ASRS American Society of Retina Specialists

July 18, 2016

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket Nos.:
FDA-2016-D-0269; Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act, and
FDA-2016-D-0271; Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; Availability

To Whom It May Concern:

The American Society of Retina Specialists (ASRS) welcomes the opportunity to comment on the Draft Guidance for Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act (Draft Guidance for Prescription Requirement) and the Draft Guidance for Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act (Draft Guidance for Hospital Compounding). We also appreciated the opportunity to present on these topics during the 2016 listening sessions on drug compounding.

ASRS is the largest retinal organization in the world, representing more than 2900 members in every state, the District of Columbia, Puerto Rico, and 59 countries. Retina specialists are board-certified ophthalmologists who have completed fellowship training in the medical and surgical treatment of retinal diseases. The mission of the ASRS is to provide a collegial and open forum for education, to advance the understanding and treatment of vitreoretinal diseases, and to enhance the ability of its members to provide the highest quality of patient care.

Retina patients are treated with a myriad of compounded therapies including injectable antibiotics, anesthetics, dyes used during surgery, and bevacizumab (Avastin). In general, retina specialists have access to these therapies either through 503B outsourcing facilities, or through 503A facilities pursuant to an individual prescription. However, in certain emergencies retina specialists have difficulty accessing medications needed for our patients. We urge the FDA to revise the proposed requirements in its Draft Guidance for Prescription Requirement and the Draft Guidance for Hospital and Health System Compounding as recommended below to ensure our patients maintain access to these critical medications.

<u>Limited access to compounded antibiotics for intravitreal injection</u>

ASRS would like to thank the FDA for acknowledging the need for retina specialists to have compounded antibiotics on hand to treat emergency infections such as endophthalmitis. This is referenced in the Draft Guidance for Prescription Requirement on page 3 (lines 103 – 110):

> "Sometimes, it is necessary for health care practitioners in hospitals, clinics, offices, or other settings to have certain compounded drug products on hand that they can administer to a patient who presents with an immediate need for the compounded drug product. For example, 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 prescriber 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."

We agree with FDA that it is necessary to have on hand compounded antibiotics for use in the case of fungal endophthalmitis. Yet, under the proposed policies in the FDA's Draft Guidance, this is not possible.

The Draft Guidance would permit pharmacists or licensed physicians to compound a drug only after receiving a valid prescription order for an individual patient. Compounding prior to receiving a prescription would be permitted only in limited quantities, based on a history of receiving valid prescription orders and if the orders have been generated solely within an established relationship between the pharmacist or physician and either the patient or prescriber. Yet, the compounded medication cannot leave the facility or be given to the patient, until the facility is sent a patient specific prescription. If office supply is needed to have on hand for immediate use, the Draft Guidance states that hospitals, clinics, and health care practitioners can obtain non-patient-specific compounded drug products from outsourcing facilities registered under section 503B. **The FDA's solution is not viable as antifungal antibiotics for intravitreal use are not currently available from any 503B facility.**

Ophthalmologists across the country usually obtain antibiotics to treat endophthalmitis via 503A compounders. As an example, the hospital pharmacy at Phillips Eye Institute in Minneapolis, MN, provides a variety of antibiotics through anticipatory compounding. The compounded drugs are frozen and stored in locked refrigerators at the surgery center, clinic, and sister hospital, to be used in the event of emergency. These antibiotics often go unused, are discarded and replaced at the expense of the hospital since patients with infectious endophthalmitis come in at unpredictable intervals. This current practice violates the Draft Guidance, however, because contrary to its requirements: (1) these 503A antibiotics are distributed without a patient-specific prescription (line 55), (2) the antibiotics are distributed to multiple locations, in excess of numbers allowed for 1 month average anticipatory compounding (lines 324-331), and (3) the outpatient surgery center, satellite clinics, and sister hospital within the same hospital system are located several miles away from the pharmacy. The Minnesota Board of Pharmacy granted Phillips Eye Institute a temporary exemption to the individual prescription requirement for ophthalmic antibiotics, pending guidance from FDA, to enable this current practice. If the FDA finalizes the onerous prescription requirement in its Draft Guidance for Prescription Requirement, this critical exemption for ophthalmic antibiotics may be withdrawn, eliminating the ability of our members to treat patients with emergencies such as fungal endophthalmitis.

