UNIVERSITY OF WARWICK

STANDARD OPERATING PROCEDURE 18

Risk-Based Quality Management of Research Studies

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Revision Chronology:	**Effective date:**	**Reason for change:**
Version 4.0	30 November 2026	Biennial review: Updated to new template. Revised the title and Scope of SOP to align with current regulatory expectations. Introduced QbD principles, including CtQfs, CDIs, DVPs and updated the process for risk identification, assessment, review and monitoring. Clarified roles and responsibilities, review and approval requirements, escalation processes and governance arrangements. For WCTU Trials, updated to reflect the new RAMP tool.
Version 3.0	26 September 2024	Biennial review. Minor updates to expand for clarity. Removal of reference to Q-Pulse to facilitate differing approaches within the University (Q-Pulse reference to remain in Guidance document).
Version 2.0	13 July 2022	Biennial review. To update text to be relevant to remote monitoring; DPIA reference change. Addition of training resource. Review to reduce repetition and excess text.
Version 1.7	28 January 2020	Review to update in accordance with the revised approach to conducting risk assessments; to review and update in accordance with requirements following NHS Digital audit.
Version 1.6	25 July 2019	Review by QA Team to ensure activities are compliant with SOP. To ensure SOP reflects additional activities in place as a result of an expanded QA team. To ensure SOP reflects the updated addendum in ICH GCP E6(R2). Addition of co-monitoring section.
Version 1.5	25 July 2016	Minor text amends; change to review/approval process, escalation process added. Change to new format.
Version 1.4	9 December 2013	Addition of process for undertaking triggered on-site visits, plus addition of process to review and approve risk assessments and monitoring plans
Version 1.3	25 May 2012	Renamed as includes risk assessment information. RSS web link updated. Minor text amends in section 3. Templates added.

Version 1.2	29 January 2010	Biennial review: RSS web page link updated.
Version 1.1	31 January 2008	Biennial review. Format change.
Version 1.0	March 2006	

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CONTENTS

1 PURPOSE AND SCOPE 4
2 ACRONYMS 4
3 DEFINITIONS 5
4 BACKGROUND 6
5 RESPONSIBILITIES 7
6 WHEN 8
7 HOW 8
7.1 DEVELOPMENT 8
7.2 REVIEW AND APPROVAL 8
7.3 CRITICAL TO QUALITY FACTORS 8
7.4 CRITICAL DATA ITEMS 9
7.5 RISK ASSESSMENT 9
7.6 DATA VALIDATION PLAN 10
7.7 MONITORING PLAN 10
7.8 TYPES OF MONITORING, CONDUCT AND COMPETENCY 11
7.9 MONITORING FINDINGS AND ESCALATION 12
7.10 TRIGGERED MONITORING 13
8 ASSOCIATED TEMPLATES AND DOCUMENTS 13

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1 Purpose and Scope

To describe the process for applying RBQM principles throughout the lifecycle of a research study. RBQM aims to ensure that quality management activities are focused on the aspects of a study that are most important to participant safety, participant rights, data integrity and reliable study outcomes. This includes the identification of CtQfs and CDIs, the assessment and management of risks, the development of monitoring and data validation activities, and the ongoing review of quality management processes.

It is applicable to all research studies sponsored by the University of Warwick and for externally sponsored studies where management of the risk-based quality system has been delegated to Warwick.

For WCTU studies, read in conjunction with **G06** WCTU RAMP Tool: Guidance.

2 Acronyms

BCP	Business Continuity Plan
CAPA	Corrective and Preventative Actions
CDIs	Critical Data Items
CDMS	Clinical Data Management System
CI	Chief Investigator
CRF	Case Report Form
CtQfs	Critical to Quality Factors
DVP	Data Validation Plan
GCP	Good Clinical Practice
UK GDPR	UK General Data Protection Regulation
HE	Health Economist
ICH	International Conference on Harmonisation
MP	Monitoring Plan
PI	Principal Investigator
QA	Quality Assurance
QbD	Quality by Design
QC	Quality Control
QTL	Quality Tolerance Limit
RA	Risk Assessment
RBQM	Risk-Based Quality Management
SAE	Serious Adverse Event
SDR	Source Data Review
SDV	Source Data Verification
SOP	Standard Operating Procedure
SPM	Senior Project Manager
S/TMF	Study/Trial Master File
S/TMG	Study/Trial Management Group
S/TC	Study/Trial Coordinator
S/TM	Study/Trial Manager
WCTU	Warwick Clinical Trials Unit

