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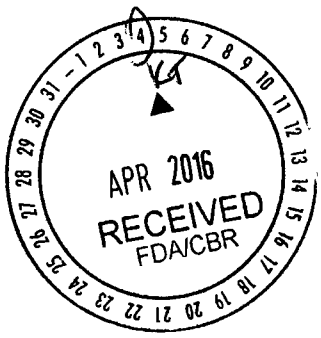
April 1, 2016



VIA ELECTRONIC MAIL AND FEDERAL EXPRESS

Ms. Diane Amador-Toro
Director
New Jersey District Office
Food and Drug Administration
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Re: Waiver Of Stokes Healthcare Inc. d/b/a Stokes Pharmacy ("*Stokes Pharmacy*") for Publication of Response to FDA Form 483 Issued February 12, 2016

Dear Director Amador-Toro:

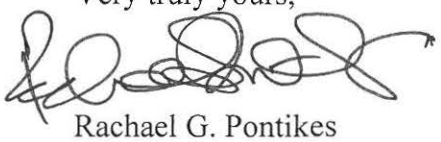
On behalf of Stokes Pharmacy, I hereby authorize the United States Food and Drug Administration ("FDA") to publicly disclose the information described below on FDA's website. I understand that the information that is disclosed may contain confidential commercial or financial information or trade secrets 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 of the information with the public.

Information to be disclosed: Stokes Pharmacy's response to the FDA Form 483 issued by FDA on February 12, 2016 (the "*Response*"). The waiver shall extend only to the Response and not to any of the supporting or underlying documents implicated or involved in the FDA Form 483 issued on February 12, 2016 or Stokes Pharmacy's response thereto.

Authorization is given to FDA to disclose the above-mentioned information which may include confidential commercial, financial, or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of Stokes Pharmacy, and my full name, title, address, 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. Thank you.

Very truly yours,



Rachael G. Pontikes

RGP:ral

Stokes Healthcare Inc. dba
Stokes Pharmacy
18000 Horizon Way, Ste. 700
Mt Laurel, NJ 08054

April 1, 2016

VIA ELECTRONIC MAIL AND FEDERAL EXPRESS

Diane Amador-Toro
District Director
New Jersey District Office
Food and Drug Administration
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

RE: STOKES HEALTHCARE, INC. D/B/A STOKES PHARMACY
RESPONSE TO INSPECTIONAL OBSERVATIONS
REQUEST FOR MEETING
FEI No: 3002815949

Dear Director Amador-Toro,

Stokes Healthcare Inc. d/b/a Stokes Pharmacy ("*Stokes Pharmacy*") thanks the Food and Drug Administration ("*FDA*") for the opportunity to respond to the inspectional observations listed on the FDA 483 issued by your office on February 12, 2016. During the most recent inspection, Stokes Pharmacy engaged cooperatively and constructively with FDA. We would like to assure FDA that Stokes Pharmacy is committed to providing patients with the highest quality compounded medications prepared in compliance with all applicable standards and that, as demonstrated herein, we take our professional responsibilities very seriously.

To that end, patient safety and wellbeing are our primary concerns, and we strive to and do provide the highest quality preparations and services. Our rigorous quality assurance and standard operating procedures ("*SOPs*") follow demonstrated pharmacy best practices and are designed to produce high-quality compounded sterile preparations. We do this to ensure that we continue to meet recognized State pharmacy requirements and other standards applicable to compounding pharmacies, and so that our patients can continue to access high-quality compounded medications to meet their individual medical needs.

Notwithstanding these and the other numerous matters described herein, Stokes Pharmacy would like to take this opportunity to briefly discuss FDA's inspection of, and application of the Form 483, to Stokes Pharmacy. Specifically, Stokes Pharmacy is a New

Jersey State-licensed pharmacy that compounds and dispenses veterinary and human medications that, where appropriate,[1] comply with Section 503A of the Federal Food, Drug, and Cosmetic Act ("*Section 503A*"). Accordingly, Stokes Pharmacy engages in pharmacy-based compounding pursuant to the guidelines set forth by the New Jersey State Board of Pharmacy and the United States Pharmacopeia ("*USP*"), which are the recognized standards for New Jersey-based compounding pharmacies. Moreover, Stokes Pharmacy has an impeccable safety record concerning the compounded medications that it prepares according to the applicable standards.

