UNIVERSITY OF WARWICK

STANDARD OPERATING PROCEDURE 04

Trial/Research Study Protocol

Version:	5.0
Approval Date:	08/07/2026
Effective Date:	22/07/2026
Review Date:	21/07/2028
Review Lead:	Greg Scott, QA Support Officer, WCTU
WCTU Reviewers:	Jill Wood, QA Manager, WCTU Donna Howe, Clinical Trial Coordinator, WCTU George Bouliotis, Associate Professor, WCTU
Sponsor Reviewers:	Mathew Gane, Research Governance & QA Manager, R&IS
WCTU approval:	Natalie Strickland, Head of Operations, WCTU
Sponsor approval:	Carole Harris, Associate Director Research Culture, Governance and Compliance, R&IS

Revision Chronology:	**Effective date:**	**Reason for change:**
Version 5.0	22 July 2026	Biennial review: Updated to new template. Updates in line with amended CT Regs and ICH E6 R3: Quality-by-Design as part of study and protocol design, built-in adaptability and risk mitigation. Amends to text to be more succinct and align with section content. Addition of new sections to make content clearer.
Version 4.0	15 March 2024	Biennial review: Format changes. Consideration of using cloud-based systems. Change from MIS to REALMS for NIHR studies. Refresh of the approval process.
Version 3.0	21 December 2021	Biennial review: Update to new format. Minor amends to text.
Version 2.2	16 August 2019	Biennial review: Minor amends to text, web links updated. Change to new format.
Version 2.1	17 January 2017	Biennial review: Minor amends to text, web links updated. Change to new format.
Version 2.0	31 July 2014	Format change. Addition of protocol writing template to include SPIRIT guidance.
Version 1.2	18 May 2010	Update web links.
Version 1.1	31 January 2008	Format change. Addition of text (protocol definition). Update web-links.
Version 1.0	March 2006	

UNIVERSITY OF WARWICK

CONTENTS

1 Purpose and Scope

The purpose of this SOP is to outline the elements that should be included in a clinical trial or research study protocol and the process for protocol development and sign-off. It is applicable to anyone involved in the protocol development process.

2 Acronyms

CI	Chief Investigator
COMET	Core Outcome Measures in Effectiveness Trials
COS	Core Outcome Set
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMC	Data Monitoring Committee
DMP	Data Management Plan
EQUATOR	Enhancing the QUAlity and Transparency Of health Research
HCP	Health Care Professional
HRA	Health Research Authority
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NIHR	National Institute for Health and Care Research
PPI	Patient and Public Involvement
PRO	Participant Reported Outcomes
RAMP	Risk Assessment & Monitoring Plan
QA	Quality Assurance
R&IS	Research & Impact Services
REC	Research Ethics Committee
SOP	Standard Operating Procedure
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
TM	Trial Manager
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee
WCTU	Warwick Clinical Trials Unit

3 Definitions

Protocol	A document that describes the objective(s), design, methodology, statistical considerations and organisation of a trial
Protocol Modification	A written description of a change(s) to, or formal clarification of a protocol
Quality-by-Design	A methodology that proactively designs quality into a trial to prevent errors that could significantly impact patient safety and data reliability
Critical to Quality	The specific processes, data points, and trial attributes essential to protecting participant safety and ensuring reliable, interpretable study results

4 Background

A well-written protocol facilitates an appropriate assessment of scientific, ethical, and safety issues before a study begins; consistency and rigor of study conduct; and full appraisal of the conduct and results after study completion. Protocols should be used for all research studies, not just clinical trials, and are especially important for projects involving the NHS or social care. All clinical trials or research studies within the NHS should have a full protocol regardless of whether they are funded or not.

The Medicines for Human Use (Clinical Trials) Regulations, as amended, has introduced a stronger emphasis on designing studies with Quality-by-Design.

Quality-by-Design means requiring engagement from all stakeholders (e.g., HCPs, patients, operational teams), putting a stronger emphasis on operational feasibility, and an explicit focus on minimising burden to trial delivery locations and participants. The process should include identifying critical-to-quality factors during setup that protect participants, ensure data and intervention integrity, and safeguard the trial's credibility.

