PHARMACY CREATIONS, LLC
Compounding and Nutritional Pharmacy

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September 3, 2013

Ms. Diana Amador-Toro, District Director
FDA Field Office, New Jersey District (NWJ-DO)
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Attn: Douglas C. Kovacs, Investigator
Michael R. Klapal, Investigator

Re: FDA 483, Pharmacy Creations of Randolph, New Jersey

Dear District Director Amador-Toro and Investigators Kovacs and Klapal,

On August 5-19, 2013, the FDA Field Office conducted an inspection of our pharmacy located at 540 Route 10 West in Randolph, New Jersey, 07869. At the conclusion of the inspection, on August 19, 2013, we received an FDA Form 483 setting forth five (5) observations. At this time, Pharmacy Creations has not received any additional correspondence related to same or any request for corrective action related to same from the FDA.

This letter is in response to the FDA Form 483. If this Form 483 appears on the FDA website, we respectfully request that this response, excluding the attached internal operating and testing procedures, be posted on the FDA's website alongside the Form 483 and be included as an additional attachment any time the FDA provides a copy of Pharmacy Creations' FDA Form 483 to anyone or any entity outside the FDA.

The observations noted on the FDA Form 483 are all requirements imposed on drug manufacturers under the Current Good Manufacturing Practices (cGMPs) for Finished Pharmaceuticals contained in 21 C.F.R. §§ 211 *et seq*., and further explained in the FDA's Guidance for Industry on cGMPs for Sterile Drug Products Produced by Aseptic Processing (2004). Similarly, 21 U.S.C. § 351(a)(2)(B), related to the "manufactured" "drugs or devices," applies only to drug manufacturers. *See* 21 U.S.C. ' 353A(a) (exempting compounding pharmacies from § 351(a)(2)(B), § 352(f)(1), and § 355).

Pharmacy Creations is licensed and permitted by the New Jersey Board of Pharmacy and subject to its jurisdiction. *See* N.J. STAT. ANN. §§ 45:14-41, 45-14-49, 45:14-73; N.J. ADMIN. CODE §§ 13:39-4.1, 13:39-11.1 *et seq*. Pharmacy Creations of New Jersey is not licensed as a manufacturer and does not engage in drug manufacturing. Pharmacy Creations engages in traditional retail drug prescription dispensing as well as pharmacy compounding of sterile products. All medications are dispensed and prepared pursuant to a prescription or prescriptive

order to individual patients based on a patient-specific prescription or in medical institution populations such as hospitals and surgery centers from a licensed practitioner, including all compounded medications. For these and other reasons, Pharmacy Creations disputes the measurement of its operations against drug manufacturing cGMPs requirements. In addition to the New Jersey regulatory regime, Pharmacy Creations is subject to Good Compounding Practices of the United States Pharmacopoeia (USP), which Pharmacy Creations follows.

Pharmacy Creations practices its compounding in full compliance with New Jersey Board of Pharmacy "compounding sterile preparations" requirements. In addition, Pharmacy Creations operates in full compliance with USP 797, and maintains accreditation with the Pharmacy Compounding Accreditation Board (PCAB). To continue our commitment to sustained improvement in pharmacy compounding, Pharmacy Creations has addressed each Form 483 observation in detail below. As noted, Pharmacy Creations disputes observations to the extent that they are premised on cGMPs requirements set forth in 21 C.F.R. §§ 211 *et seq*. However, and as noted below, Pharmacy Creations has already taken or is it the process of taking many of the corrective actions suggested by the FDA inspectors during inspection and included on the Form 483.

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<u>Observation 1</u>: An adequate number of batches of each drug product are not tested to determine an appropriate expiration date.

Pharmacy Creations was in the process of end-point, beyond use date ("BUD") testing when the FDA's inspection was conducted. Pharmacy Creations' personnel were told by both inspectors that only sterility, not both sterility and potency were necessary for preparation integrity, and results thereto have been coming in from the submitted list we gave the inspectors for proof of compliance. These results are attached as Exhibit A, which also includes a Table titled "End Point Sterility Studies." Pharmacy Creations is fully compliant with N.J. ADMIN. CODE §§ 13:39-11.10 ("Stability Criteria and Beyond Use-Dating").

<u>Observation 2</u>: Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

Pharmacy Creations has implemented additional media fill simulations, both before and after issuance of the FDA Form 483, to better assess sterile technique. Please refer to Pharmacy Creations' policy and procedure number 5.010, attached hereto as Exhibit B, which describes newly added media simulation processes for compounding with the Baxa Repeater pump and during the lyophilization process. Please also see forms A65 and A66, attached hereto as Exhibit B-1, showing newly added forms for documentation of media simulation prepared by sterile compounding staff members. Pharmacy Creations is fully compliant with N.J. ADMIN. CODE §§ 13:39-11.10 ("Stability Criteria and Beyond Use-Dating").

