RESEARCH QUALITY MANAGEMENT SYSTEM - IMPLEMENTATION AND MAINTENANCE PROTOCOL

Document ID:	9063
Version No:	1.0
Effective Date:	Date of Approval
Review Date:	22 Oct 2022
Applicable Epworth Site/s:	All

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Date:	Oct 30, 2019

RESEARCH QUALITY MANAGEMENT SYSTEM - IMPLEMENTATION AND MAINTENANCE PROTOCOL

1. PURPOSE:

The purpose of this protocol is to define, implement and maintain a clinical research quality management system (rQMS) at Epworth HealthCare

The purpose of the rQMS is to provide a quality and safety framework that mitigates research risks, guides researchers and enhances overall the quality and safety of clinical research conducted at Epworth.

2. SCOPE:

All clinical research conducted at Epworth.

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. PROCEDURE:

The Epworth rQMS is based on TransCelerate's clinical Quality Management System [1,2] and provides an integrated approach to achieve Epworth clinical research quality objectives. The rQMS takes into account strategic objectives, applicable regulatory requirements, infrastructure, organisational structure, processes and resources required to achieve these objectives.

The elements of the rQMS include:

- Standard Operating Procedures (SOPs) and Policies
- resources, roles and responsibilities
- training activities and documentation
- risk and issue management
- partnering with vendors
- oversight of clinical trial coordination
- essential documents and review of trial-related files
- process reviews
- quality metrics and objectives
- quality assurance
- knowledge management.

The rQMS requires researcher compliance with all applicable SOPs, regulatory and project requirements when conducting studies at Epworth.

4.1 Standard Operating Procedures and Associated Documents

SOPs have been developed to cover the critical clinical research business activities. Additional SOPs will be developed if a need is identified.

The review and development of the SOPs is conducted according to SOP AD-01 (SOP on SOP Creation, Implementation and Revision) taking into account the burden of implementation (including change management activities and training needs).

Role-based curricula identifies the SOP training requirements for each clinical research role at Epworth.

4.2 Resources, Roles and Responsibilities

Epworth will prospectively evaluate the resources and staff skills required to implement the Epworth Research strategy. All staff, including temporary personnel and contractors, must be qualified by appropriate education, training and/or experience to perform the clinical trial activities for which they are responsible.

The Principal Investigator (PI) is ultimately responsible for ensuring adequate resourcing is in place for the duration of their proposed research proposal, with evidence of relevant departmental support a condition of research governance authorisation (as per the Epworth Research Handbook). Epworth's management will ensure that appropriate resources are available for agreed studies, including both material resources (systems, standards, training environments) and staff.

There should be clarity in roles, responsibilities and accountability for operational effectiveness and quality at all levels throughout the organisation. Epworth managers should proactively manage clinical trial resources by anticipating resource and expertise needs according to the strategic direction of Epworth, its evolving risk profile and the evolving regulatory environment.

For all staff involved in clinical research at Epworth, current signed resumes (less than 3 years old) and archived signed CVs, position descriptions and organograms will be maintained. Certifications of all medical staff involved in clinical trials will also be maintained.

4.3 Training Activities and Documentation

The following training activities are included in the training programme for each Epworth employee:

- new employee induction by line manager or designee
- SOP training – via a curriculum, based on role as defined as either instructor-led training or as 'self-read'
- regulatory requirements for the conduct of clinical trials including ICH-GCP, 21 CFR Part 11 and Australian regulatory requirements
- functional area development training (e.g. CTA to CTC development) as identified by the line manager in the individual's performance development plan
- project specific training
- informal on-the-job training supported by mentoring of line manager or designee.
- systems training
- therapeutic area training, as needed.

Documentation of training will be maintained as described in SOP-QA-01 (Documentation of Qualifications and Training Records).

4.4 Risk and Issue Management

For all clinical research activities, risk management, including identification, evaluation, control, communication, review and reporting will be considered at all stages from study setup to closure and documented according to the project plan.

Risk management is a process through which risks are identified and characterised to permit timely and data-driven decisions about whether and how they need to be addressed. Care should be taken to distinguish between issues (events that have occurred) and risks (potential events with a range of potential consequences). Focusing on risks and their management will allow Epworth to shift to a proactive and predictive state, prioritising resources to address the most significant strategic, operational, quality and compliance-related risks. Ideally, risk management should be integrated into day-to-day decision making throughout the Epworth organisation.

An effective issue management framework is also needed to improve identification, investigation/assessment, escalation and communication of significant issues – or serious breaches. Serious breaches materially impact patient safety, rights and well-being; data integrity and/or scientific rigor; compliance with regulatory requirements; and trust in the clinical research enterprise.

The issue management framework will provide end-to-end management of issues and support an effective Corrective and Preventive Actions (CAPA) process commensurate with the impact of the issue; it will also enhance risk management strategies and drive continuous improvement through predictive analytics. A robust issue management framework will reduce the risk of serious breaches occurring, reduce resource requirements in drug development and overall, contribute to improving the quality of clinical trials.

