Current Perspective

Ophthalmology and Compounding Pharmacies

Last fall, ophthalmologists were horrified as more than 500 people developed fungal meningitis from contaminated steroids compounded at the New England Compounding Center (NECC). Many of our fellow ophthalmologists had a personal concern as well. They obtained medications, such as Avastin (bevacizumab), from NECC for intravitreal administration. Fortunately, no infections related to compounded Avastin have been reported in this case. NECC was shut down, and allegations surfaced of multiple breaches in good compounding practice and sterile technique. Patients died, suits were filed, and state and federal legislators and regulators vowed action.

This NECC tragedy followed multiple prior case clusters of endophthalmitis occurring after intravitreal injection of tainted compounded drugs. In 2005, patients at a Washington, D.C.–area Veterans Affairs hospital developed endophthalmitis from bacterially contaminated trypan blue ophthalmic solution. In summer 2011, over a dozen Miami-area patients developed streptococcal endophthalmitis following injection of contaminated Avastin obtained from a single compounding pharmacy. In early 2012, Franck's Compounding Pharmacy was implicated in an outbreak of more than 30 cases of endophthalmitis associated with use of two different intravitreal medications.

The FDA has long been concerned about the compounding pharmacy industry. A 2001 study by the FDA revealed that 31 percent of compounded prescriptions analyzed for potency were subpotent. Similar studies conducted by state boards of pharmacy have revealed an alarming prevalence of errors, with final prescriptions ranging from the very subpotent to the dangerously superpotent. The FDA's concerns are not limited to drugs for human use. Franck's Lab compounded a vitamin supplement administered by injection to polo ponies during the U.S. Open Polo Championships in April 2009. After being injected, all 21 ponies collapsed and died.

The compounding pharmacy industry is complex. Compounding was initially envisioned as the "combining, mixing, or altering of ingredients by a pharmacist in response to a physician's prescription to create a medication tailored to the specialized medical needs of an individual patient." Only about 7,500 of the approximately 56,000 pharmacies nationwide refer to themselves as compounding pharmacies, and only about 3,000 compound sterile products. Of those, only about 180 are accredited by the Pharmacy Compounding Accreditation Board. They are generally not regulated by the FDA but by state pharmacy boards.

In recent months, the issue has taken on new complexity and urgency. The FDA has recommended new legislation that will give them jurisdiction over "higher-risk" compounding—loosely described as determined by type of product, amount being manufactured, interstate shipping, and dispensing to a third party.

The states have not been silent either. At the time of press, intense regulatory scrutiny has led to legislative activity in 15 states. In early December, ophthalmology offices in Georgia were visited by agents of the Georgia Drugs and Narcotics Agency, focusing on whether compounded Avastin was being dispensed pursuant to a patient-specific prescription. Although this apparently did not represent a change in regulations, it represented a change

DAVID W. PARKE II, MD
EXECUTIVE VICE PRESIDENT/CEO

in interpretation and enforcement of existing regulations.

For ophthalmologists, while the general framework of the proposed tightening of regulations makes sense, it leaves open to interpretation the issue of anticipatory demand. How will we meet the emergent need for antimicrobials compounded for intravitreal administration in endophthalmitis cases if they are not compounded in advance? Will patients requiring Avastin be forced to wait until the compounding pharmacy ships the drug upon receipt of a valid prescription in their name? This may not only lead to delay of care but may also increase the burdens of cost and life disruption for patients and families. The American Academy of Ophthalmology has joined with other medical societies to sensitize the FDA, states, and Congressional leadership to these issues.

Ophthalmology's concerns are clear. When a physician administers a compounded medication, there must be a very high level of assurance that it is accurately compounded in a process that renders it free from microbial contamination and dangerous impurities. Existing systems have failed to provide uniformly high protection for patients and their physicians. New standards, regulatory oversight, and product testing must provide that protection. Concurrently and critically, however, regulations must not restrict the timely availability of medications when they may be urgently needed. Otherwise, patients may not receive the care they desperately need.

FOR ADDITIONAL INFORMATION

Report: Limited FDA Survey of Compounded Drug Products. Jan. 28, 2003. www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm155725.htm.

2006 Limited FDA Survey of Compounded Drug Products. Updated March 2010. www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm.

Wynkoop K. Compounded Products: Use, Regulation, and Risk. *OMIC Digest.* Fall 2012.