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Kevin Outterson
Boston University School of Law

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Boston University School of Law Public Law Paper No. 13-61

Kevin Outterson
Boston University School of Law

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The Drug Quality and Security Act — Mind the Gaps

Kevin Outterson, J.D., LL.M.

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. 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 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 compounding pharmacy 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 re-

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### Proposed Massachusetts Reforms.

<table>
<thead>
<tr>
<th>Proposed Reform</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unannounced inspections</td>
<td>With limited enforcement resources, inspections should be risk-based. Scheduled inspections fail to give a representative picture of conditions at the facility.</td>
</tr>
<tr>
<td>Mandatory reporting of serious adverse events</td>
<td>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.</td>
</tr>
<tr>
<td>Separate licenses for sterile and nonsterile compounding based on current USP standards</td>
<td>Sterile compounding entails different risks, justifying a more complete regulatory system. Most states do not require full compliance with the relevant USP standards.</td>
</tr>
<tr>
<td>Transparent reporting of enforcement actions on a public website</td>
<td>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.</td>
</tr>
<tr>
<td>Whistle-blower protections and rewards for employees of compounding pharmacies</td>
<td>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.</td>
</tr>
<tr>
<td>Mandatory reporting of the volume and scope of compounding activities</td>
<td>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.</td>
</tr>
<tr>
<td>Disclosures on labels and consent forms</td>
<td>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.</td>
</tr>
<tr>
<td>Full license requirements for out-of-state compounders shipping into Massachusetts</td>
<td>A compounding facility 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.</td>
</tr>
</tbody>
</table>

* USP denotes U.S. Pharmacopeial Convention.
forms are now urgent. Many states
do not mandate compliance with
the sterile-compounding require-
ments found in U.S. Pharmacopoeia
Chapter 797. Most states do
not carefully regulate out-of-state
compounding pharmacies, nor do
they systematically share enforce-
ment and inspection reports. The
FDA and Massachusetts enforce-
ment actions against the NECC
began in 2004 but were not widely
reported to other states, and in-
formation 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 pri-
mary regulatory responsibility for
the NECC tragedy and has spent
the past year on appropriate re-
sponses, with major reports and
proposed legislation from both
the governor and the legisla-
ture. Since the federal govern-
ment has essentially ceded much
of the regulatory landscape to
the states, it is all the more im-
portant to ensure that state regu-
lations meet minimum quality
standards while not triggering
drug shortages. Key features of
the proposed Massachusetts re-
forms are described in the table.
Each of these reforms plays an
important role in the quest to
improve the quality of com-
ounded drugs. For example, the
out-of-state license is important
because otherwise a compounding
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 stake-
holders support the FDA. For ex-
ample, the new law did not pro-
vide any additional budgetary
appropriations for inspecting com-
pounders that do not register as
outsourcing facilities. Congress
needs to adequately fund this
mission. In addition, registration
as an outsourcing facility is vol-
untary. For compounders that
fail to register, the FDA relies on
states to regulate and share in-
formation.

Finally, rather than being pas-
itive in this process, providers
and health plans could act to im-
prove the quality and availability
of compounded drugs. Purchas-
ers can demand that their sterile-
compounders be sourced exclu-
sively from outsourcing fa-
cilities regulated by the FDA.
This decision could also be in-
cluded in accreditation standards
and reimbursement contracts.
Such a market-based response
would force compounders to ac-
cede to their major customers’
demands and register with the
FDA. Alternatively, if providers
constantly seek out the cheapest
compounded drugs, then the un-
regulated compounders will have
an unfair competitive advantage
and we can expect few com-
pounders to seek FDA approval.

The Drug Quality and Security
Act may have been a good first
step, but patients will not be pro-
tected 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.

From Boston University School of Law, Bos-
ton; and the University of Iowa College
of Law, Iowa City. Professor Outterson was
a member of the Massachusetts Special Com-
mission on the Oversight of Compounding
Pharmacies, tasked with proposing respons-
es to the NECC tragedy.

This article was published on December 25,
2013, at NEJM.org.

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DOI: 10.1056/NEJMep1314691
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