DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
New Jersey District Office 10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 Ph: (973)331-4900 Fax: (973)331-4969 ORAPHARM1_RESPONSES@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	08/16/2022-10/14/2022* FEI NUMBER 3013931875

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Michael Rutkowski, General Manager Manufacturing Operations	
TO: FIRM NAME QuVa Pharma, Inc.	STREET ADDRESS 519 State Route 173
CITY, STATE, ZIP CODE, COUNTRY Bloomsbury, NJ 08804-4047	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 WE OBSERVED:

OBSERVATION 1

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

A) No documented review was performed when mold was recovered on an operator (b) (4) plate sample taken on 06/29/2022 after ISO 5 operations in Clean Room (b) (4) and the clean room experienced elevated temperature and relative humidity excursions beyond the set alarm points. This mold recovery on 06/29 was the third mold recovery on (b) (4) plates in three (3) months. In addition, a documented risk assessment was not performed on products produced after the mold recoveries in the same cleanrooms or ISO 5 hoods. Mold was recovered on operators (b) (4) after ISO 5 operations (listed below) and the product was released and/or the bulk material was used to produce Compounded Sterile Product (CSP) which were released between 05/26/2022 - 07/26/2022.

Product (Bulk /CSP)	Bulk Lot# (Expiration Date)	Date Compounded	Mold Identification on one (1) Hand (Colony Forming Units (CFU#))	CSP Lot# (Expiration Date)
Fentanyl Citrate, PF, 10 mcg/mL in NS 3 L Bulk Bag (Bulk)	Lot# (b) (4) (05/12/2022)	04/15/2022	*Rhizopus oryzae* (1)	N/A
Ketamine HCl 20 mg (10 mg/ml), 2ml in 0.9% Sodium Chloride solution in a 3ml Syringe (CSP)	N/A	05/12/2022	*Aspergillus tonophilus* (1)	Lot# (b) (4) (08/10/22)
Amiodarone HCl 1.8mg/mL in Dextrose 5% in (b) (4), 3L, Bulk Bag (Bulk)	Lot# (b) (4) (07/20/2022)	06/29/2022	*Arthrinium arundinis/sacchari* (1)	Lot# (b) (4) (08/27/22)

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		Janet A. Rajan, Investigator Annet R. Rajan, Investigator Helen Verdel, Investigator	10/14/2022

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B) Your firm's Deviation Investigation, DEV-01639, Dated: 02/22/2022, initiated due to microbial recovery on personnel monitoring plates (2 CFUs on (b) (4) , Action level (b) (4) on one (b) (4) or (b) (4) on each (b) (4)) after compounding Oxytocin 20 units added to (b) (4) 0.9% Sodium Chloride IV bag, Compound Date: 02/14/2022, Lot # (b) (4) , Expiration Date: 05/15/2022, in ISO 5 LAF (Equipment ID: NJ-LAF(b) (4)) in Cleanroom (b) (4) is inadequate. One of the two microbial recoveries were identified as *Peribacillus simplex/Brevibacterium (Peribacillus) frigoritolerans,* a spore forming bacteria, and the second microbial recovery was unable to be identified due to DNA degradation. Your firm did not evaluate the room environmental conditions, such as temperature and humidity, as part of the investigation. Additionally, no second person verification of (b) (4) colony counts is conducted and no other information, such as the morphology and/or Gram stain, about the second isolated CFU is available; your firm deemed the lot of Oxytocin eligible for release and distributed this product over the period of 03/25/2022 – 03/29/2022.

C) The environmental monitoring data for temperature and relative humidity (RH), that is captured by the (b) (4) for ISO 7 Cleanrooms in Building (b) (4) , are not reviewed and recordings exceeding alarm points are not investigated. Temperature readings exceeding the "High" and RH readings exceeding the "High High" alarm points were observed in cleanrooms in Building (b) (4) on 06/27/2022, 06/29/2022 and 07/21/2022 (listed in table below); no incident reports were initiated for these high temperature and humidity readings.

