

Protocol Amendments

Protocol amendments are necessary when a sponsor wants to change a previously submitted protocol or to add a study protocol not submitted in the original IND.

For protocol amendments that introduce a new protocol should contain the protocol itself along with a brief description of the most clinically significant differences between the new and previous protocols.

Amendments that specify changes to previously submitted protocols are required when a sponsor seeks: (1) Phase 1 modified in a manner that significant affects the safety of the clinical subjects; or (2) a Phase 2 or 3 protocol modified in a manner that significant affects the safety of the subjects; the scope of the investigation, or scientific quality of the study.

Federal regulations provide the following examples of protocol changes requiring amendments:

- any increase in the drug dosage or duration of subject's exposure to the drug beyond that of the current approved protocol, or any significant increase in the number of study subjects;
- any significant change in the design of a protocol, such as the addition or deletion of a control group;
- the addition of a new test or procedure that is intended to improve monitoring for, or reduce the risk of, a side effect or adverse event, or the elimination of a test intended to monitor safety;
- the elimination of an apparent, immediate hazard to subjects (such change may be implemented prior to an amendment submission, provided that the FDA is subsequently notified through a protocol amendment); and
- the addition of a new investigator to carry out a previously submitted protocol (the drug may be shipped to the investigator and the investigator may participate in the study prior to submission of the amendment, provided the sponsor notifies the FDA within 30 days of the investigator's first participation in the study).

PLEASE NOTE: All amendments still need to be submitted, reviewed and approved by the IRB.

Content and Format

Protocol amendments must be prominently identified in one of three ways: “Protocol Amendment: New Protocol”, Protocol Amendment: Change in Protocol”, or Protocol Amendment: New Investigator. “

- New Protocol – A copy of the new protocol and a brief description of the most clinically significant differences between it and the previous protocol.
- Change in Protocol - a brief description of the change and reference (date and number) to the submission that contained the protocol.
- New Investigator – must include the investigator's name, the qualifications to conduct the investigation, reference to the previously submitted protocol, and all additional information about the investigator's study as is required under 312.23(a)(6)(iii)(b).

For certain protocol amendments, the FDA requires sponsors to reference to specific technical information in the IND or in a concurrently submitted information amendment to the IND that the sponsor relies on to support any clinically significant change in the new or amended protocol. If the reference is made to supporting information already in the IND, the sponsor shall identify by name, reference number, volume, and page number the location of the information.

A sponsor is required submit a protocol amendment for a new protocol or a change in protocol before its implementation. Protocol amendments to add a new investigator or to provide additional information about investigators may be grouped and submitted at 30-day intervals. When several submissions of new protocols or protocol changes are anticipated during a short period, the sponsor is encouraged, to the extent feasible, to include these all in a single submission.

For additional information about IND protocol amendments please review the following regulation on this topic (21 CFR Part 312.30):

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.30>