

Good Clinical Practice Q&A: Focus on Protocol Amendments

What is the difference between a protocol revision and a protocol amendment?

Protocol revisions are not formally defined in FDA regulations or guidance documents. Generally speaking, a protocol revision refers to a minor change to the protocol—one that has absolutely no impact on risks, clinical decision-making, procedures, or a subject's decision to enroll in a study. Such minor changes might include the correction of spelling mistakes, page renumbering, or changing the name of the corporate medical director. In general, these are administrative housekeeping changes that do not require much, if anything, in the way of an IRB or FDA review. In some cases, such a revised document is called an "administrative amendment."

Protocol amendments, on the other hand, are more significant in nature, and result from sponsor and investigator concerns about deficiencies in the protocol. Such changes would include the removal or addition of an enrollment inclusion/exclusion criterion, the addition of a lab test due to safety concerns, and changes to the definition of what constitutes an adverse event (e.g., certain percentage decreases in platelet counts).

Obviously, distinctions between the significance of certain changes—and whether they are considered revisions or amendments—are not always clear. Is a protocol change that increases the targeted number of enrollees from 500 to 550 a major change, for example? Some would argue that an increase in exposure to risks associated with unapproved drugs is always major, while others might consider the 10 percent increase in patient exposure to be benign and trivial given the universe of other, more significant, changes one might make to a protocol.

All protocol revisions and amendments must be submitted to an IRB, however. Some IRBs merely acknowledge their receipt, while others actively review and approve these changes.¹

Reference

1. "Good Clinical Practice: A Question & Answer Reference Guide", Barnett International, 2007, #7.2 p. 165

Source

"Good Clinical Practice: A Question & Answer Reference Guide 2007," is available for \$39.95 at <http://www.barnettinternational.com/>