Quality Control Document:

Essential Documents Checklist

# Purpose

This document contains a checklist for studies and trials that can be used as a tool to identify the documents that should be filed in the study/trial master file (S/TMF) and/or investigator site file (ISF). The checklist will also identify what documents will be included in the sponsor file held by the Research Governance Team. For setting up a laboratory master file (LMF), please refer to Setting Up a Laboratory Master File (UoB-CRL-QCD-001).

This checklist has been written with consideration to the documents as listed in [International Conference on Harmonisation (ICH) Good Clinical Practice (GCP)](https://ichgcp.net/) and the [European (EU) recommendation on the content of the trial master file (TMF) and archiving](https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-10/v10_chap5_en.pdf). This checklist also lists documents that are expected to be part of the TMF and are based on UK specific requirements and/or University of Birmingham (UoB) specific procedures. Documents are largely grouped by topic.

The essential documents checklist will help to ensure that those documents, which individually and collectively permit the evaluation of the conduct of a trial/study and the quality of the data produced are maintained within the S/TMF and ISF.

# Instructions

1. Remove these first instruction pages.
2. Update the identifier in the header e.g. study/trial identifier or research group.
3. Update the footer, retaining the document reference information relating to this quality control document (QCD).
4. Amend the essential documents checklist by adding any additional documents that do not appear on this list but are relevant to the management of the study/trial.
5. Where sections are not applicable to the study/trial, add a comment in the applicable comment field on the checklist for the item rather than deleting the row or leaving it empty.
6. File completed versions of this record and all related correspondence in the relevant S/TMF and ISF as applicable. It is acceptable to combine some of the documents, provided the individual elements are readily identifiable.
7. Ensure the S/TMF and ISF remains up-to-date through regular review

Note: for some studies/trials (e.g. single site) it may be appropriate to merge the S/TMF and ISF. Please make a note if this is this case.

# Related documents

* UoB-CLN-PRO-QCD-002 Protocol Template for CTIMPs
* UoB-CQM-POL-001 Clinical Research Quality Manual
* UoB-CRL-QCD-001 Setting Up a Laboratory Master File
* UoB-ESD-QCD-003 Protocol Development Tool for non-CTIMP and Studies
* UoB-ESD-QCD-004 Protocol Template for non-CTIMPs and Studies
* UoB-ESD-QCD-006 Version Control Log
* UoB-ESD-SOP-001 Essential Documents Development and Maintenance

Note the UoB QMS documents can be found on the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx). Internal work instructions can be obtained from the CRCT (crct@contacts.bham.ac.uk) and/or from the RGT (researchgovernance@contacts.bham.ac.uk).

# References

* Recommendation on the content of the trial master file and archiving: <https://ec.europa.eu/health/system/files/2016-11/v10_chap5_en_0.pdf>
* ICH GCP: <https://ichgcp.net/>

