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Compliance enforcement trends for the health care industry

Data Integrity 2016 (Part 2)

In the last issue the new draft FDA Guide on Data Integrity was reviewed and found to be a clear case of increasing regulatory expectations upon electronic recordkeeping. Still, it is not out of line with GxP expectations in the EU via Annex 11. In this issue, the recently released MHRA Guide on the same subject will be reviewed and compared to the FDA standpoint. Keep in mind though that the MHRA does not speak for the European Medicines Agency, as it is a UK agency, and we know how unified Europe is.

Perhaps to emphasize the EU´s much smaller footprint in compliance enforcement, the MHRA Guide stresses, "manufacturers and analytical laboratories are not expected to implement a forensic approach to data checking on a routine basis". What it doesn´t match in enforcement is certainly compensated for by it´s propensity to formulate expectations (e.g. 16 pages text vs. 9 text pages FDA).

New from the EU

Plenty of new terms and definitions of common terms are provided, (and can only be listed here): Data; Raw Data; Metadata; Data Governance System, Data Integrity, Data Lifecycle; Primary Record; Original record / true copy; Computer system transactions; Audit Trail; Archive; Backup; Flat Files; Relational Database. Many of these terms are in common usage, but now have an almost legal definition. Most are in harmony with the FDA´s usage, but 'viva la Difference';

Despite the FDA´s painstaking past efforts to delineate what electronic records are, the MHRA Guidance mixes it up with its definition of raw data; "Original records and documentation, retained in the format in which they were originally generated (i.e. paper or electronic), or as a 'true copy'." In the EU apparently a record is any data file, which the inspector would like to see;

Audit trails are not further defined except to note that they are to be considered as metadata. Here, the MHRA seems to go back to the original concept of metadata as, "data that describe the attributes of other data, and provide context and meaning", except that data and records are now in their eyes almost synonymous. The deadline for implementing required audit trails is the end of 2017 - no more "legacy" system exclusion after this date;

"A ‚flat file' is an individual record which may not carry with it all relevant metadata (e.g. pdf, dat, doc)." Pretty weird viewpoint, but it builds up the argument that printed records are usually incomplete (missing metadata), and therefore not "true copies". Perversely, flat files are compared with a relational database – "There is an inherently greater data integrity risk

with flat files (e.g. when compared to data contained within a relational database), in that these are easier to manipulate and delete as a single file", i.e. a forensic approach after all;

Within the context of data integrity, the MHRA guide includes many special concerns and situations, e.g.:

- Proximity of printers, clocks, and terminals with data access to areas where data is being processed;
- Limitations upon employment of scribes to record the activity of someone else;
- Assignment of a Primary Record, ("where data that are collected and retained concurrently by more than one method"). In the given example, a manually entered record is compared to an electronic data capture of the same data. Here it is expected that the electronic record is to be defined as the primary record, because it is presumed to be more accurate;
- Discrete transactions of critical operations so that a time stamp of each operation is recorded. "A critical processing step is a parameter that must be within an appropriate limit, range, or distribution to ensure the desired product quality." A typical example is weighing of a component;
- "Shared logins or generic user access should not be used." No exceptions are given for this point, except where the HW/SW doesn´t provide user management. An update is expected for such systems no later than the end of 2017.

Impact

Orienting upon either the FDA or the MHRA regarding data governance will not make much difference in the implementation of a "Data Governance System" because harmonization is evident. The new guidances place many difficult technical aspects back upon center stage again. Enforcement discretion appears to be drawing to a close. The risk of noncompliance has just turned another notch.

Warning Letters of Interest

Almost as if ordered, the recently posted WLs includes an Indian API manufacturer with plenty of data integrity concerns. Megafine Pharma Limited was caught with extensive data falsification, and got an import ban already in 2015. Although the WL includes a large "Data Integrity Remediation" section, specific technical aspects as found in the guidances, e.g. audit trails, are not delineated. It is left to the hired consultant to define the measures to establish data integrity.

The WL to Italian Corden Pharma Latina indicates that expertise in aseptic processing is still not basic to the industry. Clean rooms are supposed to have cleanable surfaces, but floors with tiles and floor drains are not considered cleanable in the sense of approaching sterility. Also sampling and monitoring for bioburden is not an optional aseptic task, but rather a central one. With such basic GMP problems, data integrity concerns appear to not even reach the inspector's agenda.