COMPLIANCE NEWSLETTER 05/2016

Data Integrity 2016

Data Integrity is not a new issue, so why did the FDA issue Guidance this past April? The Warning Letters described in past issues of this newsletter often have poor data integrity, especially in connection with off-shore suppliers. But data integrity, i.e. "completeness, consistency, and accuracy of data", was also a sore point in the past with paper records. Inspectors always wanted to see and review everything that they thought could be relevant. Today with integrated IT systems and unlimited data collection, "everything" is potentially beyond anyone's ability to control, and integrated systems still need oversight.

Pragmatically, data integrity must remain focused upon record keeping. Unfortunately, this Guidance expands expectations for electronic records beyond what is required in the CFR Part 11 regulation for electronic records. It has adopted most of what the EU brought out in Annex 11, which fortunately is not actively enforced to the letter, and in the new MHRA Guidance on Data Integrity, (to be reviewed in the next issue).

Also important to note here, is that the FDA Guidance was issued by the drug enforcement wing of the FDA, and probably goes beyond the concerns of medical device enforcement, (CDRH).

What's New

- The ALCOA label, (attributable, legible, contemporaneously recorded, original or a true copy, and accurate), to describe data integrity expectations.
- Audit Trail definition: "a secure, computer-generated, time-stamped electronic record that allows for reconstruction of the course of events relating to the creation, modification, or deletion of an electronic record. An audit trail is a chronology of the "who, what, when, and why" of a record. "Why" was not specified to be recorded in Part 11. Many IT systems with an audit feature have not included a mandatory "why" field since this could require a mandatory user/machine entry with every data change.
- Definition Metadata: "the contextual information required to understand data", (not defined in Part 11). This is an open door to fault any record keeping scheme, since context can be broadly interpreted.
- Static vs. dynamic records. An example of "fixed-data" , i.e. static record is a paper record. The FDA still accepts an "electronic image" as a static record, although software for modifying images are commonplace. Dynamic records are only complete now when they have complete metadata and audit trails. The FDA seems to be avoiding addressing the complication, that dynamic records are often not stored as records and are created upon demand from the actual available data, using a reporting query.

- Formal review of audit trails, (as introduced in Annex 11) is narrowly interpreted to comprise a routine review as part of the review of the associated record.
- Validation of Workflows: When an IT system supports GxP relevant workflows, it is not sufficient to only validate the IT system. This is not a new expectation for firms with a business process orientation in their computer validation projects, but it can be interpreted to include the classic process validation expectations of consistency and repeatability, i.e. statistics.
- "True copies" of data or electronic records are expected to be in the "original format or in a format compatible with the original format". To be in compliance with the other expectations, true copies of dynamic records must include the audit trail and all metadata. A printout is practically excluded as a true copy for these kinds of records.
- Temporary records are not considered to be cGMP. "You must document, or save, the data at the time of performance to create a record in compliance with CGMP requirements."

Potential Impact

Because the FDA has retained its focus upon GxP records, it is important to also focus data integrity at this level, rather than at the level of electronic data. The electronic record should be the dominating context for any GxP data. This is at odds with some system designs, (e.g. SAP), but can be managed.

Audit trails have taken center stage again, because most electronic records are, from the definition in this guide, dynamic records. For systems which create records out of data with a reporting query (e.g. SAP), the data tables are considered to be relevant electronic records. Review of the audit trails of the data tables when reviewing and approving the GxP record would then be a GxP expectation.

Data first stored in a temporary file can be challenged if this data can be manipulated before storing it in a permanent record. This rules out business processes with local working files, (USB-sticks or files in the cloud).

True copies of electronic records in original format bring back the horror scenario commented upon in the Federal Register with the issuance of Part 11: "Persons should also be mindful of the need to keep appropriate computer systems that are capable of reading electronic records for as long as those records must be retained. In some instances, this may mean retention of otherwise outdated and supplanted systems, especially where the old records cannot be converted to a form readable by the newer systems."

Potentially affected by Data Integrity Issues?

Contact us for a Data Integrity Risk Assessment based on our Best Practice Methodology to establish your individual mitigation strategy and to take appropriate action. Our Risk Manager Training Package will enable you for execution.

No Warning Letters of Interest

The FDA website has cut back on the visibility of Warning Letters to the public. One can only browse back a few weeks in the current year. Past years are still viewable. Links to WLs given in newsletters distributed this year are still working. To be current now, one should check the "recently issued WLs" on the FDA site regularly. In the past weeks, the only relevant WLs were issued to national drug compounders and dietary supplement manufacturers.