February 11, 2019

Scott Gottlieb, MD
Commissioner
Food and Drug Administration
Attn: Division of Dockets Management (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2014-D-0779 for "Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act."

Dear Dr. Gottlieb:

The American Society of Cataract and Refractive Surgery (ASCRS) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the revised draft guidance, "Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act."

ASCRS is a medical specialty society representing nearly 9,000 ophthalmologists in the United States and abroad who share a particular interest in cataract and refractive surgical care. ASCRS members annually perform the vast majority of cataract procedures in the United States.

ASCRS appreciates that the FDA is attempting to address our concerns with policies related to office-use that require a physician to obtain a compounded drug from an outsourcing facility if he or she does not have a patient-specific prescription. However, ASCRS is concerned that the revisions made in the revised draft guidance do not address the barriers in securing ophthalmic compounded drugs needed for office-use to treat emergent conditions. While the revised draft guidance may allow outsourcing facilities to compound small batches, many outsourcing facilities have indicated that they do not intend to change their current practices and will not compound to fill small volume orders that ophthalmologists need for office-use drugs. Therefore, ophthalmologists will not have timely access to sight-saving compounded medications for patients who present an ocular emergent condition. We urge the FDA to ensure ophthalmologists have a pathway to secure compounded drugs for office-use by allowing physicians to access small quantities of compounded drugs needed to treat emergent conditions without a patient-specific prescription from 503A compounding facilities.

Obtaining Compounded Drugs in Ophthalmology

ASCRS has repeatedly advocated that ophthalmologists need to have an immediate pathway to secure drugs for office-use to treat emergent conditions; however, FDA maintains that without a patient-specific prescription, a physician must obtain compounded products from an outsourcing facility—even though many do not compound office-use products in small volume quantities needed for emergent conditions. Prior to the enactment of the Drug Quality and Security Act (DQSA), 503A

compounders were able to compound a drug in limited quantities before receipt of a valid prescription order for an identified individual patient, depending on state law. Ophthalmologists must keep a small stock of compounded drugs on hand in case a patient with an emergent condition needs a compounded medication administered immediately to prevent vision loss. However, following the DQSA, the FDA has maintained that a 503A compounder cannot compound without a patient-specific prescription. In the event of a patient presenting in a physician's office with an emergent condition, the FDA maintains that a physician may obtain a compounded medication from an outsourcing facility without a patient-specific prescription. However, as noted above, many outsourcing facilities are not willing to compound low volume orders, like those required by ophthalmologists for emergent conditions, because they are not profitable. **ASCRS is concerned that even though the revised policies in the "Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act" may allow 503Bs to produce smaller batches more easily, many outsourcing facilities will still not compound in the requested quantities needed by ophthalmologists.**

Outsourcing Facilities Will Not Produce Compounded Drugs for Office-Use

We recognize the FDA has taken steps in this revised draft guidance to address our concerns with access to office-use drugs from outsourcing facilities by revising requirements related to stability testing, including the assignment of beyond-use date (BUD) as an expiration date, and testing requirements related to batch release; however, we are concerned that the access issue will not be resolved since outsourcing facilities remain unwilling to compound in the small quantities needed by ophthalmologists to treat patients with emergent conditions. The new requirements for small batches (i.e., less than 5,000 units for non-sterile and less than 1,000 units for sterile) pertaining to certain release testing, stability testing, and BUDs where the FDA has determined that it does not intend to take regulatory action, may make it easier for outsourcing facilities to compound small orders. However, since drugs for emergent conditions are not used in ophthalmic practices on a regular basis, physicians generally order smaller quantities, which make it less cost-effective for the outsourcing facilities to manufacture. As a result, many outsourcing facilities have indicated that they do not produce compounded drugs needed for emergent conditions in the requested amounts by ophthalmologists, thus limiting physician and patient access to these drugs.

