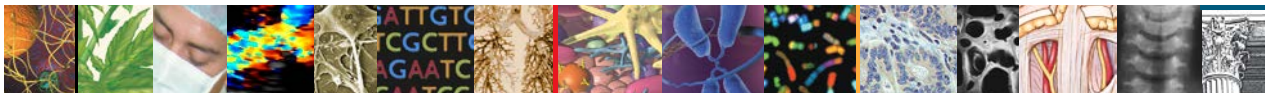

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Perspective

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The Drug Quality and Security Act — Mind the Gaps

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In November 2013, President Barack Obama signed the Drug Quality and Security Act, aimed at regulating compounding pharmacies and establishing a track-and-trace pedigree system for drugs. The law falls short of the mark on both counts. The new Food and Drug Administration (FDA) license for sterile drug compounders is entirely voluntary, and the track-and-trace requirement will be phased in over a decade, preempting a California law that would have taken effect many years earlier.

Compounding gained unwelcome attention after the 2012 fungal meningitis outbreak that was linked to the New England Compounding Center (NECC) in Framingham, Massachusetts. The Centers for Disease Control and Prevention (CDC) has now identified 751 confirmed or probable cases of fungal meningitis in 20 states, including 64 deaths in 9 states. Over the past year, beefed-up state and FDA inspections have uncovered substantial lapses at many large compounding pharmacies throughout the country.

The states with the largest death tolls from fungal meningitis did not routinely inspect out-of-state compounders, relying instead on pharmacies' home-state regulators. And it would not have been practical for inspectors from all 23 states receiving compounded drugs from the NECC to physically travel to Framingham for annual inspections. When states noticed problems with NECC products, coordination was lacking. In April 2011, Colorado filed a cease-and-desist order against the NECC, blocking sales in the state.[1] No fungal meningitis cases have been reported in Colorado, which speaks well of its regulators. But the Colorado order did not lead to quick action in other states, despite the fact that Colorado gave notice to both Massachusetts and the FDA. When compounders ship to dozens of states, no single state is in a position to adequately regulate.

Congress had responded once before, in 1997, with the passage of Section 503A of the Federal Food, Drug, and Cosmetic Act. Section 503A created a safe harbor for traditional local compounding pharmacies, exempting them from further FDA regulation. Congress distinguished traditional compounding from manufacturing on the basis of several features drawn from previous guidance documents, including whether the drug was advertised or promoted. In *Thompson v. Western States Medical Center* (2002), the Supreme Court struck down the provision prohibiting the advertising of compounded drugs, deciding that it violated the First Amendment. After that decision, the scope of the FDA's remaining authority under Section 503A was unclear.[2]

The Drug Quality and Security

Proposed Massachusetts Reforms.*

Proposed Reform	Comments
Unannounced inspections	With limited enforcement resources, inspections should be risk-based. Scheduled inspections fail to give a representative picture of conditions at the facility.
Mandatory reporting of serious adverse events	Federal law and most states do not require reporting of serious adverse events with compounded drugs, although they do require such reporting for other prescription drugs.
Separate licenses for sterile and nonsterile compounding based on current USP standards	Sterile compounding entails different risks, justifying a more complete regulatory system. Most states do not require full compliance with the relevant USP standards.
Transparent reporting of enforcement actions on a public website	Transparency will ensure that all regulators and customers can evaluate quality problems, even if they originate in other states, and give compounders a market-based incentive to improve.
Whistle-blower protections and rewards for employees of compounding pharmacies	The best source of information about quality problems is current employees. Under the federal False Claims Act, whistle-blowers may qualify for substantial rewards if a prosecution is successful.
Mandatory reporting of the volume and scope of compounding activities	Because registration as an outsourcing facility is voluntary, states should require disclosure of the type and number of drugs produced and where they are shipped and then share this information with the FDA, to permit the federal government to prioritize enforcement resources for the highest-risk compounders.
Disclosures on labels and consent forms	Physicians and patients deserve to know that a drug is compounded and whether it was produced in an FDA-regulated facility. This information should be on the label and clearly described in the patient consent form.
Full license requirements for out-of-state compounders shipping into Massachusetts	A compounder could avoid the new Massachusetts rules by relocating to a more lightly regulated state. With an out-of-state license, all compounding pharmacies selling drugs in a given state must meet the same quality standards.

