UNIVERSITY OF LEEDS / NHS The Leeds Teaching Hospitals NHS Trust Standard Operating Procedure	Title	A Researchers Guide to Source Documentation				
	Scope	Describes the process for documentation and filing of CTIMP source documentation				
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Distribution & Storage:

Distribution to:

Investigators and all members of research teams conducting or assisting with a CTIMP trial sponsored by the University of Leeds or Leeds Teaching Hospital NHS Trust.

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http://lthweb.leedsth.nhs.uk/sites/research-and-development/resources/Sponsored%20CTIMPs%20%28Quality%20Assurance%29

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Please note: *This SOP should be used and followed in conjunction with other UoL / LTHT SOPs developed for researchers to support study set up and management. These can be found on the LTHT website or by contacting R&I / QA directly. For clinical trials where Leeds is not the trial Sponsor, please refer to any Sponsor SOPs for further information.*

Section A: Introduction

1.1 This Standard Operating Procedure (SOP) will aid researchers with the documentation and management of source data when conducting a Clinical Trial of an Investigational Medicinal Product (CTIMP) sponsored by the Leeds Teaching Hospitals NHS Trust (LTHT) or the University of Leeds (UoL).

1.2 It is important for documentation of source data to be standardised across all UoL and LTHT sponsored CTIMPs to ensure integrity of trial data and adherence to Good Clinical Practice (GCP).

1.3 Documentation of source data is necessary for the reconstruction, evaluation and validation of clinical findings, observations, and other activities during a clinical trial.

1.4 This SOP serves to ensure data quality by mandating that research teams create audit trails and ensure all trial data is accurately recorded, complete and able to be verified by an auditor / monitor / inspector.

Section B: Applicability

1.1 This SOP is applicable to all members of research staff working on non-CTRU / Clinical Research Organisation (CRO) managed CTIMPs sponsored by LTHT or UoL.

1.2 The Chief Investigator has ultimate responsibility for ensuring that all applicable staff adhere to this SOP.

1.3 For CTRU managed trials, this SOP may be used as a guide but specific advice should be sought from your CTRU Head of Trial Management (HoTM).

Section C: A Researchers Guide to Source Documentation

1.0 What is Source Data?

1.1 Source data is where a data point is **first captured** and is therefore the **original record** of information.

1.2 Source data can be defined as all information in original records (and verified copies of original records) of clinical findings, observations and any other trial activities that are necessary for the reconstruction and evaluation of the trial.

1.3 Source data is a vital aspect of trial management and should be **attributable, legible, contemporaneous, original, accurate and complete** (GCP E6 R2, 4.9.0).

1.4 Source data collection methods vary depending on the type of data collected by a trial, but must be captured in accordance with any protocol mandated requirements.

1.5 Common examples of source data include, but are not restricted to;

- Annotations in paper or electronic medical notes
- Source data worksheets
- Patient completed diaries
- Blood results stored on an online server
- Clinical trial prescriptions
- Scan images stored on equipment or servers
- Laboratory data to support analysis

1.6 Source data must be retained regardless of where the data was captured. For example, if a trial participant's blood pressure was noted on a piece of scrap paper as the medical notes were not to hand, the paper **must be kept for audit trail purposes**.

1.7 How source data will be collected and where it will be stored **must** be finalised prior to the trial commencing recruitment. This must be documented in a Data Management Plan for all trials submitted to Sponsor QA from 01st October 2017 (Please see ***QCRES_07_Researchers Guide to Data Management*** for further information).

1.8 Please note: if monitored / audited / inspected **ALL** source data pertaining to the trial must be provided for review.

2.0 Where is Source Data Held?

2.1 Source Data Location Sheets

2.1.1 The location of source data varies between trials as it depends on the type of data that is collected as well as any departmental systems and processes that are in place. This must

therefore be given adequate consideration and planning during trial set up to ensure data collection methods are tailored to each trial's requirements.

2.1.2 It is the investigator's responsibility to ensure that all team members understand the data management process and are aware of the source data requirements before commencing work on the trial.

2.1.3 A Source Data Location Sheet lists each data point and where its corresponding source can be located. An example of a source data location sheet can be found in ***QCRES_07_Researchers Guide to Data Management***.

2.1.4 Source Data Location Sheets are a useful tool to ensure that all team members are consistent in their approach to source data management and to aid the source data verification process by a monitor / auditor.

2.1.5 Certain data points may require more than one location to be listed (e.g. Adverse Events may be recorded in the medical notes, source data worksheets, clinic letters etc.). It is therefore essential to list all possible locations that source may be located.

2.1.6 If the location of source changes during a trial or a new data point is added as a result of an amendment, the source data location sheet content and version control must be updated accordingly (Please see ***QCRES_05_Version Control for Trial Documentation*** for further information).