# Essential documents checklist

| Title of document | Purpose  | ISF | S/TMF | Sponsor file | Comment |
| --- | --- | --- | --- | --- | --- |
| Translations and back translations of essential documents  | To clarify which documents have been translated, and to provide evidence that the translation was appropriate.  |  | X | X (if related to documents kept in sponsor file) | Where applicable |
| Risk assessment documentation | To document the process and outcome of risk assessment, and how this informed the study/trial set up and management.  |  | X | X | Where applicable, for non-CTIMP and studies the Sponsor may request a copy of the risk assessment.  |
| Any plans and guidelines, e.g. monitor plan, communication plan, statistical analysis plan | To document the systems put in place to address study/trial risks and to ensure quality data is generated and the participant’s safety and wellbeing is safeguarded.  |  | X | X | Where applicable |
| Investigator’s brochure (IB) or Summary of Products Characteristics (SmPC) and updates\* | To document that relevant and current scientific information about the investigational product has been provided to the investigator.  | X | X |  |  |
| Signed protocol and amendments | To document investigator and sponsor agreement to the protocol/amendment(s).  | X(PI signed) | X(PI and CI signed) | X(unsigned) |  |
| **Information given to study/trial participant and any revisions thereof:** |
| * Master informed consent form
 | To document the informed consent.  | X | X | X |  |
| * Any other written information
 | To document that participants will be given appropriate written information (content and wording) to support their ability to give fully informed consent.  | X | X | X |  |
| * Advertisement for participant recruitment (if used)
 | To document that recruitment measures are appropriate and not coercive.  | X | X | X |  |
| Financial aspects of the study/trial (including funding application/award letter) | To document the financial agreement between the investigator/institution and the sponsor for the study/trial.  |  | X | X (auto) |  |
| Insurance statement  | To document that compensation to participant(s) for study/trial-related injury will be available.  | X | X | X (auto) | Where applicable; for CTIMPs insurance/indemnity cover is a legal requirement |
| **Signed Agreement between involved parties, e.g.:** |
| * Investigator/institution and sponsor (clinical trial site agreements)
 | To document agreements. | X | X | X | Where applicable, directed by the sponsor |
| * Investigator/institution and third parties, e.g. vendors, coordinating centre etc.
 | To document agreements.  | X | X(where required) | X | Where applicable |
| * Clinical trials task delegation log (CI-CTU)
 | To document agreements. |  | X | X |  |
| * Terms of Reference (or Charter) agreed by any relevant project oversight committees e.g. data monitoring committee (DMC) or trial steering committee (TSC)
 | To document expectations of both parties. |  | X |  |  |
| * Sponsor and chief investigator
 | To document expectations of both parties, e.g. via CI declaration form or CI agreement. |  | X | X |  |
| * Letter of Sponsorship
 | To document that the sponsor has agreed to take on sponsorship responsibilities for the study/trial. | X | X | X(auto) |  |
| Dated, documented favourable opinion of research ethics committee (REC) of the following including any revisions: * protocol and any amendments
* informed consent form(s)
* any other written information to be provided to the participant(s)
* advertisement for participant recruitment (if used)
* participant compensation (if any)
* any other documents given approval/ favourable opinion
* along with REC confirmation for each favourable ethical opinion
 | To document that the study/trial has been subject to *REC* review and given favourable opinion. To identify the version number and date of the document(s). To document that the favourable opinion is maintained throughout the study/trial. Documents include the application form and correspondence.  | X | X | X |  |
| NHS permissions (confirmation of capacity and capability) including application, approval letter and correspondence  | To document NHS permission was gained for an individual NHS site to participate in the study/trial. | X | X |  | Where applicable |
| Regulatory authority(ies) clinical trial authorisation, including maintaining authorisation following changes to the trial \*  | To document appropriate authorisation by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s), and to document that the authorisation is maintained throughout the trial. Documents include the application form and correspondence. | X | X | X | Where applicable |
| Other relevant approvals, e.g. ARSAC, HBRC including maintaining approval following changes to the study/trial. Application forms, approval letters and correspondence  | To document any other appropriate approvals has been obtained prior to initiation, and to document that the authorisation is maintained throughout the study/trial. Documents include the application form and correspondence. | X | X | X | Where applicable |
| Interim or annual reports to REC and authority(ies)  | Interim or annual reports provided to REC and to authority(ies).  | X | X | X | Where applicable |
| CV and/or other relevant documents including any revisions and CV for new investigators | To evidence qualifications of investigator(s) and sub-Investigator(s) and eligibility to conduct study/trial and/or provide medical supervision of participants. This includes GCP training (as required). See also *Clinical Research Quality Manual (UoB-CQM-POL-001)*.  | X | X | X (CI only) |  |
| Signature sheet  | To document signatures and initials of all persons authorised to make entries and/or corrections on CRFs. This may be combined with the delegation of responsibilities log. | X | X |  | Where applicable |
| Delegation of responsibilities log | To document what duties have been delegated by the site PI to site staff. This may be combined with the signature sheet.  | X | X |  | Where applicable, recommended |
| Normal value(s)/range(s) for medical/laboratory/technical procedure(s) and/or test(s) included in the protocol, including any updates | To document normal values and/or ranges of the tests.  | X | X |  | Where applicableSee also *Setting up a laboratory master file (UoB-CRL-QCD-001)* |
| Medical/laboratory/technical procedures/tests, including any updates* certification or
* accreditation or
* established quality control and/or external quality assessment or
* other validation (where required)
 | To document competence of facility to perform required test(s), and support reliability of results.  | X | X |  | Where applicableSee also *Setting up a laboratory master file (UoB-CRL-QCD-001)* |
| Record of retained body fluids/ tissue samples  | To document location and identification of retained samples if assays need to be repeated.  | X | X |  | Where applicableSee also *Setting up a laboratory master file (UoB-CRL-QCD-001)* |
| Sample of label(s) attached to investigational product container(s)\*  | To document compliance with applicable labelling regulations and appropriateness of instructions provided to the participants.  |  | X |  |  |
| Instructions for handling of investigational product(s) and study/trial-related materials and any updates | If not included in the protocol or IB/SmPC, to document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and study/trial-related materials.  | X | X |  | Where applicable |
