

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

<small>DISTRICT ADDRESS AND PHONE NUMBER</small> 404 BNA Dr., Bldg. 200, Ste. 500 Nashville, TN 37217-2597 (615) 366-7801 Fax: (615) 366-7802 Industry Information: www.fda.gov/oc/industry	<small>DATE(S) OF INSPECTION</small> 02/20/2013 - 02/22/2013
	<small>FEI NUMBER</small> 3004153061

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Timothy P. Rinks, General Manager

<small>FIRM NAME</small> PharMEDium Services, LLC.	<small>STREET ADDRESS</small> 913 N Davis Ave
<small>CITY, STATE, ZIP CODE, COUNTRY</small> Cleveland, MS 38732-2106	<small>TYPE ESTABLISHMENT INSPECTED</small> Producer of 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

The production area air supply lacks an appropriate air filtration system.

Specifically, there is no documentation for;

- a) the air flow studies (smoke studies) performed on the horizontal laminar flow hoods (HLAF) or in the clean room where sterile injectable drug products are processed,
- b) the performance of processing activities in the HLAF, either routine or non-routine, taking place during the dynamic smoke studies,
- c) the raw data for the HEPA filter integrity testing for these hoods and clean room.

OBSERVATION 2

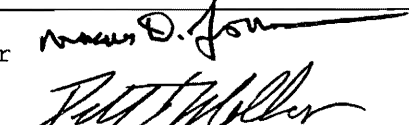
Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically, failure to perform endotoxin testing on all finished sterile injectable drug products.

OBSERVATION 3

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

Specifically, media fills are performed by the firm for equipment/process validation and employee qualification/monitoring validation. The media fills performed do not represent the continuous processes of pooling, subassembly, finished container filling, and packaging. Each media fill is performed only on one processing stage at a time and does not simulate the entire processing from the start of processing to finished packaging. Each process stage is tested separately for microbiological growth.

SEE REVERSE OF THIS PAGE	<small>EMPLOYEE(S) SIGNATURE</small> Marvin D. Jones, Investigator Dell S. Moller, Investigator	<small>DATE ISSUED</small> 02/22/2013
		

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Also, (b) (4) is used to simulate the drug product instead of microbiological growth media.

OBSERVATION 4

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.

Specifically, failure to perform finished product potency and sterility testing on each lot of finished sterile injectable drug product processed/distributed. Testing is only performed on a random basis per product family.

OBSERVATION 5

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

Specifically, there is no sterile filtration performed during the aseptic processing of sterile injectable drug products.

OBSERVATION 6

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

Specifically, on 2/20/13 we noted a rust colored build up of material behind the HEPA filter screen near the screen retaining bolts of hood #13.

OBSERVATION 7

Equipment used in the manufacture, processing, packing or holding of drug products is not suitably located to facilitate operations for its intended use.

Specifically, on 2/20/13 we observed equipment and various items blocking or partially blocking the return airflow vents for the ISO 7 clean room which contains the firm's ISO 5 hoods. Items blocking these vents included trash cans, sharps containers, and metering pumps.

SEE REVERSE OF THIS PAGE	<small>EMPLOYEE(S) SIGNATURE</small> Marvin D. Jones, Investigator <i>MDS</i> Dell S. Moller, Investigator <i>DSM</i>	<small>DATE ISSUED</small> 02/22/2013
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STREET ADDRESS

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CITY, STATE, ZIP CODE, COUNTRY

Cleveland, MS 38732-2106

TYPE ESTABLISHMENT INSPECTED

Producer of Sterile Drug Products

OBSERVATION 8

Buildings used in the processing of a drug product are not maintained in a good state of repair.

Specifically, on 2/20/13 we observed various holes, approximately 1/4 inch in diameter, in the wall near laminar airflow hoods 6 and 3 where aseptic processing occurs. We also observed an off white colored residue on this same wall, where an air return flow vent for the firm's clean room HEPA air filtration system was located.

OBSERVATION 9

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

a) failure to utilize positive and negative controls or conduct growth promotion testing for the microbiological growth media used in the (b) (4) monitoring of laminar airflow hoods, personnel glove monitoring, environmental monitoring, and media fills.

b) the procedure CPS-707, "MICROBIOLOGICAL AND ENVIRONMENTAL TESTING", implemented 9/18/12, does not include specific sampling locations for the (b) (4) sampling of microbiological environmental hood surfaces and hood air samples.

OBSERVATION 10

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

Specifically, several of the firm's finished drug products contain active drug ingredients that the manufacturer's label declares to protect from light. These finished drug products processed by this firm are placed into clear plastic containers. The firm has no testing/stability data to support that these containers provide protection from light and do not allow degradation of the finished drug product.

OBSERVATION 11

The written stability program for drug products does not include meaningful and specific test methods.

Specifically, the stability test methods used to assign expiration dating of finished sterile injectable drug products are not

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Marvin D. Jones, Investigator
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stability indicating. The firm's stability testing procedures do not include sterility, impurity, or degraded product testing. For example the firm assigns a 90 day expiration date for the sterile injectable drug product, Morphine Sulfate 1mg/ml in 0.9% Sodium Chloride packaged in a Monoject Barrel syringe.

OBSERVATION 12

Containers and closures are not tested for conformance with all appropriate written procedures. Specifically, the firm does not conduct any sampling/testing upon receipt of sterile finished injectable drug product containers or closures, they are approved/released without any testing.

OBSERVATION 13

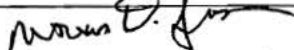
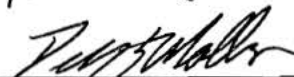
Written production and process control procedures are not followed in the execution of production and process control functions.

For example on 2/20/13, we observed;

- a) the firm's failure to follow procedure CPS-305, "PERSONNEL GOWNING AND ASEPTIC TECHNIQUE AND CONTROLS", implemented 12/6/12; in regards to;
- 1) multiple personnel leaning inside of the front edge of the laminar airflow hoods during the processing of sterile injectable drug products,
 - 2) equipment not being used, such as the (b) (4) located inside the laminar airflow hood during the processing of sterile injectable drug products,

Also, we noted an employee dragging a full trash bag across the clean room floor with laminar air flow hoods located on each side where aseptic processing activities occurring.

- b) the firm's failure to follow procedure CPS-748, "OPERATION OF THE (b) (4)", implemented 1/2/2009, in regards to environmental air monitoring of the laminar airflow hood, in which the (b) (4) device placed directly in front of the HEPA screens, which appeared to be, approximately 3 inches, instead of the (b) (4) required by this procedure.

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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 judgement, 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."