



Health & Wellness Compounding Pharmacy

Mark F. Binkley, D.Ph.
PHARMACIST/CHEMIST

RECEIVED

November 11, 2014

NOV 12 2014

NOL-DO Compliance Branch

329 21st Avenue North
Suite 3
Nashville, TN 37203

Department of Health and Human Services
Food and Drug Administration
404 BNA Drive, Building 200, Suite 500
Nashville, TN 37217-2597

***Via Fax (615) 366-7802
and Overnight Delivery***

Phone (615) 383-3784
(800) 388-7994
Fax (615) 292-2762

Attn: Patricia K. Schafer, District Director
Brandon C. Heitmeier, Investigator
Justin N. Henson, Investigator

Re: FDA Disclosure of 483 Response

mbinkley@myhwcp.com

Dear District Director Schafer and Investigators Heitmeier and Henson:

International Academy of
Compounding Pharmacists

Professional
Compounding
Centers of America

Tennessee
Pharmacists
Association

www.myhwcp.com

On behalf of Green Hills Health and Wellness Pharmacy, Inc. d/b/a Health and Wellness Compounding Pharmacy ("Health & Wellness"), I authorize the United States Food and Drug Administration (the "FDA") to publicly disclose the information described below on the FDA's web site and to include the information described below any time the FDA provides a copy of the Health & Wellness' Form 483 to anyone outside of the FDA. 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(j), 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 the FDA harmless for any injury caused by the FDA's sharing the information with the public.

Information to be disclosed: Health & Wellness' letter dated November 11, 2014, excluding all attachments, which responds to the Form 483 issued by the FDA on October 22, 2014.

Authorization is given to the 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



Health & Wellness

Compounding Pharmacy

Mark F. Binkley, D.Ph.
PHARMACIST/CHEMIST

consent on behalf of Health & Wellness and my full name, title, address, and telephone number are provided below for verification.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mark F. Binkley', written over a horizontal line.

Dr. Mark F. Binkley, BA, BS, DPh
President, Health & Wellness Compounding
Pharmacy
329 21st Avenue North, Suite 3
Nashville, TN 37203-1856
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Re: Response to FDA 483 Issued October 22, 2014 to Green Hills
Health and Wellness Pharmacy, Inc. d/b/a Health and Wellness
Compounding Pharmacy

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Dear District Director Schafer and Investigators Heitmeier and Henson:

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The United States Food and Drug Administration (the "FDA") conducted an inspection of Green Hills Health and Wellness Pharmacy, Inc. d/b/a Health and Wellness Compounding Pharmacy ("Health & Wellness"), a pharmacy located at 329 21st Avenue North, Suite 3, Nashville, Tennessee 37203-1839, between October 14 and October 22, 2014. Upon the conclusion of its inspection, the FDA provided Health & Wellness with an FDA Form 483. This letter is Health & Wellness's response to the FDA Form 483 observations. We respectfully request that this response, excluding the attachments, be posted on the FDA's website with the Form 483 and be included every time the FDA provides a copy of Health & Wellness's FDA Form 483 to anyone outside the FDA.

The FDA's observations on the 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. Part 211, and further explained in the FDA's Industry Guidance on cGMPs for Sterile Drug Products Produced by Aseptic Processing. Health & Wellness does not engage in drug manufacturing. Health & Wellness is a pharmacy licensed by the Tennessee Board of Pharmacy as a retail pharmacy with controlled substances, and is subject

medications. Prior to October 14, 2014, Health & Wellness also compounded non-sterile medications for administration in the offices of licensed Tennessee prescribing practitioners upon the receipt of orders from such prescribers, as permitted by the Tennessee Pharmacy Practice Act of 1996. Specifically, Tenn. Code Ann. § 63-10-204 defines the “practice of pharmacy” to include the “responsibility for compounding and dispensing of prescription orders” and further defines “compounding” and “dispense,” in relevant part, as follows:

(6) “Compounding” means the preparation, mixing, assembling, packaging or labeling of a drug or device:

