February 5, 2018

By Electronic Delivery

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


Dear Commissioner Gottlieb:

The American Society of Cataract and Refractive Surgery (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.

We appreciate this opportunity to provide comments in response to the FDA’s request for information on existing regulations that could be modified, repealed, or replaced to achieve meaningful burden reduction on physicians and practices. Our chief recommendations include:

• Facilitate physician access to compounded drugs for office-use from 503A compounding pharmacies for patients with emergent conditions;

• Provide access to accurate information about off-label uses of drugs and devices to physicians by eliminating policies that block communication between manufacturers and practitioners; and

• Limit the use of guidance documents, often still in draft form, because of the uncertainty of whether the described policies will be enforced.

Drug Compounding

We are very concerned that the FDA is implementing the Drug Quality and Security Act (DQSA) in a way that negatively impacts patient access to compounded medications and creates an unnecessary burden on physician practices. The practice of ophthalmology relies heavily on compounded drugs, and
it is vital that physicians have an immediate supply available in their offices to treat patients who present with emergent conditions. However, with the use of guidance documents, the FDA is placing a burden on physicians by restricting access to medications to have on hand in the office, and by not providing a guaranteed alternative pathway to obtain compounded drugs. This ultimately denies patients timely and effective treatment options.

Specifically, we are very concerned with the final guidance on “Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act,” as it will create further access issues to compounded drugs, particularly in emergency situations, as practices will experience administrative burdens when securing needed compounded drugs for patients. For office-use compounding, physicians are required to write a patient-specific prescription for any drug compounded by a 503A traditional compounder. This requirement is particularly problematic for ophthalmology practices that routinely stock small quantities of compounded drugs to treat patients who present with emergent conditions in the office setting. While physicians may access compounded drugs from 503B outsourcing facilities without a patient-specific prescription, outsourcing facilities often do not produce drugs in the limited quantities or ophthalmic solutions required by ophthalmologists.

**Timely Access to Compounded Drugs for Emergent Cases**

The guidance “Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act,” creates an unnecessary burden on practices to secure access to compounded drugs and has a secondary negative impact on patient care. It is vital for patient care that ophthalmologists have immediate access to small quantities of compounded drugs for office-use to provide treatment to patients presenting emergent conditions. If an ophthalmologist does not have access to needed compounded drugs, this could have lasting negative consequences on a patient, such as extreme ocular damage or even complete blindness. For instance, if a patient presents a bacterial endophthalmitis—an infection where bacteria has reached the inside of the eye—and is not treated within 24 hours with the injection of compounded antibiotics, he or she will almost certainly experience the loss of an eye.

We appreciate that the FDA acknowledged the medical necessity of patients’ access to compounded drugs in their physician’s office in this final guidance, while even highlighting an example from our specialty:

“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 releases final guidance that does not ensure patients’ timely access to medications. **Physicians not having access to compounded drugs creates substantial burdens for practices to secure drugs in order to treat patients, which ultimately impacts patient outcomes.**
We remind the agency that it has acknowledged in the final guidance that “writing a prescription and waiting for the drug product to be compounded and shipped to the prescriber,” also known as a patient-specific prescription, is not effective for patients experiencing a critical ophthalmic condition. This is not only an avoidable delay, but an additional burden on the practice to secure drugs to treat patients with emergent conditions.

**Barriers to Access from 503B Outsourcing Facilities**

We understand that physicians may order compounded drugs without a patient-specific prescription from 503B outsourcing facilities, however, physicians face extreme burdens in accessing compounded drugs from these facilities in the small quantities they need. Since the enactment of the DQSA, we have received dozens of reports from our members describing access issues to certain drugs for office-use from outsourcing facilities. It is clear from the final guidance and the proposed 503B pathway that the agency has ignored comments from outsourcing facilities, specifically smaller facilities expressing their inability or lack of willingness to compound in the small quantities needed by many ophthalmologists to have on hand for emergent cases. 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 produce. As a result, many outsourcing facilities have indicated that they do not produce in the requested quantities, thus limiting physician and patient access to these drugs.

We strongly urge the FDA to prioritize the needs of patients with emergent conditions by preserving physician access to compounded drugs for office-use from 503A compounding pharmacies. The FDA should ensure regulations that promote better patient outcomes by not creating additional burdens for physicians to secure needed drugs to treat patients. 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. We believe that any implementation action taken to limit access to compounded treatments goes against the intent of Congress to improve the quality of patient care. To ensure physicians are able to secure compounded drugs, without experiencing additional burdens, we ask the FDA to allow for compounding in small quantities for office-use without a patient-specific prescription.

**Off-Label Communication**

Current FDA regulations create a burden on physicians by impeding their ability to care for their patients by interfering with the flow of scientific information from drug and device manufacturers to practitioners and even among physicians themselves. ASCRS is specifically concerned with the following guidance documents: “Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices” and “Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices.” These regulations ultimately place a significant burden on physicians to obtain information about the off-label uses of medical products. We urge the FDA to open the lines of communication between manufacturers and practitioners to help facilitate the development and dissemination of accurate information about off-label use.

