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APhA

October 11, 2016

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

[Submitted electronically to www.regulations.gov]

Re: Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry (Docket ID: FDA–2016–D–1309)

Dear Sir/Madam:

APhA is pleased to submit these comments on FDA's draft guidance on Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A (the "Guidance"). Founded in 1852 as the American Pharmaceutical Association, APhA represents more than 62,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, managed care organizations, hospice settings, and the uniformed services.

APhA supports FDA's efforts to ensure drug quality and security for the provision of safe, effective medications, including compounded medications, is of paramount importance to our members. Compounding is an important part of pharmacy practice as it permits patients with unique medical needs to have access to vital medications when commercially available dosage forms do not exist. Furthermore, while we appreciate FDA providing some flexibility related to compounding of "commercially available" products, because there are a number of additional, notable situations that require the compounding of commercially available drugs, APhA requests modifications to the Guidance in order to meet patients' health care needs.

I. Drug Shortage List (Pg. 9, Lines 326-328)

Under the Guidance, the FDA does not consider a drug product to be commercially available if it appears on the FDA's drug shortage list.[1] The Guidance states that "if the drug was

[1] *See* Lines 165-172. *"We do not consider a drug product to be commercially available if • the drug product has been discontinued and is no longer marketed or • the drug product appears on the FDA drug shortage list in effect*

compounded because the approved drug products was not commercially available because it was on the FDA drug shortage list, the prescriber or compounder should include a notation on the prescription [.]" However, due to numerous factors such as agency delay, different methodology in determining what constitutes a shortage, the existence of regional or local unavailability or the lag time to obtain new drugs in the marketplace, FDA's drug shortage list is not comprehensive. Therefore, APhA recommends FDA modify the Guidance to permit the compounding of commercially available drugs, when it is reasonable, appropriate and critical to meeting the needs of patients.

There are a number of discrepancies between the drug shortage lists maintained by the FDA and the American Society of Health-System Pharmacists (ASHP)/University of Utah Drug Information Service.[2] In a comparison of the two lists, over 90 drugs appear on the ASHP/University of Utah's list, but not on FDA's list. Conversely, over 15 drugs appear on the FDA's list, but not on the ASHP/University of Utah's list. In addition, the Drug Enforcement Agency (DEA) interprets drug shortages differently than FDA.[3] Consequently, relying solely on FDA's drug shortage list for the determination of whether or not a compounded drug is "commercially available" will negatively and unjustly impact patient care.

In addition to variations in defining or determining drug product shortages, wholesalers' inability to supply drug products can also be a very real barrier to meeting patients' needs. Drug Quality and Security Act (DQSA) requirements related to trading partner verification and reporting and accessing drug supply chain records has decreased the number of wholesalers with which pharmacies work. Further limiting wholesalers and pharmacy relationships are requirements forcing system and software compatibility between trading partners. An additional factor complicating the ability of pharmacies to quickly obtain out-of-stock or scarce drugs is DQSA's restrictions on pharmacy to pharmacy transfers. Consequently, remedying a wholesaler or regional shortage is not as simple as finding a new wholesaler or pharmacy with the drug in stock. Therefore, as stated above, APhA urges FDA to allow for clinician judgement and expand the scenarios for the compounding of commercially available drugs to include when compounding is reasonable and appropriate. Additionally, to adequately document the need to compound a commercially available product that, while not on the FDA shortage list, is not available from the pharmacy's wholesalers, APhA offers that information on wholesaler unavailability can be attached to the prescription.

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under section 506E of the FD&C Act. A drug "appears on the drug shortage list in effect under section 506E" if the drug is in "currently in shortage" status (and not in "resolved" status) in FDA's drug shortage database."