3 Definitions

QbD	A systematic approach to study design and conduct that focuses on identifying the factors critical to participant safety and study integrity, engaging relevant stakeholders, considering operational feasibility, and reducing unnecessary complexity and burden.
CtQfs	The essential conditions that must be achieved or maintained to ensure participant safety, participant rights, study integrity and reliable study outcomes. CtQfs are described as positive statements of what is important for study success and form the foundation of the risk assessment process.
CDIs	Specific data elements that are critical to participant safety, trial integrity, regulatory compliance, or the evaluation of study outcomes. Examples may include participant eligibility data, primary efficacy endpoints, safety data, investigational product dosing and accountability records, treatment compliance, and drug return data.
DVP	A documented plan describing the checks and activities used to ensure that study data are accurate, complete, consistent and suitable for analysis. The DVP is informed by the identified CDIs and supports the risk-based monitoring strategy.
RA	A documented evaluation of risks to participant safety, participant rights, data reliability and study conduct, together with planned mitigations and review arrangements.
MP	A documented, risk-based plan that describes how monitoring will be undertaken throughout a study to provide assurance that participant safety and rights, data integrity, study quality and regulatory compliance are maintained. The plan defines the monitoring activities, responsibilities, frequencies, metrics, QTLs, escalation arrangements and oversight processes used to support ongoing study oversight.
QTL	A predefined threshold used to identify systematic issues that could impact participant safety, participant rights, data reliability, or the overall quality of a study. Exceeding a QTL should trigger review, investigation and consideration of corrective actions.
RAMP Tool (WCTU Only)	A structured framework tool used by WCTU to identify CtQfs, assess risks to participant safety and study integrity, document mitigations, define monitoring activities and maintain ongoing oversight throughout the study lifecycle. The RAMP incorporates CtQfs, CDIs, RA, MP, DVP and BCP within a single controlled document. BCP is covered separately in SOP 40.

4 Background

RBQM is a key principle of GCP and QbD. It promotes a systematic approach to identifying, assessing and managing risks to study quality, enabling resources and oversight activities to be focused on the area's most critical to study success.

CtQfs, RA, monitoring and data validation activities should be reviewed throughout the study lifecycle to ensure that quality management activities remain effective and proportionate.

N.B. Before University of Warwick agrees to sponsor a study, the University's Sponsorship & Oversight Committee will undertake a separate sponsorship RA which does not replace the processes outlined in this SOP.

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5 Responsibilities

Sponsor (or delegate)	• Ensure proportionate RA and monitoring activities are undertaken and documented. • Ensure appropriate delegation of risk and monitoring activities for sponsored studies.
Chief Investigator (CI)	• Ensure study-specific risk assessment, monitoring arrangements and associated documentation are developed, reviewed and approved. • Review study risks and monitoring arrangements periodically throughout the study lifecycle and ensure actions arising from risk review activities are completed and documented.
WCTU QA team (for WCTU-managed studies)	• Support study teams in the development and maintenance of risks assessment and monitoring documentation using the RAMP tool. • Maintain oversight of WCTU RAMPs to ensure risk assessments, monitoring activities and review processes remain current and appropriately documented. • Escalate issues via WCTU Governance Committee
TM or TC (where delegated by CI)	• Coordinate development, review and approval of study risk assessment and monitoring documentation. • Ensure risk assessment, monitoring and review records are maintained and version controlled. • Update risk assessments, monitoring plans and associated documentation following changes to study design, processes, identified risks or monitoring findings. • Arrange and document periodic risk review meetings with relevant personnel.
Statistician (HE where applicable)	• Contribute to the identification and review of CtQfs and CDIs. • Input into the development and review of study-specific risk assessments, monitoring strategies and monitoring metrics. • Support identification of data quality risks that could impact the integrity or interpretation of study outcomes. • Contribute to the development and review of the DVP, including validation checks relating to critical data and study endpoints. • Advise on QTLs, monitoring thresholds and escalation criteria where applicable. • Review significant data quality findings, trends and emerging risks throughout the study lifecycle, as required.
Clinical Trials Monitor (for WCTU-managed studies)	• Support the development of the risk assessment and monitoring plan. • Conduct remote and on-site monitoring activities on behalf of WCTU. • Perform monitoring as defined within the study MP. • Document and report monitoring findings and recommendations. • Escalate significant findings, risks, protocol deviations and non-compliances as required. • Follow up with study teams and site teams to ensure actions are completed within agreed timelines.

