COMPLIANCE NEWSLETTER 03/2017

Compliance enforcement trends for the health care industry

Deregulation

Donald Trump used the FDA as an example of over-regulation in his recent speech to Congress. The point taken was that new break-through medicines should not languish in a long approval process. Generalizing, he stated that per executive order under his administration, a new regulation will not be implemented unless it replaces 2 existing regulations. The relevant Code of Federal Regulations for the FDA, (Title 21) has moderately grown in the last 20 years, but compliance issues have grown dramatically with the proliferation of guidelines to these regulations. A significant decline in enforcement can only be expected if the FDA must reduce staffing. When Trump uses the FDA as an example, that may be in the cards.

The latest Mutual Recognizion Agreement between US and EU which enables utilization of each others GMP inspections of pharmaceutical manufacturing facilities might be key to lowering inspection costs and still assure inspections "in other parts of the world where there may be greater risk" (FDA News Release, March 2, 2017).

Voluntary Compliance

CDRH, the FDA division responsible for medical devices, issued a strategy plan for 2016-2017, in the final year of the Obama administration. The focus upon cooperation with industry instead of enforcement is either an experiment or an understated tectonic change, which would sit well with Trump. This may be reflected in the decline of Warning Letters issued by this agency. Whereas 10 years ago, the number issued was on par with those issued for drugs, only 1 or 2 per month is typical now. The new strategy includes a Voluntary Compliance Improvement Program (VCIP): "VCIP differs from the FDA's traditional oversight model by allowing firms to voluntarily self identify and correct possible regulatory violations instead of undergoing FDA inspection." Under Trump´s administration, this could be the new model of FDA enforcement.

Preparing for Brexit

The European Medicines Agency (EMA) has no plans for moving out of the UK, despite Brexit. However, some member states have expressed interest in hosting a new location. The FDA also has staff at the EMA headquarters. Conceivably, the EMA could remain in the UK after Brexit and is probably a bargaining chip in the negotiations. The final decision on EMAs future location will be made by the member states of the EU. The European commission secretary for the European Pharmacopoeia EDQM (European Directorate for the Quality of Medicines and Healthcare) is located in Strasbourg and is not affected by Brexit as UK is using the British Pharmacopoeia (BP).

Anti-Counterfeiting Update

Almost a year ago the status of serialization of drug products and the associated 2D-barcodes was reported, and the deadlines for implementation have not changed. 2D-Barcodes should be implemented in the US market by the end of the year and in the EU by Feb. 2019. Because verification of barcodes at the package level is currently slated for 2019 in the US, it appears like both initiatives are in the same time frame.

As the deadlines get closer, a closer look at the details makes sense. With 2D-barcodes, both regions have adopted a similar technology involving product codes and unique package serial numbers to 20 places. Given the option for alphanumeric characters, the potential number of possible serial numbers makes it unlikely that a number can be quickly guessed, (as long as used numbers are eventually decommissioned). Here again are links to the relevant legislation:

- EU Directive against Counterfeiting;
- FDA DSCSA Website (Drug Supply Chain Security Act);
- EU Commission's Questions and Answers document on safety features.

Key to the effectiveness against counterfeiting are secure databases which are needed to verify the package identifier. As can be seen in the recent DSCA Implementation Time Schedule and in the status report of the German pilot project SecurPharm, there are still many open issues which can impact upon effectiveness, such as:

- Limiting access to these databases to only authorized users, for which there will be a large number;
- Linking national databases, and/or creating a supranational repository;
- Maintaining these installations;
- Limiting exceptions to system use. For example, Belgium, Greece and Italy have the option to delay implementation by 6 years. Exported drugs are exempt from the EU legislation, and can become a huge potential source of falsified drugs.

There are important nuances to be aware of between these implementations. The FDA takes more interest in tracking and tracing of drug packages, and expects firms to maintain these records, (which can be the object of an inspection). Wholesalers must also keep these records to be in conformance with 21CFR205.50. In the EU, it is only the manufacturers who must maintain similar records, (Article 15). Generally, the EU legislation provides more technical details, and places more emphasis on detection of tampering. The requirement of the 2nd control element, an anti-tampering device is weighted equally with the unique identifier. It should inhibit reusing a registered package with a falsified medicine.

Also noteworthy is the EU requirement for complete audit trails of the repositories, but access to review these audit trails must be limited to the owners of the data, e.g. manufacturers, and to the authorities upon request, (Article 38). The focus here is upon protection of the proprietary information.

Warning Letters of Interest

The WL to Pfizer`s Hospira Inc. handles again the subject of particulate contamination in sterile injectables and their CAPA treatment, but also goes on to extensive problems of sterility control in aseptic manufacturing. FDA also noted in this recent warning letter, that similar cGMP violation have been cited at other facilities of Hospiras network in India, Australia, Italy, US.