

## PROFESSION

### Meningitis outbreak tests physician trust in compounding pharmacies

This isn't the first time compounders have been linked to safety problems. Physicians can seek out the rare accredited pharmacies or carefully question nonaccredited suppliers.

By **KEVIN B. O'REILLY**, *amednews staff*. *Posted Oct. 29, 2012.*

Michael F. Schafer, MD, a Chicago orthopedic surgeon, gives about 100 epidural steroid injections a year to help relieve back pain caused by conditions such as a herniated disk. So he was taken aback when news surfaced of a deadly fungal meningitis outbreak traced to steroids produced by a compounding pharmacy.

Dr. Schafer checked the source of the steroids he uses and found that they did not come from the drug compounder in question, Framingham, Mass.-based New England Compounding Center. His hospital, Northwestern Memorial, ordered the injectable methylprednisolone acetate from Pfizer Inc., which markets the drug as Depo-Medrol and has had no reported sterility lapses.

"I think now we've learned this is a potential problem," said Dr. Schafer, director of the orthopedic surgery residency program at Northwestern. "We're going to be more alert to where this material's coming from."

Across the country, doctors report facing questions from patients worried about the safety of their medications, especially those who receive steroid injections. Many pain clinics have seen a 25% rate of cancellations for steroid injections since the outbreak, said Robert Saenz, president of VIP Medical Consulting in San Antonio, which specializes in helping pain doctors avoid regulatory and medical liability problems.

Physicians and experts on pharmaceutical safety are urging doctors who rely on compounded medications to take care in choosing a pharmacy in light of a sterility lapse that has exposed an estimated 14,000 patients to the NECC's contaminated steroid. The Centers for Disease Control and Prevention and the Food and Drug Administration confirmed the presence of a fungus called *Exserohilum rostratum* in sealed, 80 mg/ml vials of preservative-free methylprednisolone acetate made by the compounding pharmacy.

As of Oct. 26, the CDC said nearly 340 patients in 18 states had been sickened, with 25 dying of meningitis. The medications, which were shipped to 76 health care facilities in 24 states, have been recalled. The NECC has suspended production.

The Massachusetts Board of Registration in Pharmacy released preliminary investigation findings Oct. 23, with evidence of a leaking boiler, dirty floor mats and other problems. State officials said they are moving to permanently revoke the company's licensure, as well as licenses of its top three pharmacists, and have launched a criminal investigation.

Compounded drugs account for an estimated 2% to 5% of U.S. prescriptions. Physicians often just order the compounded medications, leaving it up to retail pharmacies to secure them from pharmaceutical compounding specialists. But in many cases, pain specialists, dermatologists, sports medicine specialists, pediatricians and other doctors work directly with compounding pharmacies to obtain personalized medications to address the dosage and formulation needs of patients. For example, these pharmacists can create compounds for patients who are allergic to a medication ingredient.

#### How compounding pharmacies are regulated

About 7,500 pharmacies specialize in compounding, according to the International Academy of Compounding Pharmacists, a Missouri City, Texas-based organization that represents more than 2,700 professionals involved in drug compounding. An additional 8,200 hospital pharmacies also do compounding daily.

Unlike drugmakers such as Pfizer that must follow FDA-specified manufacturing practices, the safety and quality of compounding pharmacies is regulated by state pharmacy boards. Nearly every state incorporates all or part of U.S. Pharmacopeia standards on compounding sterile drugs such as injectables, as well as nonsterile medications such as topical anesthetics.

Ensuring that drug compounders follow USP standards is part of the process of earning accreditation from the Washington-based Pharmacy Compounding Accreditation Board, which handed out its first accreditation in 2006. David Ball, a spokesman for the International Academy of Compounding Pharmacists, said the academy considers the PCAB seal of approval "the gold standard and an important step for members to take." Yet only 162 drug compounders have earned the accreditation, said Joe Cabaleiro, RPh, the board's executive director. The NECC is not accredited.

The American Medical Association has policy stating that state pharmacy boards should require all compounding pharmacies to be accredited by the PCAB. No state has such a mandate, experts said. A bill proposed in New Jersey in October would require all pharmaceutical compounders licensed in that state to become accredited within 16 months of the bill's passage.

Accreditation is an important marker of patient safety, Cabaleiro said. The process involves verifying a pharmacy's licensure is

in good standing and an on-site evaluation to assess staff competency, facilities, equipment, records, procedures, ingredient sources and compound testing.

“The important thing for patients, prescribers and payers to know is that these pharmacies have gone the extra step and received external validation to meet national quality-control standards,” Cabaleiro said.

Short of accreditation, there are several essential questions physicians should ask of compounding pharmacies, experts said. Doctors should quiz pharmacies on their state licensure, history of infractions, drug recall procedures and how long they have been compounding various dosage forms. Another key question to ask is whether the pharmacy regularly tests its compounded preparations to ensure that the concentration on the container is what is on the label.

