



COMPLIANCE NEWSLETTER

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Compliance enforcement trends for the health care industry

Trump's Reorganization of the FDA

Trump's new administration now has a new FDA commissioner, [Scott Gottlieb](#), and he already has taken a first step in [restructuring the agency](#). The ORA (Office of Regulatory Affairs) was geographically decentralized, with most enforcement originating in the regional offices, as is quite evident from the source of Warning Letters. Regulatory enforcement should become more centralized and product-directed, as explained in this recent press release. This could have side-effects of more attention to global players, and more divergence between drugs and medical devices regarding GMP enforcement of common themes like data integrity.

The profile of S. Gottlieb reveals a focus upon economics in health care, which may have gotten him the job. The reorganization probably also has the goal of cutting operating costs. His [first directed action](#) is to bring more resources into fighting opioid abuse via prescriptions, which will put pressure on the health care providers while perhaps also reducing outlays for these drugs.

Office of Pharmaceutical Quality

Another FDA reorganization, already started under the Obama administration, was the [establishment of the OPQ](#) as an entity within CDER, as a partial replacement

of the Office of Pharmaceutical Science. "OPQ combines non-enforcement-related drug quality work into one super-office, creating one quality voice and improving our oversight of...drugs." Recently, this organization provided insight into [current compliance expectations](#). This presentation is almost completely focused upon data integrity and could be used as training on the linked Draft FDA Guidance on Data Integrity. The guide is a year old and was reviewed in the past May 2016 issue of this newsletter. From the examples given, the attention of the agency is upon laboratory records. Perhaps this focus explains the apparent lack of interest for data integrity at the CDRH, (the FDA agency regulating medical devices), as is evident in the lack of CDRH guidance about this topic and the lack of such CDRH observations in Ws. Laboratory records generally play a smaller role in the documentation of a device history record.

Brexit Positioning at the EMA

The [starting position](#) for the Brexit negotiations has now been laid out by the EMA. Basically, drugs and active ingredients originating in the UK will only be able to enter the EU via a registered importer or a licensed EU establishment. Batch release must also occur in the EU. Left unsaid, is the likelihood that exports to the UK from the EU would also be treated in this manner. Holders of existing marketing authorizations in the UK, obtained

via the centralized procedure, will need to transfer their licenses to an entity registered in the EU. Since this all takes time, the EMA is expecting the drug industry to proactively prepare for these revisions before the expected cut-over in March 2019, as explained in the [recent guidance](#).

Warning Letters Review

Excluding domestic compounders, the FDA issued in May:

- 2 Ws to foreign drug facilities;
- 6 Ws to domestic drug facilities;
- 3 Ws to domestic medical device manufacturers;
- 1 WL to a foreign medical device manufacturer.

The [WL to Huron Pharmaceuticals](#) illustrates additional concerns with COAs (Certificates of Analysis). The original COAs of the API manufacturers, along with the batch certificates, are expected to be included in the information passed on to customers. Supply chain accountability is not possible without this information. Further, Huron's own COAs were not reviewed before release.

[B. Braun Medical](#) received a WL for its site in California, which produces parenteral drugs in IV bags. Problems with leaking bags and particulates have been documented with Field Alert Reports and CAPA investigations, but have not been resolved. These are repeat findings from previous inspections, and an "Untitled Letter" was sent back in 2014. Now, escalated to a WL, the next step could be seizure and injunction.

The [WL to Swiss contract manufacturer Lonza](#) was sent to HQ, although the inspected site is in Maryland. Here, aseptic manufacturing and sterility testing expertise are needed to produce the class II medical devices. The FDA found plenty of problems in the validation of these methods, such as: lack of predefined acceptance criteria; poor sampling plans; lack of equipment and room qualifications / monitoring; lack of documentation of manual interventions (in the aseptic process); and missing cleaning validations. Apparently, HQ gave the right responses to the observations because all of them were documented to be either, "partially adequate" or "adequacy of the response cannot be determined at this time". Strangely, procedures allow for an operator to remain in the cleanroom up to six hours without exiting and re-gowning, but this extreme is not tested in the media fill testing protocols. (The candidate has yet to be found.)

Finally the [WL to Vertical Pharmaceuticals](#) cites the rare issue of PADE reports, (post-marketing adverse drug experience reports). Vertical acquired in 2014 at least some of the drugs that are missing these reports, and delegated reporting to a "Pharmacovigilance vendor". At least one of these vendors was out-of-business at the time of inspection. Three 15-day reports were documented to be late by months / years. Firms which grow via acquisitions, but have few internal resources, must have good control over their service providers to avoid such problems. Vertical merged into Osmotica Holdings in 2016, which further complicates the management issues.