ELECTRONICALLY REPRINTED FROM JUNE 2013
Pharmaceutical Executive

Pharmacy Compounding: What's Ahead for Manufacturers

Compounders are under increased scrutiny following last year's spinal meningitis outbreak.

In October 2012, a spinal meningitis outbreak caused by a tainted steroid rocked the country, and drew national attention to the Massachusetts compounding pharmacy that prepared the drug. Ever since the incident, federal and state legislators have been struggling to determine whether they should ramp up regulation of compounding pharmacies—a debate resulting in new state legislation and the introduction of the Pharmaceutical Compounding Quality and Accountability Act in the US Senate on May 15. As laws are debated at the national and local level, drug manufacturers are also evaluating the impact that increased regulation of compounders will have.

The pharmacy that caused the deadly outbreak is the New England Compounding Center (NECC), which was preparing injectable drugs despite having been cited in the past for cleanliness and safety issues. The incident shined a light on the federal regulatory landscape—and, importantly, the lack of regulation over compounders preparing high-risk drugs.

Traditional compounding

Under the traditional definition of compounding, a compounder prepares products for patients who cannot take a drug in its FDA-approved form; for instance, patients who are allergic to an inactive ingredient, or patients who cannot take the drug as prepared by a manufacturer. Traditional compounding, which takes place in state-licensed and -regulated facilities, calls for drugs to be prepared based on individual, valid prescriptions.

Because traditional compounders prepare drugs in individual batches, it is difficult to regulate their products in the same way as manufactured drugs. Compounded preparations are patient-specific and each patient has a different set of needs. Therefore, it would be nearly impossible to require a new drug application (NDA) for each drug prepared by a compounder. For this reason, and because compounders have been successful in stymieing regulation at the federal level, the FDA has unclear and limited authority to oversee compounders. In fact, at this time, there is no federal registry of compounding pharmacies—many operate outside of the FDA's notice or reach.

In certain cases, compounders have used the lack of federal regulation to act as de facto manufacturers, preparing large batches of unapproved drugs without FDA oversight. Facilities have engaged in practices that are clearly outside of the bounds of traditional, patient-specific drug preparation: preparing drugs before receiving individual prescriptions, or making compounds that are essentially copies of FDA-approved products.

Impact on manufacturers

Compounders acting as manufacturers have long competed with drug manufacturers preparing FDA-approved products, which are patented and enjoy a period of market exclusivity. Since compounded products do not have to undergo the NDA process—and because the FDA does not have clear authority to dictate their ingredients—certain compounders prepare copies of FDA-approved products for far cheaper than their manufactured counterparts.

Increased use of compounded products comes at the expense of manufactured drugs' market share—particularly in the case of costly, complex drugs. The lure of compounded products is only strengthened by ever-tightening hospital budgets. As payers shift to capitated models, hospital purchasers are looking to cut back on costs—compounded drugs can be an easy way to achieve savings.

Compounding regulation

Compounding pharmacies are currently regulated at the state level, where boards of pharmacy oversee everything from licensing to cleanliness. However, because certain compounders are acting more like manufacturers, states are often ill-equipped to regulate such facilities. This is especially true in light of many states' tightening budgets. For instance, in Texas (which, along with Missouri, is one of two states that randomly tests compounded drugs),

Michelle McGovern is an Associate in the healthcare practice of Manatt, Phelps & Phillips, LLP. She can be reached at mmcgovern@manatt.com.

the number of pharmacies given random safety tests in the state has dropped by approximately two-thirds since 2010.

Until recently, federal legislation has been strongly opposed by compounding pharmacy stakeholders. An attempt to regulate compounders under the FDA Modernization Act (FDAMA) in 1997 was challenged in court because one provision in the law prohibited soliciting prescriptions and advertising any particular compounded drug. In 2002, the Supreme Court agreed that the soliciting and advertising prohibitions were impermissible restrictions on free speech, but did not decide on whether the remaining portions of the law that (among other things) prohibited compounders from acting as manufacturers and from making copies of FDA-approved products, could stand.

As a result, the decision of the Ninth Circuit (which heard the case before its Supreme Court appeal) striking down the remaining regulations on compounders became the national standard. In 2008, the Fifth Circuit took up the issue, and came to a different conclusion—that the compounding regulations that did not relate to advertising were enforceable. However, this holding applies only in the Fifth Circuit, which covers Texas, Louisiana, and Mississippi.

