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July 25, 2016

VIA OVERNIGHT MAIL

Acting Director Dobilas
Food and Drug Administration, New Jersey Office
10 Waterview Boulevard 3rd Floor
Parsippany, New Jersey 07054

Re: Waiver of Colonia Care Pharmacy for Publication of Response to FDA Form 483 Issued April 15, 2016

Dear Director Dobilas:

On behalf of Colonia Care Pharmacy, I hereby authorize the United States Food and Drug Administration (“FDA”) to publicly disclose the information described below on FDA’s website. I understand 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. I agree to hold FDA harmless for any injury caused by FDA’s sharing the information with the public.

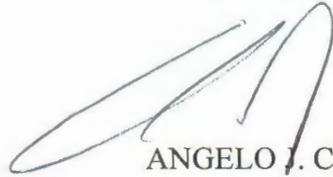
Information to be disclosed: Colonia Care Pharmacy’s Response to the FDA Form 483 issued April 15, 2016. The waiver shall extend only to Colonia Care Pharmacy’s Response to the FDA Form 483 Issued April 15, 2016 and not to any of the supporting or underlying documents implicated or involved in the FDA Form 483 issued April 15, 2016 or Colonia Care Pharmacy’s response thereto. A copy of Colonia Care Pharmacy’s Response to the FDA Form 483 issued April 15, 2016 is attached herewith for your reference.

Authorization is given to FDA to disclose the above-mentioned information which may include confidential commercial or financial or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of Colonia Care Pharmacy, and my full name, title, telephone number, and facsimile number is set out above for verification.

In the event there are any questions regarding the disclosure of such information, I hereby request pre-disclosure notification so that we can address any such questions prior to disclosure of the material.

In the interim, please do not hesitate to contact me should you have any questions.

Very truly yours,

A handwritten signature in black ink, appearing to read 'ANGELO J. CIFALDI', written over a light blue horizontal line.

ANGELO J. CIFALDI

AJC/cg

cc: Nicolas A. Violand, Investigator (Via E-Mail-Nicholas.Violand@fda.hhs.gov)

Lisa Matthews, District Recall Coordinator (Via E-Mail-Lisa.Mathew@fda.hhs.gov)

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May 5, 2016

VIA OVERNIGHT MAIL
Acting Director Dobilas
Food and Drug Administration, New Jersey Office
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

RE: Colonia Care Pharmacy
Response to 483

Dear Director Dobilas:

Please be advised that I represent the above referenced pharmacy. Please accept this submission in response to the 483 issued to Colonia Care Pharmacy. For the reasons set forth below, the pharmacy respectfully disputes portions of the FDA's factual and/or legal findings.

Please note that Colonia Care Pharmacy makes this submission without conceding the relevancy, materiality, existence, or admissibility of any document or document request, and without prejudice as to its rights to further contest the FDA's findings. In producing or making available for inspection documents in connection with this action, Colonia Care Pharmacy reserved, and continues to reserve, all claims of privilege and other such protections and further hereby expressly reserves the right to demand the return of all copies of, and object to the use of, any documents or information subject to a claim of privilege or other such protections that are inadvertently disclosed.

Additionally, please be advised that Colonia Care Pharmacy reserves the right to supplement this response and/or submit additional information as it pertains to this matter and the 483 that has been issued. This letter does not waive any rights Colonia Care Pharmacy may assert under applicable law. Furthermore, this submission should not be construed as a waiver of Colonia Care Pharmacy's rights.

As an initial matter, we also note that the pharmacy fully and voluntarily cooperated with FDA throughout the course of this matter. In addition to responding to multiple requests for

documentation, the pharmacy and its staff were also made available for multiple interviews. The pharmacy did not refuse to provide any information.

Additionally, we note that the findings contained in the 483 are based on manufacturing standards not applicable to the pharmacy. During the exit interview, Mr. Nicolas A. Violand conceded that the findings were not based upon USP Standards or New Jersey Board of Pharmacy regulations. Furthermore, even though he was unable to identify specific citations to the regulations he applied, Mr. Violand conceded that the federal regulations he generally cited pertained to facilities registered with the FDA as manufacturers.

The Form 483 observations attempt to hold Colonia Care Pharmacy to cGMP standards with which, as a matter of law, CCP is not required to comply. See 21 U.S.C. § 353a(a)(1)-(2). Colonia Care Pharmacy objects to any observation in the Form 483 which inappropriately applies cGMP standards. While Colonia Care Pharmacy is addressing all of FDA's inspectional findings, its cooperation with FDA should not be construed as Colonia Care Pharmacy agreeing that it is required to comply with cGMP.

