should be followed along with the current protocol and Funder requirements regarding reporting, dissemination and publication

The publication plan should be discussed, including establishing the authorship of the final outputs, which journal(s)s the final outputs will be submitted to, any conference presentations etc. The process of dissemination of study results to participants should be established.

Plans for reconciling all finances should be made (e.g. close down of the study grant, etc.) so that any financial reporting is compliant with the Funders' requirements and relevant BTC and University policies and procedures.

The sites should also be informed of any final actions they are responsible for (e.g. final sample shipments, archiving etc.), in accordance with the table of responsibilities in the site agreement or Organisation Information Document or any other applicable provisions. PIs and site teams should be informed of the plans, including final data deadlines and database lock dates, data cleaning process and what that will entail.

The BTC-CHK-TM-003 Study Close Down Checklist may be used by BTC study coordination teams to assist with completing activities pertinent to closedown of studies.

5.2 Early termination of the study

Before a study can terminate early the CI must seek approval from the study oversight committees (as appropriate) and then formally inform the Sponsor and Funder and all appropriate parties (e.g. PIs, Pharmacy). The CI/PI should also promptly inform the study

participants and ensure necessary care and/or follow-up for the participants. The plan for closedown should then be followed.

The Sponsor or delegate should notify the REC and MHRA if applicable within 15 days of the date of termination by submitting a declaration of the end of study form (see section 5.6). The CI must clearly explain within the form the reasons for terminating the project early.

If the early termination is for safety reasons, urgent safety measures should be followed (see BTC-SOP-TM-002 Study Conduct).

R&D offices at the participating sites should be notified in writing explaining the reason why the study was terminated early and the date on which this took place.

If the study is still recruiting, the CI (or delegate) must ensure that no further participants are recruited or randomised to the research project.

NB: If a study is completed earlier than anticipated for reasons other than safety (e.g. faster recruitment than anticipated), this is not considered an 'early termination' and the procedure for the end of study described in section 5.6 should be followed.

5.3 Data Management

5.3.1 Database Lock

Any queries which are generated as a result of data validation or any central monitoring must be addressed by the PI (or delegate). These must be documented fully.

Prior to the database being locked any data cleaning and final data reconciliation must have taken place. There should be an agreed date for the database lock, sites and other relevant stakeholders should be informed.

The CI, statistician, database manager and trial manager should decide a database lock date.

Where applicable, data held outside of the study database may be anonymised and uploaded/linked to the main database.

Further details can be found in BTC-SOP-IT-007 Database Lock

5.3.2 Providing sites access to their data

After the study database is locked, sites should be given a copy of their data and/or have access to their data at all times. Sites should confirm that they have a copy of their dataset (paper or electronic).

5.3.3 Data analysis

Final analysis of the data (following 'lock' of the study database) and report writing should commence as stated in the protocol and/or trial specific data management/statistical analysis plans as relevant.

The provisions in the relevant BTC IT SOPs (BTC-SOP-IT-007 Database Lock, BTC-SOP-IT-003 System Backup and Restoration for Clinical Research Computer Systems SOP, BTC-SOP-IT-006 Decommissioning Applications and Archiving Data) and BTC-SOP-ST-001 Statistics SOP must be followed.

5.4 Site Closure

A site can be classified as 'closed' when all study-related activities at that site are reconciled and/or complete and study site personnel are aware of ongoing responsibilities. No further changes or amendments can be made to the study for that participating site

The Sponsor or delegate should confirm in writing to the site when they consider the site to be closed.

5.4.1 Closing Sites

Once the study is ready to close as defined in the protocol the research team should start closedown procedures as detailed below.

Closedown processes should be defined in the study quality management and/or monitoring plan and all closure activities must be fully documented.

5.4.2 Sponsor or delegate tasks

All the following activities must be completed by the Sponsor or delegate:

- Conduct onsite monitoring or central monitoring ensuring:
    - essential documentation for each participating site is complete and stored in the appropriate files;
    - all site data has been collected, entered, validated;
    - original records (e.g. questionnaires, tapes of interviews) are checked for anonymity (where appropriate) and completeness;
    - all adverse events (including serious adverse events) have been adequately followed up and documented;
    - there are no open non-compliances;
    - outstanding errors and inconsistencies and all data queries have been resolved.

