

Compounding remains an FDA priority: Agency announces 2018 'Compounding Priorities Plan' and several compounding guidances, including guidance on 'essentially copies' and repackaging

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In January, FDA announced the release of its 2018 "Compounding Priorities Plan."¹ FDA also released several guidance documents in the wake of its announcement, such as its final guidance on essentially copies of commercially available drug products for Section 503A and 503B facilities, and guidance on repackaging of biologic products outside of an approved BLA.

FDA notes that "Our 2018 compounding policy priorities plan lays out how the agency will implement certain key provisions of the Drug Quality and Security Act and other provisions of the law relevant to compounders over the course of the coming year. Our policy will be part of a series of draft and final guidance documents, proposed and final rules and a revised draft memorandum of understanding (MOU) between the FDA and the states."

FDA is indeed busy in this area. The priorities include the following:

RISK BASED APPROACH TO MANUFACTURING STANDARDS FOR OUTSOURCING FACILITIES

FDA states its policy goal is to make it more efficient and lower cost for more compounding pharmacies to "voluntarily meet the higher production standards for 503B outsourcing facilities as a way to promoted more patient access to higher quality compounded medications."

Is FDA describing a "503B lite" standard for certain compounders that FDA Commissioner Scott Gottlieb hinted at last fall? Likely so. FDA states that it plans to issue proposed regulations addressing Current Good Manufacturing Processes (cGMP) requirements for outsourcing facilities.

In the meantime, however, it intends to issue revised guidance for cGMP – considering how it should apply quality standards given the differing size and scope of compounding operations. FDA's stated goal of these new requirements is to cajole more compounders to register as outsourcing facilities.

FDA states that the new draft revised cGMP guidance "will address standards critical to producing a high-quality product," while "balancing appropriate flexibility."

RESTRICTING COMPOUNDING OF DRUGS THAT ARE ESSENTIALLY COPIES OF FDA-APPROVED DRUGS

FDA announced the release of two Final Guidance Documents on compounding essentially copies of commercially available drugs.²

Although the Final Guidance documents do not seem to be materially different than what FDA released in draft form last year, FDA states that, as it moves forward with implementation and enforcement, the Agency "intends to focus its initial efforts on education and outreach" to practitioners and prescribers of compounds, who can determine whether the compounded product produces a significant or clinical difference for the patient than the commercially available product.

FDA also states it intends to prioritize review of those situations that will adversely impact the public health "such as compounding a drug using a bulk substance to produce a product than can otherwise be made by diluting an FDA-approved FDA drug according to its labeled instructions."

REGULATING COMPOUNDING FROM BULK SUBSTANCES

Not mentioning the litigation that FDA is facing in the D.C. District Court concerning whether its Interim Bulks Policy violates the Administrative Procedure Act, FDA discusses the "temporary" approach it took when implementing the interim bulks list for both 503A and 503B compounding in 2015, pending promulgation of the required final rule setting forth bulk substances that may be used in compounding. FDA again warns that it is exercising enforcement discretion concerning substances on the bulks lists.

It also states that it will continue to promulgate regulations under 503A (as it did in December 2016 addressing ten substances).



For 503B, FDA will issue (in March 2018), a draft guidance setting forth (for a third time...) criteria for making clinical need determinations for the list.

FDA states it intends to address concerns about compounding from bulk substances when the drug can be compounded from FDA-approved drugs. FDA emphasized that bulk drugs will be placed in the 503B bulks list only "when there is a clinical need to compound drugs using these substances.

It will be interesting to see whether FDA will require renominations of substances already on 503B's Bulks List 1.

SOLIDIFYING FDA'S PARTNERSHIP WITH STATE REGULATORY AUTHORITIES

FDA's announcement hints that a revised MOU under Section 503A between FDA and states (again in draft form) is forthcoming. FDA states that it will clarify "inordinate amounts" shipped interstate by a compounder if the "number of prescriptions of compounded drugs distributed interstate during any calendar month is great than 50 percent."

Importantly, instead of that number serving as a "hard limit, for state action," the 50 percent target will trigger certain reporting requirements.

The new MOU will also provide states more time to report to FDA, and flexibility on identifying when amounts are inordinate, considering the size and scope of compounding operations.

FINALIZATION OF BIOLOGICAL PRODUCTS GUIDANCE AND CLARIFYING OTHER POLICIES ON ACTIVITIES THAT COMPOUNDERS UNDERTAKE

FDA's biological products guidance was the subject of many comments, especially surrounding beyond use dating of these compounded products.

FDA announced that the new guidance is a "good example" of FDA's consideration of feedback in development of policies.

The final guidance describes a mechanism for outsourcing facilities to assign beyond use dates (BUDs) to repackaged biological products that exceed the "default" BUDs of 24 hours based on a "science and data-driven policy approach" to "support patients and their clinicians, while also protecting public health."

MISCELLANEOUS

Last but certainly not least, FDA states that it will issue guidance clarifying its "facility" guidance, and will address whether an outsourcing facility can be co-located with a Section 503A pharmacy (we thought the answer was "no" based on an earlier draft guidance³).

FDA will also soon issue long awaited guidance on repackaging radio-pharmaceuticals by a state-licensed pharmacies and outsourcing facilities. FDA will also reissue guidance describing "insanitary" compounding conditions.

Importantly, the insanitary conditions guidance will address concerns raised by pharmacies or prescribers that compound small quantities of drugs. FDA plans to "better define the circumstances" under which it believes drugs are being mixed and applied in a manner that creates "a negligible patient risk" (and thus such entities will not be subject to the same compliance policy under FDA's risk-based enforcement approach).

FDA will also update its rule setting forth withdrawn or removed drugs for reasons of safety or effectiveness.

Phew ... looks like FDA's compounding folks are in for an extremely busy 2018.

NOTES

¹ <http://bit.ly/2IbQZiM>.

² <http://bit.ly/2Ddmlw3>, <http://bit.ly/2oTaZi2>.

³ <http://bit.ly/2D9rj2x>.

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