Colonia Care Pharmacy is not a manufacturer. Colonia Care Pharmacy is a retail pharmacy licensed by the New Jersey Board of Pharmacy that compounds medications pursuant to patient specific prescriptions. Furthermore, Colonia Care Pharmacy holds an unrestricted license and is in good standing.

Notwithstanding the questionable application of federal manufacturing regulations to a retail pharmacy, we would like to assure FDA that Colonia Care Pharmacy is committed to providing patients with the highest quality compounded medications prepared in compliance with all applicable standards and that, as demonstrated herein, the pharmacy takes its professional responsibilities very seriously.

To that end, patient safety is Colonia Care Pharmacy's primary concern, and the pharmacy strives to provide the highest quality preparations and services. Colonia Care Pharmacy has an impeccable safety record concerning the compounded medications that it prepares according to the applicable standards.

Its quality assurance and standard operating procedures ("SOPs") follow demonstrated pharmacy best practices and are designed to produce high-quality compounded sterile preparations. Colonia Care Pharmacy's practices are based upon New Jersey Board of Pharmacy requirements and other standards applicable to retail pharmacies so that its patients can continue to access high-quality compounded medications to meet their individual medical needs.

Moreover, in several instances, the Form 483 and FDA's observations are on their face incorrect. There are several material errors of fact and any observations premised on these errors should be withdrawn or amended to reflect the actual facts.

In light of the above, without waiving its right to contest FDA's application of cGMPs, Colonia Care Pharmacy provides the following responses to the Observations set forth in the 483.

OBSERVATION 1

There is no written testing program designed to assess the stability characteristics of drug products. Specifically, there is insufficient test data supporting the labeled Beyond Use Date (BUD) provided for some injectable products or in-process sterile-filtered stock solutions used to prepare them. For example:

1. *Papaverine/Phentolamine/Prostaglandin-El Injection Solution ("Trimix"), lot 020216A, was prepared and filled on 2/2/16 in a multi-use vial, with a BUD of 30 days refrigerated, and 6 months when frozen. The finished product was not tested for sterility, and was made using inhouse stock solutions prepared from non-sterile starting materials, one of which was expired (Papaverine stock solution expired approx. 23 days earlier, on 1/10/2016).*

Each stock injection solution was prepared in a multi-use vial, and assigned a BUD of 1 to 6 months after filter sterilization, and stored in an unclassified area (Papaverine stock solution produced on 12/11/15, BUD 01/10/16; Phentolamine stock solution produced on 12/03/15, BUD 05/31/16; and Alprostadil stock solution produced on 12/11/15, BUD 06/08/16).

No data was provided demonstrating these stock solutions or finished sterile drug product have been evaluated for potency, purity, sterility, or endotoxin levels at the end of their labeled BUDs. The stock solutions may contain preservatives, but their effectiveness over the labeled BUDs in multi-use vials has also not been assessed.

Response:

The FDA's observation includes errors of fact. The Papaverine stock solution was not expired. As we informed Mr. Violand, the expiration date noted in the print out of the electronic record reflects a refrigerated beyond use date. It does not reflect the frozen beyond use date that actually applied to the product. The observation also fails to define material terms that on their face are not applicable to a retail pharmacy. For example, the Observation calls for "classified areas."

We acknowledge this observation but disagree with the stated conclusion. Since FDA is holding the pharmacy to a standard that is inapplicable to a compounding pharmacy under FDCA Section 503A and this pharmacy is not a manufacturer of drug for human use, the preparation of sterile aliquots and stock solutions falls within the practice of pharmacy. As such, it is within the prevailing standard of care not to test the stability, sterility, and potency characteristics of the aliquots taken from these stock solutions. Colonia Care Pharmacy does test for stability, sterility and potency characteristics. Colonia Care Pharmacy has also revised its policy for handling aliquots and stock solutions. Moving forward, Colonia Care Pharmacy will be preparing patient specific prescriptions utilizing trituration and dispensed in single dose vials with USP <797> compliant beyond use dates.