Other specific examples of compounded intravitreal antibiotics that are only available through 503A compounding pharmacies include acyclovir, amikacin, amphotericin, clindamycin, foscarnet, gancyclovir, and voriconazole (see appendix A). Intravitreal vancomycin and ceftazidime are currently available from 503B facilities for bacterial endophthalmitis, but there are no 503B available agents for fungal or viral infections or in the event a patient is allergic to cephalosporins. Furthermore, intravitreal antibiotics are low-volume products that equate to negative revenue for 503B facilities and they will not necessarily be available in the future.

FDA has argued that 503A products are less safe than those from 503B. However, if FDA restricts non-patient-specific 503A antibiotics for ophthalmic use, retina specialists will likely be tempted to return to do-it-yourself mixing of antibiotics. Twenty years ago, retina specialists mixed antibiotics in their offices with very little specific training and used techniques similar to a college chemistry lab in order to treat endophthalmitis. The FDA has discouraged "bedside compounding" and yet retina specialists would have to compound these medications in their office without availability of hoods and proper diluents. This would represent a major step backwards in terms of safety as compared to antibiotics from a 503A facility.

For the above reasons, ASRS believes that the FDA must permit in-office use of certain compounded drugs. An exception must be made to allow physicians to continue to administer critically necessary compounded drugs to patients when such drugs are not available from 503B facilities.

In its Draft Guidance for Hospital Compounding, the FDA recognizes that a hospital may need to maintain a supply of certain compounded drug products within the hospital but outside of the pharmacy (e.g., in an emergency department or operating room) in anticipation of a patient presenting with a critical need for the drug when there is no time for the hospital pharmacy to compound and provide the drug upon receipt of a prescription or order for that patient. The FDA does not intend to take action if a hospital pharmacy distributes compounded drug products without first receiving a patient-specific prescription or order provided that:

> (1) The drug products are distributed only to healthcare facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy *and that are located within a 1-mile radius of the compounding pharmacy*;
> (2) The drug products are only administered within the healthcare facilities to patients within the healthcare facilities, pursuant to a patient specific prescription or order; and
> (3) The drug products are compounded in accordance with all other provisions of section 503A, and any other applicable requirements of the FD&C Act and FDA regulations.

The ASRS appreciates this proposal, but the 1-mile radius limitation presents an obstacle to access to necessary compounded antibiotics. The FDA states that the proposed 1-mile radius policy is intended to distinguish a hospital campus from a larger health system. The FDA acknowledges that certain characteristics of hospital pharmacies distinguish them from conventional manufacturers. However, it argues that a health system pharmacy that compounds drug products without patient-specific prescriptions for facilities within its health system across a broader geographic area could function as a large manufacturing operation, but without necessary standards to assure drug quality, increasing the potential to harm many patients. **ASRS does not believe this stated rationale justifies the added obstacle to access to necessary compounded medications and the resulting harm to patients.**

As noted by the FDA, hospital and health system drug compounding and distribution practices vary. For example, some hospital pharmacies compound drugs only for use in the hospital in which the pharmacy is located (e.g., for the treatment of patients admitted to the hospital, or for use in the hospital's emergency room), while other hospital and health system pharmacies compound and distribute their compounded drug products to other facilities within their health system (e.g., to other hospitals, clinics, infusion centers, or long-term care facilities within the health system for administration or dispensing). In some cases, a hospital or health system pharmacy compounds drugs only after receipt of a prescription or order for an identified individual patient. Hospital and health system pharmacies may also compound drugs and distribute them within the hospital or health system before the receipt of a patient-specific

prescription. The hospital or health system then holds the drug products until a patient presents with a need for the drug, for example in an operating room, where emergency procedures cannot be scheduled in advance, or in emergency departments. This current practice, however, violates the 1-mile radius requirement in the Draft Guidance for Hospital Compounding because the outpatient surgery center, satellite clinics, and sister hospital within the same hospital system are located several miles away from the pharmacy, beyond a 1-mile radius.

