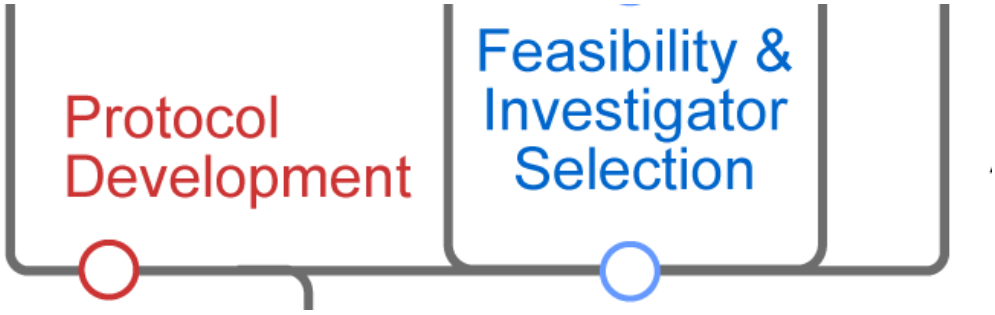
Routemap

Protocol Development



Trial Planning Phase

The Protocol Development station follows the Sponsorship station and takes place in a parallel process with R&D Consultation, the Funding Proposal, and Peer Review. Protocol Development precedes the Trial Management & Monitoring station. Protocol Development is a legal requirement which is relevant to all trials. This station is part of the 'trial planning phase' group of stations.

A protocol is defined in Part 1(2) of The Medicines for Human Use (Clinical Trials) Regulations 2004 as: "*A document that describes the objectives, design, methodology, statistical considerations, and organisation of a clinical trial*"

The protocol provides information on the background and rationale for a trial and outlines the study plan. The plan must be carefully designed to safeguard the health and safety of the participants, as well as answer the research question(s).

The protocol should describe all aspects of the trial but should also be written to be clear and concise and should also ensure that the trial avoids 'unnecessary complexity' (ICH GCP E6 R2). Protocols should include a definition of the 'end of the trial' (see End of Trial Declaration station) and information on post-trial care.

Protocols (and many other documents produced as part of a trial) should be controlled documents; version numbered and dated using a formalised convention.

Involvement of patients and the public (PPI) helps to shape fundamental aspects of the protocol to ensure it takes into account the needs of participants. Useful

information and resources about PPI can be found in the Trial Planning & Design station.

The NIHR Research Support Service (RSS) may provide support relating to aspects of protocol development such as trial design, choosing appropriate outcome measures and statistical input for researchers based in England.

To support researchers to develop high quality protocols, the Health Research Authority have produced protocol guidance and a template download to assist organisations and individuals to improve the consistency and quality of their CTIMPs. The template is in line with regulatory requirements and the SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials). Although the template is not mandatory, it contains all the elements that review bodies wish to consider, so protocols which have regard for the guidance and template are less likely to raise queries that can cause delays.

For non-CTIMP research, it is good practice for the protocol to include as much of the information in the topics/sections of ICH GCP E6 and the SPIRIT checklist, as relevant.

Both SPIRIT and the NIHR HTA Programme endorse the COMET database which contains information on published and ongoing core outcome set studies, and is regularly updated.

DIRUM is an open-access database of resource-use questionnaires for use by health economists involved in trial-based economic evaluations. DIRUM also provides a repository of methodological papers related to resource use and cost measurement.

Information on protocol review and signoff can be found in the Final Protocol station.

Further reading:

- Trial Registration station
- Final Protocol station
- Substantial Amendment station
- SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) is an international initiative that aims to improve the quality of clinical trial protocols
- Recommendations for the design of MAMS (multi-arm multi-stage) trials

- Gamble et al. (2017) recommend a minimum set of items that should be addressed and included in Statistical Analysis Plans for clinical trials.