Despite this fact, the Form 483 observations attempt to hold Stokes Pharmacy to Current Good Manufacturing Practice ("cGMP") standards with which, as a matter of law, Stokes Pharmacy is not required to comply. *See* 21 U.S.C. § 353a(a)(1)-(2). Stokes Pharmacy objects to any observation in the Form 483 which inappropriately applies cGMP standards. While Stokes Pharmacy is addressing all of FDA's inspectional findings, its cooperation with FDA should not be interpreted as Stokes Pharmacy's agreement that it is required to comply with cGMPs, thereby leaving Stokes Pharmacy exposed to repeat citations for failing to conform with cGMPs. Moreover, and in light of the above, much of the Form 483 and FDA's observations are, on their face, incorrect[2] and should be withdrawn or amended to reflect the only standards to which FDA may properly hold Stokes Pharmacy.

In the meantime, and without waiver of its right to contest FDA's application of cGMPs, Stokes Pharmacy provides the following responses to the Observations set forth in the 483.

FDA OBSERVATION NO. 1:

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically, your firm aseptically processes sterile drug products, including injectables, in two IS0-5, positive-pressure, Laminar flow safety hoods located in the same IS0-7 cleanroom. The two hoods are placed at a 90 degree angle, about 10 feet apart, on adjacent cleanroom walls. One hood is used to process cytochemical drug products, such as those used to treat cancer. These types of drug products are typically processed under negative air pressure controls. The other hood is used to process most of your sterile drug products, which are not classified as cytochemicals.

The existing design controls create conditions conducive to drug product cross-contamination, with the more significant concern being the potential for cytochemical contamination of non-cytochemical drug products.

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[1] 90% of Stokes Pharmacy's compounded medications are prepared for animal patients, and only 10% of its compounded medications are prepared for human patients.

[2] Indeed, and as further evidence that FDA is attempting to subject Stokes Pharmacy to inapplicable standards, FDA describes the pharmacy as a "producer of drug products." But Stokes Pharmacy is a State-licensed pharmacy. Moreover, "producer of drug products" is not a legally recognized FDA-regulated establishment.

Stokes Pharmacy's Response to Observation No. 1:

Stokes Pharmacy objects to Observation No. 1 because it attempts to hold the pharmacy to a standard that is inapplicable under Section 503A. Specifically, Observation No. 1 attempts to impose onto Stokes Pharmacy the cGMP requirements which are applicable to drug manufacturers. cGMP requirements are inapplicable to Stokes Pharmacy.

Nonetheless, and to further respond to this Observation No. 1, Stokes Pharmacy notes that the referenced primary engineering controls ("PECs") satisfy all applicable requirements under USP<797>. Specifically, the PECs in this Observation No. 1 identified as "positive-pressure Laminar flow safety hoods" are Class II Type A Biological Safety Cabinets and by definition operate at negative-pressure. One cabinet is designated solely for hazardous drug(s) and is the only cabinet actively in-use during the hazardous drug preparation process. Further, all of the PECs run continuously, and the ISO Class 7 buffer room operates at 72 air changes per hour ("ACPH"), which is over twice the requirement of 30 ACPH.

In addition, both Biological Safety Cabinets ("BSCs") (Stokes IDs C-1 & C-3, certified vendor test reports 93040-0116-2102-1163F & 93041-0116-2101-1163F) were certified on January 21, 2016 per CETA CAG-003-2006 (current version) and passed all requisite tests, specifically outlined in Section 10 of the CETA documents – 10.0 Biological Safety Cabinet (BSC) Certification.

Moreover, all Class II BSCs are designed to protect both the operator and environment from exposure to biohazards. In a Class II configuration, the inflow of air into the front inlet grill prevents any aerosol generated during microbiological manipulations to escape through the front opening. The vertical laminar airflow of HEPA-filtered air stream that descends downward from the interior of the cabinet continually flushes the cabinet interior of airborne contaminants. Thus, by design, the possibility of cross-contamination with the current device configuration is as remote as it possibly could be under the applicable standards. In other words, our current design more than adequately complies with all relevant requirements and ensures that the risk of possible cross-contamination is essentially non-existent.

Finally, and in addition to the above, Stokes Pharmacy has invested significant resources into a new facility, including a new clean room, based on the draft proposal for USP<800> and developing industry best practices. Among other things, our new facility and clean room will continue to ensure that our practices and procedures minimize the risk of any potential cross-contamination. We expect our new facility to be operational in the summer of 2016.

FDA OBSERVATION NO. 2:

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use and cleaning and maintenance.

Specifically, your IS0-7 cleanroom contains items that are hard to clean and sanitize such as the three vinyl chairs with wheels and the two portable power strips on the floor with several electric power cords plugged into them.

