

SUMMARY OF S. 959, THE PHARMACEUTICAL QUALITY, SECURITY, AND ACCOUNTABILITY ACT

The Pharmaceutical Quality, Security, and Accountability Act contains two titles. Title I, “The Pharmaceutical Compounding Quality and Accountability Act,” establishes a clear boundary between traditional compounders and compounding manufacturers, which make sterile products without or in advance of a prescription and sell those products across state lines. It clarifies a national, uniform set of rules for compounding manufacturers while preserving the states’ primary role in traditional pharmacy regulation. Title II, “The Drug Supply Chain Security Act,” provides a uniform, national drug tracing framework to track prescription drugs from the manufacturer to the pharmacy and raises the standards for prescription drug wholesalers across the U.S.

TITLE I – HUMAN DRUG COMPOUNDING

Section 101: Short Title

“Pharmaceutical Compounding Quality and Accountability Act”

Section 102: Regulation of Drug Compounding

Clarification of New Drug Status

This section clarifies that compounded drugs are new drugs, and therefore the Federal Food, Drug, and Cosmetic Act (FFDCA) applies.

Section 503A: Drug Compounding

This section replaces Section 503A in the current FFDCA. It clarifies the scope of compounding, and defines compounding manufacturers, and traditional compounders, and the requirements on those entities; provides for exemptions from specified sections of the FFDCA for entities that comply with this section; creates a process for the Secretary to prohibit compounding of certain drug products; refines rules around the bulk chemicals that can be used in compounding; and establishes a fee structure to cover oversight of compounding manufacturers.

Scope and Definitions

The scope of traditional pharmacy compounding is drawn from current FFDCA Section 503A. A compounding manufacturer is defined as an entity that compounds a sterile drug prior to or without receiving a prescription and introduces such drug into interstate commerce, with the exception that interstate shipment within a hospital system will not cause a hospital pharmacy to be considered a compounding manufacturer. Any entity other than a hospital or health system, or an infusion pharmacy, that pools sterile products, or that repackages sterile, single-use, preservative-free vials would also be considered a compounding manufacturer. In order to maintain clear accountability, compounding manufacturers cannot be licensed as pharmacies. Any entity compounding a product that is not a registered compounding manufacturer or a licensed traditional pharmacy would be operating outside of the new Section 503A and would not qualify for the exemptions, making it subject to the requirements of the FFDCA. Section 503A does not apply to blood and blood components for transfusion, medical gases, or human cells, tissues and cellular or tissue-based products.

Exemptions from Requirements of FFDCA

Drugs compounded by traditional compounders that meet the requirements set forth in the revised FFDCA section

503A are exempt from the FFDCA requirements regarding Good Manufacturing Practices (Sec. 501(a)(2)(B)), adequate directions for use (Sec. 502(f)(1)), the new drug provisions (Sec. 505), and Sec. 582, the drug tracing provisions added in Title II. Prescription drugs compounded by compounding manufacturers that meet the requirements set forth in the revised FFDCA Section 503A are exempt from the FFDCA requirements regarding adequate directions for use (Sec. 502(f)(1)), Sec. 582, the drug tracing provisions added in Title II, and the new drug provisions (Sec. 505), but are subject to applicable Good Manufacturing Practices.

Drugs That May Not Be Compounded

After consulting with relevant stakeholders, the Secretary may promulgate through notice and comment a regulation that designates drugs that may not be compounded. The Secretary may designate drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of that drug or category of drugs, taking into account the risks and benefits to patients. Until the regulation is finalized, the Secretary may designate drugs that meet these criteria by notice following a 60-day comment period. This interim provision sunsets when the final regulation is effective or 5 years after the date of enactment, whichever occurs sooner. Every 5 years, the Secretary must seek public input on the need for compounded drugs to be included or excluded from the list of drugs that may not be compounded, although submissions and notices to update the list are also permitted between the 5-year intervals.

Drugs removed from the market for safety and effectiveness reasons may not be compounded.

Copies of marketed FDA-approved drugs may not be compounded from bulk except in the case of a drug shortage, in which case the compounder must submit a single notice to the Secretary within 3 days of beginning compounding. Variations of marketed-FDA approved drugs may be compounded only by traditional compounders and only upon receipt of a prescription and only if that variation provides a clinical difference for that patient, as determined by the prescribing practitioner, between the compounded drug and the comparable marketed FDA approved drug.

