DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
60 Eighth Street NE Atlanta, GA 30309 (404)253-1161 Fax:(404)253-1202 ORAPHARM2_RESPONSES@fda.hhs.gov	3/28/2022-4/20/2022* FEI NUMBER 3011158388

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Lou Wood Kennedy, CEO & Owner

FIRM NAME	STREET ADDRESS
Nephron Sterile Compounding Center LLC	4500 12th Street Ext
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
West Columbia, SC 29172-3025	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 WE OBSERVED:

OBSERVATION 1

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,

a) Your firm has not conducted investigations into the majority of environmental monitoring and personnel monitoring excursions (recovery of organisms) identified as occurring in the ISO 5 environment. From January 1, 2021 to March 31, 2022, your firm had approximately 1686 instances of excursions related to work performed in the ISO 5 area to include personnel monitoring, viable air and viable surface samples.

Your firm stated that approximately 240 excursions related to monitoring of personnel who performed filling/capping and sanitizer functions, which are critical roles during the aseptic filling of sterile drug products, were not investigated.

There were approximately 51 excursions related to viable air or surface samples within the ISO 5 hood. No investigation was conducted for 48 of the 51 excursions.

Examples include but are not limited to the following.

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EMPLOYEE(S) SIGNATURE
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Demario L Walls, CSO
Saundrea A Munroe, CSO
Kemejumaka N Opara, CSO
Brandon C Heitmeier, CSO
Desiree D Clark, Chemist

X Margaret M Annes CSO Signed By: Margaret M. Annes -S Date Signed: 0 -20-2022 12:38:59

DATE ISSUED
4/20/2022

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The organism *Penicillium guizhouanum* was identified approximately 24 times in viable air, contact plate (surface) and/or personnel monitoring samples in August/September of 2021. No investigations were performed. All lots were released by QA. Examples include the following.

Sampling Date	CFU	Sample Type	Product	Lot#	BUD
08/30/2021	1	Viable Air	Hydromorphone HCl Injection, 30 mg/30 mL (1 mg/mL)	(b) (4)	180 days
09/05/2021	1	Fingertip (R)	Ketamine Hydrochloride Injection, USP 50 mg/1 mL (50 mg/mL)		150 days
09/14/2021	2 1 1 1 1	Fingertip (L) Fingertip (R) Fingertip (R) Surface Fingertip (R)	8.4% Sodium Bicarbonate Injection, USP 4.2 g/50 mL (1 mEq/mL)		365 days

On the same date that lot #(b) (4) was made, *Penicillium guizhouanum* was identified in a personnel monitoring sample and a surface sample during a media fill performed in another filling suite (Media Fill #(b) (4)). No investigation was performed for the media fill excursion and the disposition was "pass".

b) Microbiology lab excursions for excess events using rapid sterility methods are not thoroughly investigated before invalidating results and concluding no microbial contamination. Since 11/19/2019, there have been 28 excursions involving excess events for rapid sterility testing. Your firm's procedure '(b) (4) allows for (b) (4) when (b) (4) . Your firm has not established through a scientific study or other challenge the ability to detect microbes during excess

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events using the '(b) (4) " with (b) (4) . While lab error investigations are conducted, there is no assurance that test membranes with excess events are free from microbes. For some excess event investigations, no root cause could be definitively assigned. However, resampling and retesting was performed in accordance with your firm's procedure SOP-SC-MB-6204. (b) (4) event investigations with no assignable lab error include but are not limited to the following:

Excursion Report #	Product/lot	Date of QA Release
SC.ER.MB.21.109	Ketamine HCl Inj / (b) (4)	09/20/2021
SC.ER.MB.21.058	Ropivacaine HCl Inj / (b) (4)	05/06/2021
SC.ER.MB.21.075 (stability)	Phenylephrine HCl Inj / (b) (4)	06/05/2020
SC.ER.MB.21.078	0.9% buffered Lidocaine HCl Inj / (b) (4)	06/10/2021
SC.ER.MB.21.079	Labetalol HCl Inj / (b) (4)	06/17/021
SC.ER.MB.21.088	Norepinephrine Bitartrate Inj / (b) (4)	07/09/2021

c) Your firm had a stability failure at the end of shelf life timepoint for lot #(b) (4) of Oxytocin 30 units/500mL (0.06 units/mL), USP in (b) NaCl Injection. The specification for assay is (b) (4) . Your firm had a failing result of (b) (4) . At the time of the failure your firm decided not to investigate the failure because the testing occurred 10 days past the Beyond Use Date (BUD)/expiration date of 90 days for the product. The BUD for lot #(b) (4) was 11/01/2021 and the 90-day pull date for the sample was 11/09/2021 with assay testing on 11/11/21. Your firm created an addendum to the investigation (PR(b) (4)) on 4/13/2022 stating that the "Oxytocin Assay trending for (b) (4) Room Temperature was reviewed and determined that the impacted lot would remain within specification

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through its labeled Beyond Use Date (BUD) of 11/01/2021". The last passing test result for assay was at the 60-day timepoint conducted on 10/11/2021 ((b) (4)), which is 69 days past manufacturing.

