DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/25/2024-7/3/2024* FEI NUMBER 3011976853

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Robert J. Kilgore, CEO	
FIRM NAME BSO LLC	STREET ADDRESS 12860 W Cedar Dr Ste 211
CITY, STATE, ZIP CODE, COUNTRY Lakewood, CO 80228-1971	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 did not include adequate validation of the sterilization process.

Specifically,

a. Your firms sterilization validation studies used to sterilize pellets produced by your facility are inadequate.

- PQ002.01.VP, 2015 Sterile Pellets Sterilization Validation Report: Testosterone, Estradiol, Testosterone/Anastrozole, Progesterone, dated 8/13/15 (Protocol) and PQ002.01.VR, 2015 Sterile Pellets Sterilization Validation Report: Testosterone, Estradiol, Testosterone/Anastrozole, Progesterone, dated 11/04/15.

- SV002.01.VP, 2016 Sterile Pellets Sterilization Validation Protocol: Testosterone/Cholesterol, dated 122016 and SV002.01.VR, 2016 Sterile Pellets Sterility Validation Results: Testosterone/Cholesterol.

Your firm was unable to produce evidence of the material used to perform dose mapping. Dose mapping with material of (b)(4) is used to determine the minimum and maximum dose areas within a product container, thereby establishing a loading pattern to ensure the sterilization process is reproducible. Evidence provided states "Pellets in Bottles". Since the

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material is unidentified, it is unclear if the material used has the same attenuation and scattering properties similar to those of the product, material, or substance to be (b)(4) thus establishing that products of all densities received enough (b) (4) to render them sterile.

Study PQ002.01.VR is used to qualify the sterilization process for Testosterone (12.5 mg, 25 mg, 37.5 mg, 50 mg, 62.5 mg, 70 mg, 80 mg, 87.5 mg, 100 mg, 200mg), Estradiol (6 mg, 10 mg, 12.5 mg, 15 mg, 18 mg, 20 mg, 22mg, 25, 37.5 mg, 50mg), Progesterone (50 mg, 75 mg) and Anastrozole (6mg, 10 mg, 20 mg) pellets produced in your facility.

SV002.01.VR, 2016 Sterile Pellets Sterility Validation Results: Testosterone/Cholesterol, is used to qualify the sterilization process for Testosterone/Cholesterol (12.5 mg, 25 mg, 37.5 mg, 50 mg, 62.5 mg, 70 mg, 80 mg, 87.5 mg, 100 mg/ 2-4%, 200mg/ 2-4%), pellets produced in your facility.

Additionally, the impact of the sterilization method to product quality has not been adequately assessed, for example, testosterone and progesterone post-sterilization potency drops per table in validation report.

b. Your firm was unable to provide documentation or scientific justification for sterilization cycles used for Testosterone/Anastrozole pellets. Samples of Anastrozole 6mg pellets were used instead of Testosterone/Anastrozole pellets in study PQ002.01.VR, 2015 Sterile Pellets Sterilization Validation Report: Testosterone, Estradiol, Testosterone/Anastrozole, Progesterone, dated 11/04/15. During the study Testosterone/ Anastrozole did not meet the acceptance criteria.

    a. Your last manufactured batch of Testosterone/Anastrozole pellets was on (b)(4)

All pellet produced at your firm are (b)(4) sterilized by (b) (4) Your firm uses (b) (4) in lieu of sterility testing for product release.

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OBSERVATION 2

Employees engaged in the manufacture and processing of a drug product lack the training required to perform their assigned functions.

Specifically,

a. Your firm's Visual Inspection Program is inadequate. Section 6.3.2 of SOP 27, Visual Inspection for Liquid Injectables, Version 5.0, Effective Date 09/22/2023, defines *Critical Defect as a defect that*(b) (4) (b) (4) ".

Your firm maintains (b)(4) that is used for the qualification of personnel to perform visual inspection. The (b)(4) does not contain any examples of critical defects currently identified such as broken or cracked glass, particulate matter (glass particles), improper crimp (not gripping lip of vial), incorrect color or clarity. Your firm does not have documented evidence that the visual inspectors can identify critical defects of liquid injectable products produced in your facility.

