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Compliance enforcement trends for the health care industry

Novartis: Delivering Positive Patient Outcomes

Novartis has taken a strategy of moving the ball forward in the game of compliance, by pricing its drugs on the basis of positive patient outcomes. Rather than focusing on AMPs (average manufacturing prices), ASPs (average sales prices), and settling for low margins, it has negotiated pay-for-outcome agreements with US health insurance companies. Drug companies have been forced to provide post-marketing studies in the past years to provide evidence of safety. Now, Novartis has gone a step further to its own advantage by generating evidence of efficacy, in order to justify pricing. It shares now the risk of poor performance, and has to accept reduced pricing if the drug does not perform as expected. Here is the ISPE Novartis blog on the approach, which is sure to shake up the industry.

FDA Champions Safety and Effectiveness

Antibacterial soaps can no longer be marketed in the US. What other agency stands against industry for such a small issue to ensure safety and effectiveness? The press notice did not state that these soaps are a safety concern, but rather the manufacturers could not demonstrate improved safety and effectiveness, when compared to plain soap and water.

The Data Integrity Cauldron

In the compliance world this subject remains hot. The latest groups to spoon-in their positions are PIC/S and the EMEA. The new PIC Guide to GDocP, (good documentation practices), describes in detail some new terms, such as data risk and data criticality, and is a major contribution to the subject.

Almost forgotten is the security issue of system clocks, but is captured here: “General users should not have access to critical aspects of the software, e.g. system clocks, file deletion functions, etc.” This remains a problem with stand-alone computer installations.

The EMEA Q&As Data Integrity relies heavily upon the PIC/S Guide, (some text verbatim), but expands on some of its pet issues, such as managing blank forms and temporary files. The EMEA sees temporary files

as a data risk, since they usually can be manipulated without an audit trail. The widespread use of such files could be viewed as a major finding, (see below).

Pertinent to risk assessments, the PIC/S Guide suggests in section 11.2 a classification of data integrity deficiencies for inspectors to rely upon:

- A data integrity failure relating to fraud is "critical";
- Impact to product with risk to patient health is "critical";
- Impact to product with no risk to patient health is "major";
- No impact to product; evidence of widespread failure is "major";

The First Posted German Nonconformance Report

It appears now that the German regulators can also exert pressure, at least on a foreign entity, the Artemis Biotech site in India. 35 noncompliance observations are recorded, including 5 major ones, leading to a recommendation for an import ban from this API manufacturer:

- The ERP system hosts GMP data but is without QA oversight;
- Repackaging without documentation nor QA oversight;
- Inadequate control of labels for raw materials and product;
- QC lab without data integrity measures and QA oversight;
- Unacceptable computer validation of "Shimadzu LabSolutions".

Import Ban for German Medical Device Manufacturer

The WL to Spiegelberg basically lists the missing reports and documentation that the FDA expects from a firm marketing medical devices in the US. Such WLs to US firms are still common, but their products cannot be stopped at the border. Naturally, computer validation was also not documented. The firm's responses to the observations were generally inadequate, consisting basically of open promises to improve procedures and operations. An import ban cannot be considered a surprise in such a situation.

Other Warning Letters of Interest

The WL to Frontida BioPharm gives 3 examples that allow the FDA to determine a failure "to establish an adequate quality control unit" per regulation 21CFR211.22a:

- Release of potentially contaminated product;
- Inadequate investigation of stability failure;
- Discrepancies in cGMP-related records.

The last example is actually a universal problem, but at Frontida it was taken to ridiculous levels, including signing with only the first name, illegible entries, and cutting / pasting to create reports.

When novel Biotech meets GMPs, the outcome can look like the experience at Amniotic Therapies. The product is both a drug and a biological containing human tissue. The FDA needed almost a full page of the WL to Amniotic Therapies to define how these products are to be regulated. Classic concerns of hygiene and sterility of products seem to have taken this firm by surprise, which has also not registered its facility with the FDA.

The WL Unimark Remedies may be the first documented concern of "dirt and birds in the manufacturing area as well as a lizard in the controlled (b)(4) processing area", but it may not be the last from the developing economies.