(A) As the result of a prescription order or initiative based on the prescriber-patient-pharmacist relationship in the course of professional practice;

(B) In anticipation of prescription orders based on routine, regularly observed prescribing patterns;

(C) For the purpose of, or as an incident to, research, teaching or chemical analysis and not for sale or dispensing;

(D) For use in a licensed prescribing practitioner’s office for administration to the prescribing practitioner’s patient or patients when the product is not commercially available upon receipt of an order from the prescriber; [or]

(E) For use in a health care facility for administration to a patient or patients receiving treatment or services provided by that facility when the product is not commercially available upon receipt of an order from an authorized licensed medical practitioner of the facility[.]

....

(14) “Dispense” means preparing, packaging, compounding or labeling for delivery and actual delivery of a prescription drug, nonprescription drug or device in the course of professional practice to a patient or the patient's agent, to include a licensed health care practitioner or a health care facility providing services or treatment to the patient or patients, by or pursuant to the lawful order of a prescriber[.]

As noted above, prior to October 14, 2014, Health & Wellness compounded non-sterile medications for administration in the offices of licensed Tennessee prescribing practitioners upon the receipt of orders from such prescribers. We believe that this practice was in full compliance with the Tennessee Pharmacy Practice Act of 1996. Nevertheless, effective November 5, 2014, Health & Wellness amended its standard operating procedure (“SOP”), 5.10 Patient Records, and now compounds only patient-specific, sterile and non-sterile medications. See Attachment 1.

We also note that, prior to October 17, 2014, Health & Wellness compounded sterile bovine hyaluronidase injection, 150 IU/mL for administration by a single licensed prescribing practitioner's office pursuant to valid orders from the prescribing practitioner. Before the conclusion of the FDA's inspection, Health & Wellness discovered, on its own initiative, that a human recombinant form of hyaluronidase (Hyalenex, 150 USP units/mL) and an ovine form of hyaluronidase (Vitrase, 200 USP units/mL) are currently available on the commercial market.

Compounded bovine hyaluronidase generally represented a small fraction of the total number of drug dosage units dispensed by Health & Wellness during any three-month period (e.g., under 160 ml between July 14, 2014 and October 14, 2014). The bovine form of the hyaluronidase injection has not been commercially manufactured since 2010, due to a shortage of active pharmaceutical ingredient. Since 2000, the use of compounded hyaluronidase has become a more common alternative due to intermittent supply shortages caused by facility closure, product discontinuation, depleted supply of raw material, and product recalls. For example, the recombinant human hyaluronidase was the subject of a voluntary recall in 2010 after glass particles were found in vials during routine stability testing.

We do not believe that, by compounding bovine hyaluronidase, Health & Wellness was involved in compounding regularly or in inordinate amounts a drug product that is essentially a copy of a commercially available product. Nevertheless, on Friday, October 17, 2014, the day it became aware of the commercially available forms of hyaluronidase, Health & Wellness initiated a voluntary product recall of the bovine hyaluronidase injection and promptly notified the only practitioner in possession of the compounded product. All product testing for potency, sterility, and endotoxin levels had been completed prior to releasing this product to the practitioner. In response to the recall request, the clinic stated that it would do a complete count and quarantine of any unused product, and provide further information by October 20, 2014. On Monday, October 20, 2014, the clinic notified Health & Wellness that there were no remaining units of bovine hyaluronidase injection in the clinic, as all units had been used for patients prior to the recall request.

In addition, as of October 17, 2014, Health & Wellness has ceased compounding bovine hyaluronidase. Moreover, effective November 6, 2014, Health & Wellness implemented a new procedure in our SOP, 3.10 Inventory Control, which requires periodic review of any temporarily unavailable commercial product for which it receives a request for compounding. *See* Attachment 2. If a commercial product is not available through usual manufacturing channels, and compounding of that product is requested, then two forms of documentation of the shortage will be required to proceed, and, at least quarterly, updated documentation will be required to continue compounding the product.