Biologics may only be compounded starting with a licensed biologic for a patient for whom the biological product produces a clinical benefit, as determined by the prescribing practitioner, upon receipt of a prescription or practitioner order specifying that the product may be compounded, or, for emergent use in pediatric patients, in anticipation of such a prescription. Compounding manufacturers may repackage a licensed biologic product without a prescription.

Products subject to Risk Evaluation and Mitigation Strategies (REMS) with elements to assure safe use can only be compounded under these exceptions if the compounder shows the Secretary it utilizes controls that are comparable to those in the REMS.

Bulk Ingredient Qualifications and Restriction on Wholesaling

The bulk requirements in current Section 503A are preserved, with one modification. Current law requires that any drug compounded from bulk must use bulk active pharmaceutical ingredient that 1) either complies with an applicable United States Pharmacopoeia (USP) or National Formulary (NF) monograph, is part of an FDA-approved drug, or appears on a list established by the Secretary; 2) is manufactured in a registered establishment; and 3) is accompanied by a valid certificate of analysis. The revised section 503A would permit the Secretary to identify a drug that only has an applicable USP or NF monograph as not suitable for compounding based on a public health concern taking into account historical use, reports in peer-reviewed literature, or other criteria identified by the Secretary following the publication of the reasoning and consideration of comments submitted to a docket open for at least 60 days. Inactive ingredients also must comply with the applicable USP or NF monograph if such a monograph exists.

Wholesaling is not allowed for compounded drugs. Compounded drugs may only be sold by the entity that compounded that product, and all must be labeled “not for resale”. It is a prohibited act to resell a product labeled “not for resale”.

Clarification on Office Use Requirements for Traditional Compounders

A traditional compounder may compound for office use after receiving a practitioner order from an identified practitioner that specifies that the drug must be compounded. No more than 10% of the total drugs dispensed in any 30 day period may be compounded drugs dispensed to fill practitioner orders. The traditional compounder must receive the names of all the patients who received the drug no later than 14 days after it was dispensed to the physician and must maintain these records for at least 6 years. There are safe harbors to protect traditional compounders acting in good faith who make reasonable attempts to comply with these requirements. The office use products must be labeled for ‘Office Use Only’ and ‘Not for Resale’, and must state that the product must be used within 14 days from the date of dispensing. Nothing prohibits a state from making more stringent requirements regarding office use. The reconciliation provisions may be waived for public health emergencies.

Compounding Manufacturer Requirements

A compounding manufacturer must:

- Give a pharmacist licensed in the state where the compounding manufacturer is located direct oversight over the products compounded;
- Once such a list is developed, compound only non-sterile drugs that appear on a list developed by the Secretary of non-sterile drugs that may be compounded by compounding manufacturers. This list will be developed through a notice published in the Federal Register following a 60 day comment period, and must take into consideration the non-sterile products being compounded by compounding manufacturers and whether the non-sterile drug fulfills a clinical need that cannot be filled by a marketed drug;
- Register as a compounding manufacturer. FDA will make available on their website a list of the name of each compounding manufacturer along with the state where the facility is located, whether the facility compounds from bulk drug substances, and whether drugs compounded from bulk are sterile or non-sterile;
- Report to the Secretary upon registering, and every 6 months thereafter, the drugs sold in the previous 6 months;
- Be inspected by FDA according to a risk-based inspection schedule;
- Report serious adverse event experiences within 15 days, and conduct follow up investigation and reporting similar to current drug manufacturers;
- Label products with a statement identifying it as a compounded drug and other specified information about the drug.

Compounding Manufacturer Establishment and Reinspection Fees

A compounding manufacturer would pay an annual establishment fee and, if necessary, a reinspection fee, to defray the cost of compounding oversight (e.g. inspections).

The fee is \$15,000 per year with an inflation adjustment. Small businesses, defined as compounding manufacturers with under \$1,000,000 in annual gross revenue, pay one-third of that fee. FDA would then adjust the fee for the larger facilities based on the number of small businesses. Fees can only be used for the inspection and regulation of compounding manufacturers.

The Secretary will provide an annual report to Congress on the fees collected from registration and reinspections,

a description of the hiring and placement of new staff, the use of fee resources to support inspecting compounding manufacturers, and the number of inspections completed in that fiscal year.