The regulation of compounding is split between the Fifth Circuit and the rest of the country, where the FDA's authority over compounders comes in the form of a compliance policy guide issued by the agency after the 2002 Supreme Court case. While it does not carry the force of law, the guide provides the FDA with the right to take enforcement action over compounders that cross the line.

The future of federal regulation

On May 15, and after months of committee hearings with FDA and public health officials, members of the Senate Health, Education, Labor, and Pensions (HELP) Committee introduced the Pharmaceutical Compounding Quality and Accountability Act. The proposed legislation would create a new class of compounders called "compounding manufacturers," who prepare drugs for shipment in interstate commerce. So-called compounding manufacturers would be prohibited under the proposed law from, among other things, preparing drugs that are copies of FDA-approved drugs. In addition, compounding manufacturers would be required to register with the FDA, and to pay establishment fees starting at $15,000 for fiscal year 2015. This would not only create the first list of compounding manufacturers—which would provide the FDA with critical information about the facilities that it needs to inspect—but it would provide the funding necessary for the FDA to regulate such facilities.

The bill also clarifies that compounded products are new drugs subject to the Federal Food, Drug, and Cosmetic Act (FDCA)—the law that regulates manufactured drugs—and states which provisions of the law apply to compounded products. Under the proposed law, compounders would not have to comply with all traditional manufacturing regulations, but they would be held to standards set by the FDA. Finally, the bill would require compounders to investigate and report adverse events.

The recently released bill, which has bipartisan support and has received comparatively little opposition from compounders in light of the spinal meningitis outbreak, appears to present the best opportunity for federal oversight to date. However, to become law, the bill requires support in the House, where some members assert that the existing compliance policy guide provides the FDA with all the oversight authority it needs.

While the fate of federal legislation remains unclear, states have been working to tighten regulation over pharmacy compounders. For instance, in the fall of 2012, Massachusetts enacted emergency regulations increasing the state board of pharmacy's oversight of compounders, and requiring board approval of the areas where compounders prepare complex injectable drugs. In March 2013, Florida changed its definition of "office use" compounding, limiting the amount of compounded products that compounders could prepare and deliver to physician offices or hospitals in advance of a valid prescription. Finally, in New Jersey, a new statute and a complete overhaul of compounding regulations have been proposed in recent months, in an attempt to provide clearer, more comprehensive regulation over compounding pharmacies.

Product liability

Tighter regulation of compounders could also have an impact on product liability claims, which—in certain cases—can impact manufacturers as well as compounders. When patients are harmed by a compounded product, the compounding pharmacy can be sued for product liability. In the case of the NECC, where approximately 50 people have died and more than 700 others have been treated for fungal infections, the volume of ensuing litigation has played a part in crippling the now-bankrupt facility. However, the threat of litigation has yet to stop many compounders from pushing the limits of production and crossing the line into manufacturing.

In certain states, liability does not stop with the compounder. In Tennessee, for instance, a statute permits patients to sue the sellers of a defective product if the manufacturer of that product is declared insolvent. Drug manufacturers who cooperate with compounders and provide active ingredients could also be at risk of product liability claims if issues arise with the compounded products.

Looking ahead

As federal and state legislators continue to focus their attention on compounding pharmacies, it's likely that new legislation—particularly at the state level, where regulations are easier to push through—will be enacted in coming months. Federal legislation is less of a sure thing, but compounders can count on increased attention from the FDA as the debate about the proper level of regulation and enforcement continues. PE

About the Author...

Michelle McGovern is an associate at Manatt, Phelps & Phillips, LLP, specializing in the healthcare industry. She provides advice on complex regulatory and compliance issues to pharmaceutical manufacturers, hospitals, health systems, managed care plans, community health centers, insurers and other healthcare stakeholders. She also structures and negotiates transactions for healthcare clients.

Prior to Manatt, Michelle was an associate in the healthcare practice of an international law firm. In that role, she advised clients on a range of healthcare-related issues, including Medicare and Medicaid programs, fraud and abuse laws, healthcare compliance audits and tax-exempt entity structure and formation.

Michelle earned a BS and MS in journalism from Northwestern University, as well as a JD from the Northwestern University School of Law. She holds bar admissions in New York, Washington, D.C. and Illinois.

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