

## STANDARD OPERATING PROCEDURE:

### Audit and Inspection

<b>SOP REFERENCE NUMBER</b>	CLPG19 SOP 3	
<b>VERSION NUMBER</b>	Version 1	
<b>REPLACES SEPT DOCUMENT</b>	SOP15 - External Audit & Inspections (V1.0; 4 August 2014)	
<b>REPLACES NEP DOCUMENT</b>	STANDARD OPERATING PROCEDURE: Audit and Inspection v2	
<b>KEY CHANGES FROM PREVIOUS VERSION</b>		
<b>AUTHOR</b>	Research & Development Manager	
<b>CONSULTATION GROUPS</b>	R&D staff, R&D group	
<b>IMPLEMENTATION DATE</b>		
<b>AMENDMENT DATE(S)</b>		
<b>LAST REVIEW DATE</b>		
<b>NEXT REVIEW DATE</b>		
<b>APPROVAL BY CLINICAL GOVERNANCE &amp; QUALITY SUB-COMMITTEE</b>	March 2018	
<b>RATIFICATION BY QUALITY COMMITTEE</b>	April 2018	
<b>COPYRIGHT</b>	© Essex Partnership University NHS Foundation Trust 2017. All rights reserved. Not to be reproduced in whole or part without the permission of the copyright owner	
<b>SOP SUMMARY</b>		
<p>The aim of this Standard Operating Procedure (SOP) is to describe to research staff the process for preparing for, hosting and participating in an internal audit or inspection either by the sponsor's independent audit function or by the Competent Authority (CA) for clinical trials that fall under the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and the European Clinical Trials Directive (EUCTD).</p>		
<b>The Trust monitors the implementation of and compliance with this policy in the following ways:</b>		
Monitoring of implementation and compliance with this procedure will be undertaken by the Executive Medical Director, Research manager, Research lead, R&D department staff and R&D group.		
<b>Services</b>	<b>Applicable</b>	<b>Comments</b>
Trustwide	✓	
Essex MH&LD		
CHS		

**ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST**

**STANDARD OPERATING PROCEDURE:  
Audit and Inspection**

**CONTENTS**

**1. BACKGROUND**

**2. PURPOSE**

**3. PROCEDURE**

3.1. Planning the visit

3.2. Essential Documents

3.3. Source Data

3.4. Recorded in Patient Notes

3.5. Investigator File

3.6. Important points

3.7. Evidence of Compliance

3.8. Close-out of inspection

3.9. Systems Audit

**4. REFERENCES**

**5. OTHER RELATED PROCEDURES**

## 1. BACKGROUND

An audit is:

*“A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor’s Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements.” (ICH GCP 1.6)*

Throughout the audit, general information exchange between the auditor and the person(s)/institution being audited is acceptable and essentially is used as an evaluation tool. Any results obtained from an audit should be used to train staff and improve upon the quality of research conducted.

An inspection is:

*“The act by a Competent Authority of conducting an official review of documents, facilities, records, quality assurance arrangements and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor and/or Contract Research Organisation’s (CRO’s) facilities or at other establishments that the Competent Authority sees fit to inspect”. (ICH 1.29)*

An inspection is a formal process that has legal implications if non-compliance with the regulations is found. It is therefore imperative that all trial related documentation is maintained and continually updated in readiness for an inspection.

The audit involves review of the progress of the trial at intervals appropriate to the size and risks of the trial. All audit documentation must be archived within the R&D Office. Trials are audited to verify that:

- a) The rights and well-being of human subjects are protected
- b) The reported trial data are accurate, complete, and verifiable from source documents.
- c) The conduct of the trial is in compliance with the currently approved protocol/amendments(s), GCP and GCP requirements.

## 2. PURPOSE

The aim of this Standard Operating Procedure (SOP) is to describe to research staff the process for preparing for an internal audit or inspection either by the sponsor’s independent audit function or by the Competent Authority (CA) for clinical trials that fall under the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and the European Clinical Trials Directive (EUCTD). The SOP will cover the processes necessary to prepare, host and participate in a regulatory inspection by the Competent Authority.

Both audits and inspections take place to examine ‘systems’ and look for good control of processes and opportunities for process improvement.

### 3. PROCEDURE

The following Personnel, where appropriate, should be available to answer questions and to attend the final meeting before the auditor/Inspector leaves the site:

- Chief/Principal Investigator and research personnel
- Personnel from other departments involved in the audit/inspection such as pharmacy, laboratory (departments should be fore-warned if the auditor/inspector intends to visit)

An audit is an informal and planned process and can take place prior to, during or after the patient recruitment phase. An internal audit is often undertaken prior to an external inspection. A regulatory inspection is very often notified, (usually 14 days in Europe); however there are exceptions if the Competent Authority has concerns for patient safety or grounds to suspect that improper practices are occurring at a site. Under these circumstances, a “triggered” inspection will take place whereby inspectors have the legal right of entry to inspect premises at any time without notification.

Please notify R&D of any planned inspections.

