DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Cincinnati District Office 550 Main St. Suite 4-930 Cincinnati, OH 45202 513-322-0700	8/21-8/24, 9/6 – 9/7, 9/11, 9/15/2023 FEI NUMBER 3002992930
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Nicholas R. Kirkpatrick, Pharmacist in Charge	
FIRM NAME Wickliffe LLC	STREET ADDRESS 4340 Georgetown Road.
CITY, STATE, ZIP CODE, COUNTRY Lexington, KY 40511	TYPE ESTABLISHMENT INSPECTED ~~Compounder~~ **Producer of sterile and non-sterile drug products**

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 WE OBSERVED:

OBSERVATION 1

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

1) Personnel were observed conducting aseptic manipulations where the movement of "first air" in the ISO 5 area is blocked or disrupted. On 8/22/2023, in the sterile filling hood, your technician was producing Pentosan Glucosamine batch 520880. During aseptic filling your technician and/or pharmacist was observed blocking first pass air:
   a) Your technician stored the (b) (4) on a (b) (4) between the (b) (4) within the hood. First pass air over the tip of this (b) (4) was blocked throughout the aseptic filling operation. Additionally, during aseptic filling the sterile (b) (4) was held below the technician's hands on several occasions blocking first pass air.
   b) Your technician had an ISO 5 sterile glove break during aseptic filling. The technician proceeded to replace the sterile glove while open vials were sitting on the benchtop of the ISO-5 environment. These vials were then filled, capped, and sealed. According to the technician, glove changes occur as often as (b) (4) for some batches of gloves and rarely for others. Your firm does not document glove replacement for the ISO-5 gloves.

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SEE REVERSE OF THIS PAGE	Logan Williams -S Digitally signed by Logan Williams -S Date: 2023.09.26 16:17:15 -04'00'	Logan T. Williams, CSO **Stephanie Mongeluzzi, VMO** **Lauren Howard, CSO**	9/15/2023

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c) Your pharmacist reached over approximately (b) (4) empty vials to reach a spray bottle located in the back of the hood. These vials were then filled and capped.

d) Your technician handled sterile forceps below their gloved hand, blocking first pass air, while manipulating sterile stoppers. The opened bag of sterile stoppers was approached from above frequently resulting in first pass air being blocked.

2) Personnel infrequently sanitized gloves to prevent contamination. On 8/22/23, during aseptic filling of Pentosan Glucosamine batch 520880, your technician used (b) (4) to fill vials to the correct volume. The technician had to reset/manipulate the (b) (4) outside of the ISO-5 hood and then return to aseptic filling throughout the filling process. Your technician did not resanitize gloves upon re-entry into the ISO-5 (b) (4) every time. The manipulation of the (b) (4) occurred as often as 3 times in 8 minutes without resanitizing with (b) (4). During the filling of this batch the left ISO-5 glove, which was the hand used to manipulate the (b) (4), was changed due to a break.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic or sterilization process. Specifically,

1) Your media fills do not include any high-risk challenges and are performed during "routine" operations.

a) On 8/22/23, during aseptic filling of Pentosan Glucosamine batch 520880, your technician changed out a glove on the ISO-5 (b) (4), however, glove changes are not documented during media fills or reflected in the batch record. According to your technician these glove

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changes can occur frequently ((b) (4)). It is unknown if your firm has ever changed a glove during media fills.

b) Your technician overfilled a vial of Pentosan Glucosamine batch 520880 and proceeded to pour that vial's contents into another vial that was later filled and sealed. This task is not recorded during media fills.

2) Your firm's sterilization cycle for your (b) (4) and (b) (4) , that is used to render several injectable drug products sterile, has not been validated .

a) Your firm has not validated the (b) (4) cycles used for (b) (4) sterilization used in the sterilization of several drug products including Stanozolol in Water for Injection 50mg/mL, Prednisolone Acetate Injectable 50mg/mL, and Estrone Injectable 5mg/mL. Validation of the cycles includes determining appropriate loading patterns and temperature mapping of the cycle to determine worst case locations for biological indicator placement.

b) Your firm has not validated the (b) (4) cycles used for (b) (4) sterilization of several drug products including Estradiol Cypionate Injectable 10mg/mL, Iodine in Almond Oil Injectable 2%, and Altrenogest Injectable 110mg/mL. Validation of the cycles includes determining appropriate loading patterns and temperature mapping of the cycle to determine worst case locations for biological indicator placement.

3) Visual inspection limits are not based on defect criticality. An overarching (b) (4) reject threshold is set for all sterile injectable batches with no consideration for defect types that would impact sterility such as turbidity, container integrity, and extrinsic particulates, such as hair. Defect criticality has not been determined and defects found are not recorded during visual inspection. Additionally, the visual inspectors are not qualified to perform visual inspection, demonstrating that they can correctly and accurately identify known defects.

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OBSERVATION 3

Equipment and utensils are not cleaned, maintained, and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product. Specifically,

On 9/7/2023, during aseptic filling of Reserpine 2.5mg/mL, brown residue was wiped off the bottom of vials that were introduced to the sterile hood for filling. Reserpine is a clear/yellow liquid. More than 9 vials were discarded due to the brown residue. Filling, capping, and sealing of the batch was completed.