As a licensed pharmacy, Health & Wellness is required to comply with applicable Tennessee, Florida, Michigan, and Minnesota state laws and regulations governing pharmacy compounding, and with the applicable United States Pharmacopoeia ("USP") chapters <795> and <797> on pharmacy compounding. The FDA's cGMPs for finished pharmaceuticals are not applicable to Health & Wellness 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 by 21 U.S.C. § 351(a)(2)(B). 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--

(1) is by--

(A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or

(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

(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

(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.

Health & Wellness operates in compliance with the requirements of 21 U.S.C. § 353a, applicable Tennessee, Florida, Michigan, and Minnesota state laws and regulations governing pharmacy compounding, and with USP chapters <795> and <797>. Therefore, Health & Wellness is exempt from complying with cGMPs applicable to drug manufacturers under 21 U.S.C. § 351(a)(2)(B).

As noted above, Health & Wellness now requires a patient-specific prescription for all sterile and non-sterile compounded medications. However, to the extent that the FDA contends that Health & Wellness is not protected by Section 353a for patient-specific drugs prepared and dispensed to practitioners for administration, we believe that such conduct is expressly authorized by the Tennessee Board of Pharmacy. We further believe that Congress did not intend 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 the U.S. 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.

For these reasons, Health & Wellness challenges the FDA's observations on the grounds that the cGMPs are not applicable to its compounding pharmacy operations. Health & Wellness complies with all applicable state and federal laws. Health & Wellness also adheres to the USP <797> guidelines for compounding sterile drug products. Our pharmacy is dedicated to ensuring that our sterile and non-sterile drugs are prepared in a safe and effective manner. In light of Health & Wellness's commitment to self-improvement, if the FDA's observations amount to pharmacy "best practices" that, if adopted, would benefit the safety of our patients, we have considered those practices for adoption as best practices in our policies and procedures manual and have trained our staff on any newly adopted best practices.

The following Observations were cited in our 483:

1. ***Observation 1: Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.***
 - A. *Observation 1(a): Media fills performed for injectable drug products do not simulate the entire production process including but not limited to: all process steps and manipulations, and filtration performed under ISO 5 classified areas. Additionally, media fills do not include a challenge of worst case conditions including but not limited to: duration of aseptic processing and represented batch size.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> requires that a media-fill test or an equivalent test be performed under conditions that closely simulate the most challenging or stressful conditions encountered when compounding a particular risk level compounded sterile products ("CSPs").

Health & Wellness complies with USP chapter <797> standards for personnel training and evaluation.

Forward Action: Although Health & Wellness believes it is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>, we acknowledge that more stringent personnel training and evaluation is a “best practice” that would be beneficial to our patients. Accordingly, we have updated our SOP, 1.60 Orientation and Training, to specify that media-fill tests will be conducted, on a rotating basis, at the beginning, middle, and end the employee’s shift. See Attachment 3.

Timeline: Updates to the SOP, 1.60 Orientation and Training, and appropriate staff training were completed on November 5, 2014.

Responsible Individual: Pharmacist In Charge

- B. *Observation 1(b): A review of your firm’s records noted that a media fill was last performed on 05/07/2014. This media fill was the initial personnel qualification for your technician with initials “NS” however there were no repeat media fill runs to qualify the technician.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> guidelines state that, for high-risk CSPs, sterile media fills should be performed initially, at least annually thereafter for low- and medium-risk level compounding, and every six (6) months for high-risk level compounding. Health & Wellness complies with the USP chapter <797> guidelines for personnel training and evaluation.

Forward Action: Although Health & Wellness believes it is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>, we acknowledge that more frequent personnel training and evaluation is a “best practice” that would be beneficial to our patients. Therefore, in addition to the changes specified in the Response to Observation 1(a), we have updated our SOP, 1.60 Orientation and Training, to specify that media-fill testing will be performed every other month for high-risk level compounding. See Attachment 3.

