DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
8050 Marshall Drive, Suite 205 Lenexa, KS 66214 (913)495-5100 Fax:(913)495-5115	6/18/2024-6/28/2024* FEI NUMBER 3012104093

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Jason E. McGuire, Senior Vice President, Operations

FIRM NAME	STREET ADDRESS
Fagron Compounding Services, LLC dba Fagron Sterile Services	8710 E 34th St N
CITY, STATE, ZIP CODE, COUNTRY Wichita, KS 67226-2636	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed.

Specifically,

A. Your firm released batches of sterile drug products even though positive microbial growth was detected during environmental monitoring (EM) and personnel monitoring (PM) in the ISO 5 aseptic area during batch processing. For example, since 2023, your firm has released a total of 9 batches with positive growth identified on operators' gloved hands, settle plates, or active air samples in the ISO 5 areas for the following products:

- Ketamin 10 mg/ml (API) 5 ml Fill in 5 mL Syringe, Lot# (b) (4), 1 CFU of Staphylococcus capitis identified on the right surface sample
- PHENYLephrine 0.1mg/mL PF Inj Soln 10mL Syringe API, Lot# (b) (4), 1 CFU of Staphylococcus epidermidis identified on the left hand
- Norepinephrine Bitartrate 8mg added to 250mL 0.9% NaCl Bag, Lot# (b) (4), 1 CFU of Staphylococcus hominis identified on the left glove
- Succinylcholine 20mg/mL Solution, Lot #(b) (4), 1 CFU of Staphylococcus capitis identified on the left glove
- Rocuronium Bromide Inj. Solution 10mg/mL from API, Lot # (b) (4) 1 CFU of

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Peribacillus simplex identified on the left glove

- Oxytocin 30U Inj Sol 500mL Fill in 500mL 2-Port IV Bag API, Lot# (b) (4), 1 CFU of Metabacillus galliciensis identified on the left hand
- Norepinephrine Bitartrate 16mg added to 250mL 0.9% NaCl Bag, Lot# (b) (4), 1 CFU of Niallia circulans identified on the right active air sample
- Ketamine 50mg/ml (API) 1ml Fill in 3ml Syring, Lot # (b) (4) 1 CFU of Micrococcus luteus identified on the right active air sample
- Lidocaine HCl 2% 20mg/mL Sol for Inj. PF from API, Lot # (b) (4), 1 CFU of Bacillus licheniformis identified on the left glove

Your investigation indicated that syringes and IV bags were filled in a minimally exposed environment for these batches, unlike vials and eye droppers; however, there is no assurance that product sterility was maintained throughout batch processing.

B. Your qualification of the cleanrooms after construction was inadequate prior to the resumption of production of sterile products. Your firm reconstructed the production area from January 30, 2023, to February 7, 2023, including the construction of a new Filling Room (b) (4) by (b) (4) (b) (4) a(b) (4) with (b) (4). However, the Change Control 23-CC-006 was inadequate, as it only required the qualification of Filling Room (b) (4) the gowning room and the corridor, but the other (b) (4) connected filling rooms were not qualified until the July 2023 (b) (4) qualification before production resumed immediately after the construction was completed. Your firm produced approximately (b) (4) batches a day varying from (b) (4) units to (b) (4) units per batch.

C. Media fill was not conducted prior to the production of sterile products in the newly constructed Filling Room (b) (4). Your firm constructed a new Filling Room (b) (4) which is equipped with new (b) (4) filling equipment and the ISO 5 Laminar Airflow Hoods (LAFHs) transferred from Fill Room (b) (4) for the filling of sterile IV bags in February 2023. However, the initial media fill (Protocol Number: FSS-2023-

099) for this filling room was not conducted until August 2023. Despite this, the room was put into use for producing IV bags immediately after construction was completed. Your firm produced (b) (4) batches prior to the media fill in Filling Room (b) (4). For example, your firm produced the first batch of Norepinephrine Bitartrate 16 mg added to 250 mL 0.9% NaCl Bag, Lot #(b) (4), on February 13, 2023.