- All issues from previous study monitoring or audit activities must have been resolved or, if not, reasons must have been documented for failure to resolve issues.
- All financial matters must have been resolved and all site payments must have been completed as agreed and documented in study Organisation Information Document/contracts/agreements/approvals.
- Request that any samples considered to be relevant material under the Human Tissue Act (HTA) which have been collected and stored at a participating site are returned, destroyed or transferred to a biobank in accordance with the requirements of the Sponsor, the approved study protocol and the conditions of the favourable opinion from the REC.
- Update any registries, study social media accounts, websites, databases, etc.
- The Sponsor or delegate should send a formal notification that the site is closed and confirm the date of closure to the local team and R&D Office at each participating site.
- No new data may be collected at the site and by the site, once that site is closed.
- Study database should be locked; sites should be given a copy of their data and/or have access to their data at all times. Sites should confirm that they have a copy of their dataset (paper or electronic).

5.4.3 Participating site tasks

All the following activities must be completed by the site:

- Once a formal site closure notification has been received from the Sponsor no further activity can occur with the study participants at the site (i.e. no new data or samples can be collected) and no amendments concerning the site can be submitted (or implemented).
- All unused study supplies must have been returned or destroyed, in accordance with the requirements of the Sponsor and/or study protocol, unless they can be re-used/recycled.
- All research samples should be processed according to the protocol and/or applicable contractual arrangements.
- Any image acquisition and analysis should be completed.
- All essential documentation for the respective site is complete and stored in the appropriate files.
- All site data should have been collected, entered, validated.
- All adverse events (including serious adverse events) should have adequately followed up and documented.
- All data queries should have been resolved where feasible to do so.
- A copy of the site closure email or letter notification should be filed in the Investigator Site File (ISF).
- PIs must have implemented requirements such as essential document archiving and/or termination of letters of access and honorary research contracts belonging to researchers at the closing site, as appropriate.

In addition, for CTIMPs

- The Sponsor or delegate should liaise with the Trust pharmacy or equivalent (e.g. responsible individual where other facility is used for storing and/or administering the IMP) (if applicable) to ensure that all activities pertinent to closedown are completed at the site in accordance with regulatory and protocol requirements.
- The final IMP accountability must be complete for that site, and, if required, any unused IMP must have been destroyed or returned, unless full accountability may not be possible/feasible (e.g. when IMP distributed at home/in the community).
- The final IMP accountability (logs and records of returns or destruction) must have been documented in the pharmacy site file or investigator site file.

A study site visit may be necessary to verify or complete the closure process. Details of site closure visits must be documented by the person(s) conducting the visit, and any issues raised must be followed-up promptly.

A confirmation/agreement letter should be signed by the CI (or delegate) to document that all activities related to study closure are complete at a site, copies of essential documents are held appropriately and that a site visit was completed or not required.

All site closure documentation should be stored in the TMF with copies in the ISF.

5.5 Arrangements for studies involving human tissue samples

At the end of the study, the research samples must be dealt with in accordance with the approved REC application and Human Tissue Authority (HTA) regulations. The samples must be held on premises with a storage licence from the HTA, or an application made for ethical approval of another project before favourable opinion of existing project expires. Otherwise, the samples must be destroyed in accordance with the HTA Codes of Practice.

Any decision pertinent to the retention, future use or destruction of research samples must be in accordance with the participant informed consent, ethical opinion and relevant regulations.

Laboratory procedures and specific guidance pertinent to the management of the samples are detailed in the BTC-SOP-LAB-001 Laboratory SOP.

5.6 Notifying end of study to review bodies

Please refer to the HRA and MHRA websites (as applicable) for up-to-date information about how and where to submit the end of study notifications.

5.6.1 Declaration of end of study to the NHS REC and the Health Research Authority (HRA)

Where a project has HRA and HCRW Approval and has been reviewed by the NHS REC the Sponsor or delegate need to only inform the REC which gave the favourable opinion of the research when the study has ended.