In fact, when we inquired of the outsourcing community on whether the revised policies would support production of small ophthalmic orders that are used to treat patients who present with emergent conditions, the answer was no. While outsourcing facilities fill a critical gap between 503A compounders and pharmaceutical manufacturers, they are also businesses, and many decide to focus on drug products with a high volume of market demand versus low volume orders, such as those for emergent conditions. **However, the FDA maintains that without a patient-specific prescription, physicians must obtain office-use drugs from an outsourcing facility. Ultimately, this FDA policy does not make it easier for ophthalmologists to obtain compounded medications for office-use and threatens timely access to treatment for patients.**

Timely Access to Compounded Drugs for Emergent Cases

Current FDA policies for office-use compounding restrict immediate access to drugs needed for emergent conditions, which ultimately denies patients timely access to sight-saving treatments.

Since the FDA released its initial draft guidance, "Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act," ASCRS and the ophthalmic community have raised concerns related to patient safety and physician access to drugs for office-use, especially when treating an emergent condition. For instance, if a patient presents with bacterial endophthalmitis—an infection where bacteria has reached the interior of the eye—and is not treated within 24 hours with the injection of compounded antibiotics, he or she will certainly experience significant vision loss. Current treatment regimens for bacterial endophthalmitis include direct intravitreal injections of vancomycin (1.0 mg/0.1 ml) and ceftazidime (2.2 mg/0.1 ml). We have reviewed the available products to order from the major ophthalmic outsourcing facilities, and many do not offer intravitreal injections of vancomycin or ceftazidime in the quantity needed to treat an individual patient. **Therefore, the FDA's requirement for a physician to have a patient-specific prescription to obtain compounded medications from a 503A compounding pharmacy poses significant safety concerns for patients with emergent conditions who need immediate treatment.**

The FDA even acknowledges the need for timely access to ophthalmic drugs in the above final guidance:

> "If a patient presents at an ophthalmologist's office with a fungal eye infection, timely administration of a compounded antifungal medication may be critical to preventing vision loss. In such a case, the ophthalmologist may need to inject the patient with a compounded drug product immediately, rather than writing a prescription and waiting for the drug product to be compounded and shipped to the prescriber."

However, in the footnote of this example, the FDA states, "such compounding would be subject to all of the conditions of section 503A or 503B . . . ." **This is particularly alarming, as the agency has recognized the importance of the availability of compounded medications for office-use, yet does not provide a pathway to secure critical compounded medications to treat patients in a timely manner from a 503A or 503B compounding facility.**

Ensuring Access to Compounded Drugs

Ophthalmologists need to have an immediate pathway to secure drugs for office-use. ASCRS has advocated that the FDA allow 503A compounders to supply limited quantities of drugs to keep on hand for office-use to treat emergent conditions. As already indicated, the FDA has maintained that physicians may obtain compounded medications without a patient-specific prescription from outsourcing facilities; however, this is not a viable option for ophthalmologists due to outsourcing facilities' unwillingness to compound low volume drug orders needed for emergent conditions. **We strongly urge the FDA to prioritize the needs of patients with emergent conditions by allowing physicians to access compounded drugs for office-use from 503A compounding pharmacies in limited supply without a patient-specific prescription. We encourage the agency to recognize that access to compounded drugs for office-use is not only essential to the practice of medicine, but also a vital tool for patient care. This would ensure physicians have access to important compounded medications to treat patients with emergent ocular conditions.**

Conclusion

ASCRS appreciates the opportunity to provide comments regarding proposed changes to the regulations governing "Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act." We urge the FDA not to obstruct access to sight-saving drugs by allowing ophthalmologists to obtain small quantities of compounded drugs needed to treat emergent conditions without a patient-specific prescription from 503A compounding facilities, as they are not available from 503B outsourcing facilities. We would be pleased to provide further input or clarification of our comments, as needed. Please contact Allison Madson, manager of regulatory affairs, at 703-591-2220 if you have any questions or would like to arrange a meeting.

Sincerely,

Thomas W. Samuelson, MD
President, ASCRS