STANDARD OPERATING PROCEDURE (SOP)

TITLE: MANAGEMENT OF SERIOUS BREACHES AND CAPA PROCESS

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1. PURPOSE:

The purpose of this SOP is to describe the handling of serious breaches of GCP or the protocol (i.e. deviations that have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated) and the subsequent development, implementation and closure of corrective and preventive actions (CAPA) at Epworth HealthCare (Epworth).

Where non-compliance is identified but is not considered to meet the reporting requirements of a serious breach by the Sponsor or Epworth, the principles outlined within this SOP can be used to ensure quality improvement within Epworth.

2. SCOPE:

All clinical trials conducted at Epworth involving therapeutic goods.

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 Reporting Serious Breaches

- Epworth expects all parties engaged in clinical research to be familiar with and abide by the *NHMRC guideline: Reporting of Serious Breaches of GCP or the Protocol for Trials Involving Therapeutic Goods – 2018*[2].
- However, some serious breaches may be identified by Epworth staff who may wish to report directly to the reviewing HREC rather than through the Sponsor. This would usually be appropriate if:
    - the PI has good evidence that a serious breach has occurred but the Sponsor disagrees with their assessment and is unwilling to notify the HREC
    - the PI has become aware that the Sponsor may have committed a serious breach
- It is the PI's responsibility to:
    - Ensure that the trial team is aware of the process for reporting serious breaches.
    - Report any suspected breaches to the Sponsor within 72 hours of becoming aware of the suspected breach.

- Report all serious breaches that have been confirmed by the Sponsor as occurring at the site to Epworth via Riskman, and to Research Development Governance Unit (RDGU) within 72 hours of being notified of the serious breach.
- Provide any follow-up information as required.
- Work with Epworth or the Sponsor, as appropriate, to implement any CAPA that may be indicated.

5.2 Corrective and Preventative Actions (CAPA)

The need for CAPA may be identified as a result of the following, but is not limited to:

- Sponsor audit
- Regulatory inspection
- Process review
- Monitoring
- Participant complaint or report

Not all identified issues will require a formal CAPA plan.

5.3 Issue Identification and Risk Assessment

Once an issue is identified, a risk assessment should initially be performed by the trial team to determine the impact of the issue on patient safety, rights or well-being and/or trial data credibility.

The level of risk of the issue will determine if the issue should be escalated to Epworth senior management by the staff member. If in doubt, the staff member should report the issue immediately to their line manager and/or senior managers.

For serious breaches and critical and major audit findings, the Research Development and Quality Officer (RDQO) must be notified for centralised management.

5.4 Root Cause Analysis of Non-Compliance Issues

As a minimum, all serious breaches, and critical findings from audits/inspections, will require a root cause analysis. Senior managers at Epworth will appoint an individual from the trial team to act as the 'owner/CAPA author' of the issue(s). When a root cause analysis is performed by the trial team, the root causes will be documented in a CAPA form. Some Sponsors may provide their own template or process for documenting CAPAs. If such a template is not provided, the CAPA Form Template 01 should be completed.

The root cause analysis will consider the following:

- What is the problem?

- What events/contributing factors led to the problem?
- When did the problem first occur?
- Who/what is impacted by the problem?
- Where is the problem occurring?
- How widespread is the problem?
- How was the problem identified?

5.5 Documentation of CAPA

All CAPA actions must have a responsible person identified to complete the action and a due date for implementation/completion of the actions. All actions should be specific, measurable, attainable, realistic and timely. There must be evidence or documentation in place to support the actions proposed.

5.6 Review of CAPA Responses

Once CAPA responses have been received, the responses should be reviewed by the CAPA Author and senior management. For serious breaches of the protocol and/or GCP and critical audit findings, the RDQO must also review the CAPA responses prior to finalisation.

5.7 Implementation, Follow-up and Closure of CAPA

All actions in the CAPA must be completed by the responsible person within the documented timeframe. There must be documented evidence of this completion. If the timeline cannot be met, there must be justification for extension of the timeline and a revised CAPA issued.

5.8 Effectiveness of CAPA

The effectiveness of the CAPA over time should be assessed by the RDQO to ensure continuous quality improvement has occurred as a result of the CAPA.

5.9 Tracking and Trending of CAPAs

The RDQO will maintain a centralised CAPA tracker for Epworth clinical research where the non-compliance is a serious breach of the protocol or GCP and/or based upon critical and major audit findings.

The completed CAPA forms will be filed by the RDQO in a confidential file.

6. REFERENCES:

1. NHMRC: Reporting of Serious Breaches of GCP or the Protocol for Trials Involving Therapeutic Goods - 2018 https://nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods
2. Epworth Incident Management Protocol

7. RELATED DOCUMENTS:

7.1 Related Forms and Templates

- SOP-QA-02-Template-01: Corrective and Preventive Actions (CAPA) Form

7.2 Related SOPs

- SOP-Glossary-of-Terms

8. VERSION CONTROL

Document History	
Version	**Summary of Changes**
1.0	N/A First Issue
2.0	**Section 5.1** – Requirement to report incident in Riskman emphasised. Reference to Epworth Incident Management Protocol added.

9. APPENDIX

N/A