

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

DISTRICT ADDRESS AND PHONE NUMBER 404 BNA Dr., Bldg. 200, Ste. 500 Nashville, TN 37217-2597 (615) 366-7801 Fax: (615) 366-7802 Industry Information: <a href="http://www.fda.gov/oc/industry">www.fda.gov/oc/industry</a>	DATE(S) OF INSPECTION 03/18/2013 - 03/22/2013
	FET NUMBER 3007045542

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

FIRM NAME PharMEDium Services, LLC.	STREET ADDRESS 6100 Global Drive
CITY, STATE, ZIP CODE, COUNTRY Memphis, TN 38141-8385	TYPE ESTABLISHMENT INSPECTED Producer of Injectable 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**

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

For example, on 3/18/13 during the processing of injectable drug products, we observed;

a) failure to follow procedure CPS-305, "PERSONNEL GOWNING AND ASEPTIC TECHNIQUE AND CONTROLS", effective 3/13/13, in regards to;

- 1) multiple personnel with exposed facial areas leaning inside of the front edge of the LAFH during the processing of injectable drug products,
- 2) personnel examining uncapped syringes after filling less than the required (b) (4) inside the hood,
- 3) at least 8 LAFHs in which processing was occurring noted trash containers and/or sharps containers directly against the air intake for the LAFH
- 4) multiple personnel continually resting their hands on worksurfaces of the LAFH without re-sanitizing their hands,
- 5) personnel processing ampule product moving their hand in front of and over the previously opened ampules,

b) failure to follow procedure CPS-606, "SERVICE CODE CONTROLLED SUBSTANCE COMPOUNDING PROCESS", issued 3/13/13, in regards to properly sanitizing the (b) (4) unit before moving this unit into the LAFH. This employee lightly sprayed only the front of the unit with alcohol and did not wipe down all accessible areas of the unit as required by this procedure.

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**OBSERVATION 2**

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

Specifically,

- a) the airflow studies (smoke studies) performed on the firm's (b) (4) laminar airflow hoods (LAFH) and in the clean room where injectable drug products are processed are only documented by schematic drawings,
- b) there is no documentation of the processing activities in the LAFHs taking place during dynamic smoke studies,
- c) there is no documentation of the raw data for HEPA filter integrity testing for these hoods and clean room.

**OBSERVATION 3**

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

Specifically,

- a) there is no filtration step performed during the final filling operations of the finished product containers for sterile injectable drug products.
- b) there is no procedure to specifically require sanitizing packaging components prior to placing them in the LAFH. On 3/18/13, during the processing of injectable drug products, we observed;
  - 1) an employee sanitizing only the front and back of a stack of approximately 15-20 plastic IV bags prior to placing in the LAFH,
  - 2) an employee only lightly spraying with (b) (4) the top layer of empty PCA syringe packaging components (still in the manufacturer's packaging), and then turning over a small portion of them and again lightly spraying with (b) (4) before placing them in the LAFH.
- c) procedure CPS-305, "PERSONNEL GOWNING AND ASEPTIC TECHNIQUE AND CONTROLS", effective 3/13/13, does not have requirements for complete covering of the facial area. During this inspection, we noted several employees with their head inside LAFHs with exposed facial areas.

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Memphis, TN 38141-8385

TYPE ESTABLISHMENT INSPECTED

Producer of Injectable Drug Products

#### OBSERVATION 4

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

Specifically,

a) the upper and lower potency limits, established by the firm, for the injectable drug products are based on multiple criteria including a combination of: (b) (4)

variations are added to USP monograph specification (for example: +/-10% if applicable) to give a wider specification range than the active ingredient specification established by the drug product manufacturer. For example, Fentanyl Citrate 2mcg/mL, the firm specification is: (b) (4) mcg/mL and the U.S.P. specification is 90.0-110.0% (1.8mcg/mL-2.2mcg/mL) of label claim; and Hydromorphone 10mcg/mL, the firm specification is: (b) (4) mcg/mL and U.S.P. specification is 95.0-105.0% (9.5mcg/mL-10.5mcg/mL) of label claim. The firm has various limits established for each finished injectable drug product.