6 When

RBQM should be embedded across the whole study life cycle, with risks to CtQfs identified and assessed at the time of protocol development.

RBQM is an ongoing, dynamic process. Risks should be reviewed regularly throughout the study lifecycle to ensure that mitigations, monitoring and data management activities remain appropriate, effective and aligned with emerging knowledge and experience.

7 How

7.1 Development

Appropriately qualified and experienced members of the study team should contribute to the identification of study specific CtQfs, CDIs, RA, monitoring activities and supporting quality management documentation. Where appropriate, a multi-disciplinary approach should be adopted.

Whilst this SOP describes each component separately for clarity, the process should not be considered strictly linear. Information developed during one activity may inform, refine or necessitate updates to another. The identification of CtQfs should normally be undertaken first, as these drive the identification of CDIs, RA, monitoring activities and supporting plans, ensuring that quality management activities remain risk-based and proportionate.

For WCTU managed studies, these activities are documented within the RAMP tool. Alternative documentation may be used for non-WCTU managed studies, provided the requirements of this SOP are met.

7.2 Review and Approval

The identified CtQfs, baseline RA and associated quality management documentation (e.g. monitoring and data validation documentation where applicable) should be reviewed and approved prior to study initiation through completion of the Green Light to Commence Clinical Research Study form (**T18**). Evidence of approval should be retained within the TMF.

Reviews should be proportionate to the level of risk, with high-risk or time-dependent items reviewed more frequently. Additional reviews should be considered following significant changes to the study, protocol modifications, non-compliances or significant changes to study resources. Completion of key milestones (e.g. end of pilot phase, end of recruitment, end of study) should also prompt review. Changes to CtQfs, CDIs, RA, monitoring activities, the DVP and associated documentation should be documented and retained as part of the study records.

For WCTU-managed studies any reviews and amendments should be recorded within the 'Review Summary' worksheet within the RAMP tool, to maintain an auditable record of decisions and updates.

See **G06** WCTU RAMP Tool: Guidance for further details.

7.3 Critical to Quality Factors

CtQfs define the aspects of a study that are essential for participant safety, rights and study integrity. The Identification of CtQfs should be undertaken early in the study design phase to inform the development of study processes and controls. The identification and review of CtQfs should involve

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individuals with appropriate qualifications and expertise in study conduct, quality management, statistics and relevant clinical or technical disciplines. These should be documented in the TMF with approval from the CI.

For WCTU-managed studies, CtQfs are discussed during a multidisciplinary meeting held during study set-up and should include; the CI, a member of the QA team, SPM, TM/TC, statistician and any other relevant staff (e.g. HE, pharmacist, lab technician, radiologist, clinicians) associated with the study. A record of the agreed items will be documented in the RAMP tool.

7.4 Critical Data Items

CDIs are the data required to demonstrate that CtQfs are being achieved and maintained throughout the lifecycle of the study.

Identification of CDIs may occur alongside development of CRFs, database specifications, RA activities or other study design activities. The proposed CDIs should be agreed by the study team and documented (within the RAMP tool for WCTU managed studies) and should inform the development of the DVP, and monitoring activities.

