DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973) 331-4900 Fax: (973) 331-4969 Industry Information: www.fda.gov/oc/industry	06/12/2015 - 07/13/2015* FEI NUMBER 2242985

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Walter T. Kelso, Center Manager

FIRM NAME	STREET ADDRESS
PharMEDium Services, LLC	43 Distribution Blvd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Edison, NJ 08817-6005	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

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

Specifically, investigations into environmental monitoring excursions and nonconformance investigations do not include all details relating to the occurrence, does not require the documentation of the affected product name and lot number on the forms, do not include all activities of the investigation, do not include supporting documentation for training that was reported to have occurred, assessment of impact to drug product, and corrective/preventative actions. For example:

a. There were 2 personnel fingertip plates collected [redacted] (b) (4) during compounding that exceeded the alert limit in September and October of 2014. The microorganisms from these plates were identified as *Bacilus gibsonii* and *Bacilus sonorensis*, both spore forming microorganisms. During the retest of one of the operators, their gowning plates also exceeded the alert limits. The Microbiological Action Reports for these occurrences do not include details of what had occurred, does not include the identification of the microorganism observed on the retest plate, does not include training performed, or assessed if there is any product impact since the operators were processing at the time of testing. In addition, Procedure CPS-301, Facility Cleaning, does not include a surface contact time when using [redacted] (b) (4) as a sporicide for an environmental monitoring excursion or during the [redacted] (b) (4) cleaning rotation.

b. A nonconformance investigation was not issued for the invalidation of sterility testing results by the contract testing laboratory for the following products:
   i. Vancomycin HCL 1.25 g, Lot 15086004E, expiration date 04/26/15
   ii. Vancomycin HCL 1.5 g, Lot 15099004E, expiration date 05/09/15
   iii. Cefazolin 2 g, Lot 15096046E, expiration 05/06/15
   iv. Cefazolin 2 g, Lot 15111030E, expiration 05/21/15

OBSERVATION 2

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

Specifically, in September of 2014, personnel engaged in sterile processing had excursions observed on the contact plates for gowning qualification. All personnel underwent a gowning re-qualification in [redacted] (b) (4). During September and November of 2014, personnel were allowed to continue to process sterile drug products despite not being qualified. In

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addition, 2 employees during this time period were reported with fingertip test plates collected during processing exceeding the alert limit and were identifed as spore forming microorganisms. Another 3 employees were not documented to have passed the gowning re-qualification in (b) (4) and were not re-qualified until (b) (4)

OBSERVATION 3

The control systems necessary to prevent contamination or mix-ups are deficient.

Specifically, there are no investigations or thoroughly documented events for alarms triggered within (b) (4), the building monitoring system.

a. On 10/06/14, an alarm was activated for low pressure between the clean room (ISO 6) door and the pass through (ISO 8). There is no investigation into the alarm or corrective actions to ensure the ISO 6 clean room was not compromised. In addition there is no procedure for the corrective actions when the pressure differentials are out of specification.
b. On 03/07/15, multiple alarms were activated for "Total power loss" and for the generator. There were 5 total power loss alarms and 3 generator alarms. There is no investigation, no description of what occurred, no root cause analysis, no assessment of potential product impact, or the corrective actions. In addition, the data recorded by the system for this day was not thoroughly reviewed; for example the lowest temperature for Walk in Refrigerator (b) was recorded at -204.88°F and its highest was 44.85°F.
c. On 01/31/15, an alarm was activated for low relative humidity within the ISO 6 clean room. There is no investigation, no description of what occurred, or an assessment of potential product impact.
d. On 02/20/15, an alarm was activated for low temperature within the ISO 6 clean room which extended into 02/21/15. The temperature of the ISO 6 clean room was recorded at its lowest at 27.71°F. There is no investigation, no description of what occurred, no root cause analysis, or the corrective/preventative actions.
e. The walk-in refrigerator (b) used to store raw materials had two alarms for low temperature on 12/18/14 and 02/04/15. The recording from the chart recorder was used to assess product impact but there is investigation into the cause of the excursion by the electronic system.
f. From 03/25/15 through 05/05/15, there were 5 alarms for low temperature of Incubator (b) (Set Range: (b) (4)). The temperatures were recorded as low as -0.02°F. The recording from the chart recorder was used to assess product impact but there is no investigation into the cause of the excursion by the electronic system.

OBSERVATION 4

The flow of components, drug product containers, closures, in-process materials, and drug products though the building is not designed to prevent contamination.

Specifically,

a. The wheels of the Batch Cart used to contain and transport all the materials needed for a batch is not sanitized before being transferred into the ISO 6 clean room. The Batch cart is loaded with all the needed materials within the unclassified Staging Room. The Batch Cart is transferred from the unclassifed Staging Room to the unclassified Prep Room. In the Prep Room, the materials for the batch are verified by a Pharmacist before it is placed within the

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ISO 8 Pass In. There is no sanitization of the wheels or cart in the ISO 8 Pass In before being taken into the ISO 6 clean room.

b. All materials such as drug product, pooling supplies, IV bags, etc. are not sanitized before being placed into the ISO 5 laminar flow hood.
c. Particulate shedding and contamination sources such as paper batch records in folders, pens, and hardboard clipboards are used within the ISO 6 clean room. The folders with the batch records are stored and transported on the Batch Cart throughout the process.

