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EVERWELL℠
SPECIALTY PHARMACY

September 19, 2016

Susan M. Turcobski, District Director
Joshua P. Wireman, Investigator
Department of Health and Human Services
Food and Drug Administration
555 Winderly Place, Suite 200
Maitland, FL 32751

Via Overnight Delivery

Re: Response to FDA Form 483 Issued August 31, 2016,
to Pensacola Apothecary, Inc., d/b/a Everwell Specialty Pharmacy

Dear Ms. Turcobski and Mr. Wireman:

The Food and Drug Administration ("FDA") conducted an inspection of Pensacola Apothecary, Inc., d/b/a Everwell Specialty Pharmacy ("Everwell Specialty Pharmacy"), located at 6506 N. Davis Highway, Pensacola, Florida 32504, between August 22 and August 31, 2016. Upon the conclusion of its inspection, the FDA provided Everwell Specialty Pharmacy with an FDA Form 483 detailing five observations. Please accept this letter as Everwell Specialty Pharmacy's response to the observations raised in the FDA Form 483.

Everwell Specialty Pharmacy hereby requests that the FDA publicly disclose this response, excluding the exhibits, whenever the FDA provides a copy of Everwell Specialty Pharmacy's FDA Form 483 to any individual or entity outside the FDA. In addition, Everwell Specialty Pharmacy asks that this information also be posted on the FDA's website next to the Form 483. Everwell Specialty Pharmacy understands that the information that is disclosed may contain confidential commercial or financial information or trade secrets within the meaning of 18 U.S.C. § 1905, 21 U.S.C. § 331(y)(2) and 5 U.S.C. § 552(b)(4) that is exempt from public disclosure under those statutory provisions and/or relevant FDA regulations. Everwell Specialty Pharmacy agrees to hold the FDA harmless for any injury caused by the FDA's sharing the information with the public.

It is the understanding of Everwell Specialty Pharmacy that the FDA considered it to be an outsourcing facility during the inspection process and based its observations on the current Good Manufacturing Practices ("cGMPs") for finished pharmaceuticals. Please note that, to the extent the observations cited within the FDA Form 483 are based on cGMPs, such cGMPs are

inapplicable to the operations of Everwell Specialty Pharmacy. The cGMPs are requirements imposed upon either drug manufacturers or outsourcing facilities. Everwell Specialty Pharmacy does not engage in drug manufacturing nor has it registered as an outsourcing facility under 21 U.S.C. § 353b. Everwell Specialty Pharmacy remains a traditional pharmacy licensed by the boards of pharmacy in the states in which it conducts business as a retail pharmacy and is subject to their jurisdiction.

The FDA's cGMPs for finished pharmaceuticals are not applicable to Everwell Specialty Pharmacy or any compounded medications it prepares. 21 U.S.C. § 353a specifically exempts a compounding pharmacy from the cGMP requirements imposed on a drug manufacturer or outsourcing facility by 21 U.S.C. § 351(a)(2)(B). In particular, 21 U.S.C. § 353a states:

> (a) In General.-- Sections 351(a)(2)(B), 352(f)(1), and 355 shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding--
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> (1) is by--
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> (A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or
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> (B) a licensed physician, on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or
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> (2)
>
> (A) is by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and
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> (B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between--
>
> (i) the licensed pharmacist or licensed physician; and

(ii)

(I) such individual patient for whom the prescription order will be provided; or

(II) the physician or other licensed practitioner who will write such prescription order.

Everwell Specialty Pharmacy operates in compliance with the requirements of 21 U.S.C. § 353a, applicable state laws and regulations governing pharmacy compounding, and with the appropriate United States Pharmacopoeia ("USP") chapters. The pharmacy compounds primarily patient-specific prescriptions in compliance with the laws of states where it conducts business. Everwell Specialty Pharmacy also prepares non-sterile medications for administration in the offices of licensed prescribing practitioners in Florida upon the receipt of their orders as permitted by Florida state law. Specifically, Fl. Rule 64B16-27.700(3) states, in part, that a "pharmacist may dispense and deliver a quantity of a compounded drug to a practitioner for office-use by the practitioner in accordance with this section ...." To the extent that Everwell Specialty Pharmacy is in compliance with the Florida Board of Pharmacy's rules regarding office-use compounding, it is also exempt from complying with cGMPs applicable to drug manufacturers and outsourcing facilities under 21 U.S.C. § 351(a)(2)(B).

