Federation of American Hospitals®

May 25, 2018

The Honorable Scott Gottlieb, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug and Cosmetic Act

Submitted electronically to www.regulations.gov

Dear Commissioners Gottlieb:

The Federation of American Hospitals (FAH) is the national representative of more than 1,000 investor-owned or managed community hospitals and health systems throughout the United States. Our members include teaching and non-teaching full-service community hospitals in urban and rural parts of the United States, as well as inpatient rehabilitation, psychiatric, long-term acute care, and cancer hospitals. The FAH appreciates the opportunity to provide comments to the Food and Drug Administration (FDA) about the referenced Draft Guidance on the Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug and Cosmetic Act (Draft Guidance).

We appreciate and share the FDA's commitment to ensuring the safety and reliability of pharmaceutical products and the supply chain. Our hospitals' mission is to provide the highest quality care to our patients and the availability of safe drug products is essential to that mission. Given historic increases in drug prices and persistent shortages in widely used drug products, this is a particularly challenging time for hospitals as they seek to meet the clinical needs of their patients. Compounding is an essential resource to providing patients with safe and reliable drug products and we hope the FDA will consider our views on the Draft Guidance as it considers changes to the document.

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Clinical Need Standard

Patient safety should be the primary test when determining clinical need. We encourage the FDA to consider factors that impact patient safety that are not explicitly considered in the Draft Guidance. Drug product scarcity, precipitated by shortages and backorders, continues to induce human risk factors into care delivery which can result in medication errors. These supply chain issues require hospitals to make frequent changes in the delivery of the drug products based on the availability of product in an effort to absorb the effect of these fluctuations and minimize negative risk factors on the patient. As a result, drug delivery ends up changing through adaptations in vial size, volume, concentration, and delivery system. These changes increase the risk of errors and thus adverse drug events due to the disruption from standardized forms of delivery. Under normal conditions, hospitals have standardized these variables to reduce instances of error and harm. In some instances, a compounded product can result in the avoidance of these errors, offering a superior safety environment for patients. For example, commercially available phenylephrine is not provided in the concentration needed in the operating room requiring manipulation prior to use. Hospitals can utilize compounding to provide standardized, ready to use concentrations of phenylephrine in prefilled syringes providing an added measure of safety for the patient. An additional example includes the practice of some compounding pharmacies of color coding products as an added safety feature.

In other instances, an FDA approved product may be medically unsuitable for a patient resulting in the need for a compounded product. While the Draft Guidance notes the potential need for a compounded product due to certain attributes incompatible with certain patients, we are concerned that the standard the Draft Guidance proposes would result in a delay in treatment or the inability for certain drug products to be administered. As such, we encourage the FDA to consider the safety and clinical implications the Draft Guidance could have on patients.

Bulk Designation Nomination Timeline

We encourage the FDA to include in the Draft Guidance a clear and transparent timeline by which nominations for bulk drug substance will be reviewed and determined. While the FDA lays out the policy it will use to make determinations on bulk drug substance designation, it does not specify a timeline by which these decisions will be made. This information is imperative to all entities within the drug product supply chain that are making decisions about product purchasing and administration. The ability to understand potential drug product availability into the future helps inform health care providers as they determine how to best treat their patients in both the short- and long-term. Without such information, providers are left to make near-sighted decisions that could be better informed by a transparent timeline for bulk drug substance nomination determinations.

Provider Capability

The Draft Guidance delineates a standard that acknowledges the need for compounding from a bulk substance where the difficulty and complexities of removing an ingredient from a finished drug product are too great. However, the Draft Guidance contrasts this complexity with

the ability to formulate an FDA-approved drug in a lower concentration – expressing that this process can often be completed with minimal, simple manipulations. We caution that not all providers have the capability to perform the type of manipulation required to create these lower concentrations from FDA-approved drug products. This new standard could result in those providers inability to provide optimal care to certain patients.

Recognize Earlier Signs of Drug Product Scarcity That Can Lead to Shortages

We appreciate that the FDA recognizes in the Draft Guidance that drug product shortages are a permissible reason for compounding for bulk drug substances. However, we encourage the FDA to take a more expansive view of shortages, how they originate and how they first appear in the supply chain. By the time a drug product is listed on the FDA's drug shortage list, providers have often already been managing the impacts of that shortage for some time. As laid out by the Draft Guidance, in a circumstance where a drug shortage is identified, making it eligible for compounding, but where no bulk drug substance has already been approved and listed by the FDA, it is unclear how long providers would have to wait for a compounded version of the drug to be available for patient use. Under the circumstances laid out by the FDA, providers would be waiting for the FDA to first determine whether the bulk drug substance was available for use in compounding, with no timeline for that decision laid out in the Draft Guidance, and then for the compounding pharmacies to manufacture the drug product. Under the best circumstances, once the bulk drugs substance was made available, it could take compounding pharmacies three months or more to formulate, develop, validate and launch the product. The lack of early recognition could result in months or even years of delay and could lead to the type of errors we described earlier.

We encourage the FDA to either improve its identification of drug product shortages long before they reach a crisis point or consider factors, like long-term and persistent backorders, when determining whether a drug product can be compounded by bulk drug substances. A policy that results in the persistent unavailability of the most appropriate drug product for a patient, could result in unnecessary patient harm.

Drug Pricing and Cost

As we have noted in the past, rising drug costs continue to strain patients, health care providers and the nation's health care system generally. There are many instances where compounded versions of a manufactured drug product are hundreds of percent less expensive without compromising patient safety. For example, compounded syringes of commonly used drug products used in the operating room like ephedrine sulfate, glycopyrrolate, neostigmine and succinylcholine are safely provided in the appropriate size, concentration and strength at dramatically less cost than the manufactured vials of the same drug product. We appreciate that the FDA is taking steps to help bring down the prices of drug products. However, more needs to be done, especially in light of the fact that the FDA is not taking price and cost into account when determining the availability of bulk drug substances for use in compounding.

Thank you for the opportunity to comment, should you have questions please do not hesitate to contact me.

Sincerely,

Claudia Salzberg, Ph.D.
Vice President, Quality