

## What's New in GCP? Lapse in IRB Approval Does Not Necessarily Have To Result in Trial Suspension or Termination

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The lapse of institutional review board (IRB) approval due to a failure to complete continuing review and obtain re-approval prior to expiration of the prior approval "does not automatically constitute a suspension or termination of IRB approval," an FDA draft guidance on IRB continuing review states.

However, the failure to meet continuing review obligations may be grounds for suspension or termination under 21 C.F.R. §56.113, "in particular where the lapse of approval is not the first to occur in a study. If the IRB notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions," the guidance said.

IRBs must report to the FDA any instance of serious or continuing non-compliance with the regulations or IRB requirements or determinations, and any suspension or termination of IRB approval (21 C.F.R. §56.108(b) (2) and (3), and 21 C.F.R. §56.113). The FDA evaluates the reports and inspects the site, investigator or IRB, as needed, to assess compliance with the human subject protection regulations.

### Suspension, Termination Criteria Listed

The guidance noted that IRBs have the authority to suspend or terminate approval of clinical investigations that are:

- not conducted in accordance with the IRB's requirements (21 C.F.R. §56.113); or
- associated with unexpected serious harm to subjects (21 C.F.R. §56.113).

"Suspension of approval may be appropriate when a significant issue is first identified and while the IRB investigates the matter," the guidance said. In addition, IRBs "may determine whether it is appropriate to notify subjects, and if so, when, given that complete information may not be available," the guidance added.

Any suspension or termination of IRB approval must include the reasons for the IRB's actions and be promptly reported to the clinical investigator, institutional officials, and the FDA (21 C.F.R. §56.113). When reporting suspensions or terminations of IRB approval to FDA, IRBs should include the:

- name of the drug, biologic, or device;
- investigational new drug or the investigational device exemption number/non-significant risk (NSR) status of the device;
- full name of the research protocol;
- name(s) and address(es) of the clinical investigator(s); and
- reason(s) for the suspension or termination.

When IRB approval of a clinical investigation is suspended or terminated, the FDA said the IRB should establish procedures to ensure that the rights and welfare of enrolled subjects

are protected, that subjects are not put at risk, and that subjects receive appropriate care during any period in which the IRB and clinical investigator are attempting to resolve the issues.

“For example, the IRB should determine on a case-by-case basis whether currently enrolled subjects should continue receiving the test article, be transferred to another investigator or site, or obtain care from a health care provider who is not part of the clinical investigation,” the guidance said. “Continuation of subjects on the test article may be appropriate, for example, when the test article holds out the prospect of direct benefit to the study subjects or when withholding the test article poses increased risk to study subjects. If the IRB decides that enrolled subjects should continue to receive the test article, it should also ensure that data collection (especially safety information) continues for such subjects.”

In addition, “if follow-up of currently enrolled subjects is necessary to ensure their rights, safety or welfare, the IRB should ensure that the investigators inform the subjects, and report any unanticipated problems to the IRB, the sponsor, and the FDA” (21 C.F.R. §56.108(b)).

### **To Find Out More**

The FDA guidance is available at  
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM197347.pdf>.

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