D. The qualification of ISO 5 Laminar Airflow Hoods used for aseptic production was inadequate. Your (b) (4) certifications of HEPA filters conducted in January 2024 and January 2023 revealed multiple occasions of HEPA filter leaks in the ISO 5 aseptic processing areas, deviations in air velocity and discoloration. HEPA filter leaks were detected during the January 2024 qualification in the following locations: LFH-FSS-(b) (4), Fill Room (b) (4); LFH-FSS-(b) (4) Fill Room (b)(; LFH-FSS(b) (4), Fill Room (b)(4 and LFH-FSS-(b) (4), Fill Room (b)(4 Additionally, HEPA filter leaks were detected during the (b) (4) qualification in the following locations: LFH-FSS-(b) (4), Fill Room (b)(4 and LFH-FSS(b) (4) Fill Room EM for viable air, surface and PM found positive growth in multiple ISO 5 LAFHs associated with those HEPA filters. There is no assurance your sterile drug product were produced under controlled aseptic conditions. A total of (b) (4) batches were produced before the January 2024 qualification of the cleanroom related to those deviations are still within their expiry dates. For example, Ropivacaine 0.50% (API) 20mL fill in 20mL Syringe, Lot#(b) (4) was produced on January 22, 2024 with an assigned BUD on July 23, 2004.

E. Validation of disinfectant efficacy was inadequate. Your firm conducted a disinfectant efficacy study (Protocol Number: FSS-2022-022, dated 10/18/2022) of (b) (4) used for disinfecting supplies and equipment on three materials surfaces: vinyl flooring, acrylic, and stainless steel, simulating surfaces of the ISO 5 LAFHs and floor. However, this study did not include surfaces of IV bags and gloves made from (b) (4). (b) (4) is used to disinfect the surfaces of IV bags before they are introduced from the dispensing area to the ISO 8 area and from the ISO 7 area to ISO 5 area. It is also used to disinfect gloves in the ISO 5 area. Additionally, (b) (4) (b) (4) was used to sanitize supplies introduced from the ISO 8 area to the ISO 7 area and from the ISO 7 area to the ISO 5 area; however, no study has been conducted to validate its

effectiveness.

F. The procedure for General Aseptic Technique, SOP FSS-SOP-0002 , Revision 3, Effective Date: January 26/2024 was not followed. The Section 7.2.1 of this procedure requires avoiding leaning over work area and open containers when working in the cleanroom area; however, production operators heads covers were observed entering the (b) (4) ISO 5 LAFH during batch processing of Fentanyl Citrate 2mcg/ml / Bupivacaine IV Bag, 0.0625%/ 250 bag, Lot# (b) (4) on June 18, 2024, Expiration Date: December 14, 2024.

G. According to FSS-SOP-0015, Environmental Monitoring of Clean Room Facility, personnel monitoring does not require monitoring of sleeves and heads covered by gowns during production of sterile syringes and IV bags. However, operators' sleeves were inside the (b) (4) ISO 5 LAFH throughout the Production. For example, during the production of PHENYLephrine 0.1mg/mL PF Inj Soln 10mL Syringe API, Lot# (b) (4) , dated June 3, 2024, operators sleeves were observed inside the LAFH in the production video.

OBSERVATION 2

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

Your investigations of out-of-specification (OOS) results in environmental monitoring (EM), visual inspection failures, and consumer complaints were inadequate for the following:

- Since 2023, your firm has reported 22 deviations due to OOS results of gloved hands, settle

plates, or active air monitoring in the ISO 5 areas during aseptic batch processing. No definite root causes were identified and therefore no CAPAs were initiated for any of these EM OOS results. For example, your firm reported 1 CFU of Chaetomium globosum on the right glove of an aseptic technician during the production of Norepinephrine Bitartrate 8mg added to 250mL0.9% NaCl Bag, Lot# (b) (4), dated February 1, 2024 (DEV-2024-0174). Since no definite root causes have been identified for the OOS result, the batch was rejected, and no CAPA was initiated.

- Since 2023, your firm has rejected approximately 30 batches of ketamine syringes due to visual inspection failures. Although your firm suggests the cause might be a combination of factors such as (b) (4) the units, No definite root causes have been identified. Your firm continues to produce commercial batches of this product.