Stokes Pharmacy's Response to Observation No. 2:

As its response to this Observation No. 2, Stokes Pharmacy notes that it thoroughly researched and procured cleanroom seating that met established design qualifications. The seats in question were tested by the manufacturer and, as set forth on the attached documentation, were determined by the manufacturer to be suitable for ISO Class 3 environments under static conditions and ISO Class 5 environments under dynamic conditions while the seat cushion is compressed. *See* Exhibit 1 hereto. Thus, the chairs identified in Observation No. 2 satisfy applicable standards and are appropriate for use in their current locations.

Additionally, Stokes Pharmacy has established policies and procedures that address processes for cleaning equipment, including chairs and power strips, in the sterile processing areas. As part of that process, and as evidenced by Observation No. 2, our power cords and power strips are not grouped together because that setup allows us to efficiently and thoroughly clean and decontaminate those items during our regular cleaning/decontamination procedures. Further, Stokes Pharmacy logs a visual observation of completed cleaning activities, meaning that staff could have raised concerns if any cleaning was inadequate (which they did not do).

Finally, Stokes Pharmacy notes that its continuous environmental monitoring data has not indicated that the current position of the cords or chairs poses any risk of contamination. Nonetheless, and although our current processes and procedures are more than adequate, we have considered the strategic placement of outlets for our new facility design and expect that design to further the ease of cleaning outlets.

FDA OBSERVATION NO. 3

Written procedures are not followed for the identification, handling, and approval of closures.

Specifically, your firm uses two types of eye-dropper tips, one is designed to dose aqueous formulations and one is designed with a larger orifice to dose oil based formulations. Your complaint files indicate that for at least one year your cleanroom personnel intermittently mismatched the dropper tips to the drug product formulations for Tacrolimus and Cidofovir eye drops for veterinary use. When oil based drug products accidentally received an aqueous tip you received complaints that the product was hard to dispense (e.g. complaint Dl50519-2, dated 5/19/2015). During the period between 04/07/2014 and 07/01/2015, your firm received at least eight complaints where you recorded complaint statements such as "drops are pouring out of the bottle ... drops are coming out of the bottle too quickly ... tacrolimus is coming out in stream instead of a drop" (e.g. Lots: 01142014@66; 03262015@8; 03042015@111; 04022015@1; 02022015@74 and 05012015@160).

Stokes Pharmacy's Response to Observation No. 3:

Before providing its response to this Observation No. 3, Stokes Pharmacy would like to provide further information as to the observation itself. Specifically, Stokes Pharmacy historically used one style of dropper tip because that tip was determined to be acceptable for use with "droptainers" used by its existing clients. Eventually, however, Stokes Pharmacy retained several new clients who used different droptainers. Those clients submitted complaints

concerning the dropper tips even though our technicians had been following all approved procedures for the packaging of compounded preparations. Importantly, none of our clients' complaints related to the sterility or potency of our compounded medications.

We thereafter conducted a thorough and timely investigation of the client complaints according to our standard pharmacy policy. Based on that investigation, and as part of our ongoing commitment to total quality improvement, we determined that the root cause of customer complaints was that clients were using our dropper tip with refill eye drop prescriptions provided by the pharmacy. Those refills were provided in different droptainers than those previously used by our clients. This combination of both new and old droptainers created a situation where less pressure was required to dispense the medication provided. But our clients were unaware of that fact, and therefore the clients did not apply proper pressure when dispensing the medication. We also learned as a result of our investigation and analysis that we could provide a better dropper tip for our new clients' droptainers. Finally, we concluded that a new dropper tip would be better suited for all patients, and would allow the new patients to dispense medication more consistently. Accordingly, to respond to the client complaints and accommodate the new dropper tip, we updated our policies, procedures, and work instructions to ensure that this implementation would be the most successful.

As its further response to this Observation No. 3, Stokes Pharmacy acknowledges the importance of maintaining thorough processes at all times. Accordingly, we are in the process of developing a more extensive quality system process work-flow for recognizing and trending complaints (such as the ones at issue in Observation No. 3) that are indicative of product or process control deficiencies. Our goal in doing so, as always, is to ensure that our processes and procedures continue to meet our patients' expectations and allow us to provide quality preparations. Stokes Pharmacy is in the process of completing its review, analysis, and development of this new process, in coordination with an upgrade of its computer software. We are working closely with our software vendor to assure that this upgrade and software enhancement is seamless, and that all data and trending information is preserved on a go-forward basis.

FDA OBSERVATION NO. 4:

Written procedures describing the handling of all written and oral complaints do not include provisions for review to determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to the Food and Drug Administration.