* USP denotes U.S. Pharmacopeial Convention.

Act reenacts Section 503A with the advertising provisions removed. Traditional compounders can now operate without fear of federal enforcement. By inference, the FDA now has stronger authority to proceed against any compounder that exceeds the limits of Section 503A. These rules have been on the books since 1997 but have never been enforced, because of the *Western States* litigation. Now, after more than 16 years, the FDA can use Section 503A.

The more disappointing provision of the new law is found in Section 503B, which creates an optional new license for sterile compounders, to be known as "outsourcing facilities." This new license applies tougher standards than those applied to traditional compounders but is less stringent than the full rules applied to drug manufacturers. In the Senate bill, the outsourcing-facility license was mandatory, but the final act followed the House bill, making the license entirely voluntary. Over the past year, most of the debate in Congress has centered on how to draw the line between traditional compounding and activities that require the new license. The legislative compromise leaves that choice up to the compounder.

Few compounders will eagerly embrace the new license. Outsourcing facilities are subject to higher expenses than traditional compounders. They must comply with current Good Manufacturing Practices and, for the first time, report serious adverse events that occur with compounded drugs. Production and sales information must be provided to the FDA, and the company must pay a user fee for FDA inspections. If most large compounders opt out, Section 503B will have little effect.

If another tragedy similar to the one involving the NECC is to be avoided, additional action is needed. Public health requires new legislation in the states, robust enforcement by the FDA, and greater vigilance for patient safety by plans and providers.

First, states bear great responsibility for enforcement of compounding quality standards. Although a few states have modified rules in the wake of the 2012 fungal meningitis outbreak, most have not yet acted.[3] In light of the new federal law, state legislative reforms are now urgent. Many states do not mandate compliance with the sterile-compounding requirements found in U.S. Pharmacopeia Chapter 797. Most states do not carefully regulate out-of-state compounding pharmacies, nor do they systematically share enforcement and inspection reports. The FDA and Massachusetts enforcement actions against the NECC

began in 2004 but were not widely reported to other states, and information about them was not transparently available to health care providers. If these steps had been taken, the NECC might have seen reduced sales in out-of-state markets, prompting improvements in quality control.

Massachusetts accepted primary regulatory responsibility for the NECC tragedy and has spent the past year on appropriate responses, with major reports and proposed legislation from both the governor and the legislature.[4,5] Since the federal government has essentially ceded much of the regulatory landscape to the states, it is all the more important to ensure that state regulations meet minimum quality standards while not triggering drug shortages. Key features of the proposed Massachusetts reforms are described in the table. Each of these reforms plays an important role in the quest to improve the quality of compounded drugs. For example, the out-of-state license is important because otherwise a compounder like the NECC could avoid the new Massachusetts rules by relocating to a more lightly regulated state. With an out-of-state license, all compounding pharmacies selling in Massachusetts must meet the same quality standards.

Second, the FDA now has clearer authority, especially over outsourcing facilities, but will be successful only if other stakeholders support the FDA. For example, the new law did not provide any additional budgetary appropriations for inspecting compounders that do not register as outsourcing facilities. Congress needs to adequately fund this mission. In addition, registration as an outsourcing facility is voluntary. For compounders that fail to register, the FDA relies on states to regulate and share information.

Finally, rather than being passive in this process, providers and health plans could act to improve the quality and availability of compounded drugs. Purchasers can demand that their sterile-compounded drugs be sourced exclusively from outsourcing facilities regulated by the FDA. This decision could also be included in accreditation standards and reimbursement contracts. Such a market-based response would force compounders to accede to their major customers' demands and register with the FDA. Alternatively, if providers constantly seek out the cheapest compounded drugs, then the unregulated compounders will have an unfair competitive advantage and we can expect few compounders to seek FDA approval.

The Drug Quality and Security Act may have been a good first step, but patients will not be protected unless states, the FDA, and health care providers and plans act quickly to fill in the gaps left by Congress.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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Accelerating the Adoption of High-Value Primary Care — A New Provider Type under Medicare?

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A bipartisan, bicameral proposal from the Senate Finance Committee and House Ways and Means Committee to repeal and replace the Medicare sustainable growth rate formula (SGR) for physician payment would begin to reform provider payment to reward high-value care.[1] It calls for replacement of the SGR with a 10-year freeze on physician payment levels and, beginning in