The (b)(4) does not contain examples of all Major Defects identified in Table 1, section 7.1 of WI 27-01, Liquid Injectables Visual Inspection Procedures, Version 2.0, Effective Date 09/22/2023. Missing Major defects include Broken Caps, and Under-crimped caps. Additionally, the (b)(4) does not have examples of Minor defects such as Superficial scratches or chips on outside of vial and dropped vials. Your firm does not have documented evidence that the visual inspectors can identify all major and minor defects in liquid injectable products produced in your facility.

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Liquid Injectable products include Testosterone Cypionate/Anastrozole 200mg/0.5 mg; Testosterone Cypionate/Anastrozole 200mg/1mg; Testosterone Cypionate/DHEA 200mg/10mg.

b. SOP 12, Visual Inspection for Pellets, Version 21.0, Effective Date 05/03/2024 is deficient as it does not contain sufficient instruction for using the (b)(4) during visual inspection. The SOP requires all pellets to be inspected against a (b)(4) as (b)(4). I observed technicians performing visual inspection by placing an (b)(4), and then (b)(4)" on (b)(4). The pellets are not held against (b)(4) for a specified amount of time. The use of the (b)(4) to hold the pellets, negate the use of the (b)(4) as intended in the SOP. This initial visual inspection step for is especially critical for products that use amber vials such as Anastrozole and Estradiol pellets.

OBSERVATION 3

Time limits are not established when appropriate for the completion of each production phase to assure the quality of the drug product.

Specifically,

Your firm failed to establish a hold times between start of batch manufacturing and (b)(4) sterilization for Anastrozole 10 mg (for example Lot (b) (4) Expiration Date: 05/08/2025) and Anastrozole 20 mg (for example Lot (b) (4) Expiration Date: 05/08/2025). Both lots of Anastrozole were held for a period of (b) (4) prior to sterilization.

OBSERVATION 4

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There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically,

You have not conducted investigations to identify the source of particulates identified as major defects during the initial 100% Visual Inspection of your liquid injectable products.

Sec 6.3.3.3 of SOP 27, Version 5.0, Effective Date 09/22/2023, states (b)(4) *" Section 6.4.6. The Quality Manager will determine if an investigation, deviation, or assessment is warranted.*

For example, Testosterone Cypionate/DHEA 200mg /10 mg/ ml (Lot (b) (4), Expiration Date: 10/15/2024), rejected 95 vials for Major defect (Particle in solution: Black, white, or any color fiber, etc.). No investigation was opened to determine the source of the particle. Testosterone Cypionate /Anastrozole 200mg /1 mg/ ml (Lot #(b) (4) Expiration Date: 10/15/2024), rejected 99 vials for Major defect (Particle in solution: Black, white, or any color fiber, etc.). No investigation was opened to determine the source of the particle.

For example, Testosterone Cypionate/DHEA 200mg /10 mg/ ml (Lot(b) (4) Expiration Date: 10/15/2024), rejected 95 vials for Major defect (Particle in solution: Black, white, or any color fiber, etc.) No investigation was opened to determine the source of the particle. Testosterone Cypionate /Anastrozole 200mg /1 mg/ ml (Lot # (b) (4) Expiration Date: 10/15/2024), rejected 99 vials for Major defect (Particle in solution: Black, white, or any color fiber, etc.) No investigation was opened to determine the source of the particle. Both lots were released without investigation.

SOP 27 does not establish limits for each type of critical defect to initiate an inspection to the source and

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extrinsic, intrinsic, or inherent nature of the defect.

OBSERVATION 5

The written stability testing program is not followed.

Specifically,

Your firm lacks stability data to support the 360-day BUD for Anastrozole 10 mg and 20 mg doses. Your firm currently distributes Anastrozole 6 mg, 10 mg, and 20 mg pellets.

***DATES OF INSPECTION**

6/25/2024(Tue), 6/26/2024(Wed), 6/27/2024(Thu), 6/28/2024(Fri), 7/01/2024(Mon), 7/02/2024(Tue), 7/03/2024(Wed)

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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."