If the FDA finalizes the requirements in its draft guidance documents that create obstacles to patient access, retina physicians will be unable to treat patients with emergencies such as fungal endophthalmitis. The critical exemption granted to Phillips Eye Institute by the Minnesota Board of Pharmacy for ophthalmic antibiotics may be withdrawn or curtailed. **With the 1-mile radius restriction, ophthalmic antibiotics could not be distributed to locations such as outpatient surgery centers, satellite clinics, and sister hospitals within the same hospital system if they are located several miles away from the pharmacy. While these locations are not within a 1-mile radius of the pharmacy, they are in relatively close proximity to the pharmacy and share the same ownership and control. ASRS believes that a 1-mile restriction is arbitrary and would do more harm than good as it would deny prompt access to urgently needed intravitreal antibiotics for many patients.**

As the FDA recognizes in the Draft Guidance; "certain characteristics of hospital pharmacies differentiate them from pharmacies that are not owned and controlled by hospitals, and from conventional manufacturers, greatly reducing certain risks. For example, generally, the scope of distribution of drug products compounded by hospital pharmacies is limited. Hospital pharmacies usually compound drug products based on orders from practitioners who work in the hospital, distribute the drug products only within the hospital or to related healthcare facilities under common ownership and control and located within close proximity to the hospital, and administer them only to patients within the hospital or healthcare facility. Because the hospital or healthcare facility and the pharmacy are under common ownership and control, the hospital or healthcare facility is responsible for both the compounding of the drug and treatment of the patient, and the cause of any compounding-related adverse events can be more readily identified." The FDA stated that it "believes that the policies set forth in this guidance, based on the way a hospital pharmacy normally functions with regard to compounding for its patients, will prevent hospital pharmacies from operating like conventional manufacturers." **ASRS believes that the 1-mile radius requirement should be eliminated as it is arbitrary and does little to enhance the assurances already provided by the above noted characteristics of hospital and health system pharmacies.**

<u>Streamlining the prescription process for 503A compounded drugs</u>

In its Draft Guidance for Prescription Requirement, the FDA recommends including the following statement along with a prescription for a compounded medication (Draft Guidance line 277-278):

"Per [type of communication] with [name of prescriber] on [date], [name of prescriber] has advised that compounded [name of drug] is necessary for the treatment of [name of patient]."

Writing and transmitting this sentence for each prescription is time consuming for the physician and staff without enhancing the safety of the medication or the prescription process. Furthermore, the statement should reflect information that is already part of the patient's electronic or paper record. ASRS suggests that FDA not include this recommendation in its final guidance.

Recommendation

The ASRS urges the FDA to uphold its stated position that certain compounded drug products must be on hand to administer to a patient with an immediate need or emergency (such as fungal endophthalmitis) by allowing office use of compounded drugs obtained without a patient specific prescription from 503A facilities when such drugs cannot be obtained from 503B facilities. Without, this critical revision, retina specialists cannot ensure appropriate emergency vision saving treatment for patients. We also recommend that the requirement for physicians to include a specific statement with a prescription for a compounded medication be eliminated as it increases administrative burden for physicians without enhancing care or patient safety. Last, ASRS urges the FDA to eliminate the 1-mile radius requirement from its Draft Guidance on Hospital Compounding so compounded drug products may be distributed to all healthcare facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy. It should delete the words on lines 213 and 214: "and that are located within a 1-mile radius of the compounding pharmacy."

Please contact Jill Blim, ASRS Executive Vice President, at jill.blim@asrs.org, if you have any questions.

Sincerely,

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