Timeline: Updates to the SOP, 1.60 Orientation and Training, and appropriate staff training were completed on November 5, 2014.

Responsible Individual: Pharmacist In Charge

2. ***Observation 2: Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the equipment to produce aseptic conditions.***

Specifically, the cleaning and disinfecting agents PeridoxRTU and AccelTB used to clean the ISO 5 areas are not sterile.

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. According to USP chapter <797>, “a residue-free disinfecting agent such as sterile 70% [isopropyl alcohol (IPA)]” must be used within the ISO 5 environment. Health & Wellness uses sterile 70% IPA to clean the ISO 5 area, in accordance with USP chapter <797>. Although Health & Wellness uses PeridoxRTU and AccelTB to clean areas outside the ISO 5 area, it does not use these non-sterile products to clean the ISO 5 area.

Forward Action: We acknowledge that the use of other sterile disinfecting agents is a “best practice” that would benefit the safety of our patients. Therefore, Health & Wellness has elected to amend its SOP, 1.40 Compounding Area Requirements (Sterile), to require a daily wipe of each hood with a sterile sporicidal pre-soaked towel. See Attachment 4.

Timeline: Updates to the SOP, 1.40 Compounding Area Requirements (Sterile), and appropriate staff training were completed on November 5, 2014.

Responsible Individual: Pharmacist In Charge

3. Observation 3: *Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.*

- A. *Observation 3(a): Surface, air, and personnel monitoring of the ISO 5 areas is not performed for each day sterile drug products are produced. Currently, surface, viable air, and personnel monitoring is only performed every two weeks.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> guidelines require viable air sampling at least every six (6) months, surface sampling on a periodic basis, and personnel sampling initially, at least annually thereafter for low- and medium-risk level compounding, and every six (6) months for high-risk level compounding. Our current policy for viable air, surface, and personnel sampling meets and significantly exceeds USP chapter <797> requirements.

Health & Wellness is currently in compliance with USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 3(a).

- B. *Observation 3(b): Non-viable air monitoring of the ISO 5 areas is not performed for each day sterile drug products are produced. Currently, non-viable air is only monitored during certification of laminar airflow hoods and biological safety cabinets every 6 months.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> requires non-viable air sampling be performed every six (6) months. The certification documents provided to the inspectors demonstrate that non-viable air sampling is conducted in compliance with USP chapter <797> and otherwise confirm that our test results are within USP chapter <797> guidelines.

Health & Wellness is currently in compliance with USP chapter <797> with respect to non-viable air sampling. Accordingly, we do not believe additional action is required for Observation 3(b).

- C. *Observation 3(c): Disinfectant neutralizers are not used to assure microbial contamination can be detected in environmental monitoring samples months.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> states that “[m]edia used for surface sampling must be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA [tripticase soy agar] with lecithin and polysorbate 80).” In compliance with USP chapter <797>, Health & Wellness’s current SOP, 1.40 Compounding Area Requirements (Sterile), requires the use of TSA with lecithin and polysorbate 80, to ensure microbial contamination can be detected in environmental monitoring.

Health & Wellness is currently in compliance with USP chapter <797> with respect to environmental monitoring. Accordingly, we do not believe that additional action is required for Observation 3(c).

- D. *Observation 3(d): Raw data for dynamic smoke studies performed in the laminar air flow hoods and biological safety cabinet was not documented and retained.*

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> guidelines require that smoke studies “demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions.” Health & Wellness uses a cleanroom compliance certification company, Southeastern Certification, Inc., to perform smoke studies on a semiannual basis. The raw data is based on visual observation, which is documented during the certification process. Test results reflecting compliance with USP chapter <797> were provided to the investigators. USP chapter <797> does not require videotaping of smoke studies.

Health & Wellness is currently in compliance with USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 3(d).

4. ***Observation 4: Equipment for adequate control over air pressure is not provided when appropriate for the manufacture, processing, packing or holding of a drug product.***

Specifically, air pressure in classified areas is not continuously monitored during production of sterile products. Currently, pressure differentials for ISO 5, ISO 7, and ISO 8 areas are only checked once a day.