Where a project has HRA and HCRW Approval and REC review was not required, the Sponsor or delegate will need to email the HRA (approvals@hra.nhs.uk) when the project has ended, including the study IRAS ID and contact information (phone and email) of the individual submitting the notification.

For non-CTIMPs, the ‘Declaration of the end of a study form’ can be downloaded from the HRA website.

The appropriate form must be sent to the REC that gave a favourable opinion within 90 days of the end of the study.

No further amendments can be made once the end of study has been declared to the REC/HRA.

Relevant correspondence must be filed in the TMF.

5.6.2 Notification of end of study to Confidentiality Advisory Group (CAG)

If an application with the CAG was made for the study, when the study is completed the Confidentiality Advice Team has to be notified as soon as possible in writing. Once received the Confidentiality Advice Team will review the information provided, update the approval register and write to confirm receipt of the application closure notice.

5.6.3 Declaration of end of a CTIMP to the MHRA

For CTIMPs submitted through the combined review service, the 'End of Trial' report should be completed via IRAS. This automatically submits the notification to the REC and MHRA. Information on how to submit the report can be found on the IRAS user guide.

For CTIMPs not submitted through the combined review service, you will need to complete the 'Declaration of the end of a trial' form available on the MHRA website and email this to the MHRA and REC.

The declaration of the end of the clinical trial must be sent to the MHRA by the Sponsor or delegate within 90 days of the global end of the trial (i.e. when the trial has ended in all member states/countries concerned) and within 15 days of the global premature end of the trial.

Any trial activities (such as follow-ups, visits) must be completed before the submission of the global end of trial declaration form.

No further amendments to the trial, or the Development Safety Update Reports (DSUR), may be submitted once the end of trial declaration has been received by the MHRA.

The MHRA will acknowledge receipt of the end of study declaration. This receipt must be filed in the TMF.

5.6.4 Declaration of end of a clinical investigation of a medical device to MHRA

Manufacturers (or delegates) are required to notify the MHRA via email when a clinical investigation comes to an end.

5.6.5 Notification of end of study to a Higher Educational Institution (HEI) REC

For studies not suitable for NHS REC where ethical review was sought from an academic institution REC, the specific requirements of the HEI REC should be followed to notify the end of study.

5.6.6 Notification of end of study to other review bodies

The CI, Sponsor of delegates should determine whether there are any requirements for notifications to other review bodies that need to be observed at the end of a study.

5.7 Communication to research participants at the end of study

At the end of the research study the investigators (CI and PI(s)) will be expected to fulfil commitments made to research participants. This may include:

- Ethical and practical issues regarding care after research, in particular when participants may wish to continue on the study intervention after the study.
- Providing information about the outcome of the study: participants should be given information at the end of a study explaining when they can expect the summary findings

to be made available. All participants should be informed as to how they can access the study findings. The summary of the findings made available for the participants should be written in lay terms. Ensure that those participants who opted out of the process are not sent such communication.

- Disclosing (if participants wish) their randomisation assignment i.e. which treatment they received whenever it is possible to do so without harming the integrity of the study.
- An acknowledgement of the contribution they have made to research and the improvement of healthcare.

5.8 Final Report, Results Dissemination and Publication

5.8.1 General considerations

The exact format of the final report is decided by the research team based on the type of the study, any Funder requirement, the intended recipients of the report and the format of other reports or publications produced at the end of the study.

Authors should use relevant reporting standards e.g. guidelines provided by the EQUATOR (Enhancing the Quality and Transparency of Health Research) Network.

Randomised controlled trials (RCTs) should be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement (available on the CONSORT website).

Prospective observational studies should be reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (available on the STROBE website).

Diagnostic tests should be reported in accordance with the Standards for the Reporting of Diagnostic accuracy studies (STARD) statement.

5.8.2 Final study report to Funder

Reports to the Funder should be submitted by the CI or delegate according to the terms and conditions of the grant (e.g. according to timeframes). The NIHR state that the draft final report should be provided to the relevant research programme team within 14 days of contract completion date or date of termination.