#### 3.1 Planning the visit

Prior to an inspection taking place a co-ordinator should be appointed to organise and plan the visit. All records must be made available (direct access) for monitors, auditors and regulatory authorities. It is important to address the following:

- Establish the name(s) of the inspector(s), the scope of the inspection and agree all dates in advance. It is essential that sufficient notice should be given to those expected to attend the inspection, with dates for availability of all involved agreed well in advance. The hosting co-ordinator should be given a timetable of events and all roles and responsibilities agreed. For commercial trials that have been assigned an external monitor, they will act as a key liaison between the sponsor (if commercial company) and the Investigator’s study team, providing support to ensure that the personnel and site are ready for an inspection.
- Identify and book suitable accommodation for the inspection to be conducted in, including space for all trial documents to be reviewed. Ensure that the room is tidy before the inspection.
- Provide photocopying facilities
- Organise refreshments such as tea/coffee/biscuits but no lunch or extras as this can be viewed as an enticement
- Respond to requests for specific documents, visits to specific departments e.g. labs, pharmacy.
- Provide Inspection training/mock interviews for staff to prepare for an inspection and document in their training records.

An inspector will be looking for a number of things during the inspection process including:

### 3.2 Essential Documents

*‘...those documents which permit evaluation of the conduct of the trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and the monitor with the standards of GCP and with regulatory requirements’*

### 3.3 Source Data

- Records should be accurate, complete, legible, attributable, original and timely
- Data should be consistent with the source documents, or discrepancies explained.
- Document all deviations from protocol and explain.
- Any changes should be initialled, dated and signed
- Document all dose/therapy modifications, visits and tests not conducted
- Data verification will check CRF's for completeness, looking at data queries, lab results, ECG's , X-rays etc., protocol details/ number in notes, date of birth, vital signs, all visit dates, medical examinations, concomitant medication, cognitive assessments intervention provided, IMP administered/dispensed, adverse events, new medical conditions and changes, adherence to study specific procedures, laboratory requisition forms, biosample storage temperature log.

Essential documents should be retained for 2 years following last approval of marketing application in the ICH region.

### 3.4 Recorded in patient notes

- Signed and dated copy of consent form and Patient Information Leaflet
- Verbal consent from patient and caregiver for clinical study continuation
- Laboratory results, X-ray results etc. related to participation in the clinical trial
- Title of the trial including the drug to be received
- Visit dates
- Concomitant medicines taken
- Any adverse events
- A letter informing the GP that the patient has been enrolled in the clinical trial
- Other relevant correspondence- i.e. GP and other speciality professionals

### 3.5 Investigator File

- Approval and correspondence- ethics approval with all correspondence between ethics and Trust, MHRA notification and MREC approval
- Laboratory – manual, reference normal ranges, reports, accreditation records and procedures
- Documentation – Protocol and amendments (signed and dated), Information leaflet and consent form (all current updated versions), previous version of protocols, indemnity and all correspondence between sponsor and investigator, sample CRF, study safety reports.
- Personnel – CV's (signed and dated) of those working on study, training record (such as GCP)

## CLPG19 SOP3 – Audit & Inspection

- Drugs – Shipping record, drug receipt (possibly held in pharmacy), sample of labels, accountability, security and dispensing log
- Patient Details – Screening/enrolment/identity logs, randomisation log, SAE reports
- Signed and dated completed Informed Consent Forms (originals)
- Decoding procedure for blinded trials
- Interim or annual reports to Ethics Committee of the trial status
- Any monitoring documentation
- Local Department/Third party providers- manual, training materials, forms and reports, lists/logs, correspondence. Data collection training documentation, eCRF completion guidelines
- Signature/delegation list

### 3.6 Important points

It is important that:

- Documents are up to date, reviewed and that staff are familiar with location and content
- There is a clear Audit trail
- Relevant documents bear dates and version numbers
- A Tracking log is kept, if documents are updated (evidence of distribution and receipt)
- Patient hospital notes should include up to date annotations, copy of consent form, General Practitioner (GP) letters, laboratory results, X-ray results etc. related to participation in the clinical trial
- There are Pharmacy/drug accountability records
- Staff delegation logs are kept up to date for any change of personnel

### 3.7 Evidence of Compliance

- SOPs/Guides/Work instructions/trial procedures manuals etc.
- Centre Delegation Log - old versions should be kept to reflect past and present staff
- Trial Master Files
- Investigator Centre Files
- Databases
- Archiving
- Contracts
- Training records/CV's
- SOP's for related departments
- Equipment and calibration records
- Security
- Emergency out of hours procedures

### 3.8 Close-out of inspection

At the end of the inspection a close out meeting will take place and the inspector will provide verbal feedback of the findings, followed by a detailed written inspection report. Each finding will be labelled, 'Critical, major, minor or For Note'. Each finding is referred to the particular regulation/guideline to which it is attributed. **A reply to the report is required.**

Dissemination of Inspection findings should be used to evaluate research practices, and assist in staff training. Improving upon the quality of research conducted by implementing solutions to remedy the findings should be a priority after an inspection.

### 3.9 Systems Audit

A systems audit is an assessment of a sample of clinical trials to verify the compliance of procedures and system set up within the Trust to conduct clinical trials. The systems audit will identify any deficiencies within the existing system that leads to non-compliance with sponsor, GCP, regulatory and Trust requirements.

The audits will be carried out by the R&D Office on a selected number of projects based on risk assessment methods.

## 4. REFERENCES

ICH Harmonised Tripartite guideline for Good Clinical Practice (1996)

The Institute of Clinical Research - Principles of Clinical Research (2001)

## 5. OTHER RELATED PROCEDURES

CLPG19 SOP 4 - Case Record Form Completion

CLPG19 SOP 18 - Study Files and Filing for Externally Sponsored Clinical Trials