July 14th, 2023

Mrs. Monica Maxwell
U.S. Food and Drug Administration
Acting Program Division Director
Office of Pharmaceutical Quality Operations Division II
404 BNA Drive, Building 200, Suite 500
Nashville, TN 37217

On behalf of Surgery Pharmacy Services, Inc., I authorize the United States Food and Drug Administration (FDA) to publicly disclose the information described below. 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 (0), 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 of this information with the public.

Information to be disclosed: Surgery Pharmacy Services' letter dated 07/14/2023 excluding attachments/exhibits, which responds to the FDA's Form 483 dated 07/07/2023.

Authorization is given to the 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 Surgery Pharmacy Services, Inc.

Sincerely,

Hunter Eaves, PharmD.
President/Owner
Surgery Pharmacy Services, Inc.
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Mrs. Monica Maxwell,

Per FDA inspector Mr. Jared Stevens instructions, this letter comprises Surgery Pharmacy's response to the FDA Form 483 Observations which were issued on July 14th, 2023 following an inspection of Surgery Pharmacy Services, Inc.

Surgery Pharmacy Services, Inc. is a sterile compounding pharmacy operating pursuant to rules and regulations of The Tennessee Board of Pharmacy, and relevant United States Pharmacopeia (USP) 797 standards. Surgery Pharmacy Services, Inc. operates as a 503A sterile compounding pharmacy preparing compounded preparations for identified patients upon receipt of a patient-specific prescription order. Our facility holds secondary accreditation through the American Commission for Healthcare (ACHC) by meeting all standards set forth by the commission. This accreditation was renewed on August 13th, 2022 (see ACHC Certification 2022). These standards meet and exceed the current USP chapter <797> requirements for compounding pharmacies.

Surgery Pharmacy Services, Inc. appreciates the thorough inspection by Mr. Jared Stevens, and has made and will continue to make improvements in our processes as described below.

OBSERVATION 1:

Smoke studies were inadequately performed under dynamic conditions.

Specifically, your videos of the smoke studies conducted on April 13, 2023 do not show manipulations or conditions performed that would be representative of the dynamic process used in actual compounding processes using the Exactamix Compounder.
For example, the manual additions of volumes deemed too small to be added to the final products; the connection of the TPN bag to the tubing, the powered on state of the Exactamix and scale; and connections made to all twenty-four component stations are not performed during the smoke study.

RESPONSE:

Surgery Pharmacy Services contracts with Controlled Environment Certification Services, Inc., a subsidiary of Steris corporation (Steris), to perform recertification of both our LAFW hoods and Cleanroom/anteroom suite. Recertification occurs every 6 months to maintain compliance with the current USP <797> chapter. This certification is performed according to the requirements set forth by the CETA certification guide for sterile compounding (CAG-003-2006).

Every certification cycle, an airflow visualization test is performed by Steris on the laminar flow hoods located in the ISO 7 Cleanroom. All Steris reports include documentation outlining the procedures and results of the airflow visualization test (see Steris Airflow Test Form), and indicates visualization tests are conducted under dynamic or operable conditions as required by USP <797>.

As noted in our firm's previous 483 response letter (see 483 response 2019) written December 26, 2019, proposed changes to our previous airflow visualization testing were implemented in response to the inspection findings. These changes include both a more thorough smoke study of our EM2400 compounder to be conducted on biannual recertification, and shifting of vials and spikes to ensure they are bathed in first air at all times, even when no critical sites are exposed. These proposed changes were implemented following our 483 response, and have been a part of our firm's operating procedures to date.

In response to the above observation, our firm will further improve the process of airflow visualization studies conducted by Steris. On each subsequent biannual recertification, smoke studies will be conducted and filmed that will encompass visualization of airflow during manipulations performed on every spiked vial/bag on the EM2400 compounder, all ports on the EM2400 valve set, sterile EVA bag connections, and manual additions of volumes too small to be pumped by the EM2400. Future smoke studies will seek to mimic the compounding process of the most complex solution produced by the EM2400 compounder.