Some funding bodies specify their own final report template to be used; where this is the case that template should be followed.

For some studies a report of the study published in a peer-reviewed journal may be sufficient while other studies may require a more extensive document.

5.8.3 Final study report submission to the REC

The CI or delegate should submit the final research report to the main REC within 12 months of the declaration of end of the study. All studies reviewed by an NHS Research Ethics Committee (REC) within the UK complete the same final report. The report requires a lay summary of results which will be published alongside the rest of the research summary on the HRA website.

For studies submitted through combined review, the final report can be found and submitted in IRAS. For all other studies the final report form is completed and submitted via the HRA website.

Information on the processes for submitting final reports to REC can be found on the HRA website.

5.8.4 Submission of study summary results to the MHRA (CTIMPs)

The Sponsor is responsible for uploading the trial summary results to the relevant Portal. This may be delegated.

The time frame for posting the summary is within six months of the end of trial for paediatric clinical trials or within one year of the end of trial for non-paediatric clinical trials.

Summary results should be published in the public register where the study is registered. The clinical trial summary report does not need to be sent to the MHRA as well; however, for CTIMPs not using the combined review service, you must send a short confirmatory email to CT.Submission@mhra.gov.uk once the result-related information has been uploaded to the public register and provide a link. If your clinical trial is not on a public register, summary results should be submitted to the MHRA.For studies submitted through the combined review service the final report can be found and submitted in IRAS.

Guidance on clinical trial summary results is available on the HRA and MHRA websites.

5.8.5 Submission of study summary results to MHRA (Medical Devices)

A copy of the final report of a clinical investigation of a device should be sent to the MHRA (Medical Devices) when available.

5.8.6 Publication and dissemination of findings

The CI should ensure that study findings are published and disseminated appropriately, regardless of findings.

The results of the study should be disseminated to the research community through publication in peer-reviewed scientific journals, and/or presentation at scientific meetings/conferences.

Findings should be disseminated to the public by, for example, publication on a website, by a letter to all participants, publication in a newsletter or in leaflets for distribution in hospital or GP waiting rooms.

All individuals who have made a substantial contribution to the research project without fulfilling the authorship criteria should be acknowledged, usually in an ‘Acknowledgements’ section, detailing their contributions.

Some Funders require to be named and acknowledged appropriately when submitting a paper, article or report for publication. Where a format for this acknowledgement has been specified by the Funder(s) this must be followed (e.g. NIHR). It may be necessary to include an appropriate disclaimer (e.g. Funder’s disclaimer) when reporting research findings or opinions.

Authors should include details of the Sponsor, ethics committee and other approvals (e.g. MHRA) within the manuscript. Where applicable, all study reference numbers (REC, MHRA, etc) shall be stated in the publication.

The BTC-TEMP-TM-010 Publication Policy template may be used by BTC study coordination teams to assist with publication and dissemination.

5.8.7 Data sharing

Consideration should be given to the use of data and tissues obtained in the course of a study for future research, in line with the consent provided by participants. Where consent has not been obtained for future retention, only anonymised data can be retained. The application to the HRA/REC (and CAG, where relevant) should have set out the commitments for future use.

Requests for data to be shared may need to go to the Study Management Group for prior agreement.

Relevant information is provided in the BTC-WI-TM-005 Data Sharing Guidance document.

The BTC-TEMP-TM-012 Archiving Record Form may be used to assist with archiving.

5.9 Archiving

5.9.1 General considerations

The Sponsor has overall responsibility for archiving essential documentation. All essential documents must be archived. Archiving applies to both participating research sites and the BTC as the central coordinating office.

Arrangements for archiving should be agreed prior to the commencement of the study. These will include costs, responsibilities, duration and where study documents will be archived.

For CTIMPs, the Clinical Trials Regulations require that all clinical trial information shall be recorded, handled and stored in a way that allows accurate reporting, interpretation and verification, and that the confidentiality of records which could identify subjects shall be protected, in accordance with the requirements of the General Data Protection Regulation (GDPR) and Data Protection Act (2018).