Increasing State and FDA Communication

The Secretary will encourage States to identify entities licensed by the State that appear to be entities required to be registered as compounding manufacturers, shall designate a point of contact at FDA for state boards of pharmacy, and establish a process for States to notify the Secretary of such entities. If the Secretary determines that the entity is a compounding manufacturer it will notify the State within 15 days, and will make the determination available on FDA's website. The Secretary will encourage direct communication between the states regarding traditional compounders.

GAO Reports

This section requires GAO to conduct a study on the quality of non-sterile and sterile drugs compounded within hospitals and health systems, to be submitted to Congress no later than July 31, 2016. It also requires the GAO to conduct a study on the safety of animal drug compounding, to be submitted to Congress no later than November 1, 2016.

Enforcement

Violation of Section 503A is a prohibited act under the FFDCFA. Reselling compounded drug labeled "not for resale;" failure to register or list products; intentionally falsifying prescriptions, practitioner orders or patient names required for reconciliation; and violating the office use provisions are also not permitted.

Section 103: Other Requirements Relating To Compounding Manufacturers

This subsection clarifies that a drug is misbranded if it is not labeled in accordance with this Act, if the advertising or promotion of such drug is false or misleading in any particular, or if it is made by a compounding manufacturer that has not paid fees as required. It also clarifies the pharmacy exemption in Section 704 inspection authorities would not apply to compounding manufacturers.

Section 104: Implementation

The Secretary must consult with stakeholders regarding implementation of everything within this title. Any regulations promulgated under this title must be done through the rulemaking process (no interim final rules) and the final regulation must be published within 18 months of the proposed regulation.

Section 105: Effective Date

The effective date of this title is one year from the date of enactment.

TITLE II – DRUG SUPPLY CHAIN SECURITY

Section 201: Short Title: "The Drug Supply Chain Security Act"

Section 202: Pharmaceutical Distribution Supply Chain

Section 581: Definitions

This section adds a new section to the FFDCA. This section sets forth definitions for the Drug Supply Chain Security Act (Act).

Section 582: Requirements

This new section in the FFDCA sets forth product tracing requirements for “downstream” pharmaceutical supply chain members: drug manufacturers, repackagers, wholesale distributors, and dispensers. These entities will be required to pass certain information and representations about pharmaceutical transactions when there is a change of ownership. Entities in the supply chain may only accept product if this information is provided. These entities will also engage in verification and notification activities in circumstances pertaining to suspect and illegitimate product. Once product is serialized, manufacturers, repackagers, and wholesale distributors will respond to requests to verify product at the unit level in circumstances pertaining to suspect and illegitimate product and must also verify product at the unit level for saleable returns. Third party logistics providers that warehouse or provide other logistics services, but do not take ownership of the product, will accept information from the owner of the product before taking possession, and alert the owner in the case of a suspect or illegitimate product.

Entities across the supply chain also must promptly respond to requests for information from the Secretary, or another State or Federal official, in the event of a recall or investigation of suspect or illegitimate product, and to keep records of investigations of suspect and illegitimate product. However, rather than imposing one-size-fits-all requirements, requirements are tailored to the supply chain members to reflect the different and unique roles that each sector plays in the pharmaceutical distribution supply chain. Four years after the date of enactment of this Act, manufacturers will provide transaction information, transaction history, and transaction statements in an electronic format to their trading partners. To further strengthen pharmaceutical supply chain security, not later than 1 year after the date of enactment of this Act, the trading partners of drug manufacturers, repackagers, wholesale distributors, third-party logistics providers, and dispensers must be properly registered or licensed.

The timeline for serializing product and accepting and transferring only serialized product is phased in: manufacturers are responsible for these requirements 4 years after the date of enactment of this Act; repackagers in 5 years; wholesale distributors and third-party logistics providers in 6 years; and dispensers in 7 years. This section also sets forth how grandfathered product will be addressed, both with respect to serialization and tracing requirements.

Section 203: Enhanced Drug Distribution Security

Section 582: Requirements

This section further amends Section 582, as added by this Act, to require interoperable, electronic unit level product tracing 10 years after the date of enactment of this Act. This section lays out an appropriate pathway to achieve unit-level traceability. The unit-level product tracing requirements are tied to guidance issued by the Secretary on unit level product tracing and standards for interoperable data exchange, which are informed by public meetings and pilot projects. Specific procedures for the issuance and revision of such guidance are set forth in this section.