Not all study data will be classified as critical. The identification of CDIs should focus on those data items that are essential to participant safety, participant rights, the assessment of study outcomes, regulatory compliance, or the overall integrity and reliability of the study conclusions. Other data may still be important, but oversight and quality management activities should be prioritised towards identified CDIs.

7.5 Risk Assessment

RA should be informed by the identified CtQfs and associated CDIs, a RA meeting should be held during protocol development and before study initiation. The purpose of the RA is to identify, assess and document study-specific risks that could impact participant safety & rights, study integrity, data quality, study delivery or regulatory compliance. Attendance should include individuals with appropriate expertise in study conduct, quality management, statistics and relevant clinical or operational disciplines. Wherever possible, attendance should be consistent with the CtQfs assessment process. The RA should consider:

- Factors that may increase the likelihood or impact of identified risks
- Existing and planned controls or mitigations
- Novel, complex, high-risk or operationally challenging aspects of the study.

Risk control and mitigation measures should, where possible, be embedded within the study protocol, study procedures, training activities, monitoring activities or other study documentation, to demonstrate the application of QbD.

As the study progresses, emerging knowledge and experience may alter the likelihood or impact of identified risks. Allocating a review date to individual risk items (rather than a single over-arching review date for the study) enables a proportionate approach to risk management, ensuring that resources and mitigation activities are focused appropriately.

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For WCTU-managed studies, the outcome of the risk assessment should be documented in the RAMP tool. This provides a framework for risk discussion. For more details see **G06**.

7.6 Data Validation Plan

The DVP should describe the validation checks required to ensure that study data are accurate, complete and suitable for analysis, with priority given to CDIs and checks that are not otherwise automated within the CDMS (or equivalent system). Further information on CDMS functionality can be found in SOP 14 and SOP 42.

The DVP should be developed following identification of CDIs and prior to database finalisation. Validation checks should be defined and executed by appropriately qualified members of the study team, with input from statistics and other relevant subject matter experts as required. The DVP should be documented and retained in the TMF. For WCTU-managed studies, the RAMP tool will capture this information.

The DVP should be reviewed and updated throughout the study lifecycle as required.

7.7 Monitoring Plan

The MP should take a systematic, prioritised, risk-based approach, that is appropriate to the study design. Monitoring activities should be proportionate to the identified risks, with particular focus on activities that could impact participant safety & rights, study integrity, data quality, study delivery or regulatory compliance.

The MP should be documented and retained in the TMF (within the RAMP tool for WCTU studies) and describe:

- The extent, nature and frequency of monitoring activities
- Monitoring metrics, QTLs, and associated actions
- The responsibilities of those involved in monitoring activities.

The MP should be developed and reviewed by people with an appropriate level of knowledge about the study. Consideration should be given to monitoring critical data and any aspects of the study that fall outside of SOPs.

QTLs should be considered and defined to identify systematic issues that may impact participant safety or the reliability of study results. Monitoring metrics that exceed predefined QTLs should trigger review and escalation to the CI or TMG, as appropriate. For more details see **G06**.

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7.8 Types of Monitoring, Conduct and Competency

Various approaches may be used e.g. central monitoring, remote monitoring, on-site monitoring, triggered monitoring and site self-monitoring checks. Monitoring activities should be conducted in accordance with the study MP and should clearly define responsibilities, methods, frequency and escalation arrangements.

Central Monitoring
Performed away from the investigator research site, usually at the CTU/Sponsor's office. It involves an evaluation of accumulating data, performed in a timely manner. These data are examined by qualified and trained persons such as the data entry clerk, TM/TC or statistician, to identify anomalies, outliers or deviations and inconsistencies. All activities should be clearly defined and documented upon completion, with evidence of any findings and escalation.

***On-site Monitoring**
Performed at researcher sites where the study is being conducted. It requires access to medical records and other source documents of study participants for the purpose of source data review (SDR) - to ensure compliance with the protocol and GCP, and source data verification (SDV) - to confirm the accuracy of data transcription and to verify the existence of participants. On-site visits may be routine or triggered.