2. *Methylcobalamin and Acetylcysteine Injection Solution, lot 120715M, was prepared and filled on 12/07/15 in pre-filled syringes, with a BUD of 30 days refrigerated, and 6 months when frozen. The finished product was not tested for sterility, and was made from an in-house stock solution, with BUD 04/05/16 (prepared 10/08/15), which is stored in an unclassified area. No data was provided demonstrating the stock solution, or finished sterile drug product have been evaluated for potency, purity, sterility, or endotoxin levels at the end of their labeled BUDs, or that the container-closure system (syringes); used for the finished drug product is suitable for its intended use.*

Response:

Colonia Care Pharmacy incorporates by reference its response to paragraph one of Observation 1 (see above). Moving forward, Colonia Care Pharmacy will be preparing patient specific prescriptions dispensed in syringes, pursuant to the literature sources previously produced by the pharmacy, with USP <797> compliant beyond use dates. We note that as it relates to this compound, it is not prepared by way of trituration. We also note that Acetylcysteine Injection is a commercial product that was utilized as part of this compound.

3. *Dexamethasone 24mg/ml Injectable, lot 031716N, was aseptically filled on 3/17/2016, with instructions to provide a BUD of "45 days after compounding date" but was labeled "06/01/16 Frozen", instead of the specified "5/1/2016" in the record. There was no sterility, potency, purity, or endotoxin testing performed to support the labeled BUD.*

Response:

The FDA's observation includes errors of fact. The product is labeled "'5/1/2016" not "06/01/16"

OBSERVATION 2

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

Specifically, not all finished sterile drug products are tested for sterility and endotoxin levels, where appropriate, and there is no testing schedule. For example:

- a) *Papaverine/Phentolamine/Prostaglandin-EI Injection Solution ("Trimix"), lot 020216A, was prepared and filled on 2/2/16, and given a BUD of 30 days refrigerated, and 6 months when frozen. There was no testing of sterility or endotoxin levels of the finished drug product.*

Methylcobalamin and Acetylcysteine Injection Solution, lot 120715M, was prepared and filled on 12/07/15, and given a BUD of 30 days refrigerated, and 6 months when frozen. There was no testing of sterility or endotoxin levels of the finished drug product.

Atropine Ophthalmic Solution, lot 020316J, was prepared and filled on 02/03/16, and given a BUD of 3 months. There was no testing of sterility of the finished drug product.

Hydrogen Peroxide Injectable, lot 010516G, was prepared and filled on 01/05/16, and given a BUD of 1 month. There was no testing of sterility or endotoxin levels of the finished drug product.

Response:

Colonia Care Pharmacy acknowledges the importance of safe and potent compounded medications. As a compounding retail pharmacy, Colonia Care Pharmacy is governed by USP chapter <797>, which does not require potency testing for every lot or otherwise specify when potency testing is required. Nevertheless, Colonia Care Pharmacy proposes to test all high-risk level CSPs prepared in groups of more than 25 units for sterility, endotoxin, and potency. In addition, prior to dispensing any CSP, Colonia Care Pharmacy complies with USP chapter <797> guidelines for verifying the correct identify and quality of CSPs. Its current policy on potency testing meets and exceeds USP chapter <797> guidelines.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically, in the laminar flow glovebox, which is located in an unclassified room and is used for aseptic filling of sterile drug products, the evaluation of unidirectional airflow continuity (e.g., smoke studies), airborne viable and non-viable particle counts, and surface monitoring for microbiological contamination are not performed under dynamic conditions that represent routine usage.

Response:

The FDA's observation includes errors of fact. The pharmacy utilizes a service that performs "Visual smoke study during dynamic conditions." Nonetheless, Colonia Care Pharmacy acknowledge this observation. The policy and procedure is under review and will be revised to current CAG-003-2006v13 05 20 2015 CETA Certification Guide for Sterile Compounding Facilities. Smoke testing under dynamic conditions has been and will continue to be performed during each and every certification.

The air and surface monitoring are performed twice annually during recertification of the laminar flow glovebox when it is not being used, and not routinely during aseptic filling, which may occur daily or multiple times throughout the week. In addition, personnel monitoring consists of gloved fingertip monitoring (sterile gloves are donned over the gauntlet-gloves) every six months, and is performed as an independent operation, not after completion of aseptic filling, to represent routine conditions.