2.1.7 Source data location sheets are mandated for all trials submitted for approval from 01st October 2017. It is recommended that any trial approved prior to this date also implements a source data location sheet.

2.2 Source Data Worksheets

2.2.1 Source Data Worksheets mimic the Case Report Form (CRF) and can be useful if there is a high volume of data to be collected for a trial or the data is not commonly collected as part of standard of care.

2.2.2 If a team choose to create source data worksheets, it is important that these are not confused with paper CRFs. The CRF is a formal, anonymised record of trial participation for a clinical trial whereas source data worksheets can be used as a method to ensure all information required by the CRF is captured at source.

2.2.3 **Source data worksheets must be filed in the medical notes in a timely manner** as soon as the data for that specific visit / assessment is recorded on the CRF for audit trail purposes.

2.2.4 It is not acceptable to file these separately to the medical notes as they contain patient data that may be required by another department.

2.2.5 Where a team has concerns that there is potential for source data worksheets to be lost from the medical notes, they may wish to also scan the worksheets onto PPM+ for backup purposes.

2.3 Electronic Data

2.3.1 Source data held centrally on computer systems (e.g. lab results, PPM+ annotations etc.) must remain accessible for inspection purposes. Consideration must therefore be given as to how electronic data will be provided to a monitor / auditor / inspector.

2.3.2 PPM+ access can now be provided to a monitor / auditor / inspector for review. To do this, the research team must complete a "PPM Inspector Access Application" form at least 10 working days in advance of the visit. This form can be located on the LTHT R&I intranet page (please contact LTHT R&I if assistance is required). Once approved, the monitor / auditor / inspector will be granted time-limited access to the requested patient data for the visit dates specified.

2.3.3 An audit trail to evidence timely investigator review of any electronic data (e.g. blood results, ultrasound etc.) must also be visible to any individual reviewing the trial data. This may be noted in paper medical notes or via a PPM+ annotation, however the method(s) of documenting investigator review must be noted on the Source Data Location Sheet.

2.4 Direct CRF Entry

2.4.1 Although the CRF is normally used for transcribing data from source, occasionally a research team may wish to directly enter data onto the CRF. In these instances, at least part of the CRF then becomes a source document.

2.4.2 Any data points to be directly entered onto the CRF **must** be clearly defined in the Sponsor approved protocol, source data location sheet and Data Management Plan (for trials submitted for approval from 01st October 2017) to alert a monitor / auditor / inspector that there will be no corresponding source to the data point(s).

3.0 Source Documentation

3.1 What Needs to be Documented at Source?

3.1.1 All protocol mandated data must be evident at source unless any direct entry to the CRF has previously been agreed (please see section 3.0).

3.1.2 All entries made to source documentation must be initialled and dated for audit trail purposes.

3.1.3 Data entry must be performed by authorised study personnel and all data entries must be traceable to an individual.

3.2 Approaching and Recruiting Trial Patients

3.2.1 All approaches to potentially eligible patients must be recorded in their medical notes.

3.2.2 The patients notes should be annotated to reflect when and how the current Patient Information Sheet (PIS) was provided (e.g. by clinic appointment or via post), the date the patient was first approached and by who, what was discussed and the next planned visit (if applicable).

3.3 Documentation of Patient Consent and Eligibility

3.3.1 If a patient shows willingness to participate in the study the entire consent and eligibility process must be documented at source.

3.3.2 An ideal entry in the medical notes to document patient consent and eligibility would include the following points (Please note these annotations do not need to be detailed transcriptions and can be brief statements of fact):

- Date of consent, name of consenting clinician and the version and date of the PIS and consent form provided
- Evidence of discussion prior to consent and that the patient had ample time to consider the trial and ask any questions
- Evidence that a copy of the signed consent form was provided to the patient
- Date of screening / baseline visit and a record of all protocol related assessments undertaken and results required to deem the patient eligible
- **Clear statement of eligibility by a <u>medically qualified doctor prior to dosing</u>**
- Confirmation of the patient's willingness to participate in the trial

3.3.3 As well as providing the patient a copy of the fully signed and dated consent form, a copy must also be added to the patients' notes along with a copy of the PIS and GP letter. ***Please note,*** different protocols may request additional information / documentation to be stored.

3.3.4 Unless specifically approved by the Research Ethics Committee, research nurses are not authorised to obtain informed consent on CTIMPs sponsored by UoL or LTHT.

3.3.5 Eligibility must be confirmed **by a medically qualified Doctor on the delegation log prior to dosing** with the trial IMP. If research nurses are authorised to obtain informed consent (as approved by the REC) eligibility must still be assessed by a medically qualified clinician.

3.3.6 Once a patient has consented to the trial, a yellow clinical trial notification sticker (a supply of which is sent out with the LTHT Confirmation of Capacity and Capability) must be attached to the inside cover of each volume of the patient medical notes. This identifies the patient as a clinical trial participant and ensures the notes are archived in accordance with sponsor policy.