To the extent that the FDA contends that Everwell Specialty Pharmacy is not protected by Section 353a for medications prepared and dispensed to practitioners for administration in their office, we reiterate that such practice is expressly authorized by the Florida Board of Pharmacy. Furthermore, Congress never intended to allow the FDA to prohibit pharmacy compounding for office-use in states where it is expressly allowed and regulated. In a letter to the FDA dated June 27, 2014, members of Congress clarified its intent as follows:

> Pharmacies that produce small amounts of compounded products in advance of receiving a patient-specific prescription and practice within States where office-use is authorized and regulated by State Boards of Pharmacy should not be the focus of FDA oversight. Expecting these small pharmacies that practice in accordance with State law to register as outsourcing facilities solely because products are intended for office-use is unreasonable. As FDA prioritizes its resources in a way that best protects public health, we believe the focus should be on manufacturers, not small pharmacies providing safely-compounded products for the physicians and hospitals in their communities.[1]

[1] Letter from H. Morgan Griffith, et al., to U.S. Food and Drug Administration (June 27, 2014).

In the House Agriculture Appropriations Committee Report dated July 14, 2015, the U.S. Congress again reiterated its belief that the FDA has, by attempting to regulate office-use compounding, overstepped its statutory authority.[2] Specifically, Congress stated that office-use compounding is authorized in "the vast majority of states and was intended to be allowed" under 21 U.S.C. § 353a and subsequently directed the FDA to issue guidance allowing pharmacies to engage in office-use compounding before the receipt of a patient-specific prescription in a manner consistent with the provisions of Section 353a.[3]

Most recently, on June 20, 2016, Congress stated in a letter to the Commissioner of the FDA that "[i]t is unacceptable that the FDA would ignore the Congress and continue to take the position that Section 503A specifically prohibits office-use compounding, despite clear congressional intent to the contrary and despite previous FDA actions that directly contradict that position, including the recent statement by Health and Human Services Secretary Burwell that also directly conflicts with FDA's current position on 'office-use.'"[4] As a pharmacy that neither engages in drug manufacturing nor is registered as a 503B outsourcing facility, it is improper to deny Everwell Specialty Pharmacy the exemptions afforded to traditional retail pharmacies under Section 353a in light of Congress's expressed intent. For these reasons, Everwell Specialty Pharmacy challenges the FDA's observations on the grounds that the cGMPs are not applicable to its compounding pharmacy operations. Rather, Everwell Specialty Pharmacy adheres to the requirements and recommendations set forth in the USP chapters as well as the rules established by the state boards of pharmacy. Please note that Everwell Specialty Pharmacy has no desire or intent to become an outsourcing facility to which cGMP requirements apply.

Notwithstanding Everwell Specialty Pharmacy's objection of the FDA's classification of its operations as an outsourcing facility, it would like to assure the FDA that it is committed to providing patients with the highest quality prescription medications and services. Accordingly, Everwell Specialty Pharmacy has ceased compounding any non-sterile medications for office-use as of August 23, 2016, and practitioners were notified accordingly. Please note that the compounding of non-sterile medications for office-use constituted only a small component of Everwell Specialty Pharmacy's operations. In the three months prior to cessation, such compounding accounted for only 0.3 percent of its prescriptions processed at the pharmacy. Everwell Specialty Pharmacy ceased compounding sterile medications for office-use several years prior.

Our responses to the observations raised in the FDA Form 483 are as follows:

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[2] H. Rep. No. 114-205 (2015).
[3] Id.
[4] Letter from Chris Stewart, et al., to Dr. Robert M. Califf, M.D., Commissioner, U.S. Food and Drug Administration (June 20, 2016).

1. ***Observation 1: Personnel donned gowning apparel improperly, in a way that may have caused the gowning apparel to become contaminated.***

   Specifically, the gowns worn during aseptic production are stored on a shelf next to a sink in the anteroom where they can be splashed with water during handwashing.

   Response: The current USP chapter <797> does not provide specific and detailed guidance regarding the storage of gowning apparel utilized by pharmacy personnel during aseptic production. Specifically, USP chapter <797> does not provide guidance or instructions on the placement of gowning apparel in relation to its distance from a sink in the anteroom. Rather, USP chapter <797> states only that gowns should be donned by compounding personnel prior to entering the compounding area.

   Notwithstanding the above, we acknowledge that stricter garbing policies and procedures are a best practice that may provide greater assurances of patient safety. Accordingly, we have moved all gowning apparel to the opposite side of the anteroom, approximately eight feet away from the sink utilized by pharmacy personnel for hand washing purposes. Photographs of the new storage location of the gowning apparel are provided as Exhibits A and B.

2. ***Observation 2: Equipment, material, and/or supplies are not disinfected prior to entering the aseptic processing areas.***

   Specifically, General Aseptic Technique SOP 5.2.1 states that work surfaces of the aseptic production area shall be cleaned prior to use. While observing the production of Lot: 08242016@18 it was noted that the inside surface of the ISO 5 Unit was not sanitized prior to production.

