STANDARD OPERATING PROCEDURE (SOP):

TITLE: CLINICAL TRIAL INTERNAL QUALITY ASSURANCE

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STANDARD OPERATING PROCEDURE (SOP):

TITLE: CLINICAL TRIAL INTERNAL QUALITY ASSURANCE

1. PURPOSE:

The purpose of this SOP is to describe the process for the planning, preparation, conduct, reporting and response to quality assurance reviews conducted by the Research Quality Coordinator (RQC) or delegate. In compliance with the International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines[1] (hereafter referred to as GCP), audits performed by Epworth HealthCare will be a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial related activities were conducted, and the data recorded, analysed and accurately reported according to the protocol, Epworth procedures and policies, GCP and applicable regulatory requirements.

2. SCOPE:

Audits may be conducted on any clinical trial being performed at Epworth as well as internal clinical trial processes or third party vendors contracted to perform clinical trial activities.

3. APPLICABILITY:

This applies to all Epworth employees, non-employed staff and Visiting Medical Officers (VMOs) and to all relevant external persons and parties engaged in the research activity at Epworth.

4. GLOSSARY OF TERMS:

Please refer to Epworth SOP Glossary of Terms (see Related Documents).

5. PROCEDURE:

5.1 Audit Planning

The type and frequency of internal audits shall vary, depending on the risk or process being audited. Audits will be performed according to the applicable annual Quality Plan prepared by the RQC and approved by the Group Director of Research and Development. Additional audits may be undertaken if significant potential or actual quality and/or safety issues arise.

The RQC or a delegate who is 'independent' (i.e. not a member of the trial team) will act as the auditor.

The selection of trials, processes and/or vendors to be audited may be decided on the following risk-based considerations:

- the number of patients recruited
- the phase/complexity of the study
- the status of the trial
- concerns regarding data integrity
- experience of Clinical Trial Coordinator (CTC)/Research Nurse/ Principal Investigator (PI)

- turnover of staff
- findings from Sponsors
- high incidence of Serious Adverse Events (SAEs)
- periodic audit cycles
- new vendor; change in location.

5.2 Audit Preparation

Prior to an audit being undertaken, the RQC or delegate shall contact individuals concerned (auditees, for example CTCs, PIs, vendors) to agree a convenient date and time for the audit.

5.3 Clinical Trial Audits

For clinical trial audits, the auditor should send a confirmation letter/email to the PI and CTC/Research Nurse to confirm the audit date(s) and notify them of the upcoming audit and to state any specific needs for the audit.

The auditor should meet with the CTC/Research Nurse to gain access to the following documents, information, systems and training, if applicable:

- trial protocol
- protocol amendments
- Case Report Form (CRF) – if an eCRF is being used, the auditor should discuss the ease of getting access to the eCRF or whether the printing of line listings from the database is best for reviewing the data
- trial manual, including worksheets and source data specific templates
- CRF guidelines and any other study related plans
- monitoring follow-up visit letters
- a listing of SAEs and Protocol Deviations
- trial specific Patient Informed Consent Forms (PICFs)
- trial status overall
- Investigator Site File (ISF), including Pharmacy documents
- participants' source data and medical records
- communications
- other documents, as required.

The CTC/Research Nurse should arrange appointments for the auditor with supporting departments (e.g. Pharmacy, Pathology, Imaging), if applicable.

5.4 Clinical Trial Process Audits

The auditor will notify any relevant staff of a process audit and request documentation, as required.

5.5 Clinical Trial Vendor Audits

As part of the oversight process for vendors, audits of vendors may occur to initially determine whether to use the vendor as well as determining their ongoing suitability for clinical trial work.

The auditor will notify the vendor and agree on a specific date(s) and time. The auditor will request documents pertaining to the vendor's processes as well as any documents related to specific trials.

5.6 Conducting the Audit

5.6.1 Introductory Meeting

An introductory meeting with the auditees may be held at the beginning of the audit so that the auditor can:

- introduce themselves
- discuss the scope and objectives of the audit
- review and confirm the audit schedule
- ascertain how the trial and/or processes are conducted and confirm roles and responsibilities
- confirm the availability of personnel for the audit, including vendors, as applicable
- indicate the tentative time and date for the closing meeting.