OBSERVATION 5

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

Specifically, the environmental monitoring program performed in the ISO 5 laminar flow hoods and ISO 6 clean room is inadequate. For example,

a. The personnel working within the ISO 5 laminar flow hood are monitored (b) (4) and not on a daily basis or after every batch of drug product produced.
b. The ISO 5 laminar flow hoods are not monitored for viable air or surface samples on a daily basis during operating conditions.
c. Environmental monitoring of surfaces in the ISO 6 clean room adjacent to the ISO 5 laminar flow hoods such as doors, walls, and supply carts are only performed on a (b) (4) basis. Procedure CPS-707, Microbiological and Environmental Testing require this (b) (4) monitoring to be performed for the evaluation of the cleaning and sanitizing process. Environmental monitoring of these surfaces are not being performed to evaluate daily operating activities.
d. The (b) (4) monitoring of floor surface samples does not include the documentation of specific locations. In addition, Procedure CPS-707, Microbiological and Environmental Testing does not include a schematic of the clean room illustrating specific sampling locations to ensure that the floor samples collected are of areas that are the most used.
e. The non-viable air monitoring within the ISO 5 and ISO 6 areas are not performed under operating conditions.
f. The environmental monitoring program for the (b) (4) and (b) (4) routine testing of the floors within the ISO 6 and ISO 8 areas do not evaluate the areas during operating conditions. Procedure, CPS-707, Microbiological and Environmental Testing, requires the (b) (4) and (b) (4) surface sampling of the floors to be performed after cleaning to evaluate the cleaning and sanitizing process.
g. The personnel gowning qualification requires the employees to spray their gloved hands with (b) (4) (b) (4) before collecting the surface samples of their gloves. This sampling does not demonstrate whether each employee is proficient in donning sterile gloves.

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OBSERVATION 6

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically, there is no training program to assure the Pharmacy Technicians and Pharmacists inspecting finished drug product are trained to detect particulate matter in the IV bags and syringes.

OBSERVATION 7

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically, sterility testing is not performed for each batch of finished drug product produced. Sterility testing is only performed on [redacted] batches from each of the [redacted] (b) (4) [redacted], not of the [redacted] drug products. Sterility samples are sent for testing or placed on test [redacted] (b) (4) [redacted].

OBSERVATION 8

Clothing of personnel engaged in the manufacturing, processing, packing, and holding of drug products is not appropriate for the duties they perform.

Specifically,on 06/12/15, a Pharmacy Technican was observed donning sterile gloves in a manner that compromises sterility. The employee used their sterile gloved hand to touch the inner cuff of the glove as they were applying it. The observed practice was not preformed as described and illustrated in procedure, CPS-305, Personnel Gowning and Asetic Technique and Controls.

OBSERVATION 9

The batch production and control records are deficient in that they do not include specimen and copy of labeling.

Specifically, batch production records do not include the shipper label and intermediate labels which contains pertinent product information, such as adverse event reporting contact information, not included on the product label.

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OBSERVATION 10

The labels and containers of your outsourcing facility's drug products do not include information required by section 503B(a)(10)(A) and (B).

Specifically,

The following information is not found on some of your drug product labels, as required by 503B(a)(10)(A):

1. The date that the drug was compounded.
2. The inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

The following information is not found on the container labels for products you produce, as described in 503B(a)(10)(B).

1. Information to facilitate adverse event reporting: ---www.fda.gov/medwatch and 1800FDA1088 <http://www.fda.gov/medwatch and 1800FDA1088>.

Examples of drug product labels that do not contain this information include:

- Magnesium Sulfate 2 g in 50 mL 5% Dextrose Injection USP
- Vancomycin HCl 1.25g in 250 mL 0.9% Sodium Chloride Injection USP
- Diltiazem 250mg in 250 mL 5% Dextrose Injection USP
- niCARdipine 125 mg in 250 mL 0.9% Sodium Chloride Injection USP
- OxyTOCIN 20 units in 1000 mL Lactated Ringer's Injection USP
- Potassium CHLORide 20 mEq and Lidocaine HCl 10 mg added to 5% Dextrose 100 mL
- Vasopressin 100 units added to 100 mL 0.9% Sodium Chloride Injection USP
- Vasopressin 60 units added to 100 mL 5% Dextrose Injection USP
- Calcium GLUCOnate 1g in 0.9% Sodium Chloride Injection USP
- Potassium CHLORide 40 mEq added to 0.9% Sodium Chloride 500 mL

For purposes of 503B(a)(10)(B) container labeling, the clear plastic bag (e.g., [redacted] *(b) (4)* Overwrap) enclosing some of your products should be considered the "container" for purposes of this requirement and bear the information required by 503B(a)(10)(B).

*** DATES OF INSPECTION:**
06/12/2015(Fri), 06/16/2015(Tue), 06/17/2015(Wed), 06/18/2015(Thu), 06/19/2015(Fri), 06/23/2015(Tue), 06/26/2015(Fri), 06/29/2015(Mon), 07/13/2015(Mon)

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