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What's New in GCP?
FDA Proposes Tighter Data Falsification Rules

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The FDA proposed amending its regulations Feb. 19 to require sponsors to report possible study data falsification to the agency within 45 days of becoming aware of the information.

"This proposal is necessary because ambiguity in the current reporting scheme has caused confusion among sponsors," the agency said, announcing the amended regulations that would cover pharmaceutical, biotech, device and food manufacturers, as well as dietary supplement makers and veterinary products (75 Fed. Reg. 7412). "It is critical that participants in the product development process assist FDA in detecting falsification of data."

The agency said the ambiguity of the present regulations related to: the extent to which possible falsification of data had to be reported to the FDA; the amount and type of information that sponsors must report when a study and/or an investigator's participation in a study has terminated; whose falsification of data must be reported; and the timing of reporting.

The revised regulations would require "sponsors to report information indicating that any person has, or may have, engaged in the falsification of data in the course of reporting study results, or in the course of proposing, designing, performing, recording, supervising, or reviewing studies that involve human subjects or animal subjects conducted by or on behalf of a sponsor or relied on by a sponsor."

The reporting requirement would cover before and after study completion, including after the review, approval or authorization of the affected product or labeling.

The requirement would be added to the FDA's regulations on good laboratory practice for nonclinical laboratory studies (21 C.F.R. Part 58), color additive petitions (21 C.F.R. Part 71), petitions for nutrient content and health claims (21 C.F.R. Part 101), premarket notification for a food contact substance (21 C.F.R. Part 170), food additive petitions (21 C.F.R. Part 171), dietary supplements (21 C.F.R. Part 190), investigational new drug applications (21 C.F.R. Part 312), new animal drugs for investigational use (21 C.F.R. Part 511), food additive petitions (21 C.F.R. Part 571), and investigational device exemptions (21 C.F.R. Part 812).

Help To Protect Human Subjects

The proposed rules are "intended to help protect research subjects by making it less likely that persons who falsify data will continue to conduct studies, come in contact with research subjects, or jeopardize the rights, safety and welfare of such subjects through unsound scientific practices," the agency said.

The FDA intends to use the information from sponsors "to identify patterns, potential signals, or other indications of misconduct, so that we can conduct further investigations. These investigations, in turn, may form the basis of administrative or enforcement actions, such as excluding clinical trials from consideration by FDA, placing a clinical trial on hold, or initiating disqualification of investigators or criminal proceedings." The agency added that "taking effective action in response to falsification could lessen the magnitude and impact of

the falsification in a current study, reduce the potential for delays or compromise to other studies and applications (including studies and applications from other sponsors for whom such a person might also be working), and protect the rights, safety and welfare of research subjects."

The agency listed several examples of falsification that would be reportable under the proposed regulations:

- Creating data that were never obtained (e.g., making up data or results and recording or reporting them; reporting enrollment in a study of a subject who did not exist; forging the signature on an informed consent form);
- Altering data by replacing original data with something different that does not accurately reflect study conduct or results (e.g., changing a laboratory measurement to a less extreme deviation from normal);
- Recording or obtaining data from a specimen, sample or test whose origin is not accurately described or in a way that does not accurately reflect the data (e.g., changing the date of a specimen, sample or test; adding a substance not called for in the study to a specimen or sample; identifying a specimen, sample or test as coming from a specific subject when it came from a source other than the subject); and
- Omitting data that were obtained and would be appropriate for recording based on study design and conduct (e.g., not recording exclusionary medical history or prohibited concomitant medications or treatments; omitting data so that a statistical analysis yields a result that would not have been obtained had all data been analyzed).

The announcement said sponsors would not be required to "specifically characterize the falsification" in reports to the agency. The FDA also "purposely" did not propose a specific "information threshold that must be met before the reporting requirements are triggered, such as the exact form, quality or reliability of information about possible falsification that would require a sponsor to report to FDA."

"Unintentional Errors" Are Not Reported

The FDA noted the proposed regulations are "designed to address falsification of data rather than unintentional errors in recording and reporting information." The agency is soliciting comments on whether to include additional descriptions of what the agency considers as "errors" and specific examples of such errors.

The agency said that the proposed rules "would not require a sponsor to determine definitively that data have been falsified, nor would [they] require that a sponsor determine the intent of the person who has, or may have, falsified data." The agency invited specific comments on whether the regulation "should specify some form of evidentiary standard or minimum threshold."

The FDA said that it does not intend to impose additional monitoring responsibilities under the proposed rules.

Under the proposed regulations, reports would include:

- the name of the person who has, or may have, falsified data;
- the last known address(es) and phone number(s) of that person;
- the specific identity of the potentially affected study, including, when applicable, application information, such as the application number, investigational protocol number, study title, study site(s), and study dates; and
- information suggesting that falsification occurred and describing the falsification.

The agency noted that it is considering whether to require additional information, such as the National Clinical Trial (NCT) number assigned to a study when it is registered with ClinicalTrials.gov.

Under the proposal, data includes, but is not limited to: individual facts, tests, specimens, samples, results, statistics, items of information, or statements made by individuals.

The regulations would apply to data from studies conducted by or on behalf of a sponsor or relied on by a sponsor. “Thus, it would apply not only to data from studies conducted by a sponsor, but also to data from studies not sponsored or conducted by a sponsor but cited in a petition, new dietary ingredient notification, or application to FDA in support of a claim, product marketing, or other regulatory action, such as reclassification of a device,” the agency said.

To Find Out More

The announcement is available at http://edocket.access.gpo.gov/2010/pdf/2010-3123.pdf.

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