

FDA Revises Compliance Program Manual for Sponsors; Adds Information on Foreign Inspections

The FDA revised its Compliance Program Guidance Manual for inspections of sponsors, contract research organizations and monitors (CP 7348.810) to include information on foreign inspections.

The manual was last revised in 2001. The FDA revised its manual for investigators in 2008 (see App. III and “FDA Revamps Regulatory Processes for Trial Investigators Who Fail To Comply,” May 2009, p. 18). The agency also is expected to update its manual for institutional review board inspections, which has not been updated since 1994.

The revised manual specifies that domestic inspection assignments are issued to the FDA district offices and international inspection assignments are issued to the Division of Foreign Field Investigations (DFFI). “International inspections of sponsors are generally assigned when the sponsor is located outside of the United States and an overall view of the conduct of the study, as provided at the sponsor site, is critical to decision-making on product approval,” the manual stated.

The revised manual also specifies the items that should be identified in the inspection assignment, such as the type and purpose of the inspection, the background materials, specific issues or concerns to be addressed and the due date of the completed establishment inspection report.

The new manual also goes into detail on the communications between the FDA product centers and the districts prior to an inspection, during an inspection and after an inspection. It also details the responsibilities of field investigators, inspection team leaders and headquarters participants.

The manual noted that “if there is disagreement among members of the inspection team, the issue should be discussed off-site and resolved cooperatively. Any difficulties in conducting team inspections should be discussed with both district management and the assigning center, and, if not resolved, immediately referred to the Division of Domestic Field Investigations for domestic inspections and DFFI for foreign inspections.”

It also discusses inspections of Veteran’s Administration sponsored FDA-related clinical trials.

Discussion of Classification Criteria

The new manual also provides additional information on the criteria that are relevant to the agency’s classification of inspections into no action indicated, voluntary action indicated and official action indicated (OAI).

“When applying the classification criteria,” the manual said, “center reviewers will evaluate the impact of the sponsor’s deficiencies on the general conduct of their clinical trials, with particular attention to the safety, rights and welfare of study subjects and the integrity of the resulting data.”

The manual now includes 12 examples of violations that “alone or in combination would be considered significant and may warrant OAI classification.”

The manual also has a new section on follow-up inspections that states that “centers should evaluate whether the violations found [in an inspection] indicate systemic problems with the conduct of the study or the reliability of the data and whether additional inspection assignments should be issued,” such as to the investigators participating in the study or an institutional review board.

The manual added that “following issuance of a Warning Letter, centers should be alert to information indicating that a Warning Letter recipient is the sponsor/CRO/monitor responsible for the conduct of other clinical

See *Manual*, p. 4

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