b) failure to utilize positive and negative controls or conduct growth promotion testing for the microbiological growth media used for daily, weekly, or monthly monitoring of LAFHs, personnel monitoring, environmental monitoring, and media fills,

c) the procedure CPS-707, "MICROBIOLOGICAL AND ENVIRONMENTAL TESTING", effective date 3/14/13, does not include specific sampling locations, including establishment of the worst case sampling sites, for routine environmental monitoring.

#### OBSERVATION 5

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

Specifically, the firm does not conduct endotoxin testing on any finished injectable drug products.

#### OBSERVATION 6

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 performed by the firm for equipment/process validation and employee qualification/monitoring do not represent the continuous process of pooling, subassembly, finished product 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

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finished packaging. Each process stage is tested separately for microbial growth.

### OBSERVATION 7

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/sterility testing on each lot of finished injectable drug product processed/distributed. Testing is only performed annually on a random basis per drug product family.

### OBSERVATION 8

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 injectable drug products are not stability indicating. The firm's stability testing procedures do not include sterility, impurity, or degradant product testing. For example,

- a) a review of the Final Report for Fentanyl Citrate, dated 12/4/07, noted the stability samples were not produced at this location and were only tested for visual inspection, assay, pH, and particle counts through (b) days. Also, only 1 drug product lot was tested. This product has 90 day expiration dating, assigned by the firm.
- b) a review of the Final Report for Propofol in the 20 mL syringe, dated 11/15/10, noted the stability samples were not produced at this location and were tested for visual inspection, pH, average globular size, assay, related compounds A and B through (b) days. Also, only 1 drug product lot was tested. This product has 30 day expiration dating, assigned by the firm. Furthermore, no nitrogen overlay blanket was used in this testing and no comparison testing with and without nitrogen was conducted. Per record review, this a highly oxidative product and should be processed and packaged under a nitrogen blanket.

### OBSERVATION 9

Certificates of testing of containers and closures are accepted in lieu of testing without establishing the reliability of the supplier's test results through appropriate validation of the test results at appropriate intervals.

Specifically, the firm does not conduct any sampling/testing upon receipt of finished injectable drug product containers or closures, they are approved/released without any testing. During a review of complaints for 2012 and 2013, we noted numerous complaints for leaking IV bags and cassettes.

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**OBSERVATION 10**

The quality control unit lacks authority to fully investigate errors that have occurred.

Specifically, for incubator temperature monitoring charts, there is no evidence to show temperature excursions have been detected,

- a) between May 8 and May 15, 2012 incubator # 2, used to incubate media fills, had a recorded temperature at or above 100 degrees F. This temperature exceeded the temperature limits set for this incubator of (b) degrees F,
- b) between August 9 and August 16, 2012 incubator # 2, used to incubate media fills, had a recorded temperature below 85 degrees F. This temperature exceeded the temperature limits set for this incubator of (b) degrees F,
- c) between May 1 and May 8, 2012 incubator # 3, used to incubate environmental monitoring media plates, did not record any temperatures.

These records were signed off as being reviewed and the quality unit failed to detect and perform corrective actions required in procedure CPS-712, "TEMPERATURE MONITORING", issue date 1/31/13.

**OBSERVATION 11**

There was a failure to handle and store components at all times in a manner to prevent contamination.

Specifically, on 3/18/13, we observed IV diluent bags containing 0.9% Sodium Chloride solution improperly stored, uncovered and unprotected in a gray tote in the unclassified warehouse area.

**OBSERVATION 12**

Reserve drug product samples are not retained and stored under conditions consistent with product labeling.

Specifically, the firm does not maintain reserve samples of finished injectable drug products.

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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."