OBSERVATION 2:
Failure to conduct media fills that closely simulate aseptic production operations under the worst-case, most-challenging, and stressful conditions.

Specifically, your media fills are not representative of production in that manipulations made during production are not reproduced with the media fill process. For example, manipulations not represented are the addition of volumes deemed too small for inclusion via the Exactamix Compounder machine.

RESPONSE:

Surgery Pharmacy Services as part of initial and continued competency training requires all compounding personnel to perform media fill assessments in accordance with USP Chapter <797> (see SPS Policy 3 Updated). This is performed in conjunction with fingertip sterility for new compounding employees, and every 6 months thereafter for continued assessment of compounding personnel's aseptic technique. In addition to our response to the 483 observations made on December 26, 2019 detailing the proposed implementation of a revised media fill that simulates the most strenuous media CSP at our firm (see 483 response 2019), two separate and distinct media fill assessments have since been implemented. These media fill assessments seek to simulate our most strenuous compounding process, as well as our most frequent compounding process. Our firm has chosen to utilize the QI Medical QuickTest system to perform our most frequent CSP media fill assessment.

The QI Medical QuickTest system QT1000 is designed to assess aseptic process validation of compounding personnel while using a medical compounder. Per QI Medical's instructions (see QI Medical QuickTest information), The QI QuickTest is attached to the compounding valve set of the EM2400, a representative solution is pumped into a waste bag, the QuickTest is then aseptically removed from the EM2400 valve set after pumping, and included GroMed TSB media is attached to the QuickTest to purge admixture from the chamber and replace with

growth media. The included growth media contains a certificate of analysis and method suitability by lot (see QI GroMed CofA Example). Any contaminants introduced during compounding will be captured by the QuickTest filter chamber and produce growth. During our inspection, it was found that the process of manual additions may not be evaluated by this method

In response to the above observation, our firm will amend our media fill procedures when using the QI Medical QuickTest system to include steps to evaluate volumes added to admixture solutions that are too small to pump through the EM2400 compounder. The QuickTest fill chamber provides a needle port that can be used to inject representative amounts of manual addition volumes into the chamber for incubation (see QI QuickTest photo 1, 2). Our procedures will be revised to include the use of this port to simulate manual injections into the chamber to produce a more accurate representation of our most frequent compounded product for evaluation.

OBSERVATION 3:

Your facility is designed and operated in a way that may permit the influx of lesser quality air into a higher quality air area.
specifically, material flows directly from an unclassified area into a ISO 7 classified room in which sterile production occurs via a pass-through portal which consists of an un-powered refrigerator with a door on each end.
On 6/21/2023, materials were used in compounding total parenteral nutrition (TPN) products that included a calibration kit, tubing, and bags which had entered the ISO 7 area via the pass-through as well as finished TPN products leaving the ISO 7 area into the unclassified space via this unfiltered pass-through. This pass through is located within close proximity, approximately three feet, to an ISO 5 hood used in sterile compounding of TPN products.

RESPONSE:

Surgery Pharmacy Services utilizes a monitored pass through cabinet (previously refrigerated) to move products and equipment from the general pharmacy to the Cleanroom. According to the currently applicable USP 797 chapter (see USP 797 excerpt 1, 2, 3), pass through cabinets require frequent cleaning, monitoring, as well as provisions to prevent the opening of both doors (interlocking) simultaneously. Our firm follows and exceeds these requirements as demonstrated in the following points.

Viable air/surface sampling is conducted more frequently than required by USP 797, with air sampling being conducted bimonthly (six month requirement) and surface sampling monthly (see Q2 2023 air sampling report). USP 797 also requires pass through cabinets to be disinfected daily, but only requires the use of sporicidal agents on a monthly basis. Our firm uses sporicidal cleaning agents daily on the pass through cabinet, exceeding the chapter's requirement. Currently, PeridoxRTU is used as the sporicidal agent for our firm (see PeridoxRTU 1, 2).