   Response: The technician observed by the FDA during its inspection had cleaned the immediate work surface area, the base of the isolator, prior to beginning compounding activities. However, the technician failed to properly sanitize the inside surface of the equipment in accordance with Everwell Specialty Pharmacy's policies and procedures. Everwell Specialty Pharmacy acknowledges the importance of properly ensuring the sterility of equipment utilized in the sterile compounding process. SOP 5.2.1, *General Aseptic Technique*, requires that applicable compounding personnel are required to clean all interior work surfaces and sides prior to and after each use of the equipment. A copy of the SOP 5.2.1 is provided as Exhibit C. In addition, all pharmacy personnel involved in sterile compounding operations have been retrained and instructed on the required procedures of SOP 5.2.1. The signed acknowledgements from the

appropriate personnel regarding their review and understanding of SOP 5.2.1 are provided as Exhibit D.

3. ***Observation 3: Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.***

Specifically, finished nonsterile products are not tested for potency and unacceptable microorganisms. For example lot#06102016@12 was not tested for potency and unacceptable microorganisms.

Response: Everwell Specialty Pharmacy acknowledges the importance of safe and potent compounded non-sterile medications. Please note that USP chapter <795> does not require the testing of finished non-sterile medications for potency and microorganisms. Rather, USP chapter <795> requires only that a "reliable BUD is established to ensure that the finished preparation has its accepted potency, purity, quality, and characteristics, at least until the labeled BUD." When assigning a BUD to a compound, USP chapter <795> recommends that the compounder refer to information provided by the manufacturer, applicable literature, and stability factors set forth in USP chapter <1191> as well as his or her own "compounding education and experience." With regards to lot#06102016@12, Everwell Specialty Pharmacy reviewed pertinent information and determined that a BUD of 180 days was appropriate. Thus, Everwell Specialty Pharmacy is in compliance with the requirements of USP chapter <795>.

4. ***Observation 4: There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.***

Specifically, mixing instructions do not include duration of mixing to assure the replication of the process. For example, the logged formula worksheet instructions for Capsule lot 08182016@10 state to mix all powders with agitation in the Turbula, however the mixing time is not included in the instructions.

Response: Everwell Specialty Pharmacy acknowledges the importance of specifying the duration of mixing for a compounded pharmaceutical in order to ensure an accurate replication of the preparation as compounded. Everwell Specialty Pharmacy utilizes the Turbula for all mixing processes. At the time of inspection, the mixing times using the Turbula were listed on the equipment itself

and varied based on the powder load being mixed and the size of the prescription or batch being prepared.

However, as a best practice, Everwell Specialty Pharmacy has amended its compounding formula worksheets so as to specifically detail the duration of mixing for the particular compound. An example of the amended compounding formula worksheet is provided as Exhibit E. In addition, SOP 4.13.1, *Compounding of Capsules*, has been revised to include the specific Turbula mixing times. A copy of the amended SOP 4.13.1 is provided as Exhibit F.

5. ***Observation 5: Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.***

Specifically, the cleaning and maintenance of the Non-Sterile Compounding Area SOP 4.15.1 has not been validated to assure removal of residual product and sanitizing agents and prevent crossover between batches.

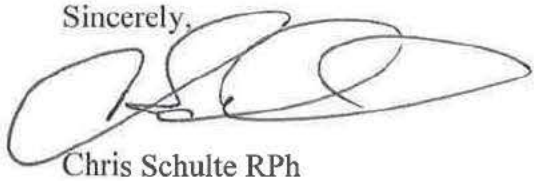
Response: Everwell Specialty Pharmacy is in compliance with USP chapter <795> requirements for compounded non-sterile preparation which do not require the testing of the compounding area for residual products or sanitizing agents. Rather, USP chapter <795> requires only that the areas used for compounding be maintained in "clean, orderly, and sanitary conditions ...." In addition, equipment utilized in the compounding process are to be "appropriately cleaned" after each use. Unlike USP chapter <797> for sterile compounding, USP chapter <795> does not require or recommend the use of a specific sanitizing or cleaning agent. SOP 4.15.1, *Cleaning and Maintenance of the Non-Sterile Compounding Area*, provides for monthly and daily cleaning by pharmacy personnel. In addition, pharmacy personnel are required to "clean and sanitize the exposed work surfaces before and after each batch preparation and immediately should a spill occur." A copy of SOP 4.15.1 is provided as Exhibit G. To the extent that the pharmacy's cleaning policies and procedures for its non-sterile compounding area is compliant with the requirements of USP chapter <795>, no additional corrective action is necessary.

Conclusion

With this response, Everwell Specialty Pharmacy has sought to address all of the FDA's observations and concerns. While cGMP requirements are not applicable to the pharmacy's current operations, Everwell Specialty Pharmacy has viewed the FDA's observations as suggestions for improvement and has implemented additional best practices to the extent feasible and compatible with its obligations under state law and applicable USP guidelines. If the FDA

requires additional information or communication from Everwell Specialty Pharmacy, please contact me at 855-507-2560 or Chris@everwellrx.com.

Sincerely,



Chris Schulte RPh
President and Owner
Everwell Specialty Pharmacy

Enclosures