OBSERVATION 2

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

a) Your firm has no documentation for the justification of action levels for personnel and environmental monitoring. Per your firm's written procedure SOP-SC-MB-4511 Environmental and Personnel Monitoring, version 25 implemented 1/17/2022, action levels for environmental monitoring in ISO 5 areas are (b) (4) for viable air and (b) (4) for viable surface. Action levels for personnel monitoring are (b) (4) for fingertips of sterile gloves and (b) (4) for forearm of sterile sleeves. Your firm does not perform investigations into the majority of excursions for recoveries that are below these action levels with a few exceptions such as when an objectionable organism is identified.

b) Your firm performed a desiccation study for (b) (4) plates used for viable air sampling in the (b) (4) to establish the maximum time the plates can remain in the active air sampler. There was no written and approved protocol and no requirement to demonstrate that the plates would support microbial growth for time limit of (b) (4) as was determined by the study. The plates were (b) (4) with challenge organisms to demonstrate that the plates will support viable microbial growth after (b) (4).

OBSERVATION 3

Test procedures relative to appropriate laboratory testing for sterility are not written and followed.

Specifically, your firm's procedure '(b) (4))

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allows for (b) (4) .
Your firm has not established through a scientific study or other challenge, the ability to detect microbes during excess events using the "(b) (4) " with (b) (4) .

OBSERVATION 4

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

Specifically,

a) Your firm has not performed a media fill simulating all most stressful/challenging conditions. For example, your firm did not perform a media fill simulating the filling of drug products simultaneously in (b) different ISO 5 laminar flow hoods (LFH) within the same ISO7 filling suite.

b) We observed the (b) media fill read conducted on 03/30/2022 for media fill lot (b) (4) in 20mL syringes. The personnel looking at the media filled syringes were inconsistent with their process of reading them. We observed one inspector to initially stand during the reading holding the vial above the light source and then later sit. We also observed both primary inspectors to sometimes shake or invert quickly the syringe before initially looking at the syringe which may make it difficult to detect slight or low levels of contamination.

OBSERVATION 5

All records of production and control associated with a batch of drug product were not maintained at (b) (4) after the expiration date.

Specifically, surveillance video is used by your firm for investigation of production discrepancies including but not limited to environmental and personnel monitoring excursions. Video recordings of gowning and production activities are described and referenced in written investigation reports and have been used to establish root

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cause. However, these video recordings are not maintained by your firm. Examples include but are not limited to the following:

Excursion Report #	Reason For Excursion	Product/lot	Date of QA Release
SC.ER.MB.20.207	TNTC - (b) (4) Plate (ISO 5)	Phenylephrine HCL / Lot (b) (4)	11/18/2020
SC.ER.MB.21.035	7 CFUs, viable air (ISO 5)	del Nido Cardioplegia / (b) (4)	03/10/2021
SC.ER.MB.21.060	TNTC Sleeves of Sterile Filling Technician (ISO 5)	Succinylcholine Chloride Injection / (b) (4)	05/18/2021
SC.ER.MB.21.141	8 CFUs, Sleeves of filling technician (ISO 5)	(b) (4)	10/16/2021
SC.ER.MB.22.020	(b) (4) non-viable air (ISO 5)	Morphine Sulfate Injection / (b) (4)	02/23/2022

OBSERVATION 6

Laboratory records are deficient in that they do not include the initials and signature of the (b) (4) person reviewing the record for accuracy.

Specifically, (b) (4) person verification is not performed for sterility testing of drug products using (b) (4) methods. On 03/30/22, the analysis of Ketamine HCL 1 mg/mL lot (b) (4), Dexmedetomidine HCl 4mcg/mL lot (b) (4), Labetalol Hydrochloride 5mg/mL lot (b) (4), and (b) (4) was observed. There was no (b) (4) person verification via microscopic examination for (b) sessions identified as (b) (4) and (b) (4) for Ketamine lot (b) (4). The events were all determined by (b) analyst with initials (b) to be particles and the events were not verified by a (b) (4) analyst via microscope. Additionally, your firm's procedure '(b) (4)) does not require (b) (4) person verification of (b) (4) with events.

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OBSERVATION 7

Your outsourcing facility compounds drug products using bulk drug substances that cannot be used in compounding under section 503B because they (a) are not used to compound drug products that appear on the drug shortage list in effect under section 506E of the Act and (b) do not appear on a list developed by FDA of bulk drug substances for which there is a clinical need. Specifically, your firm compounds glycopyrrolate.

*DATES OF INSPECTION

3/28/2022(Mon), 3/29/2022(Tue), 3/30/2022(Wed), 3/31/2022(Thu), 4/01/2022(Fri), 4/04/2022(Mon), 4/05/2022(Tue), 4/06/2022(Wed), 4/07/2022(Thu), 4/08/2022(Fri), 4/11/2022(Mon), 4/12/2022(Tue), 4/13/2022(Wed), 4/15/2022(Fri), 4/18/2022(Mon), 4/20/2022(Wed)

X Demario L Walls
CSO
Signed By: Demario L. Walls -S3
Date Signed: 04-20-2022 12:39:46

X Saundrea A Munroe
CSO
Signed By: Saundrea A. Munroe -S
Date Signed: 04-20-2022 12:41:18

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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."