The Secretary is required to contract with a private, independent consulting firm to conduct an assessment of the feasibility of unit level product tracing requirements on dispensers with 25 or fewer full-time employees. The Secretary, taking into consideration this assessment, shall provide for alternative methods of compliance, including establishing a process by which a dispenser may obtain a waiver from any of the requirements if the Secretary determines that such requirements would result in undue economic hardship. The Secretary is also required to establish one or more pilot projects to explore and evaluate methods to enhance the safety and security of the pharmaceutical distribution supply chain. The transaction history requirements sunset 10 years after the

date of enactment of the Act, when the interoperable, electronic unit level product tracing requirements begin.

Section 204: National Licensure Standards for Prescription Drug Wholesale Distributors

Section 503(e)/Section 583: Licensure Standards

This section amends Section 503(e) of the FFDCFA to increase the minimum wholesale distributor licensure standards under current law by regulation. Beginning 1 year after the date of enactment of the Act, any person who owns or operates an establishment that engages in wholesale distribution shall report to the Secretary, on an annual basis, regarding each State by which the person is licensed and the name and address of each facility at which the person conducts business. Not later than 1 year after the date of enactment of this Act, the Secretary shall establish a database that identifies each wholesale distributor by name, contact information, and the State where the wholesale distributor is licensed and make this database available on the Internet Website of the Food and Drug Administration. If a State chooses not to license a wholesale distributor to the standards set forth in the newly added Section 583 of the FFDCFA, the Secretary shall license qualified wholesale distributors in that State and collect reasonable fees to cover the costs of this licensing program. This section also makes clear that a third-party logistics provider is not required to obtain a license as a wholesale distributor. The amendments made in Section 4 go into effect 1 year after the date of enactment of the Act.

Section 205: National Licensure Standards for Third-Party Logistics Providers; Uniform National Policy

Section 584: National Licensure Standards for Third-Party Logistics Providers

This section sets forth new minimum third-party logistics provider licensure standards in the FFDCFA. Beginning 1 year after the date of enactment of the Act, a facility of a third-party logistics provider shall report to the Secretary, on an annual basis, regarding the State by which the facility is licensed and the name and address of the facility. If a State chooses not to establish a licensing program for a third-party logistics provider, the Secretary shall license the third-party logistics provider and collect reasonable fees to cover the costs of administering a federal licensing program for entities in such States. The Secretary is required to issue regulations regarding the minimum licensure standards, including establishing a process by which a third-party accreditation program approved by the Secretary, shall upon request by a third-party logistics provider, issue a license to a third-party logistics provider that meets the minimum requirements set forth in this Act. If the Secretary is not able to approve a third-party accreditation program because no such program meets the Secretary's requirements, the Secretary shall issue a license to a third-party logistics provider consistent with this section.

Section 585: Uniform National Policy

This section makes explicit that, beginning on the date of enactment of this Act, the product tracing requirements set forth in this Act preempt State product tracing requirements, including paper or electronic pedigree systems. This section also makes clear that, beginning on the date of enactment of this Act, no State may establish or continue any standards, requirements, or regulations with respect to wholesale prescription drug distributor or third-party logistics provider licensure requirements less stringent than the standards and requirements set forth in Sections 503(e) and 584. This section makes clear that pre-emption of product tracing shall not be construed to pre-empt State requirements related to the distribution of prescription drugs if such requirements are not related to product tracing as described in this Act.

Section 206: Penalties

This section amends Section 301(t) of the FFDCFA to add failure to comply with the requirements under Sections 582 and 584 as prohibited acts. It also amends Section 502 to make a product misbranded if it fails to bear a product identifier as required under Section 582.

Section 207: Conforming Amendment

This section makes a conforming amendment to Section 303(b)(1)(D) to update the cross cite in current law to wholesale distributor licensure requirements in Section 503(e).

Section 208: Savings Clause

This section makes clear that except as provided in the amendments made to wholesale distributor licensure requirements in Section 4(a) and the penalties in Section 6(a), nothing in this Act (including the amendments made by this Act) shall be construed as altering any authority of the Secretary of Health and Human Services with respect to a drug subject to Section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act under any provision of such Act or the Public Health Service Act.