What's Going on Legislatively, Judicially, and by way of Enforcement? A 2017 – 2018 Pharmacy Law Update:

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Governing Laws, Regulations, and Rules

503A "Traditional Compounder"	503B "Outsourcing Facility"
USP <795> and <797>	USP <795> and <797>
State boards statutes, regulations, and rules	State boards statutes, regulations, and rules, if applicable
But Note: FDA Compounding Policy Priorities Plan: 5 areas FDA intends to address before year-end to continue implementation of regulations and policies: (i) Quality standards for outsourcing facilities (503B) (ii) Restrictions on essential copies (503 A&B) (iii) Regulations for compounding bulk (503A & B) (iv) MOU with state authorities (503A) (v) Additional guidances for specific areas of concern	21 CFR Parts 210 and 211 (cGMP). But see One Policy Priority: Quality Standards • to make it more efficient & lower cost for more compounding pharmacies to voluntarily meet the production standards for 503B outsourcing facilities; • to issue proposed regulations on CGMP requirements that outsourcing facilities must meet • In the interim: revised draft guidance to describe new flexible, risk-based approach to CGMP, considering how CGMP should be applied in light of size and scope • The hope: smaller compounders will register under 503B, which will allow them to compound drugs with or without patient-specific prescriptions

Exemptions if ALL Statutory Conditions are Met

503A "Traditional Compounder"	503B "Outsourcing Facility"
Section 501(a)(2)(B) (current good manufacturing practice requirements)	Section 502(f)(1) (labeling with adequate directions for use)
Section 502(f)(1) (labeling with adequate directions for use)	Section 505 (new drug approval requirements)
Section 505 (new drug approval requirements)	Section 582 (drug supply chain security requirements)

Types of Compounders

503A(a) Compounding is by a Licensed pharmacist or physician in a	503B(a) & (d)(4)(B) Compounding is by or under the direct supervision of a
state-licensed pharmacy, or	licensed pharmacist in an outsourcing facility
federal facility, or	outsourcing facility, itself, is not required to be a licensed pharmacy
Licensed physician	But see New FDA Guidance re: Outsourcing Facility “Definition”

Prescriptions and Orders

503A(a)	503B(d)(4)(C)
"drug product compounded for an identified individual patient based on the receipt of a valid prescription order or notation"	WITH or WITHOUT prescription for identified individual patients
See FDA's final guidance on the prescription requirement, which appears to conflict with other statute provisions (i.e., the difference between dispensing & distributing)	Office use is clearly allowed
anticipatory compounding is different: limited quantities before receipt of RX and based on history between compounding pharmacist/physician and patient or physician/practitioner	

Bulk Drug Substances

503A(b)(1)(A)	503B(a)(2)
(a) comply with an applicable USP or NF monograph, if one exists, and the USP chapter on pharmacy compounding; OR (b) if USP/NF monograph does not exist, be a component of an FDA-approved drug; OR (c) if USP/NF monograph does not exist and the substance is not a component of an FDA-approved drug, appear on a list of bulk drug substances that can be compounded. See FDA's guidance	(a) appear on a list developed by FDA of bulk drug substances that can be used in compounding; See FDA's guidance; OR (b) the drug compounded from the bulk drug appears on FDA's drug shortage list at the time of compounding, distribution, and dispensing. **Comply with any USP/NF/compendium monograph, if recognized for 503B(a)(2)
Valid C of A	Valid C of A
Purchased from FDA registered manufacturer	Purchased from FDA registered manufacturer

Drugs Withdrawn or Removed from the Market and Drugs Presenting Demonstrable Difficulties for Compound

503A(b)(1)(C) and 21 CFR 216.24 (rule with list)	503B(a)(4) and 21 CFR 216.24 (rule with list)
• Shall not compound a drug product that appears on a list published by FDA in the Federal Register of drug products withdrawn or removed from the market because such drug products or components have been found to be unsafe or not effective.	• The Secretary has authority to include drugs on a list that cannot be compounded of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or ineffective.
503A(b)(3)(A). Requires an implementing regulation	503B(a)(6). Requires an implementing regulation
• May be compounded only if – such drug product is not identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product	• May be compounded if not identified on a do not compound list by FDA through regulatory process. • Can include drugs or categories of drugs that •present demonstrable difficulties for compounding reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug/ category, taking into account the risks and benefits to patients • OR is compounded in accordance with applicable conditions identified on FDA list that are necessary to prevent drug/category from presenting demonstrable difficulties.

