

APC BRIEF: 503A and 503B Bulk Ingredient Lists

The Drug Quality and Security Act of 2013 (DQSA) established criteria for the active ingredients that “503A” traditional state licensed compounding pharmacies and “503B” FDA-registered outsourcing facilities can use in human compounding. Below is a short summary of the criteria for each and concerns APC has expressed with FDA about the procedure and substance of the ingredient nomination and approval process thus far. The FDA is also working on a “negative list” of substances that neither 503As or 503Bs can compound with because they have been removed from the market for safety reasons.

503A: The DQSA requires that 503A pharmacies use only substances that meet one of the following criteria be as active ingredients in compounding:

- Have an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph
- Are a component of an FDA-approved drug
- Are on the FDA’s 503A Bulk Substances List (sometimes referred to as the “positive list”)

Nominated substances are considered by the Pharmacy Compounding Advisory Committee (PCAC) that then makes recommendations to the FDA as to whether they should be included on the positive list through the rulemaking process (posted in the federal register for public comment before final). Although hundreds of substances have been nominated, only 10 have made it through the process and been accepted (6) or rejected (4) by FDA to date. While FDA works to finalize the list of substances for the positive list, an interim guidance document establishes FDA’s policy on three categories of nominated substances that determine whether the substance can be used while under consideration for the positive list. (link to GFI and categories here): <https://www.fda.gov/media/94155/download>.

APC’s main concern with the 503A criteria has been that FDA does not consider substance with a USP or NF dietary supplement monograph to be “applicable” for purposes of the criteria, and therefore have to be nominated for inclusion. APC has also expressed concerns that the PCAC and FDA have taken an overly restrictive view of the substances nominated and that the make-up of the PCAC has not included sufficient representation from community compounding pharmacists. (link to 503A positive list).

503B: FDA registered outsourcing facilities may only compound using substances that:

- Are used to compound drug products that appear on FDA’s drug shortage list at the time of compounding, distribution, and dispensing; or
- Appear on FDA’s list of bulk drug substances for which there is a clinical need.

The FDA has accepted nominations for substances for which there is a clinical need for compounding and through an interim guidance document, established criteria by which they will allow compounding by outsourcing facilities of some of the nominated substances while the list is finalized. (link to categories and GFI here): <https://www.fda.gov/media/94164/download>. APC has expressed concerns that FDA’s review of nominated substances for 503B bulks list has taken a very restrictive view of the “clinical need” determination in a way that greatly favors the use of finished (FDA-approved) product in compounding over bulk ingredients.

Comments or questions? Contact APC at info@a4pc.org.