*Off-Label Uses in Ophthalmology and the Distribution of Scientific Information*
ASCRS is very concerned with the burdens placed on physicians by the draft guidance, “Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices,” as it inappropriately hinders physicians’ ability to access scientific information provided by manufacturers on the safe and effective use of medical products (including drugs, devices, and biologics). The off-label use of drugs and devices is very common in the everyday practice of medicine, especially in ophthalmology. In fact, failure to use off-label medications or devices would quickly place many physicians at risk for a malpractice lawsuit. In ophthalmology, routine use of postoperative antibiotics after cataract surgery, the use of mitomycin-C as a surgical adjunct, application of adhesives for the closure of wounds, and even the treatment of infectious corneal ulcers with effective topical antibiotics represent off-label use. With restrictions placed on physicians to access this information, patients are negatively impacted and experience reduced treatment options.

While physicians and manufacturers know that drugs and devices work well for alternative uses not included in their approved label, the FDA does not allow pharmaceutical companies to actively distribute any key clinical information, even if it is related to the on-label indication, unless it is explicitly referenced in the package insert. Therefore, any new information—such as observational data, subpopulation information, comparative data derived from clinical trials other than randomized controlled trials, and pharmacoeconomic or comparative cost data—cannot be shared proactively with physicians, unless such data is directly referenced in the package insert. This is particularly alarming for ophthalmology, as many drugs and devices are used off-label in this specialty. Limiting knowledge to new scientific information of off-label uses not only burdens physicians, but ultimately impacts patient outcomes.

Furthermore, the label on medical products represents the results of clinical trials that are designed by the manufacturer to obtain FDA approval in the most certain and expeditious way possible. These motivations are not the same as physicians’ motivations to provide the best medical care to patients. Clinical trial results, therefore, often do not represent all appropriate indications for a product. The product label not only reflects limited clinical data influenced by business considerations, but it also represents a summary of knowledge that is frozen in time. We urge the FDA to ensure that access to scientific information from manufacturers on off-label use of medical products is not disrupted and does not create additional burdens for physicians.

Off-Label Communication Between Physicians

ASCRS is very concerned with the guidance document “Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices,” as it restricts off-label communication among physicians, creating an unnecessary burden by placing the onus on physicians to submit requests for information to access facts about off-label uses of medical products. According to this guidance, if a physician is affiliated with a company, he or she may not present off-label use data to colleagues at a sponsored event, as this could be considered a “solicited request” and evidence of a company’s intent to use that drug or medical device for a use other than the FDA approval. Because of off-label communication policies, physicians can only publicly access new information about potential off-label uses if the educational material or event does not receive any sponsorship from the manufacturer. This is particularly alarming, as the most common way physicians stay current on off-label uses is by sharing their experiences with one another.
ASCRS believes that limiting access to information about off-label uses places an unnecessary burden on physicians to constantly review and research information, ultimately impacting patient care and patient outcomes. By restricting physicians’ access to new information on medical products, physicians’ knowledge of a medical product is directly impacted. While there are limited incidences of complications from drugs and devices used off-label, they must be balanced by the sight-saving treatments that benefit a significant patient population. We urge the FDA to stop restricting new information about the uses of medical products, as it places unnecessary burdens on physicians to continually submit requests for information on off-label uses. Additionally, patients are negatively impacted by off-label regulations, experiencing reduced treatments options and harmful patient outcomes.

Limit Use of Guidance Documents

Unfortunately, the FDA’s use of guidance documents has created significant burdens for physicians and other stakeholders by creating an environment in which they feel forced to comply even though the documents are not finalized. The implementation of off-label communication regulations and the DQSA showcase a larger pattern of regulatory overreach by the FDA that has involved the use of guidance documents, often still in draft form, that are not finalized. These guidance documents, while neither nonbinding or technically enforceable, create an environment of ambiguity, as new requirements are often cited in these documents without the benefit of notice or comment from the public. As a result, physicians and other stakeholders feel forced to comply due to the weight the agency and courts give these guidance documents. Furthermore, the implications of complying with some guidance documents, particularly those mentioned above, may be burdensome for physicians and practices.

These guidance documents create significant financial and administrative burdens on physicians and other stakeholders. The Administrative Procedure Act’s (APA) rulemaking process does not apply to “interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice.” Therefore, guidance documents do not consider estimates of costs, economic burdens, and administrative burdens before expecting stakeholders to comply. We believe that policy decisions by the FDA should be conducted through the formal APA rulemaking process, should be consistent with the intent of Congress when the law was passed, and should not create additional burdens.

We thank you for the opportunity to bring these matters to your attention. We support the agency’s efforts to reduce regulatory burdens on physicians. 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,

Bonnie An Henderson, MD
President, ASCRS