Submitted electronically via: http://www.regulations.gov

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

Docket No. FDA-2016-D-1309

RE: Draft Guidance - Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Dear Sir or Madam:

Thank you for the opportunity to submit our comments on the Food and Drug Administration's (FDA) Draft Guidance for Industry – Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug. As FDA considers finalizing the proposed new guidance for pharmacy compounding, the International Academy of Compounding Pharmacists (IACP) appreciates the opportunity to share our perspectives and to work with FDA in the future on this very important issue.

IACP is an association representing more than 3,600 pharmacists, technicians, students, and members of the compounding community who focus on the specialty practice of pharmacy compounding. Compounding pharmacists work directly with prescribers including physicians, nurse practitioners and veterinarians to create customized medication solutions for patients and animals whose health care needs cannot be met by manufactured medications.

IACP understands and supports the need to protect public health. However, when providing guidance, it is essential that FDA adheres to the plain language of statutes and Congressional intent to preserve patient and prescriber access to vital compounded medications. Providing clear direction as to the FDA's thoughts regarding this important subject help not only guide Agency investigators during inspections but gives additional insight to the pharmacy industry as a whole on what the FDA expects from this practice of pharmacy.

IACP is concerned with several main points of the proposed guidance, which we outline below, and we look forward to starting a dialog with the Agency on proposed solutions to the issues raised by our Academy.

1. **The guidance appears to require the pharmacy to surrender the records exemption provided in Section 704(a)(2) of the FD&C Act.**

While the guidance does not r*equire* the production of records created by the pharmacy attempting to comply with several parts of this guidance (e.g. reviewing prescription records for essential copies of commercially available medication, calculating the number of times a pharmacy dispensed an essential copy, reviewing documentation on the clinical need for an essential copy, etc.), one can certainly envision FDA requiring a pharmacy to produce those records to demonstrate compliance with the guidance. This places the pharmacy in an impossible situation – either produce the records and theoretically waive the records exemption provided in Section 704(a)(2) or not produce the records and face further scrutiny from the FDA.

A balance must be struck between the agency's inspection authority, the State Boards' authority over licensees and the exemptions provided by Federal law to pharmacies "in conformance with any applicable local laws regulating the practice of pharmacy…" If the FDA is conducting a "routine" inspection in which the FDA has no knowledge the pharmacy has violated any State law, rule or regulation, the records exemption remains intact. A pharmacy should not be forced to volunteer the records exemption in an attempt to show compliance with a non-binding and not legally enforceable document. IACP urges the FDA to continue working with State Boards of Pharmacy to develop a framework to identify cases of compounding essential copies of commercially available drugs.

2. **Reliance solely on the FDA's Drug Shortage database will lead to decreased patient access to potentially lifesaving medications.**

In lines 169-172 of the guidance, the Agency states they do not consider a drug product to be commercially available if the "drug product appears on the FDA drug shortage list in effect under section 506E of the FD&C Act." While this provision certainly helps ensure patient access to drugs which are currently not available but are still marketed by FDA-registered manufacturers, the guidance does not take into effect the very real situations prescribers face on a daily basis of other drug shortages which currently occur in the marketplace.

In research done on or about July 19, 2016, FDA's drug shortage list was compared to a drug shortage list accessible on the American Society of Health-System Pharmacists (ASHP) website. This list is maintained in conjunction with the University of Utah Health Care Drug Information Service and unlike the FDA's drug shortage list, does not rely solely on notification from manufacturers on when a particular drug product is or will be in short supply. In the comparison, we found a total of ***ninety-three*** drug products which ASHP has deemed to be either not available in the market or in very limited supply. Conversely, the FDA's drug shortage list reflected ***sixteen*** items as "in short" which did not appear on the ASHP list.

Therefore, reliance solely on the FDA's drug shortage list for identification if a drug product is not currently available in the marketplace creates the potential for decreased patient access to potentially lifesaving drugs. **IACP urges the FDA to expand the references compounders can use to satisfy this portion of the guidance and, additionally, allow for compounders to document drugs which may be in short supply regionally.** Many drugs have experienced a

"regional shortage" where suppliers are unable to fill orders based on current inventory in regional warehouses across the country. A patient should not be denied access to these medications if a compounder can document that all available sources for the FDA-approved medication have been exhausted and the patient has no other option but to turn to a compounded medication to either start or continue their therapy. Once the FDA-approved medication is available in the marketplace, IACP agrees that the compounding of the medication identified in short supply should cease, unless other conditions exist where switching the patient to the FDA-approved medication would be clinically detrimental to their health.

3. **"Same Route of Administration" requirement may be problematic, depending on FDA enforcement.**

The guidance describes a situation where an FDA-approved medication is available on the market and the patient's condition could be treated by using the medication via a route of administration which is not approved nor appears in the labeling for the drug. While IACP generally agrees with the example outlined in the section (lines 261-267), we fear implementation and enforcement by the Agency regarding this provision could be problematic.

For example, if an FDA-approved cream is labeled "for intravaginal use only," but the prescriber would like to use the medication topically for treatment of a skin condition on the patient's arm, would the pharmacy be required to dispense the FDA-approved medication or would this cream be allowed to be compounded? If an FDA-approved otic drop is currently available, are pharmacies required to dispense the approved drug if it is to be used orally or topically on the skin?

While IACP generally agrees with the example provided within the "Same Route of Administration" provision, **we strongly urge the Agency to develop more detailed practice standards in future draft guidances** to provide clear direction to compounders as to what this provision does or does not entail.