Health & Wellness acknowledges the importance of a safe and sterile compounding environment. USP chapter <797> requires that pressure differential monitoring be “reviewed and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a continuous recording device.” Health & Wellness currently has one work shift per day; therefore, pressure differentials in classified areas are monitored on a daily basis. We are

compliant with USP chapter <797> requirements. Currently, USP chapter <797> allows, but does not require, continuous recording device as an alternative to visual monitoring.

Forward Action: Although our pressure differential monitoring conforms to the Tennessee Board of Pharmacy requirements and USP chapter <797> guidelines, we acknowledge the critical role that pressure differential serves in the compounding process. Therefore, we are currently considering a device or digital application to monitor pressure and send alerts when power outages occur.

Responsible Individual: Pharmacist In Charge

5. ***Observation 5: Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance with the final specifications and identity and strength of each active ingredient prior to release.***

- A. *Observation 5(a): Potency testing is not performed on every lot of sterile drug products produced by your firm. According to your firm's procedures, 6.10 Total Quality Management, potency testing on finished drug products is not required for every lot.*

Health & Wellness acknowledges the importance of safe and potent compounded medications. As a compounding pharmacy, Health & Wellness complies with USP chapter <797>, which does not require potency testing for every lot or otherwise specify when potency testing is required. Nevertheless, as discussed in more detail in the response to Observation 5(b) below, Health & Wellness tests 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, Health & Wellness complies with USP chapter <797> guidelines for verifying the correct identify and quality of CSPs. Our current policy on potency testing meets and exceeds USP chapter <797> guidelines.

Health & Wellness is currently in compliance with USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 5(a).

- B. *Observation 5(b): Sterility and endotoxin testing is not required on every lot of sterile drug products produced by your firm according to your firm's procedure, 6.10 Total Quality Management. This procedure states that sterility and endotoxin testing is only required for sterile preparations with a lot size of 25 or more or preparations which have been exposed to temperatures of 2-8C for 12 hours or 6 hours at warmer temperatures.*

As a compounding pharmacy, Health & Wellness complies with USP chapter <797>, which requires sterility and endotoxin testing as follows:

All high-risk level CSPs that are prepared in groups of more than 25 identical individual single-dose packages (e.g., ampuls, bags, syringes, vials) or in multiple-dose vials (MDVs) for administration to multiple patients or that have been exposed longer than 12 hours at 2° to 8° and longer than 6 hours at warmer

than 8° before they are sterilized shall meet the sterility test before they are dispensed or administered.

....

All high-risk level CSPs, except those for inhalation and ophthalmic administration, that are prepared in groups of more than 25 identical individual single-dose packages (e.g., ampuls, bags, syringes, vials) or in MDVs for administration to multiple patients or that have been exposed longer than 12 hours at 2° to 8° and longer than 6 hours at warmer than 8° before they are sterilized shall be tested to ensure that they do not contain excessive bacterial endotoxins.

Furthermore, USP chapter <797> guidelines state that “sterility tests for autoclaved CSPs are not required unless they are prepared in batches of more than 25 units.” Health & Wellness’s SOP, 6.10 Total Quality Management, complies with the USP chapter <797> requirements for sterility and endotoxin testing and the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies. We have also been approved as a sterile compounding pharmacy by the Tennessee Board of Pharmacy and our policies and procedures otherwise comply with Tennessee requirements for sterile compounding pharmacies.

Health & Wellness is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 5(b).

- C. *Observation 5(c): Sterile drug product lots produced by your firm and sampled for laboratory testing are sometimes released and distributed before receiving laboratory confirmation of potency, sterility, and endotoxin tests meeting final specifications.*

As a compounding pharmacy, Health & Wellness complies with USP chapter <797>, which does not require holding CSPs until receipt of test results. USP chapter <797> states:

When high-risk level CSPs are dispensed before receiving the results of their sterility tests, there shall be a written procedure requiring daily observation of the incubating test specimens and immediate recall of the dispensed CSPs when there is any evidence of microbial growth in the test specimens.

