

Information required in trial protocol

1. Contents of the protocol

The draft guidelines on the principles of good clinical practice in the conduct of clinical trials, ENTR/6416/01¹ section 8, recommends that the contents of a trial protocol should generally include the following information:

- General information
- Background information
- Trial objective and purpose
- Trial design
- Selection and withdrawal of subjects
- Treatment of subjects
- Assessment of efficacy
- Assessment of safety
- Statistics
- Direct access to source data/documents
- Quality control and quality assurance
- Ethics
- Data handling and record keeping
- Financial and insurance matters
- Publication policy
- Supplements.

2. Protocol identification: code number, version number, version date

a. Protocol code number

A protocol code number is required on each protocol. These code number must be unique. This number is used as the unique identifier for the protocol when the EudraCT number is issued and therefore a protocol code number should be allocated that is unlikely to have been used for other trials, e.g. trial acronym and year (MAG98).

Host institutions (Trusts, University etc) need to devise unique numbering systems for their protocols. Discuss this matter with your research services office or R&D department. Simple consecutive numbers like 1, 2, 3 should not be used as these are likely to be duplicated by other trials.

If an [ISRCTN](#), has been obtained for the trial then it is recommended that the number be used as the protocol code number. Alternatively, the grant reference number could be used, if applicable.

¹ http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2002/July/gcp_51_july.pdf

b. Protocol version numbers and version dates

It is advisable to allocate version numbers and version dates for protocols during the drafting process.

The final protocol that is submitted to the ethics committee should ideally be numbered version 1.0 and dated with the date of finalisation of the protocol.

If any protocol amendments are made, then the protocol version number and date must be updated accordingly.

Similarly, Patient Information Sheets and Consent Forms should be marked with the appropriate version numbers and dates.

3. Other guidance for good protocol development

a. Serious adverse events

In order to minimise unnecessary work, it is recommended that all expected adverse drug reactions and all expected serious adverse events are listed in the protocol (otherwise they will have to be reported as SUSARs).

Sometimes, unexpected adverse drug reactions and unexpected serious adverse events become 'expected' during the trial, in which case the protocol should be amended and such events would not need reporting. The Sponsor² and Chief Investigator and Data Monitoring Committee, if applicable, should determine whether any events become 'expected' during the course of the trial and apply for MHRA and Ethics Committee approval for a substantial amendment.

See [Pharmacovigilance Station](#)

b. Definition of end of trial

The sponsor must notify the MHRA of the end of a clinical trial within 90 days of its completion. The definition of the end of the trial must be provided in the protocol. Any change to this definition for whatever reason should be notified as a substantial amendment. In most cases, the end of the trial will be the date of the last visit of the last patient undergoing the trial. Any exceptions to this should be justified in the protocol.

NB Trialists can separate the treatment and immediate follow-up period from the long-term follow-up period, providing the follow up phase does not include

² The Sponsor is defined in the Directive as an individual, company, institution or organisation which takes responsibility for initiating, financing and /or managing a clinical trial. A group may take on the responsibilities of sponsorship and the UK Regulations are expected to specify how these responsibilities may be allocated/delegated to individuals or organisations responsible for specific aspects of the trial. See 'Quality Partnerships' for latest information on sponsorship.

any 'trial specific' tests, and define the end of the trial as the last treatment visit for the last patient. This will minimise the MHRA charges. Any long-term follow-up phase should be defined as a non-interventional phase in the protocol. Appropriate informed consent should be obtained at the start of the trial to ensure the participant is aware of both phases of the trial.

c. *Protocol amendments*

If the protocol is substantially amended after initiation, then there are certain procedures to follow. Protocol amendments must be reported and fees will apply. Therefore it is wise to minimise the likelihood of [protocol amendments](#) in the first version of the protocol, where possible.

It will be important to consider the strictness of the eligibility criteria and consider whether any flexibility should be incorporated into the protocol to minimise the need for protocol amendments that are considered substantial by the MHRA's definition, but that are not substantial in terms of the safety or physical or mental integrity of the subjects, the scientific value of the trial, the conduct or management of the trial and/or the quality or safety of any IMP used in the trial. For example, changing the age range in a trial from, say, 18-70 to 18-75 in order to increase the rate of accrual in a trial is less likely to affect the safety of a trial than a change in age range from, say, 18-70 to 14-70.