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What's New in GCP?
FDA Issues Final Guidance on Electronic Source Data

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The FDA released final guidance on electronic source data in clinical investigations Sept. 18.

The guidance, which helps sponsors, clinical research organizations, and investigators ensure the reliability, quality, integrity and traceability of data, extends from electronic source to electronic regulatory submission. An earlier draft guidance dealt only with electronic source collection.

Examples of electronic data include clinical data initially recorded in electronic health records (EHRs) maintained by healthcare providers and institutions, electronic laboratory reports, electronic medical images from devices, and electronic diaries completed by study subjects.

As it did in the draft guidance, the agency said capturing source data electronically should help eliminate unnecessary duplication of data; reduce the possibility for transcription errors; encourage entering source data during a subject's visit, where appropriate; eliminate transcription of source data prior to entry into an electronic case report form (eCRF); promote real-time access for data review; and aid the collection of accurate and complete data. The final guidance adds another benefit — aiding the remote monitoring of data and extending those benefits to transmitting the data to the eCRF.

Unlike the draft, which said that sponsors and investigators should co-develop and maintain a list of all authorized data originators, the final guidance makes it clear that developing and maintaining the list is the sponsor's responsibility and should be made available at each clinical site. The final guidance adds that, "in the case of electronic, patient-reported outcome measures, the subject (e.g., unique subject identifier) should be listed as the originator."

The final guidance expands the FDA's discussion of direct entry of data into the eCRF and provides an example in which, at an initial visit, a clinical investigator might ask a subject about underlying illnesses and proceed to enter the illness(es) in an eCRF. During an FDA inspection, a record may be requested for evidence of testing or the use of medications to corroborate a diagnosis.

The final guidance noted that, "typically, images (e.g., CT scans) are not included as data elements in an eCRF, but rather the clinical interpretation of the image is included as a predefined data field. When an image is sent to a central reading center for clinical interpretation and the radiologist is authorized to enter data directly into the eCRF, the radiologist's assessment is the data element as predefined in the eCRF, the radiologist is the data originator, and the CT scan is the pertinent clinical record. However, when the radiologist sends a report to a clinical investigator(s), who transcribes the data into the eCRF, the clinical investigator(s) is the originator and the source is the radiologist's report."

The final guidance also goes into more depth regarding the transmission of data from patient-reported outcome (PRO) instruments to the eCRF, saying, "when a PRO instrument is used by a subject to transmit data elements directly to the eCRF, the subject is the data originator and the eCRF is the source. If a process is used by which the subject uses the

instrument to transmit data to a technology service provider database, the service provider database is the source," the guidance said.

The guidance states that "only a clinical investigator(s) or delegated clinical study staff should perform modifications or corrections to the eCRF data." The draft guidance said that modified and/or corrected data elements should have data element identifiers that reflect the date, time, originator and reason for the change. The final guidance said the modified and/or corrected data elements must have those data element identifiers.

The final guidance adds that, "automatic transmissions should have traceability and controls via the audit trail to reflect the reason for the change" and that "clinical investigator(s) should have the ability to enter comments about issues associated with the data. Sponsors should describe (e.g., in a data management plan) the electronic prompts, flags and data quality checks that are designed to address, for example, data inconsistencies, missing data, and entries out of range."

The final guidance also notes that the "use of electronic signatures must comply with 21 C.F.R. Part 11" and that "the clinical investigator(s) should provide FDA Electronic Source Data inspectors with access to the records that serve as the electronic source data." It also adds that, "in some studies, specific administrative data (e.g., code lists) might be exempt from review."

The final guidance emphasizes that "only those individuals who have documented training and authorization should have access to the eCRF data."

The FDA said, "adequate controls should be in place to ensure confidence in the reliability, quality and integrity of the electronic source data. The determination of whether a computer system used in a clinical investigation is suitable for its intended purpose might not be under the control of the clinical investigator(s) or sponsor (e.g., EHRs). The performance standards for these computer systems may be regulated by other authorities and under the control of, for example, healthcare providers or institutions. FDA does not intend to assess the compliance of EHRs with Part 11."

To Find Out More

The final guidance is available at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM328691.pdf.

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