5.6.2 Clinical Trial Audits - Conduct

Information to be reviewed by the auditor includes (but is not limited to):

- the ISF, including Pharmacy documents, if applicable
- PICFs
- regulatory and ethics correspondence
- participant source data
- protocol deviations
- adverse events
- Investigational Product receipt, accountability, storage and disposal

- management of biological samples
- equipment maintenance
- qualifications and training of staff.

Comparison of source data against the data entered into the CRFs will occur. The number of CRFs reviewed will be dependent upon the number of participants recruited and the risk profile of the trial.

Trial team members may be interviewed regarding the conduct of the trial.

5.6.3 Clinical Trial Processes – Conduct

Clinical trial processes may be audited including, but not exclusively, the process for taking informed consent, SAE reporting, drug storage, documentation of a trial, coordination of the trial, training processes and compliance etc. etc. The audit process for these procedural audits will be determined depending on the process being audited.

5.6.4 Clinical Trial Vendor Audits – Conduct

Clinical trial vendors may be audited including, but not exclusively, vendors providing clinical trial services of imaging, pathology and pharmacy. The audit process for vendor audits will be determined by the specific services a vendor provides for the clinical trial.

5.6.5 Exit Interview

At the end of an audit, an exit meeting will be held with the auditees to present and discuss the observations from the auditing activities. The auditor will emphasise the critical and major observations. The exit interview will also provide the auditee with an opportunity to ask questions and clarify the observations from the audit.

5.6.6 Preparation, Approval and Distribution of the Audit Report

The auditor is responsible for the preparation of a draft audit report within 10 working days after the completion of the audit. Audit observations will be classified as:

- **Critical**: Where significant and unjustified departure(s) from applicable regulatory requirements has occurred with evidence that (1) the safety or wellbeing of trial participants either have been, or have significant potential to be, jeopardised and/or (2) the clinical data are unreliable. Critical observations may include serious breaches of the protocol or GCP as defined in SOP-QA-02 (see Related Documents). Formal documented corrective and preventive actions are required as per SOP-QA-02. Immediate suspension of the practices or trial may be required. Immediate escalation to Epworth senior management is required.

- **Major**: If not resolved or left unaddressed, the observation(s) could adversely impact the safety or wellbeing of trial participants or the integrity or reliability of the site's data. Major observations may include serious breaches of the protocol or GCP. Formal documented

corrective and preventive actions are required and site practices must be modified as per SOP-QA-02. Major observations may also include repeated or frequent occurrence of minor findings or known non-compliance which has not been corrected or the corrective action has been ineffective.

- **Minor**: Although requiring attention, the observation(s) would not significantly impact the integrity of the site's data or jeopardise the safety or wellbeing of the trial participants. Documentation of the deviation is required and site education or modification of site practices may be advisable. Formal corrective action is required.

- **Recommendations**: A suggestion (not non-compliance) for improvement to a current process, procedure, operation and/or quality system.

The audit report will be reviewed by the Group Director of Research and Development within 10 working days of receipt from the auditor.

The approved audit report will be distributed to the relevant auditees and/or the Research Operations Manager. The auditees should review the audit report and respond to the auditor within 20 working days of receipt from the auditor.

Once the auditor deems the responses to the audit report are adequate, the auditor will finalise the audit report and close the audit.

Final, signed audit reports will be stored securely with restricted access by the RQC.

5.7 Sharing Audit Observations with Sponsors

The audit report and responses from internal Epworth audits will not generally be distributed to external trial Sponsors. It is the responsibility of the CTC and/or the PI to communicate with the Sponsor on the audit observations in line with trial-specific requirements. Issues confirmed as critical must be escalated to the Sponsor immediately.

6. REFERENCES:

1. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2) https://www.tga.gov.au/publication/note-guidance-good-clinical-practice

7. RELATED DOCUMENTS:

7.1 Related Forms and Templates

N/A

7.2 Related SOPs

- SOP-QA-02 Management of Serious Breaches and CAPA Process

- SOP-Glossary-of-Terms

8. VERSION CONTROL

Document History	
Version	**Summary of Changes**
1.0	N/A First Issue
2.0	• Removal of reference to internal supporting templates. • Minor formatting and grammatical corrections.

9. APPENDIX

N/A