- Your firm has received four complaints regarding Lidocaine-Epinephrine-Tetracaine (L.E.T.) topical gel (Lot # (b) (4) being discolored. The investigation identified the root cause as inappropriate storage conditions, leading to the oxidation of epinephrine and the resulting color change. However, retention samples stored at your facility were also found to be discolored, which is defined as a critical defect. No definite root causes have been identified for discoloration of products.

OBSERVATION 3

The quality control unit lacks responsibility to approve and reject all procedures or specifications impacting on the identity, strength, quality and purity of drug products.

Specifically,

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A. Your (b) (4) certifications of HEPA filters conducted in January 2024 and January 2023 identified HEPA filter leaks and/or discoloration in the ISO 5 aseptic processing areas; however, no CAPA has been initiated to prevent similar situations from reoccurrence.

B. No risk assessment or change control has been initiated for the impact of ongoing adjacent construction on sterile manufacturing. Your firm plans to construct an adjacent (b) (4) expansion to the east of the FSSE facility at 8720 East 34th St. North, (b) (4) facility upon completion. The construction has started in the second quarter of 2024, with a target completion date of (b) (4). However, your firm has not initiated a change control for this project, stating that a change control will be initiated once the new construction (b) (4) (b) (4). Your firm claims there is no impact on current manufacturing before the new construction is completed, but there are no documented records of risk assessment and its impact on current manufacturing.

OBSERVATION 4

Complaint records are deficient in that they do not include the findings of the investigation and follow-up.

Specifically,

Customer complaint investigations are inadequate because your firm did not thoroughly investigate batches and provide supporting data to determine if a complaint is related to a quality issue. Since 2022, your firm has received complaints about potential infections after using sterile drug products produced at your facility, as follows:

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	Taichun Qin, Investigator X Taichun Qin Investigator Signed By: 2001324646 Date Signed: 06-28-2024 16:22:28	6/28/2024

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- COMP-2023-0581: inflammation resulting in vision loss following the administration of TRIAMcinolone acetonide 40 mg/mL Inj Susp PF 2mL SDV, Lot#: (b) (4), dated August 25, 2022
- COMP-2022-0423: endophthalmitis following the administration of Avastin Solution for Injection, 2.5 mg/0.1 mL. 0.12mL Fill, Lot# , (b) (4), dated June 22, 2022
- COMP-2023-0671: infection flowing the administration of Moxifloxacin HCl(Avelox) 1.6mg/mL 1mL fill in 3mL Syringe, Lot# (b) (4), dated September 14, 2023
- COMP-2023-0680: spinal meningitis following the administration of TRIAMcinolone acetonide 40 mg/mL Inj Susp PF 1mL SDV, Lot# (b) (4), dated September 18, 2023
- COMP-2024-0250: diffuse corneal swelling following the administration of Lidocaine 1%/Phenylephrine 1.5% BSS PF/SF Inj Soln 1mL SYR, Lot# (b) (4), dated May 17, 2024

Your firm conducted an investigation for each case without identifying any deficiencies; however, no sterility tests were performed on retention samples from the batches related to these adverse event reports.

OBSERVATION 5

Laboratory controls do not include the establishment of scientifically sound and appropriate designed to assure that conform to appropriate standards of identity, strength, quality and purity.

Specifically,

During the walkthrough of the warehouse where (b) (4) incubators were located, I observed that all environmental monitoring (b) (4) plates were placed in a (b) (4) for incubation without any visible gaps. For example, I observed EM plates for Moxifloxacin HCl (Avelox) 1.6mg/mL 1mL fill in 3mL Syringe, Lot# (b) (4) were placed in a (b) (4) for incubation. Currently, all

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environmental monitoring samples collected during production of sterile drug products were placed in (b) (4) for microbial growth testing in these (b) (4) incubators. However, your firm has not validated this method using known bacterial strains under the same conditions. Your growth promotion testing was conducted in the microbiology laboratory in a different location using (b) (4) plates that were unsealed. There is no documented evidence or study demonstrating the impact of this practice on bacterial and fungal growth.