Specifically, your procedures do not include provisions for filing Adverse Drug Events (ADE) reports. While reading through your complaint files at least one complaint (D 150206-2) was noted where you were required to file an ADE Report, and one was not filed. On 02/06/2015, your firm received a complaint that a cat died after being administered Buprenorphine 0.5 MG/ML Injection, Lot# 05302014@29, Exp. 02/24/2015.

Additionally, your Complaint Handling SOP Number 5.030 (Version 1.0 Effective 02-27-10) does not establish a system for recognizing and trending complaints that are indicative of product or process control deficiencies, such as the repeated use of the wrong dropper tips as cited above under Observation #3.

Stokes Pharmacy's Response to Observation No. 4:

Stokes Pharmacy respectfully disputes this Observation No. 4 for a number of separate and independent reasons.

First, this Observation No. 4 appears to be an attempt to require Stokes Pharmacy to comply with FDA's Draft "Guidance for Industry Compounding Animal Drugs from Bulk Drug Substances." But FDA's "guidance" is not enforceable against Stokes Pharmacy because, among other things, that guidance is still in draft form, specifically provides that it "contains nonbinding recommendations," and has not been promulgated into any final regulation. Moreover, even the reporting Form 1932a referenced in the "guidance" affirmatively provides that it relates to "VOLUNTARY reporting" (emphasis in original) and that "***you are not required to report***" (emphasis added). In other words, FDA's own documents and statements confirm that Stokes Pharmacy is not required to satisfy the alleged reporting requirement set forth in Observation No. 4.

Second, to the extent Observation No. 4 seeks to require Stokes Pharmacy to submit MedWatch reports, any supposed MedWatch requirement is also inapplicable. Specifically, the adverse event at issue related to a veterinary medication, and therefore was not reportable to MedWatch. *See, e.g.*, MedWatch Online Voluntary Reporting Form, *available at* https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home (last accessed Mar. 15, 2016) (confirming that "reporting on veterinary medicine products" is one of the items that should *not* be reported through MedWatch).

Third, and contrary to Observation No. 4, Stokes Pharmacy has in place written policies and procedures that describe the handling of all written and oral complaints and which are more than adequate under applicable requirements. *See* SOP 9.080 and SOP 1.030, attached hereto as Exhibit 2. Stokes Pharmacy adhered to its processes with respect to the complaint at issue. Accordingly, no corrective actions are warranted.

Specifically, Stokes Pharmacy contacted the prescriber that submitted the complaint to request further information about the animal's medical record (which was not otherwise available to the pharmacy) and to present the prescriber with pharmacy compounding documentation. Included in this documentation were several reports that supported the quality of the medication which were supplied by qualified and independent third-party laboratories. Independent testing confirmed that the medication at issue complied with USP<71> and <85> as to both sterility and bacterial endotoxins. The certificate of analysis also reflected a potency value of 99%, further demonstrating that the labeled concentration was within specification. Stokes Pharmacy requested that the prescriber provide a complete dosing record to aid in its investigation. Finally, we reminded the prescriber that the medication at issue must be disposed of within 28 days after it is opened. Thus, and contrary to Observation No. 4, the complaint in question was thoroughly investigated, and Stokes Pharmacy confirmed that the medication was compounded within all applicable specifications. The prescriber was also educated as to the medication at issue and, once those steps were complete and no further information was provided, the investigation was closed in accordance with its policy and procedures.

Fourth, and as stated above, Stokes Pharmacy is in the process of completing its review, analysis, and development of a more extensive quality system process work-flow for recognizing and trending complaints, in coordination with an upgrade of its computer software. It is working closely with its software vendor to assure that this upgrade and software enhancement is seamless, and that all data and trending information is preserved on a go-forward basis.

In closing, Stokes Pharmacy wants to emphasize that it takes patient safety and its professional responsibilities very seriously. Stokes Pharmacy shares FDA's goal of ensuring that patients in need of custom compounded medications receive the highest quality preparations. To that end, and although it is not required to do so, Stokes Pharmacy voluntarily chose to and did take the corrective actions identified herein even though certain of those corrective actions exceed the standards to which Stokes Pharmacy is held as a Section 503A pharmacy. Thus, Stokes Pharmacy trusts that the above actions that have been or will be taken should more than adequately address FDA's observations, and otherwise should exceed FDA's expectations in this matter.

Thank you for your attention to this matter.

Sincerely,

Emmett McVey, R.Ph.
Pharmacist-In-Charge

cc: Rachael G. Pontikes, Esq.
Elinor H. Murárová, Esq.
Duane Morris LLP