3.3.7 All consenting patients must be flagged as clinical trial participants on PAS (Patient Administration System) and any other departmental electronic databases (e.g. PPM+).

3.4 Documentation of Patient Participation (screening and trial specific visits)

3.4.1 It is important to document every trial visit in full to allow reconstruction of the patients' participation and to demonstrate compliance with the protocol.

3.4.2 Important milestones to record can include (but are not restricted to) date and dose of trial IMP, dose modifications, adverse events and patient withdrawals / end of trial participation.

3.4.3 Trial visits must be clearly referenced in the notes with the trial name, visit number and date.

3.4.4 All trial visits must be held in accordance with the timescales outlined in the trial protocol. Any deviation to this must be reported to QA in accordance with ***QCRES_02_ Researchers Guide to Protocol Deviations, Violations and Potential GCP Breaches.***

3.4.5 All trial tests must be completed and evidence must be available in the medical notes to confirm all results were reviewed **prior** to the patient being deemed eligible for trial entry / to progress to the next stage of the trial. For example, lab reports could be printed, signed and dated by a medically qualified clinician and filed in the notes, or an annotation could be added to PPM+ confirming the date of review and clinician who reviewed the results.

3.4.6 Where printing a high volume of lab reports within the screening window is not feasible, please ensure a statement is added to the patient medical record confirming the results have been reviewed and deemed acceptable by a medically qualified Doctor.

3.4.7 Any tests to be performed at a particular time point must be referenced in the medical notes. If a particular test could not be performed this must be reported in accordance with ***QCRES_02_Researchers Guide to Protocol Deviations, Violations and Potential GCP Breaches.***

3.4.8 Treatment details including date of dose, dose regimen and any dose modifications must be documented. (If the patient is self-administering please ensure a diary card is maintained and collected to ensure compliance with the protocol and dosing regimen).

3.4.9 It is good practice to confirm a patients on-going willingness to participate in the trial (e.g. 'Trial discussed, patient continues to be happy to participate').

3.5 Adverse Events

3.5.1 The investigator is required to document and report any adverse events (including abnormal laboratory results) that are identified in accordance with the protocol's requirements.

3.5.2 All relevant information regarding reported adverse events, SAEs/SUSARs (Serious Adverse Events / Suspected Unexpected Serious Adverse Reaction) must be recorded in the medical notes including start/stop dates, tests performed and any changes to trial treatment.

3.5.3 Checks must be undertaken at each trial visit to identify any adverse events reported since the last patient contact. All possible locations of source for adverse events must be checked (e.g. verbal questioning, medical notes, PPM+, clinic letters etc.).

3.5.4 Please refer to ***QCRES_01_A Researchers Guide to Pharmacovigilance*** for further information on the recording and reporting of AEs, SAEs and SUSARs.

3.6 Withdrawal

3.6.1 Details regarding patient withdrawals must be documented in the medical notes including the date the patient was withdrawn and the reason why. Please refer to the protocol for further information regarding patient replacement and data collection following withdrawal.

4.0 Correcting Errors on Trial Documentation

4.1 Any errors made to clinical trial documentation must be correct and amended in a timely fashion. Corrections must be made by drawing a single line through the incorrect information to leave the original entry still visible, initialling and dating the change and stating the reason for change (if necessary).

4.2 Source data **must not be altered retrospectively** and original documents must never be destroyed even if they require error correction.

4.3 Pencil must not be used to record trial data and correction fluid must not be used to obscure trial documentation.

Section D: References

MHRA Good Clinical Practice Guide (2012)
QCRES_01_A Researchers Guide to Pharmacovigilance
QCRES_02_Researchers Guide to Protocol Deviations, Violations and Potential GCP Breaches
QCRES_05_Version Control for Trial Documentation
QCRES_07_Researchers Guide to Data Management

Section E: Acronyms

AE	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTRU	Clinical Trials Research Unit
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
LTHT	Leeds Teaching Hospitals NHS Trust
MHRA	Medicines and Healthcare products Regulatory Agency
PAS	Patient Administration Service
PIS	Patient Information Sheet
PPM	Patient Pathway Manager
QA	Quality Assurance
R&I	Research and Innovation
REC	Research Ethics Committee
SAE	Serious Adverse Event

SOP Standard Operation Procedure
SUSAR Suspected Unexpected Serious Adverse Reaction
UoL University of Leeds

Section F: Previous versions of Document

Version no.	Valid from	Approved by	Date approved
1.0	21/10/2013	Stephen Smye & Clare Skinner	16/01/2014 & 20/01/2014
2.0	03/10/2018	Louise Harris & Clare Skinner	24/10/2018 & 25/10/2018