OBSERVATION 6

The labels of your outsourcing facility's drug products do not include information required by section 503B(a)(10)(A) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Specifically,

The dosage form is not included on some of your drug product labels.

For example, labels for the following drug product do not contain this information:

- Tropicamide 1%/Cyclopentolate 1%/Phenylephrine 2.5%/Ketorolac 0.5%, 5 mL in Multi-Dose Dropper Bottle (NDC# 71266-8240-05)
- Fentanyl Citrate 2 mcg/mL (100 mcg/50 mL)/Ropivacaine HCl 0.15% (1.5 mg/mL) (75 mg/50 mL), PF, for epidural use only (NDC# 71266-9235-01)

OBSERVATION 7

The container of your outsourcing facility's drug products does not include information required by section 503B(a)(10)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

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Specifically,

Your containers do not include the following information:

A. Directions for use, including, as appropriate, dosage and administration. Specifically, the route of administration is not included on your containers.

Examples of your container labels that do not contain this information include:

- Lidocaine 1% (10 mg/mL)/Phenylephrine 1.5% (15 mg/mL) in BSS, PF/SF Injection, 1 mL in 3 mL Single-Use Syringe (NDC# 71266-6360-01)
- Epinephrine (1 mg/mL), Sterile Solution for Injection, PF/SF, 1 mL in Single-Use Syringe (NDC #71266-8120-01)
- Phenol Injection 6% (60 mg/mL), In Sterile Water for Injection, 10 mL in Multi-Dose Vial (NDC# 71266-6519-01)
- Iohexol (Omnipaque) 300 mgI/mL, Sterile Aqueous Injection, PF, Repackaged, 3 mL in Single-Use Vial (NDC# 71266-6488-03)
- Iohexol (Omnipaque) 240 mgI/mL, Sterile Aqueous Injection, PF, Repackaged, 5 mL in Single-Use Vial (NDC# 71266-6487-05)
- Sodium Citrate Injection 4% (40 mg/mL), 30 mL in Multi-Dose Vial (NDC# 71266-6641-01)
- Sodium Citrate 4% (40 mg/mL) containing Gentamicin 320 mcg/mL Injection, 30 mL in Multi-Dose Vial (NDC# 71266-6670-01)
- Sodium Citrate 4% (40 mg/mL) Injection containing Gentamicin 320 mcg/mL, 3 mL in Single-Use Syringe for Injection (NDC# 71266-6670-03)
- Sodium Citrate 4% (40 mg/mL) Injection containing Gentamicin 320 mcg/mL, 5 mL in Single-

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Use Syringe for Injection (NDC# 71266-6670-04)

- Dexamethasone Sodium Phosphate (dexamethasone phosphate equivalent), 10 mg/mL, Solution for Injection, PF, 2 mL in Single-Dose Vial (NDC# 71266-1041-02)
- Dexamethasone Sodium Phosphate (dexamethasone phosphate equivalent), 4 mg/mL, Solution for Injection, PF, 2 mL in Single-Dose Vial (NDC# 71266-1051-02)
- Methylprednisolone Acetate, 80 mg/mL, Injectable Suspension, PF, 1 mL in Single-Dose Vial (NDC# 71266-1075-01)
- Triamcinolone Acetonide, 40 mg/mL, Injectable Suspension, PF, 1 mL in Single-Dose Vial (NDC# 71266-1080-01)
- Betamethasone Sodium Phosphate, Sterile Solution for Injection, 6 mg/mL, 2 mL in Single-Dose Vial (NDC# 71266-1025-02)

***DATES OF INSPECTION**

6/18/2024(Tue), 6/19/2024(Wed), 6/20/2024(Thu), 6/21/2024(Fri), 6/24/2024(Mon), 6/25/2024(Tue), 6/26/2024(Wed), 6/27/2024(Thu), 6/28/2024(Fri)

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	Taichun Qin, Investigator X Taichun Qin Investigator Signed By: 2001324646 Date Signed: 06-28-2024 16:22:28	6/28/2024

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."