<u>Observation 3</u>: Drug product containers were not sterilized to remove pyrogenic properties to assure that they are suitable for their intended use.

Pharmacy Creations currently employs a Depyrogenation Method, which is both valid and accepted by the USP and scores of authoritative compounding resources. *See, e.g.*, REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (22d Ed. 2013); TURCO SJ., STERILE DOSAGE FORMS: THEIR PREPARATION AND CLINICAL APPLICATION (4th Ed. 1994); GROVES MJ., PARENTERAL TECHNOLOGY MANUAL: AN INTRODUCTION TO FORMULATION AND PRODUCT ASPECTS OF PARENTERAL PRODUCTS (1985). At the time of the FDA inspection, Pharmacy Creations was in the process of validating its Depyrogenation Method with two outside labs. Validation of a depyrogenation method can be accomplished through the use of the Limulus Amebocyte Lysate (LAL) test. The ultimate test on the efficiency of depyrogenation is the result obtained from endotoxin testing for the sterile preparations. Please see the copy of the study report titled "Beaker and Vials Endotoxins" performed on controls, rinsed and heat depyrogenated samples, attached hereto as Exhibit C. Please also see the document titled "Depyrogenation Study #2," attached hereto as Exhibit C-1, which describes the study being conducted by Dynalabs, an independent laboratory. Preliminary Results from that testing, attached hereto as Exhibit C-2, demonstrate that Pharmacy Creations' method will be effective in reducing "pyrogens to acceptable levels." At the time of this writing, results on endotoxin levels on the control are pending, however results of the heated and rinse-method depyrogenation samples are identical. The FDA's inspector's also suggested a "spiked control test" to demonstrate a "3 log reduction." Pharmacy Creations has initiated and undertaken this test. Results will be submitted as an addendum hereto as soon as they become available. Pharmacy Creations is fully compliant with N.J. ADMIN. CODE §§ 13:39-11.10 ("Stability Criteria and Beyond Use-Dating").

<u>Observation 4</u>: Each batch of drug product purporting to be sterile is not laboratory tested to determine conformance to such requirements.

Growth media promotion/challenge was being conducted by Pharmacy Creations at the time of the FDA's inspection. The Pharmacist in charge was not aware that documentation was available at the time of the inspection. We have since added additional controls for all new lots of media. Potency testing is performed annually for each preparation type and new formulation to determine accuracy of formulation and BUD dating as per New Jersey state regulations and PCAB standards. We will increase periodic and routine potency testing per our policy and procedures. Please see Pharmacy Creations' policy and procedure number 5.140, attached hereto as Exhibit D, which describes the procedures and documentation of media fill challenges to be performed on each new media lot. Form A67, attached hereto as Exhibit D-1, demonstrates the documentation process for recording the results of the media challenges. Pharmacy Creations is fully compliant with N.J. ADMIN. CODE §§ 13:39-11.10 ("Stability Criteria and Beyond Use-Dating").

<u>Observation 5</u>: Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

As noted, *supra*, Pharmacy Creations of New Jersey is not licensed as a drug manufacturer and does not engage in drug manufacturing. Pharmacy Creations is licensed as a traditional pharmacy, permitted by the New Jersey Board of Pharmacy, and subject to that Board's jurisdiction. New Jersey regulation 13:39-11.24 requires that air and surface sampling for microbial organisms in an ISO class 5 clean room and related areas be performed twice annually, which Pharmacy Creations has done using an approved outside certifier, Charles Solana & Sons. Pharmacy Creations also operates in full compliance with USP 797. Periodic and routine non-viable particle testing, as observed by the FDA inspectors, is not found in the USP and is required per the parameters of the NJ regulation above. Because Pharmacy Creations is licensed and permitted as a traditional compounding pharmacy it is not subject to or required to comply with FDA cGMPs as those regulations and associated guidance are set forth for pharmaceutical manufacturers. Pharmacy Creations is fully compliant with N.J. ADMIN. CODE §§ 13:39-11.10 (Stability Criteria and Beyond Use-Dating) and N.J. ADMIN. CODE §§ 13:39-11.24 (Air and Microbial Organism Testing) per above.

If I can provide any additional information, please do not hesitate to contact me at any time.

Sincerely,

<u>/s/ Scott Karolchyk</u>

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