Any serious breaches of GCP or the protocol or critical and major audit/regulatory findings should be reported and followed according to SOP-QA-02 (Management of Serious Breaches and CAPA Process).

These issues will be reported to the Sponsor as agreed and as appropriate.

All serious breaches/critical and major audit/regulatory findings will be reviewed to assess impact on other participants and trials at the time of identification.

As part of risk management, relevant identified issues will be incorporated into training module development, SOP revision and ‘lessons learned’ sessions.

4.5 Partnering with Vendors

Epworth will prospectively consider the needs, expectations and limitations of all parties involved in a partnership as well as the risks posed by the activities to be carried out in such partnerships. A common understanding will be established between Epworth and vendors regarding their

specific roles in the overall quality of the partnered activities and how oversight of quality will be maintained. This will include their respective roles and responsibilities and how issues will be managed and escalated. Epworth and its vendors will prospectively document their agreement (in relevant service agreements or work orders) regarding expectations for how activities will be conducted and overseen, communications (including escalations) will be managed and performance will be measured

4.6 Oversight of Clinical Trial Coordination

Oversight of clinical trial coordination will be conducted by the line manager. For new clinical trial coordinators (CTCs), an assessment of their competency will be performed by their line manager observing the conduct of trial visits, reviewing the patient trial specific files and other trial-related activities. An annual assessment of each clinical trial coordinator will be conducted by the line manager.

4.7 Essential Documents and Review of Trial-Related Files

All Epworth staff are responsible for maintaining appropriate files for the clinical trials they work on. CTCs must conduct periodic reviews of the Investigator Site Files (ISF) for their designated studies in accordance with SOP-TM-02 (Investigator Site File and Essential Documentation).

4.8 Quality Reviews/Audits

Epworth management and the Research Quality Coordinator (RQC) will determine if and when areas of the business or specific clinical trials require a quality review/audit for ongoing improvement or as a result of operational issues.

Quality reviews may form part of the vendor selection process for activities that are outsourced.

4.9 Quality metrics and objectives

Quality metrics will be maintained and analysed by the RQC and provided to the Group Director of Research and Development (GDRD), Research Operations Manager (ROM), Epworth Research Advisory Committee (ERAC), Epworth management team and Clinical Institute Directors on half yearly basis. These may include:

- tracking of compliance with timelines for data entry
- tracking of incidence and closure of issues and trending of issues across a clinical trial.

In addition, both quantitative and qualitative metrics will be maintained across all audits and inspections conducted at Epworth.

The analyses from the quality metrics will be used to monitor performance, to initiate process improvements and to identify areas for training and revision of SOPs.

4.10 Quality assurance

Quality assurance is conducted in accordance with SOP-QA-01, SOP-QA-02, SOP-QA-03, SOP-QA-04 and SOP-QA5.

All audit findings, whether conducted internally or by Sponsors or Third Parties, are circulated to the GDRD, ROM, RQC, PIs and Clinical Trial Coordinators. Senior management and Clinical Institute Directors will be notified where there are any critical findings identified (see SOP-QA-02, SOP-QA-05).

4.11 Knowledge management

A knowledge management framework enables the effective and successful implementation of a rQMS. A knowledge management framework includes strategies and processes designed to identify, capture, structure, value, leverage and share the organisation's intellectual assets to enhance the clinical development organisation's performance, and the performance of rQMS elements such as issue and risk management.

The goal of managing knowledge is to improve organisational performance by getting the right information to the right people at the right time. Loss of knowledge or the failure to apply knowledge may have negative consequences for organisations and most importantly, for participants.

To assist with knowledge management, Epworth staff will ensure that all study-related correspondence and documents are stored in the ISF or on an accessible shared drive rather than on personal computer drives.

The Epworth staff will also initiate a 'lessons learned' session at the end of each trial and document what went well and what needed improvement (see SOP-TM-12 Trial Closeout). A copy of the meeting minutes will be circulated to the RQC.

The RQC will report findings from serious breaches, audits as well as relevant 'lessons learned' feedback on a 6 monthly basis. Findings from reported events will inform risk management, process improvements and will help identify future training needs.

5. REFERENCES:

1. O'Connell, A.M. et al., TransCelerate's Clinical Quality Management System: From a Vision to a Conceptual Framework. Therapeutic Innovation & Regulatory Science 2016, Vol. 50(4) 397-413

2. http://www.transceleratebiopharmainc.com/assets/quality-management-system-assets/

6. RELATED DOCUMENTS:

6.1 Related SOPs

- SOP-Glossary-of-Terms
- SOP AD-01 SOP Creation, Implementation and RevisionSOP-QA-01 Documentation of Qualifications and Training Records
- SOP-QA-02 Management of Serious Breaches and CAPA Process
- SOP-QA-04 Vendor Assurance and Oversight
- SOP-QA-05 Clinical Trial Internal Quality Assurance
- SOP-TM-02 Investigator Site File and Essential Documentation
- SOP-TM-12 Trial Closeout

7. VERSION CONTROL

Document History	
Version	Summary of Changes
1.0	N/A First issue

8. APPENDIX

N/A