For CTIMPs, the Clinical Trials Regulations require the Sponsor to appoint a Nominated Archivist who is responsible for overseeing the archiving of trial documentation which is part of the TMF, and who controls access to archived material. The Archivist should have a clearly documented role and be appropriately trained and supported to carry out their role. If this is a delegated responsibility for BTC, the nominated archivist will be the QA team.

Essential documents must be retained for sufficient periods after the study ends to allow for audit and inspection by the study Sponsor and/or regulatory authorities. As such, archived essential documents have to be readily available.

Individual research organisations, Sponsors and Funders may each have their own policies for archiving study documentation, and these should be followed, as applicable.

Where the Sponsor delegates their responsibility for archiving to sites/PIs, this should be documented in writing, usually in the site agreement and/or the Organisation Information Document. The PI must make the Sponsor (or delegate) aware of their local storage

arrangements. If the site/PI is unable to store their essential documents, the Sponsor (or delegate) should be notified in writing so that alternative arrangements can be agreed.

Where a third party archive facility is used, a contractual agreement should be in place.

5.9.2 Suitability of archiving facility

The Nominated Archivist is responsible for ensuring the integrity of all archived data in their custody. The Archivist shall assess the storage facilities to consider:

- Size and location: are facilities large enough with appropriate off-floor shelving?
- Environmental conditions/pests: is the risk of fire, flood and pests minimised?
- Confidentiality and security: is there controlled access and are appropriate authorised records maintained of all removals, requests for review, relocation and/or return?

5.9.3 What to archive

Both essential documents and relevant source documentation must be archived (see definitions).

The TMF, including the ISF, Laboratory and Pharmacy Files (if applicable), all data forms (case report forms), electronic data files and staff training records, study mailbox, should be archived according to the site agreement or Organisation Information Document or any other applicable provisions.

PIs must liaise with any relevant support departments at the earliest opportunity to determine archiving arrangements.

It is essential that arrangements are made to ensure that patient medical records, and the source data held within, are retained throughout the archiving period.

5.9.3.1 Paper documents

The following procedure should be followed when archiving paper documentation:

- Any alteration of records should be traceable, and all essential documents should be legible and accurate.
- Documents need to be stored in a way which preserves their integrity and readability.
- Documentation should be packed in archiving boxes or other appropriate storage container, which should be labelled with the study details including showing the start and end date of the archiving period.
- A record of archived documentation must be completed with details of the contents of each box. Once completed, this document should be filed for reference.
- Archive boxes should be stored in a secure and dry location, accessible to authorised personnel only.
- If no suitable on-site facility is available, a sub-contractor (e.g. a commercial archive) can be used. As the Sponsor remains responsible for the quality, integrity, confidentiality and accessibility of the documents, an audit of the potential sub-contractor is recommended.

5.9.3.2 Electronic data

In certain circumstances the trial Sponsor may request for essential documentation to be scanned and stored electronically.

- Where essential trial documents are digitised, images of paper records will be stored on a secure network with password protection and/or on an independent storage device in a secure location.
- A record of the secure location where digitised images and independent storage devices are stored should be kept.
- The University of Bristol Research Data Storage Facility (RDSF) can be used to store research data securely over the long term.
- Data that is collected in a study database will need to be moved to long term storage at the end of the study.
- The data management team that set up the study database can provide database specific processes. At a minimum, data must be exported to an open-source format (typically CSV or XML).
- To permit the study to be re-opened or longer-term follow-up, it is also prudent to create a database backup/restore file and instructions for returning the database to live status.
- All export/backup files must be saved to the appropriate study folder on the relevant drive/location. When a study folder is no longer required a request should be made to the IT service desk to archive the study folder.

5.9.4 Archive duration

Specific retention periods for study documentation will be stated in the study protocol and be documented in the IRAS application. The following guidance summarises the requirements for archive duration however it is always important to consult the Funder requirements, regulatory agencies (especially when other countries are involved) and local policies to ensure that any extended requirements are met.