		Approximate (b) (4) Recording (Temperature: High Alarm Point: (b) (4), High High Alarm Point: (b) (4) (Humidity: High Alarm Point (b) (4) High High Alarm Point: (b) (4))	
Date	Room# (Clean Room (CR-#))	Temperature (°C)	Humidity (%)
06/27/2022	(b) (4)	20	78
06/29/2022		22	78
07/21/2022		22	78
06/27/2022		21	78
06/29/2022		23	78
07/21/2022		22.8	78
06/27/2022		21	79

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06/29/2022		(b) (4)	23.5	78
07/21/2022			22.8	79
06/27/2022			21.2	80
06/29/2022			23.8	76
07/21/2022			22.6	79
06/27/2022			20.8	80
06/29/2022			23.2	79
07/21/2022			22.8	79
06/27/2022			21.2	77
06/29/2022			23.4	77
07/21/2022			23	77

D) Your firm did not initiate an Incident Report (IR) when low pressure gauge readings in the ISO 5 hood and light brown stain on the HEPA filter of the ISO 5 hood were observed. On 06/16/2022, a Work Order ((b) (4)) was created for ISO 5 Hood (Equipment ID: NJ-LAF(b) (4)) due to "hood gauge reading is significantly low. Almost at 0". On 07/23/2022, (b) (4) was generated to address drug splashes in the ISO 5 Hood (Equipment ID: NJ-LAF-(b) (4)); during the maintenance a one (1) inch by half (1/2) inch "Light Brown Stain in the Center Section" of the HEPA filter was observed. No IRs were generated for either incident and no retrospective review of batches compounded using the same equipment was conducted.

OBSERVATION 2

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

Your firm's environmental and personnel monitoring program does not include sampling of all potential routes of microbial contamination. For example:

A) On 08/16/2022, during our observation of sterile filling of Epinephrine, Preservative Free (PF), 10mcg/ml in 10ml Dextrose 5% in (b) (4)(D5W) Syringe, Lot# (b) (4) , Expiration Date: 11/14/2022 within the ISO 5(b) (4)

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Laminar Air Flow (b) (4) syringe filling machine (Equipment ID: NJ- (b) (4)), located in Cleanroom (b) (4) (ISO 7), we observed the operator place their upper left side of the body (including head, chest, and sleeves) into the ISO 5 area within the syringe filler. However, only (b) (4) samples are collected at the completion of each production lot. We also witnessed the operator open the Zone (b) (4) and Zone (b) (4) doors (located behind the bulk product source bag) of the (b) (4) fill machine into the ISO 7 area; however, no surface samples are collected from the Zone (b) (4) or Zone (b) (4) doors.

B) On 08/18/2022, during our observation of the sterile filling of Fentanyl PF, 10 mcg/ml in 100 ml Normal Saline (NS) IVB, Lot# (b) (4) , Expiration Date: 11/16/2022, within the ISO 5 (b) (4) hood (Equipment ID: NJ-LAF-(b) (4)) located in Cleanroom (b) (4) (ISO 7), we observed the operator placing sleeves, chest, and forehead under the hood. However, only (b) (4) samples are collected at the completion of each production lot. Additionally, the (b) (4) plate is placed at the far-right or far-left corner of the (b) (4) and is not placed close to the area of operation most prone to contamination.

OBSERVATION 3

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,

Your firm's visual inspection procedure utilized during Inspection, Labeling and Packaging (ILP) of sterile products, are deficient for the following reasons:

A) The (b) (4) and defect (b) (4) that is used to train and qualify visual inspection operators and AQL visual inspectors do not include representative defects for "debris" and "excessive liquid between plunger ribs". For example, your firm categorizes "particulates" and "debris" as two different defects to identify during (b) (4) . The defect (b) (4) used to qualify operators for visual inspection includes seed material for particulates such as (b) (4) , (b) (4) , (b) (4) , (b) (4) and (b) (4) ; there are no seed materials or examples representative of debris in the defect (b) (4) or defect (b) (4) respectively. Debris was identified in (b) (4) of Ropivacaine HCl, Epinephrine, Clonidine HCl, Ketorolac Tromethamine (R.E.C.K) 50 ml in Sodium Chloride 50ml syringe, Lot# (b) (4) , Expiration Date: 11/02/2022 and in (b) (4) during inspection of Phenylephrine HCl 1 mg (100 mcg/ml) 10 ml in 0.9% Sodium Chloride solution 10ml

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syringe KCT, Lot# (b) (4), Expiration Date: 11/07/2022. Additionally, the Quality Assurance AQL Inspection Form "NJ- (b) (4) " used by AQL visual inspectors include the following minor defect to identify during AQL visual inspection: Excessive liquid between plunger ribs. However, (b) (4) and the defect(b) (4) does not include representative defects for "excessive liquid between plunger ribs". There is no assurance that all visual inspectors can accurately identify debris or excessive liquid between plunger ribs in syringes.