[2] *See* FDA. Current and Resolved Drug Shortages and Discontinuations Reported to FDA. Available at: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm. Also, *See* University of Utah/ASHP. Drug Shortages: Current Drugs. Available at: http://www.ashp.org/drugshortages/current/

[3] For example, DEA and FDA disagree about what constitutes a shortage. DEA officials said that they do not believe FDA appropriately validates or investigates the shortage information it posts on its website and that posting this information encourages manufacturers to falsely report shortages to obtain additional quota. Given such barriers to coordination, DEA and FDA cannot effectively act to prevent or alleviate shortages. *See*, Drug Shortages. Better Management of the Quota Process for Controlled Substances Needed; Coordination between DEA and FDA Should Be Improved. GAO-15-202: Published: Feb 2, 2015. Publicly Released: Mar 4, 2015. Available at: http://www.gao.gov/products/GAO-15-202

II. Drug Strength (Pg. 6, Lines 234-243) (Pg. 8, Lines 279-283)

The Guidance states that a compounded drug that combines two commercially available oral drug products "that are within 10% of the strengths of the respective commercially available products to be essentially a copy of the commercially available drug product, unless a prescriber determination of significant difference has been documented." In addition, the Guidance goes on to discuss easily substitutable strength. APhA is concerned that these provisions are problematic for pharmacists and their patients, as patients may not be able to "easily" tolerate substituted strengths or doses. For example, elderly, blind and pediatric patients may require compounded medications to avoid multiple doses or pill splitting. Alternatively, physicians frequently base the dose for pediatric prescriptions on the patient's weight and for certain vulnerable populations, 10% can be significant and/or toxic. In cases of children needing high doses of Omeprazole, while Omeprazole is commercially available as 2mg/ml, many physicians want a more concentrated form to avoid such a large volume to be administered in each dose, which is not only more convenient, but can affect compliance and health outcomes. Accordingly, APhA urges FDA to recognize the role of health care practitioners and modify its Guidance to allow clinicians more flexibility in meeting the special needs of their patients, even when the drug may be considered commercially available.

III. Four or Fewer Prescriptions Exemption (Regularly/Inordinate Compounded Amounts) (Pg. 10, Lines 361-380)

The Guidance states that a drug product is not eligible for the compounding exemptions under section 503A of the FD&C "if it is prepared by a pharmacist or physician who compounds "regularly or in inordinate amounts (as defined by the Secretary) [.]" The FDA provides that it "does not intend to take action against a compounder for compounding a drug product that is essentially a copy of a commercially available drug product regularly or in inordinate amounts if the compounder fills four or fewer prescriptions for the relevant compounded drug product in a calendar month." While APhA appreciates FDA providing flexibility, we do not believe the language in the Guidance is adequate for pharmacists and others to meet the individualized needs of patients through reasonable and appropriate compounding practices.

The "four or fewer" target does not include prescriptions in which a significant difference for the patient is noted. Inherently, a prescriber would not prescribe a drug unless it already made a significant difference for a patient, which makes this new requirement unnecessary. Furthermore, if the Guidance goes unchanged, when a drug is not available, but fails to appear on the FDA's drug shortage list, the compounder would be arbitrarily restricted to helping only a limited number of patients. In addition, the FDA does not include additional refills under this policy and intends to consider each refill as an additional prescription, which contradicts many existing State Pharmacy Practice Acts across the country and would make it more difficult for compounders to provide essential medications to patients.

Finally, as FDA understands, prescribers often turn to compounding pharmacists because their patients have special needs. Thus, a compounding pharmacy specializing in pediatrics or with a large number of patients with a particular disease state(s) is likely going to have a high percentage of drug products that fall outside the norm. Therefore, APhA strongly urges FDA to remove or modify the potential factor of "more than a small number of prescriptions…" to

identify when a pharmacist or physician is compounding regularly and inordinate amounts, as this is not an appropriate way to evaluate compounders, particularly those meeting specialized or individualized needs.[4]

Thank you again for the opportunity to provide comments on this important issue. APhA looks forward to continuing to work with the FDA and other stakeholders to construct a compounding framework that ensures patient access to appropriate, safe and effective compounded drug products. We hope to be a resource for FDA and are happy to be of assistance in any way possible. If you have any questions or require additional information, please contact Michael Baxter, Director of Regulatory Affairs, at mbaxter@aphanet.org or by phone at (202) 429-7538.

Sincerely,

Thomas E. Menighan, BSPharm, MBA, ScD (Hon), FAPhA
Executive Vice President and CEO

cc: Stacie S. Maass, RPh, JD, Senior Vice President, Pharmacy Practice and Government Affairs

[4] *See* Lines 361-363. *"The compounded drug product amounts to more than a small number of prescriptions or a small percentage of the compounded drug products that a physician or prescriber prepares or provides to patients."*