For CTIMPs the Sponsor should determine which requirements apply to the respective trial in relation to the start and end dates and whether the trial is used, or intended to be used, to support a marketing authorisation, as the retention requirements are dependent on these factors, as follows:

Essential documents from trials that are not to be used to support a marketing authorisation should be retained for at least five years after completion of the trial. These documents should be retained for a longer period if required by the applicable regulatory requirement(s), the Sponsor or the Funder of the trial.

For trials to be included in regulatory submissions the essential documents should be retained for at least fifteen years after completion or discontinuation of the trial or for at least two years after the granting of the UK marketing authorisation . These documents should be retained for a longer period if required by the applicable regulatory requirement(s) or if needed by the Sponsor.

In addition to these retention times for the trial documentation, documents relating to the full traceability of an advanced therapy medicinal product (ATMP) have longer retention periods: 30 years after the expiry date of the product or longer if required by the clinical trial authorisation. This will include the relevant documentation contained in the Sponsor and investigator TMF as well as the trial participants' medical records.

All other studies shall be archived as stated in the protocol, or Sponsor's institutional guidelines. Individual Sponsor's policies should be consulted for their requirements.

Site-specific archiving requirements, as detailed by each NHS Trust's R&D Department must also be taken into consideration for each study.

For paediatric studies, the NHS code of practice requests retention until each patient's 25th birthday (or 26th if the young person was 17 at conclusion of treatment) or 8 years after death. You should check the archiving period for paediatric studies with the Sponsor as this may vary by Sponsor organisation.

5.9.5 After the archive period

At the end of the archive period, destruction and disposal of essential documents should be done in a way that maintains participants' confidentiality.

The Sponsor should notify the BTC/University of Bristol in writing when the BTC central records can be destroyed.

The Sponsor (or delegate) should notify local PIs in writing when their study records can be destroyed.

Once authorisation for destruction of records is given by all parties concerned, the records should be destroyed as confidential waste and the destruction should be logged as appropriate.

The record of destruction should be retained for a further 5 years.

6. SUPPORTING DOCUMENTS

Number	Title
BTC-RES-TM-001	Definitions and Acronyms
BTC-RES-TM-002	Website References (Trial Management SOPs)
BTC-SOP-TM-001	Study Start Up SOP
BTC-SOP-TM-002	Study Conduct SOP
BTC-SOP-IT-003	System Backup and Restoration for Clinical Research Computer Systems SOP
BTC-SOP-IT-006	Decommissioning Applications and Archiving Data SOP
BTC-SOP-IT-007	Database Lock SOP
BTC-SOP-ST-001	Statistics SOP
BTC-SOP-LAB-001	Laboratory SOP
BTC-CHK-TM-003	Study Close Down Checklist
BTC-TEMP-TM-012	Archiving Record Form
BTC-WI-TM-001	Archiving Work Instructions
BTC-WI-TM-005	Data Sharing Guidance
BTC-TEMP-TM-010	Publication Policy

7. CHANGE HISTORY

Previous version and date	New version and date	Brief summary of review
NIL	V1, 14 July 2021	New document
V1, 14 July 2021	V2, 9 February 2022	Addition of Sponsor responsibility to notify CAG when the study is completed, where this is applicable Minor clarifications to bring the requirements in line with changes in HRA/MHRA processes Requirement to refer to the HRA and MHRA websites (as applicable) for up-to-date information about how and where to submit the end of study notifications and reporting Mention of templates and guidance produced internally which may be used by the study coordination teams; these have been listed in Section 6 Supporting Documents Clarification that requests for data to be shared may need to go to the Study Management Group for prior agreement

V2, 9 February 2022	Vx xx/xx/xxxx	Reference to the BTC Sharepoint was removed and replaced with BTC Teams site Updated with new HRA and MHRA processes for the notification of the end of study report and final report. Additional information added regarding the NIHR requirements for submission of the final study report. Sections of the SOP have been moved for flow purposes. A new section on data sharing with sites has been added Reference to the BTC publication policy template and archiving form added.