“Doctors can ask the pharmacy to show the test results on sterility, potency and endotoxins,” Cabaleiro said. “Pharmacies should be able to have some program to demonstrate this — it’s not an unreasonable question.”

Drug compounding has an important place in medical treatment, so long as the correct safety protocols are followed, said Timothy Deer, MD. He uses compounded medications in his Charleston, W.Va., pain medicine practice. One use is for infusion therapy for a patient with cancer-related pain who requires a mixture of two drugs, he said.

“If you have a patient need that is medically appropriate, then it makes perfect sense to use a compounding pharmacy that is accredited and has to adhere to high standards of pharmaceutical safety, infection control and concentration control,” said Dr. Deer, who sits on the American Academy of Pain Medicine’s board of directors. “If it’s not accredited, the doctor must ask himself whether he needs to use that compounded drug.”

The NECC case is reminiscent of another compounding incident that made negative headlines in 2002. In that instance, the CDC traced a fungal meningitis outbreak that sickened five patients to a contaminated steroid produced by a South Carolina compounding pharmacy. One of the physicians involved in treating those 2002 patients, John Perfect, MD, said the 2012

outbreak is a painful reminder of the importance of sterile compounding. He said it is clear that pharmaceutical compounding regulations need to be revisited.

“With 20/20 hindsight, not as a physician but just as a layperson, I would ask, ‘Why didn’t we fix this?’” said Dr. Perfect, chief of the division of infectious diseases at Duke University Medical Center in Durham, N.C. “This should have been prevented.”

The CDC and the FDA continue to investigate the NECC case. Meanwhile, the U.S. House Energy and Commerce Committee is conducting its own investigation, and several Democratic and Republican members of the committee have called for hearings on pharmaceutical compounding safety. The Drug Safety Enhancement Act of 2011, proposed last year, would require on-site FDA inspections of compounding pharmacies at least once every four years. It was referred to the Commerce panel’s health subcommittee and has not seen further action.

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#### ADDITIONAL INFORMATION:

### What it takes to become an accredited compounding pharmacy

Physicians sometimes order directly from compounding pharmacies to obtain specialized dosages or forms of medications that are not otherwise commercially available. Experts advise ordering from a pharmacy recognized by the Pharmacy Compounding Accreditation Board. As part of the accreditation process, the board:

- Verifies that the pharmacy is properly licensed in each state where it does business.
- Verifies that the pharmacy does not have outstanding state pharmacy board sanctions for issues related to compounding quality, public safety or controlled substances.
- Conducts an extensive on-site evaluation.
- Assesses the pharmacy’s system for assuring and maintaining staff competency.
- Reviews facilities, equipment, records and quality procedures.
- Verifies that the pharmacy uses ingredients from Food and Drug Administration-registered or -licensed sources.
- Reviews the pharmacy’s program for testing compounded preparations.

Source: “Choose an Accredited Pharmacy Fact Sheet,” Pharmacy Compounding Accreditation Board ([pcab.org/cms/wp-content/uploads/2012/03/How-to-Choose-an-accredited-pharmacy-fact-sheet.pdf](http://www.pcab.org/cms/wp-content/uploads/2012/03/How-to-Choose-an-accredited-pharmacy-fact-sheet.pdf))

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#### WEBLINK

Centers for Disease Control and Prevention investigation on multistate fungal meningitis outbreak ([www.cdc.gov/HAI/outbreaks/meningitis.html](http://www.cdc.gov/HAI/outbreaks/meningitis.html))

“Iatrogenic Fungal Meningitis: Tragedy Repeated,” *Annals of Internal Medicine*, Oct. 18 ([www.ncbi.nlm.nih.gov/pubmed/23080380/](http://www.ncbi.nlm.nih.gov/pubmed/23080380/))

“JAMA Update on Fungal Meningitis Outbreak,” *The Journal of the American Medical Association*, Oct. 17 ([jama.jamanetwork.com/SS/fungal\\_meningitis\\_outbreak.aspx](http://jama.jamanetwork.com/SS/fungal_meningitis_outbreak.aspx))

“New England Compounding Center (NECC) Preliminary Investigation Findings,” Massachusetts Board of Registration in Pharmacy, Oct. 23 ([www.mass.gov/eohhs/docs/dph/quality/boards/necc/necc-preliminary-report-10-23-2012.pdf](http://www.mass.gov/eohhs/docs/dph/quality/boards/necc/necc-preliminary-report-10-23-2012.pdf))

Pharmacy Compounding Accreditation Board’s fact sheet on choosing an accredited pharmacy ([www.pcab.org/cms/wp-content/uploads/2012/03/How-to-Choose-an-accredited-pharmacy-fact-sheet.pdf](http://www.pcab.org/cms/wp-content/uploads/2012/03/How-to-Choose-an-accredited-pharmacy-fact-sheet.pdf))

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