Response:

We acknowledge your observation but disagree with your conclusion. Colonia Care Pharmacy is in compliance with USP 797: Viable and Nonviable Environmental Sampling (ES) Testing, "Environmental Particle Testing Program" - Engineering Control Performance Verification that states "Certification procedures such as those outlined Certification Guide for Sterile Compounding Facilities (CAG-003-2006) shall be performed by a qualified individual no less than every 6 months and whenever the device or room is relocated or altered or major service to the facility is performed." And Total Particle Count (same reference) Certification is within established guidelines shall be performed no less than every 6 months." See Clean Room Certification Report dated March 12, 2016.

USP<797> requires initial gloving competency evaluation; re-evaluation of all compounding personnel for this competency shall occur at least annually for personnel who compound low- and medium-risk level CSPs, and semi-annually for personnel who compound high-risk level CSPs. It also requires using one or more sample collections during any media fill test procedure before they are allowed to continue compounding CSPs for human use. Colonia Care Pharmacy complies with these standards concerning gowning and gloving evaluations and re-evaluations, and media fills. Documentation of personnel testing has been previously produced.

OBSERVATION 4

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include validation of the sterilization process.

Specifically, twice-annual media fill testing is performed to support aseptic filling practices, in which 100ml of soybean casein digest media is prepared, sterile filtered, and filled into an unspecified number of "10 ml" vials, with a 5 ml control sample. This does not represent the most challenging conditions, in that up to 30 vials may be filled at one time. For example, Dexamethasone 24mg/mL Injectable, lot 031716N, was prepared on 3/17/16, and filled into 30 vials.

Response:

We acknowledge your observation of not performing process simulations but disagree with your conclusion. Once again, FDA is holding the pharmacy to a standard that is inapplicable to a compounding retail pharmacy under FDCA Section 503A. The observation mirrors 21 C.F.R. § 211.113(b). (Specifically, that section of 21 C.F.R. part 211 requires: "Appropriate written procedures designed to prevent microbial contamination of drug products purporting to be sterile shall be established, written, and followed. Such procedures shall include validation of any sterilization process.") FDA's cGMP regulations are inapplicable because Section 503A pharmacies are exempt from cGMP.

Notwithstanding the inapplicability of FDA's cGMP standard, Colonia Care Pharmacy will review its processes, revise current procedures for process simulation testing, and follow appropriate

New Jersey Board of Pharmacy regulations and expand methods of testing operators performing high risk manipulations.

Consideration of worst case aseptic processing conditions will be included in the formulation of procedures, as well as include follow up procedures in the event of positive results. Revised testing process will be representative of processes performed when compounding from non-sterile powder as well as complex manipulations as USP<797> requires a media fill test that represents the most challenging or stressful conditions actually encountered by the personnel being evaluated when they prepare low-, medium-, and high-risk level CSPs. In addition, process simulation media fill evaluations are a semi-annual event for high-risk compounding and are part of the Competency Manual; specifically, the Orientation and Annual Competency. Documentation of completion is contained in each employee file.

OBSERVATION 5

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

Specifically, the filling record for Papaverine/Phentolamine/Prostaglandin-E1 Injection Solution, lot 020216A, executed 2/2/16, notes "Protect from light", but the finished drug product is prepared in "30ml Clear Sterile vial". There is no assurance the drug is adequately protected from light.

Response:

We acknowledge FDA's observation but disagree with the findings. The preparations, while prepared in glass vials, are then dispensed in a standard pharmacy USP approved amber vial. Accordingly, the issues raised in this observation do not apply. Nonetheless, Colonia Care Pharmacy has implemented a review of the final containers to confirm the proper final container for the CSP.

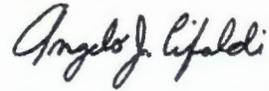
In closing, we respectfully submit this response to explain and distinguish Colonia Care Pharmacy's operational processes and to clarify what may have been misinterpreted by the FDA field investigator who visited the pharmacy.

Colonia Care Pharmacy emphasizes that it takes patient safety and its professional responsibilities very seriously. Colonia Care Pharmacy shares FDA's goal of ensuring that patients in need of custom compounded medications receive quality preparations. To that end, and although it is not required to do so, Colonia Care Pharmacy has voluntarily taken corrective measures identified herein.

We respectfully submit that these measures more than adequately address FDA's observations, and otherwise should exceed FDA's expectations in this matter. We look forward to discussing this matter with you.

In the interim, please do not hesitate to contact me should you have any questions.

Very truly yours,



ANGELO J. CIFALDI

AJC/cg

cc: Nicolas A. Violand, Investigator (via e-mail)
Lisa Matthews, District Recall Coordinator (via e-mail)