***Remote Monitoring**
Follows the same principles as on-site monitoring but performed at a location away from the Investigator site. This may be in the form of a telephone or MS Teams video call with the site, via a self-monitoring checklist or through requesting copies of study documents/redacted source data. This may also include direct access to electronic healthcare records, if appropriate security measures are in place. This may be the initial approach for a routine or a triggered monitoring visit and has the potential to be escalated to an on-site visit if required.

*Where remote or onsite monitoring will be conducted, Investigator sites should be provided with clear information regarding monitoring expectations, usually communicated during site activation processes. Guidance may be provided to support source documentation and study record keeping, irrespective of whether source data verification is planned. (G16). Specific monitoring tools and checklists may be developed where appropriate (T58).

Individuals conducting monitoring activities must be appropriately trained and have sufficient knowledge relevant to their assigned responsibilities. Appropriate training may include study specific training, SOP training and supervised practical experience. Evidence of training should be retained.

Monitoring-specific training resources are available from the UK Registered CTU Network.

On-site or remote visits involving more than one staff member may be undertaken for training, competency assessment or quality assurance purposes. Where a second individual is attending a remote or on-site visit, the site should be informed in advance of who will be attending, their role/job title and the purpose of their attendance. Monitoring may involve lone working, where this is the case, **T12** – Lone Worker Visit details should be completed and the monitor should familiarise themselves with the WMS lone worker guidance and follow the relevant procedures.

7.9 Monitoring Findings and Escalation

Monitoring activities may identify findings, trends, deviations, non-compliances, quality issues, or other risks requiring further investigation or action. Findings may arise from central monitoring activities, remote monitoring visits, on-site monitoring visits, data reviews, quality control activities, study oversight meetings, or other monitoring processes.

Monitoring findings should be documented and include sufficient detail to describe:

- The activity performed
- Findings identified
- Any associated risks or impacts
- Required actions
- The individual(s) responsible for completing actions
- Timelines for completion of actions

Monitoring findings should be communicated in a timely manner to relevant study personnel and where appropriate, investigator sites, the CI, TMG, Sponsor or other oversight committees.

For remote or on-site visits a report should be created to include the author, date, site, name of the monitor, and name of the investigator(s) or other individuals present, as well as a summary of what was reviewed.

For WCTU managed studies, an approved monitoring report template should be used where appropriate and should be reviewed by a QA Manager prior to sending to site, CI and Sponsor.

Actions arising from monitoring activities should be addressed within agreed timelines. Responsibility for oversight of actions should be clearly assigned and progress monitored until satisfactory resolution has been achieved.

Where action owners are unresponsive, or findings remain unresolved, escalation should occur in accordance with the study MP and applicable governance processes. For WCTU managed studies, the QA team can support these escalation strategies with support from the Governance Committee. Where concerns remain unresolved, the issue should be discussed with the CI to agree appropriate actions. This may include engagement with the site PI, discussion at the TMG, escalation through governance routes, suspension of specific activities, or consideration of site closure (where participant safety, data integrity or study conduct may be compromised).

Monitoring findings should be used to inform:

- CAPAs.
- Staff training requirements.
- Study process improvements.
- Updates to risk assessments.
- Review of monitoring activities and mitigations

Where monitoring findings indicate potential non-compliance, follow the procedures outlined in SOP 31 ‘Deviations, Violations, Misconduct and Serious Breaches of GCP and/or Protocol’.

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7.10 Triggered Monitoring

Triggered monitoring may be undertaken where study oversight activities identify indicators of increased risk. These may include data anomalies, repeated protocol deviations, delayed safety reporting, unusually high withdrawal rates, predefined QTL breaches, non-compliance investigations or other significant findings.

Triggered monitoring should be proportionate to the issue identified and focus on the relevant activity, process or issues of concern. Depending on the circumstances, this may be conducted remotely or on-site.

Findings arising from triggered monitoring should be documented, communicated and managed in accordance with Section 7.9.

8 Associated Templates and Documents

G06	WCTU RAMP Tool: Guidance
T19	WCTU RAMP Tool [Available from QA Team on request]
T18	Green Light to Commence Clinical Research Study form
T58	Trial Monitoring Checklist
T12	Lone worker visit details
G16	Source Data

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