Health & Wellness complies with USP chapter <797> when any high-risk level CSPs are dispensed prior to the receipt of laboratory testing. Our current SOP, 4.30 Sterile Preparations, states that, when any high-risk level CSP is dispensed before receiving sterility test results, sterility results must be checked daily and, if there is any evidence of microbial contamination, an immediate recall should be issued following the procedure in SOP, 5.50 Recalls.

Health & Wellness is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 5(c).

6. ***Observation 6: There is no written testing program designed to assess the stability characteristics of drug products.***

Specifically, your firm assigns Beyond Use Dates (BUDs) of up to 90 days for preservative free sterile drug products and up to 180 days for preservative containing sterile drug products. Stability studies have not been performed to support these BUDs. Additionally, no studies have been performed for antimicrobial effectiveness of preservatives over the labeled shelf life.

The FDA's observation is referring to stability study requirements for drug product expiration dates, a process reserved for pharmaceutical manufacturers. As a compounding pharmacy, we do not assign expiration dates, but rather determine BUDs for sterile products in accordance with USP chapter <797>. All sterile preparations are carefully reviewed to observe the recommended USP dating for BUDs. For high-risk sterile preparations, BUDs do not exceed twenty-four (24) hours at controlled room temperature, three (3) days under refrigerated conditions, and forty-five (45) days in a solid frozen state, in accordance with USP chapter <797>. For other CSPs, Health & Wellness determines BUDs by a review of scientific literature, direct testing on our compounded products, and vendor-established BUD studies, in accordance with USP chapter <797>.

Health & Wellness is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 6.

7. ***Observation 7: Equipment and utensils are not maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.***

Specifically, hold time studies have not been performed on equipment that has been autoclaved and depyrogenated and stored for future use. Currently, bulk process equipment and containers used in the production of sterile drugs are given a 90 day expiration, but no studies have been performed to support these hold times.

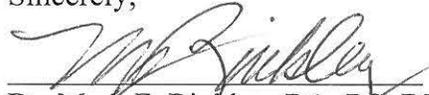
As a compounding pharmacy, Health & Wellness complies with USP chapter <797>, which does not require or otherwise address hold time studies for glassware, utensils, or metal devices used to compound CSPs. USP chapter <797> states that, prior to autoclaving, "plastic, glass, and metal devices [should be] tightly wrapped in low-particle-shedding paper or fabrics or sealed in envelopes that prevent post-sterilization microbial penetration." USP chapter <797> further provides that "[g]lass and metal devices may be covered tightly with aluminum foil, then exposed to dry heat in an oven at a mean temperature of 250° for 30 minutes to achieve sterility and depyrogenation. Such items are either used immediately or stored until use in an environment suitable for compounding Low-Risk Level CSPs and Medium-Risk Level CSPs."

Health & Wellness's SOPs, 2.10 Autoclave and 2.220 Oven (Convection), comply with USP chapter <797> guidelines. Under our procedures, equipment that has been autoclaved and depyrogenated remains in the autoclaving bag or wrapped in aluminum foil, which is placed in a tightly closed container and stored in a designated location within an ISO Class 7 environment. This procedure is designed to ensure the sterility of equipment while in storage, and glassware and devices that are steam sterilized or depyrogenated by dry heat contain biological indicators appropriate for use.

Health & Wellness is currently in compliance with the Tennessee Board of Pharmacy requirements for sterile compounding pharmacies and USP chapter <797>. Accordingly, we do not believe additional action is required for Observation 7.

In this response, Health & Wellness has sought to address all of the FDA inspector's observations and concerns. If the FDA requires additional information or communication from Health & Wellness, it is welcome to contact Dr. Mark F. Binkley, Health & Wellness's President, at (615) 383-3784.

Sincerely,



Dr. Mark F. Binkley, BA, BS, DPh
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