4. **"Same Characteristics as Two or More Commercially Available Drug Products" ignores the ability of compounders to combine medications, which could possibly increase patient compliance to prescribed drug regimens.**

Again, while IACP generally agrees with the overall premise the Agency provides that compounding two or more commercially available drugs should be considered an essential copy, the guidance completely ignores the ability of compounders to provide such a combination where the patient has compliance issues with his or her current drug regimen. Additionally, IACP has concerns regarding when this provision would be enforced, especially when it comes to multiple ingredient compounds. For example, a commonly compounded medication, Mary's Magic Mouthwash, can be compounded in one of two ways – either by combining three or more FDA-approved medications or by utilizing Active Pharmaceutical Ingredients (APIs) that either have USP or NF monographs or appear in FDA-approved drugs. IACP is concerned the guidance disallows the use of APIs when compounding this formulation. Is it the Agency's intention to limit multiple ingredient compounding utilizing APIs for prescriptions like Mary's Magic Mouthwash? Utilizing APIs for compounds such as this eliminates unnecessary excipients and

allows for more accurate drug concentrations which can be tailored to meet the patient's medical needs. We recommend **allowing for combinations of commercially available drugs to be incorporated into a single compounded preparation when the prescriber has determined the clinical significance of ensuring patient compliance with the prescribed regimen. IACP also recommends for the allowance for compounding from APIs when a multiple ingredient compound has been prescribed and not restrict compounders to only use FDA-approved drugs.**

5. **Provisions with the "Statement of Significant Difference" ignore the issue of rising drug costs in the United States which negatively impact patients and their healthcare and which ignores the Agency's prior actions regarding compounding because of cost.**

Lines 302-308 clearly state that "…lower price, is not sufficient to establish that the compounded drug product is not essentially a copy of the commercially available product." This statement is provided in the guidance in the section covering the "Statement of Significant Difference." IACP argues that cost should be factored in as a significant difference, and past Agency actions support this idea.

In a time of skyrocketing drug costs, compounding can provide a solution to those patients who otherwise cannot afford potentially lifesaving medication. Many of these patients, parents and caregivers have decided to either turn to foreign countries to obtain their medication (and thus, obtaining non-FDA approved drugs) or have decided to not take the prescribed drug at all. When a solution is so readily available to patients and prescribers alike, the Agency should look to allow "compounding on the basis of cost" instead of rejecting the idea outright.

Historically, the FDA has allowed "compounding on the basis of cost." In a published statement on March 30, 2011[1], in response to a marked increase in the cost of an FDA-approved form of hydroxyprogesterone caproate, the Agency said:

> "In order to support access to this important drug, at this time and under this unique situation, FDA does not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate based on a valid prescription for an individually identified patient unless the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products."

Therefore, FDA itself has identified at least one case in recent history where cost was an acceptable factor in which to compound an essential copy of a commercially available medication. IACP additionally argues that cost is a "significant difference" when it serves as a barrier as to whether a patient will be able to afford the prescribed medication. If the patient cannot afford the medication, the negative consequences to the patient's health could be

[1] FDA Statement on Makena. (2011, March 31) Retrieved from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2011/ucm249025.htm on October 10, 2016

substantial, leading to either an associated increase in other health care costs (additional physician visits, hospital admittance, long term care, etc.) or even patient death.

IACP urges the FDA to work with key stakeholders regarding this issue in order to develop a sound and smart policy which would allow compounders to help those patients who otherwise cannot afford their prescribed medication or are turning to foreign sources for their medications.

6. **The limitations described in relationship to inordinate amounts are arbitrary and, without further insight, appear to be completely unsubstantiated.**

While IACP appreciates a clearly defined amount as the "ceiling" for what would be considered an inordinate amount, the terms used within this section are confusing and, when coupled with the issue of drug shortages as described above, could be problematic for compounders to provide essential medications to patients.

In the footnote referenced in this section (16), the Agency describes "each refill of a prescription as an additional prescription." This is confounding to the day-to-day terms used in the practice of pharmacy and, moreover, could be misconstrued by State Boards of Pharmacy as a differing definition for the term "refill" as found in the various Pharmacy Practice Acts across the country. **IACP urges the FDA to rework this section to provide more clarity and to work with the Boards of Pharmacy to ensure the guidance does not contradict current State laws or regulations.**

Additionally, the "four or fewer prescriptions" limitation per month could cause great issues if the drug shortage issue described above is not resolved in a more pragmatic way. If an FDA-approved drug is not available to patients, pharmacies and prescribers but fails to appear on the Agency's drug shortage list, the compounder would be artificially limited in being able to provide compounded medications to those patients who need it most. Even worse, the compounder would be forced to pick and choose which patients would receive the compounded medication, a decision no healthcare professional should be required to make, especially when compounded options are available, because of this artificial limitation. **Again, we urge the Agency to dutifully consider the addition of other resources to allow the compounder to determine whether or not an FDA-approved medication is available in the marketplace.**

7. **IACP requests the Agency produce a flow chart, much like what is published in the guidance for essential copies for 503B Outsourcing Facilities, in order to more clearly show the process in which the FDA would determine if a medication is an essential copy of a commercial drug or not.**

The provision of a flow chart will provide clarity for the "decision tree" FDA would use in making this important determination.

Thank you for the opportunity to submit our comments on this guidance. IACP looks forward to working with the FDA in the future on this very important issue.

Sincerely,

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Executive Vice President
International Academy of Compounding Pharmacists