B) The ILP section of the Batch Production Record (BPR) for syringe products such as (b) (4) 50 ml in Sodium Chloride 50ml syringe (Lot# (b) (4), Expiration Date: 11/02/2022), Phenylephrine HCl 1 mg (100 mcg/ml) 10 ml in 0.9% Sodium Chloride solution 10ml syringe KCT (Lot# (b) (4), Expiration Date: 11/07/2022) and Lidocaine HCl PF 1%, 100 mg/10 mL, 10ml syringe (Lot# (b) (4), Expiration Date: 09/29/2022) does not include a section for operators to identify and record defects related to leaking syringes. Regarding actively leaking units, Work Instructions NJ-WI-PO-0020 "Identification and Definition of Defects in Products During Visual Inspection" Revision 2, Effective 10 Aug 2021 states, " (b) (4) ". According to management, leaking syringes are recorded in the "other" defects section; however, the batch record does not include a section for the description of "other" defects identified during (b) (4) .

OBSERVATION 4

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Specifically,

A) During review of user access rights for the(b) (4) (Equipment ID: (b) (4) (b) (4)), in Building(b) (4) which are used to test the (b) (4) of the (b) (4) used to sterilize in process bulk, it was observed that all operators access the software with the (b) (4) and share a common username and password. We also observed that the (b) (4) function for the results was enabled for the (b) (4) . Additionally, the(b) (4) equipment ID is not recorded in the Batch Production Records.

B) During review of user access rights on the (b) (4) Endotoxin Unit (Equipment ID: NJ-END-(b) (4)), which is used for finished product release endotoxin testing for all compounded sterile product, it was observed that all microbiologists who perform endotoxin testing have (b) (4) user privileges to

the (b) (4) where results generated from the (b) (4) Software are stored; the (b) (4) permission permits users to delete files and folders.

C) During walkthrough of the QC laboratory and review of data in the (b) (4) software, we observed that Senior Chemist (b) (6) who routinely conducts analytical testing of finished sterile products, and raw materials, had (b) (4) roles assigned and has final data review and approve privileges in (b) (4) enabled. Prior to (b) (6) role as a Senior Chemist, (b) (6) functioned as a Reviewer; however, Senior Chemist (b) (6) has not functioned in the capacity of a reviewer for approximately (b) (4).

OBSERVATION 5

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

A) Smoke studies conducted on 09/08-09/10/2021 in the ISO 5 (b) (4) syringe filler (Equipment ID: NJ(b) (4)-(b) (4)) and on 02/24/2022 in the ISO 5 LAF Hood (Equipment ID: NJ-LAF-(b) (4)) are inadequate. Specifically, during the smoke studies, the (b) (4) system was not turned on during dynamic study to demonstrate that the (b) (4) system does not alter or impede the unidirectionality of air from the HEPA filter to the ISO 5 area of the (b) (4) syringe filler or laminar air flow hoods where products are aseptically processed.

B) During observation of sterile production activities, the following deficiencies in aseptic behaviors and gowning were observed:

i. On 08/16/2022, during the sterile filling of Epinephrine, Preservative Free (PF), 10mcg/ml in 10ml Dextrose 5% in (b) (4) Syringe, Lot# (b) (4), within the ISO 5 (b) (4) Air Flow (b) (4) syringe filling machine (Equipment ID: NJ- (b) (4)), located in Cleanroom (b) (4) (ISO 7), we observed the operator's sterile gown was not zipped completely and was not buttoned at the collar while performing operations in the ISO 5 area. We also observed the operator place their upper left side of the body (including head, chest and sleeves) into the ISO 5 area within the syringe filler. Additionally, the operator did not clean the Zone (b) (4) and Zone (b) (4) doors of the syringe filling machine after opening the doors to the ISO 7 room to perform interventions and prior to closing the doors.

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ii. On 08/18/2022, during the sterile filling of Fentanyl PF, 10 mcg/ml in 100 ml Normal Saline (NS) IVB, Lot# (b) (4), within the ISO 5 (b) (4) LAF ((b) (4)) hood (Equipment ID: NJ-LAF (b) (4)) located in Cleanroom (b) (4) (ISO 7), we observed the operator placing sleeves, chest and forehead under the hood. Additionally, we observed the operator use one (1) sterile wipe to clean the ports on all (b) (4) bags placed in the ISO 5 hood; however, Section 3.2.30 of work instructions NJ-WI-PO-0021 "Batch Preparation and Dosing of IV Bags", Revision 16, Effective 28 Feb 2022, states to (b) (4). We also observed an operator's sterile gown was not zipped completely and was not buttoned at the collar while performing operations in the cleanroom.

***DATES OF INSPECTION**

08/16/2022 (Tue), 08/18/2022 (Thu), 08/22/2022 (Mon), 08/24/2022 (Wed), 08/26/2022 (Fri), 08/31/2022 (Wed), 09/01/2022 (Thu), 09/06/2022 (Tue), 09/07/2022 (Wed), 09/08/2022 (Thu), 10/05/2022 (Wed), 10/14/2022 (Fri) (12 Days).

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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."