5 Responsibilities

Chief Investigator (CI) (or delegate)	• Produce the protocol and gain the applicable approvals prior to use. This is usually in collaboration with other personnel e.g., Co-applicants, Senior Project Managers, Research Fellows, Statisticians, Health Economists, Quality Assurance Team, Trial Managers/Coordinators etc. • Responsible for the submission, approval and implementation of modifications • Responsible for documentation and assessment of any deviations from the protocol
Sponsor	• Review and approval of protocol prior to submission to authorities for approvals

6 When

It is good practice to produce the first draft during the study design phase and to do this concurrently with conversations about what is critical to quality and identifying critical risk items for the study as each process can inform the other. However, some funding bodies do require an abbreviated protocol (or detailed project description) to be submitted as part of the application process, so researchers must be aware of their funding bodies requirements. An approved version of the protocol should be in place throughout the life of the study.

7 How

The following template protocol writing documents are available on the WCTU website and should be used to ensure that all necessary items are included:

- **T15**: Protocol Writing Template Document non-CTIMP
- **T16**: Protocol Writing Template Document CTIMP
- Also see the HRA Qualitative Protocol Guidance and Template: HRA Protocol Guidance

The HRA website also provides further guidance on the requirements for protocols for CTIMPs.

Emphasis should be on operational feasibility to reduce protocol deviations and unnecessary modifications with built-in adaptability allowing for pre-defined adjustments without requiring formal amendments.

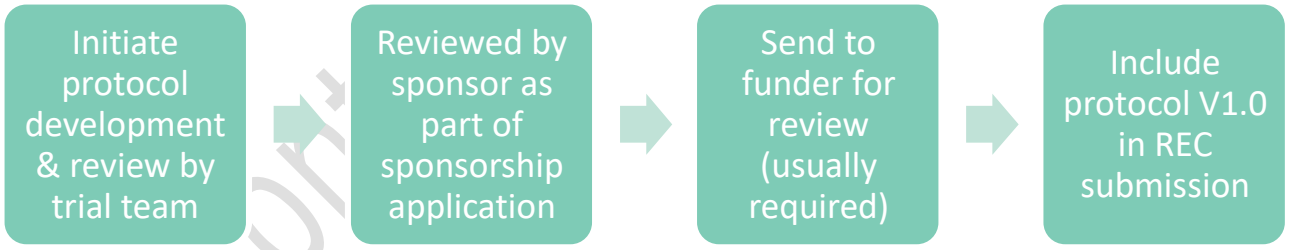
Risk mitigation should be built into the protocol design to identify and mitigate risks to participant safety and data integrity. This includes identifying critical-to-quality factors, their associated risks and risk mitigation in the trial and a summary of monitoring processes. These may be documented elsewhere e.g., RAMP, DMP, and referenced in the protocol.

Additional guidance for producing a protocol includes:

- The SPIRIT Initiative has the primary aim of improving protocol content. The main output is the SPIRIT 2025 Statement, providing guidance for key content and minimum recommended protocol items. Details and the content checklist are available online.
    - The SPIRIT recommendations support the development of high-quality, transparent, and complete study protocols. Following SPIRIT improves clarity and usefulness for all stakeholders, including investigators, participants, sponsors, funders, ethics committees, journals, registries, policymakers, and regulators.
    - Protocol writing templates have been developed which take the SPIRIT Statement into account, including SPIRIT PRO.
- The COMET Initiative (Core Outcome Measures in Effectiveness Trials) which brings together researchers interested in the development and application of agreed standardised sets of outcomes, known as a 'core outcome set' (COS).
- The equator network (Enhancing the QUAlity and Transparency Of health Research) contains guidelines for the reporting of all main study types.

Funding bodies may require different formats and review processes for protocols. Researchers should ensure they are aware of the funding body's requirements.

7.1 Procedure for the generation, review and approval of a research protocol



Protocols should be drafted (using the appropriate template) by an individual with an appropriate level of knowledge and experience. The draft document should be circulated for review by other personnel who have relevant knowledge or experience sufficient to comment on the content of the document (this may include but is not limited to: statisticians, health economists, QA staff, co-applicants, funding body, oversight committee etc.). Departmental consideration should be given to using a cloud-based system to facilitate simultaneous document review in a single location. Permissions to access/edit the file should be set appropriately.