Pressure monitoring is not a requirement set forth by USP 797 for pass through cabinets, however such monitoring would help to demonstrate positive pressure within the cabinet leading

from higher quality to lower quality air areas as well as the principle of HEPA filtered air continuously washing over the cabinet and any contents contained within. As such, our firm will utilize a redundant, annually calibrated pressure monometer (see pass through Monometer 1, 2) to measure the active pressure between the pass through cabinet and the general pharmacy. This monometer has been installed, and will be added to our firms daily pressure monitoring routine.

Measurements were taken on 7/19/2023 to validate positive pressure gradients between higher quality air spaces to lower quality air spaces. The measurement taken from the pass through cabinet to the general pharmacy was recorded to be positive 0.16 inches of water column (in/wc). To determine whether this pressure would indicate the flow of air would move as expected from the ISO 7 Cleanroom to the general pharmacy, and not influx the opposite direction, a pressure reading was taken from the calibrated monometer that measures the pressure differential between the ISO 7 Cleanroom to the ISO 8 anteroom (see Cleanroom Monometer 1). the pressure measured from the ISO 7 Cleanroom to ISO 8 anteroom was found to be 0.17 in/wc. In order to determine the positive pressure from the ISO 7 Cleanroom to the general pharmacy, a pressure tube was placed on the low end of the Cleanroom monometer and routed into the general pharmacy to obtain an approximate pressure of positive 0.27 in/wc (see Cleanroom Monometer 2). This value would be expected as the pressure reading between the ISO 8 anteroom and general pharmacy was found to be 0.09 in/wc and the ISO 7 Cleanroom to ISO 8 anteroom was found to be 0.17 in/wc which would yield 0.26 in/wc from the ISO 7 Cleanroom to the general pharmacy (see Anteroom Monometer 1, 2; Cleanroom Monometer 1). To determine the pressure differential between the ISO 7 Cleanroom and the pass through cabinet, the Cleanroom's pressure of 0.27 in/wc is reduced by the pass through cabinet's previously recorded pressure of 0.16 in/wc to obtain a positive pressure gradient of 0.11 in/wc from the ISO 7 Cleanroom to the pass through cabinet. This value is more than five times higher than the minimum pressure of 0.02 in/wc set by USP 797 for pressure differentials between ISO 7 clean rooms and ISO 8 anterooms (see USP 797 excerpt 4).

In response to the above observation, our firm feels that our current Cleanroom suite as designed and operated has proven to prevent the influx of lower quality air to higher quality air areas, and does not need to be redesigned or altered. Currently our firm not only meets, but exceeds currently applicable laws governing 503A Cleanroom pharmacies. On the contrary, if our Cleanroom suite was to be altered from its current design, it may negatively impact patient safety as such a change may inadvertently create a situation in which lower quality air could influx into higher quality air spaces.

As an addition to the above response, our firm is in the final stages of construction of a new Cleanroom facility. This facility has been designed and constructed by a third party, Cleanroom's International, to modernize all aspects of our firms current Cleanroom operations. Specifically related to the operation of the pass through cabinet, the new facility is designed and constructed with the pass through cabinet located in the ISO 8 anteroom, and placed further away from ISO 5 hoods due to a larger floor plan. In conjunction with previously stated monitoring, cleaning, and

testing procedures that will continue to be conducted by our firm, this redesigned Cleanroom suite should only further mitigate any possibilities of air influx.

We appreciate your thorough inspection of our pharmacy, and for allowing us to respond to the observations noted during our FDA inspection. We respectfully request that this letter of response be publicly posted along with the FDA form 483 observations.

Sincerely,

Hunter Eaves, PharmD.
President/Owner
Surgery Pharmacy Services, Inc.