The last 3 batches of 30mL vials being filled were Altrenogest lot 517601 on 8/4/23, Stanozolol lot 517465 on 8/7/23, and Altrenogest lot 520197 on 8/18/23. Altrenogest is a (b) (4) sterilized oil-based product and has an orangish/brown color when dry according to the Pharmacist in Charge. The batch of Altrenogest on 8/4/23 was rejected due to overfilling and the seals popping off during (b) (4) sterilization. Following the rejected Altrenogest (b) (4) cycle, a lot of 30mL vials was loaded into the (b) (4) for (b) (4). Similarly, following the Alrenogest lot on 8/18/23, a lot of 30mL vials was loaded into the (b) (4) for (b) (4). These 30mL vials are then run through (b) (4) cycle for sterilization and use in other 30mL vial batches.

There is no documentation for (b) (4) or (b) (4) cleaning of (b) (4) which is used for (b) (4) of vials as well as (b) (4) sterilization for oil-based drug products such as Altrenogest 110mg/mL injectable, Estradiol Cypionate Injectable 10mg/mL, Estradiol Cypionate Injectable 2mg/mL and Iodine in Almond Oil Injectable 2%. Additionally, a white residue was seen along each of the walls and back of (b) (4) on 8/23/23.

OBSERVATION 4

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Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet each appropriate specification as a condition for their approval and release. Specifically,

Your firm only tests potency of a product the first time it is compounded. Once the first batch is successfully produced for potency then all subsequent batches are not tested for potency. On 5/24/2023, your firm received passing potency results for Estrone Injectable 5mg/mL, lot 499797. Since then, your firm has produced and released (b) (4) additional lots of Estrone Injectable 5mg/mL with no additional potency testing performed. (b) (4) additional batch of Estrone 5mg/mL, lot 504414, was produced after initial potency but was not released due to a sterility failure.

OBSERVATION 5

Investigations of a failure of a batch or any of its components to meet any of its specifications did not extend to other batches of the same drug product or other drug products that may have been associated with the specific failure or discrepancy, Specifically,

1) Your firm did not determine a root cause or investigate batches that failed during visual inspection for leaking vials due to excessive seals popping off during (b) (4) sterilization. Your firm has rejected two batches in the past year due to seals leaking. On 7/5/23, Estradiol 2mg/mL lot 511677 was rejected due to excessive vial seals popping off. On 8/4/23, Altrenogest 110mg/mL lot 517601 was rejected due to excessive vial seals popping off.

2) Your firm produced Estrone injectable 5mg/mL batch 497879 that failed potency at 83% with a specification of (b) (4) . This batch was discarded. The investigation into batch 497879 concluded that "not setting the (b) (4) plates on the proper (b) (4) ended up with some vials filled with less Estrone concentration than 5mg/ml." The following Estrone 5mg/mL production, batch 499797, was produced using the same batch instructions and no documented

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retraining. Appropriate preventative actions were not implemented to assure that this product and other similar products consistently meet potency specifications.

3) Your firm did not expand the investigation of a sterility failure of Estrone Injectable 5mg/mL lot 504414 to other batches of aseptically filled products from around the same period. The investigation corrective actions included running biological indicators to verify cycle efficiency and running an additional (b) (4) cycle on each (b) (4) . According to the investigation "Follow up was done with the following batch and shall be done with successive batches each time", however actions for follow up were not identified nor recorded in the investigation.

OBSERVATION 6

There is no written testing program designed to assess the stability characteristics of drug products. Specifically,

Batches are not put on stability that have been prescribed for office stock. Products prescribed for office stock include Doxycycline Hyclate in Oil Suspension 500mg/mL and Methimazole Suspension 2.5mg/mL. Potency over time or (b) (4) is tested for new sterile products, however, other drug quality attributes are not evaluated under long term storage conditions such as impurities formed over time. No stability testing has been performed for non-sterile products.

OBSERVATION 7

Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess. Specifically,

1) On 9/6/2023, during non-sterile observation of Doxycycline (as Hyclate) Powder 5gm/TBSP lot 521872, your firm (b) (4) mixed the batch and weighed out scoops to determine if adequate mixing

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had occurred. Your scoop weights did not meet specification ((b) (4)) during initial weighing of approximately (b) (4) scoops. The batch was (b) (4) mixed and an additional (b) (4) scoops were weighed to verify scoop weight was met. The (b) (4) scoops were within the tolerance of (b) (4) of scoops weighing within specification. The initial (b) (4) scoops were weighed out by a different technician than the following (b) (4) scoops.

This process is (b) (4) and has not been validated to assure that each operator can successfully perform adequate mixing and weighing. Processing instructions state to mix by (b) (4) in an appropriately sized (b) (4) and to mix thoroughly. Mix times and mixing technique are not described.

Scoops weights are used to assure that each scoop contains the desired amount of active ingredient and ingredient adjustments to the formulation are made when scoops weights are not being met. Additionally, the firm did not keep the (b) (4) scoop weight data and only reported the (b) (4) scoops that passed specification in the compounding record.

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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."