The draft protocol should be sent to the sponsor for review as part of the sponsorship application.

If the project is funded by the NIHR, the relevant Programme Manager may also need to review the initial protocol before documents are submitted to the REC. Documents must be uploaded to the appropriate NIHR management system for review. All funding opportunities contain links to the relevant awards management system, so you can check the details of the funding opportunity if you are not sure which system to log into.

When, after appropriate review, the document is ready to be finalised, there should be a formal sign-off by the CI and those involved in its production and the new document changed to become version 1.0 **before** being submitted for ethical (and regulatory if applicable) approvals.

Sign-off should be in place prior to submission to authorities for approval with an agreed process for each study. An audit trail of the process should be retained using an appropriate system and retained within the TMF. This may include using the approval system in a SharePoint eTMF site, a paper or electronic review/approval form (**T09**), or email confirmation from appropriate staff using a professional (non-personal) email account. See **G33** Email Approval Guidance for more information.

For externally sponsored studies and/or non-NIHR funded studies, appropriate review and approval processes should be established on a case-by-case basis, ensuring adherence to the relevant sponsor's SOPs and the funder's requirements for the review of key study documents.

7.2 Statistical input to a research protocol

Best practice is that text within the statistics section of a protocol should be reviewed and checked by another suitably trained statistician and the checks documented.

For WCTU managed studies, documentation of double checks of elements of the statistics section of the protocol (and any subsequent modifications if changes to the section are required) will be evidenced with a clear audit trail (e.g. using a review/approval form or email approval following **G33**). The Statistical Processes for a Clinical Trial Checklist (**C13**) is also available to support this process.

7.3 Modifications to a research protocol

Where a **modification** to the protocol is required, the process described above should be followed for its generation, review and approval. It is good practice to prepare a summary of the changes, so that those undertaking the review can easily identify what changes have been made (this may be a table indicating page numbers or sections where amends have been made and details of the previous and new text). The WCTU protocol templates have a protocol version log where a summary of changes should be entered. Otherwise, consider adding an appendix to the protocol to provide a summary of the changes made for each version.

The TMG should discuss all modifications and identify if any other study documents or the Risk Assessment/Monitoring Plan will be impacted by the modification and ensure they are revised as appropriate (e.g. Participant Information Sheets, Consent Forms). The statisticians should also check that any modification does not impact on the statistical section, and approve any changes as required. This process should be documented.

See also SOP 6 'Modifications to Approved Study Documents' for further details.

If the project is funded by the NIHR, the relevant Programme Manager may also need to be made aware of any substantial modifications before documents are submitted to the REC. See section 7.1 for details on sharing documents with the Programme Manager.

7.4 Version control of a research protocol

The protocol should be version controlled (version number and dated) to ensure the current approved version is in use. The new version number must be added to the cover page and footer, with superseded versions listed on the protocol version log (also usually on the cover page).

Appropriate version control measures should be implemented to ensure distinction between each version (e.g., 1st draft = v0.1, second draft = v0.2, first approved version = v1.0, subsequent drafts = v1.1, v1.2 etc. until the final version is saved as v2.0). If a cloud-based system is used, consideration should be given to this process using automated version control. For more information see SOP 45 'Document Management'.

7.5 Terminology

A research study may be referred to as a 'trial' or 'study' as appropriate, but one or other term should be used consistently throughout the protocol.

The amended Clinical Trials Regulations now require the use of 'participant' rather than 'subject'.

The amended regulations have expanded the definition of who may act as an investigator and a chief investigator to now include 'health care professionals'. A list of who a 'health care professional' is defined as can be found in this HRA guidance.

8 Associated Templates and Documents

T09	Key Document Review/Approval Form
T15	Protocol Writing Template Document non-CTIMP
T16	Protocol Writing Template Document CTIMP
C04	Protocol Checklist
C13	Statistical Processes for a Clinical Trial Checklist
G33	Email Approval Guidance
Qualitative Protocol Guidance and Template – link to HRA website	