| Shipping records for Investigational Product(s) and study/trial-related materials and any updates # | To document shipment dates, batch numbers and method of shipment of investigational product(s) and study/trial-related materials. Allows tracking of product batch, review of shipping conditions, and accountability.  | X | X |  | Where applicable |
| Certificate(s) of analysis of investigational product(s) shipped including certificates of analysis for new batches (and QP release for CTIMPs) | To document identity, purity, and strength of investigational product(s) to be used in the study/trial.  |  | X |  | Where applicable |
| Proof of (investigational product(s)) storage condition monitoring # | To document that the required storage conditions of the investigational product(s) are maintained at site. Note that this is especially important where storage conditions vary from normal practice, e.g. use of refrigerator/freezer. | X | X |  | Where applicable |
| Investigational product(s) accountability at site # | To document that the investigational product(s) have been used according to the protocol. To documents the final accounting of investigational product(s) received at the site, dispensed to participants, returned by the participants, and returned to sponsor.  | X | X |  | Where applicable |
| Documentation of investigational product destruction # | To document destruction of unused investigational products by sponsor or at site.  | X(if destroyed at site) | X |  | Where applicable |
| Decoding procedures  | For blinded trials only, to document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining participants treatment.  | X | X(third party if applicable) |  | Where applicable |
| Master randomisation list  | To document method for randomisation of study/trial population. Note this may be a programme rather than a list and may be held by the trial statistician. In this case, a NtF should be added to the TMF, document the name and contact details of the trial statistician, and the parameters of the randomisation. |  | X(third party if applicable) |  | Where applicable |
| Treatment allocation and decoding documentation  | Returned to sponsor to document any decoding that may have occurred.  |  | X |  | Where applicable |
| Pre-study/trial monitoring report | To document that the site is suitable for the study/trial. This may be combined with initiation monitoring report. |  | X |  | Where applicable |
| Study/trial initiation monitoring report  | To document that study/trial procedures were reviewed with the investigator and the investigator’s staff. This may be combined with the pre-study/trial monitoring report.  | X | X |  | Where applicable |
| Monitoring visit reports  | To document site visits by, and findings of, the monitor.  |   | X |  | Where applicable |
| Final study/trial close-out monitoring report  | To document that all activities required for study/trial close-out are completed, and copies of essential documents are held in the appropriate files.  |  | X |  | Where applicable |
| Audit certificate (if available)  | To document that audit was performed.  |  | X |  | Where applicable |
| Relevant communications other than site visits:* letters
* emails
* meeting notes
* notes of telephone calls
 | To document any agreements or significant discussions regarding study/trial administration, protocol violations, study/trial conduct, adverse event (AE) reporting.Note this may include communications amongst the trial management group (TMG) members, between TMG and DMC. etc., including meeting minutes. | X(where required) | X |  | Where applicable |
| Participant screening log  | To document identification of participants who entered pre-study/trial screening.  | X | X(where required) |  | Where applicable |
| Up to date participant identification code list  | To permit identification of all participants enrolled in the trial by investigator/institution in case follow-up is required. List should be kept in a confidential manner and for agreed upon time. | X |  |  | Where applicable |
| Participant enrolment log  | To document chronological enrolment of participants by study/trial number.  | X |  |  | Where applicable |
| Signed informed consent forms  | To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each participant in study/trial. Also to document direct access permission. | X | X (where applicable) |  |  |
| Source documents  | To document the existence of the participant and substantiate integrity of study/trial data collected. To include original documents related to the study/trial, to medical treatment, and history of participant.  | X |  |  |  |
| Sample CRFs and any updates thereof | To record study/trial related observations.  | X | X |  |  |
| Completed CRF (signed & date, where required) | To document that the investigator or authorised member of the investigator’s staff confirms the observations recorded.  | X(copy) | X(original) |  | Where applicable |
| Documentation of CRF corrections  | To document all changes/additions or corrections made to CRF after initial data were recorded.  | X(copy) | X(original) |  | Where applicable |
| Analytical data and supporting records relating to clinical trial analysis\*  | To enable the conduct and quality of the data to be evaluated to ensure that the research has been conducted in accordance with GCP and all applicable regulations. |  | X |  | Where applicableSee also *Setting up a laboratory master file (UoB-CRL-QCD-001)* |
| Notification by originating Investigator to Sponsor of serious adverse events (SAEs) and related reports  | To document notification by originating investigator to sponsor of serious adverse events and related reports. | X | X | X(where reportable) |  |
| Notification by sponsor and/or investigator, where applicable, to regulatory authority(ies) and REC(s) of unexpected serious adverse drug reactions (in CTIMPs: SUSARs)and of other safety information  | To document notification by sponsor and/or investigator, where applicable, to regulatory authorities and IRB(s)/IEC(s) of unexpected serious adverse drug reactions and of other safety information.  | X(where required) | X | X |  |
| Notification by sponsor to investigators of safety information | To document notification by sponsor to investigator of safety information.  | X | X |  |  |
| Final report by Investigator to REC  | To document completion of the study/trial.  |  | X | X | Where required and also where applicable, to the regulatory authority(ies) |
| End of study/trial Declarations submitted to authority and REC at the end of the study/trial | To document completion of the trial. |  | X | X |  |
| Clinical study report  | To document results and interpretation of study/trial.  | X (if applicable) | X | X |  |

Notes:

\* Applicable to CTIMPs only.

# Many non-commercial trials use pharmacy supplies of medicinal products that have a marketing authorisation and the tracking of product batches, shipping conditions and accountability, storage and dispensing instructions and the need for reconciliation between medicinal products supplied, used and returned before destruction as well as the process for destruction will be part of the pharmacy’s standard operating procedure (SOP) for handling clinical trial materials. If this applies, provided the pharmacy SOP conforms to the applicable legislation and guidance, including retention of records, it may be noted in the TMF and ISF.

Columns marked ‘X (auto)’: the underlying processes are dealt with by the UoB central offices (Research Governance Team (RGT), research finance office) and the information will be automatically captured in the Sponsor Files.