Commercially Available

• Shall not compound, regularly or in inordinate amounts (as defined by the Secretary), any drug products that are essentially copies of a commercially available drug product.	• Shall not compound a drug that is essentially a copy of one or more approved drugs. • "approved drug" = a drug approved under 505 and not on the list of drugs or components withdrawn or removed as unsafe or ineffective (see last slide)
• "essentially a copy of a commercially available drug product" does not include a drug product in which there is a change, made for identified individual patient, which produces for that patient a significant difference, as determined by physician, between compounded drug and commercially-available drug. 503A(b)(1)(D) and 503A(b)(2) See also FDA's final guidance	• "essentially a copy of an approved drug" means: (a) drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to 503B or 505, unless the drug appears on the drug shortage list of 506E at the time of compounding, distributing, & dispensing OR (b) drug, component of which is a bulk drug substance that is a component of an approved drug or a marketed drug not subject to 503B or 505 unless there is a change that produces for an individual patient a clinical difference, as determined by physician, between compounded drug and approved drug. 503B(a)(5) and 503B(d)(2) See also FDA's final guidance.

Wholesaling

503A	503B(a)(8)
No language addresses it within 503A – however, state wholesaling language may be applicable.	• The drug will not be sold or transferred by an entity other than the outsourcing facility that compounded such drug. • This paragraph does not prohibit office use and the administration of a drug in a health care setting or dispensing a drug pursuant to a prescription. Note: methods for stability testing must be validated and vendors must be vetted

Labeling

503A	503B(a)(10)
No label requirement in 503A, but be sure to comply with State boards of pharmacy	Compounded products must be labeled: -- “This is a compounded drug” -- “Not for resale” or “Office Use Only”, when applicable -- Outsourcing facility contact information -- Drug specific information (see 503B(a)(1) for list of information required regarding the drug and the container) -- other information deemed necessary by FDA through a regulatory process

Registration and Listing/Reporting

503A	503B(a)(1)
No registration required, see 510(g) exemption: • maintain establishment in conformance with local law • regularly dispense prescription drugs, on prescriptions of licensed practitioners for patients under their care • do not manufacture, prepare, propagate, compound, or process drugs for sale other than in regular course of their business of dispensing or selling drugs at retail Note: identical inspection exemption, 347(a)(2)(A)	Per 503B(b)(1): Registration • Must register with FDA annually between October 1 and December 31 • Must indicate whether it intends to compound drugs that appear on the drug shortage list during the subsequent calendar year • FDA will make registration information of outsourcing facility available on its website See FDA guidance
No reporting requirement in 503A. For both, be sure to follow rules of state boards & DEA	Per 503B(b)(2): Reporting • Between June and December, must identify drugs compounded during previous 6 months and provide specifics about each drug (see 503B(b)(2) listing)

Fees and Adverse Event Reporting

503A	503B(a)(9) & (b)(5)
No fee requirement for 503A	• Annual inspection fees & reinspection fees: -- $15,000 if not small business -- $5,000 if small business ($1 million or less) • Note: separately responsible for state board fees if also registered as a pharmacy
No adverse event reporting requirement within 503A, but be sure to check y our state boards.	• Adverse event reports to FDA in accordance with the content & format requirements established through guidance or regulation under 21 CFR 310.305 (or any successor regulations). See FDA's final guidance

Interstate Distribution Limitations

503A(b)(3)(B)	503B(a)(9) & (b)(5)
Default Rule (no MOU): limits interstate distribution of compounded drugs to 5% or less of total prescription orders dispensed or distributed or more	No limitation within 503B.
2018 Compounding Policy Priority: New MOU 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 greater 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. FDA Website: FDA does not intend to enforce the 5% limit until issuing a final MOU and making it available to the states.	

Enforcement for the Last Year

Form 483s	Warning Letters	State Board Referrals
More than 30	About 5	About 10

FOR MORE INFORMATION
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