

**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: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

07/06/2015 - 07/16/2015*

FEI NUMBER

3004153061

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Brenda L. Womak, Plant Manager

FIRM NAME

PharMEDium Services, LLC.

STREET ADDRESS

913 N. Davis Ave

CITY, STATE, ZIP CODE, COUNTRY

Cleveland, MS 38732-2106

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 I OBSERVED:

OBSERVATION 1

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically, you use non-sterile cleaning agents ((b) (4) (b) (4)) in the cleaning and sanitization of the ISO 7 room. One of the ingredients in the (b) (4) is not sterile and (b) (4) is not sterile. Your procedure, CPS-301 does not include contact times for cleaning.

You do not successfully control for spore-forming organisms. During our review of your environmental monitoring records since the beginning of 2015, you have had 48 action ((b) (4)) or alerts ((b) (4)) with 1 cfu to too numerous to count cfus with several different species identified for both personnel and ISO 5 monitoring. Species include, but not limited to, *Bacillus simplex*, *Bacillus circulans*, *Bacillus niabensis*, *Bacillus amyloliquefaciens* and *Bacillus cereus*.

In addition, as stated in CPS-306, you (b) (4) ((b) (4)) This (b) (4) is stored in the ISO 7 area during operations for that day. ((b) (4)) ((b) (4)) ((b) (4)) The wipes are used to clean the laminar flow hoods (ISO 5) for each technician throughout the day. During this inspection we observed wipes to be hanging out of the tote with the lid closed on them. This could allow for microbial introduction into the hood.

OBSERVATION 2

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

Specifically, you did not fully investigate when your met or exceeded an action or alert level for environmental monitoring. You continued to release products without determining the effect of the microorganism on finished products.

**SEE REVERSE
OF THIS PAGE**

EMPLOYEE(S) SIGNATURE

Claire M. Minden, Investigator

Claire M Minden

DATE ISSUED

07/16/2015

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

DISTRICT ADDRESS AND PHONE NUMBER		DATE(S) OF INSPECTION
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		07/06/2015 - 07/16/2015*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED		FEI NUMBER
TO: Brenda L. Womak, Plant Manager		3004153061
FIRM NAME	STREET ADDRESS	
PharMEDium Services, LLC.	913 N. Davis Ave	
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED	
Cleveland, MS 38732-2106	Outsourcing Facility	

OBSERVATION 3

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

Specifically, your environmental procedure does not require daily monitoring of employees. Employees' gloves are tested (b) (4) and gowns (b) (4).

****THIS IS A REPEAT OBSERVATION.****

OBSERVATION 4

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

Specifically, media fills do not simulate actual production, quantities and different drug product containers. You initially qualify your technicians by (b) (4). You did perform a media validation but this validation does not simulate the entire production. It simulates (b) (4).

We also observed personnel engaged in operations in the aseptic processing area on July 6 and 8, 2015 place their heads under the laminar flow hood (ISO 5), touch non-sanitized equipment or items with arms without changing gown or sanitizing arm then proceeded to continue aseptic operations and lean against the laminar flow hood which is contrary to your written procedure, CPS-305. We also observed an environmental technician contaminate the ISO 5 area when setting up environmental monitoring equipment by touching the surface of all of the laminar flow hoods after arms and elbows touched carts in the ISO 7 area without proper sanitization of arms and elbows.

****THIS IS A REPEAT OBSERVATION.****

OBSERVATION 5

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, you release all products without any laboratory analysis. You only perform (b) (4) verification. You do not wait for the analytical results of the partial testing you conduct per drug family to release product. Without analytical results, the complaints you received about lack of effectiveness could not be fully investigated.

****THIS IS A REPEAT OBSERVATION.****

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Claire M. Minden, Investigator <i>CMM</i>	07/16/2015

**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: www.fda.gov/oc/industry		DATE(S) OF INSPECTION 07/06/2015 - 07/16/2015*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Brenda L. Womak, Plant Manager		FEI NUMBER 3004153061
FIRM NAME PharMEDium Services, LLC.	STREET ADDRESS 913 N. Davis Ave	
CITY, STATE, ZIP CODE, COUNTRY Cleveland, MS 38732-2106	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility	

OBSERVATION 6

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

Specifically, you do not perform sterility and endotoxin testing on each lot of product prior to release and distribution. You only perform endotoxin testing (b) (4). In addition, you only perform sterility testing on (b) (4). You produce sterile injectable drug products including epidural and intrathecal injections and components labeled for IV use only.

THIS IS A REPEAT OBSERVATION.

OBSERVATION 7

Drug products do not bear an expiration date determined by appropriate stability data to assure they meet applicable standards of identity, strength, quality and purity at the time of use.

Specifically, your firm failed to ensure that its drug products bore an expiration date that was supported by appropriate stability testing. A review of the Stability Summary and Final Report for Succinylcholine Chloride only included results for (b) (4).

THIS IS A REPEAT OBSERVATION.

OBSERVATION 8

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, you have not validated your production process to demonstrate each batch of drug product meets the identity, strength, quality and purity it purports to be.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Claire M. Minden, Investigator	DATE ISSUED 07/16/2015
	<i>cm</i>	

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

DISTRICT ADDRESS AND PHONE NUMBER		DATE(S) OF INSPECTION
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		07/06/2015 - 07/16/2015*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED		FEI NUMBER
TO: Brenda L. Womak, Plant Manager		3004153061
FIRM NAME	STREET ADDRESS	
PharMEDium Services, LLC.	913 N. Davis Ave	
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED	
Cleveland, MS 38732-2106	Outsourcing Facility	

OBSERVATION 9

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 dosage form
2. Statement of quantity
3. The date that the drug was compounded.
4. 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:

- Methadone HCl 1 mg per mL in 0.9% Sodium Chloride
- Meperidine HCl 10 mg per mL (1000 mg per 100 mL) in Sodium Chloride 0.9%
- PHENYLEphrine 40 mcg per mL (0.4 mg per 10 mL) in 0.9% Sodium Chloride
- Lorazepam 1 mg per mL (50 mg per 50 mL) in a 250 mL Aviva Bag in Sodium Chloride 0.9%
- 1 mg/ml HYDROmorphone HCl in 0.9% Sodium Chloride (Total Dose 30 mg/30 mL)
- Cisatracurium Besylate 2 mg per mL (20 mg per 10 mL)
- ePHEDrine 5 mg per mL (25 mg per 5 mL)
- morphine sulfate 5 mg per mL (500 mg per 100 mL) in Sodium Chloride 0.9%
- Midazolam HCl 1 mg per mL (100 mg per 100 mL) in a 150 mL Intravia Bag in Sodium Chloride 0.9%
- 0.2% Ropivacaine HCl in 0.9% Sodium Chloride
- Bupivacaine HCl 0.1% in a 250 mL Yellow Cassette Res. Flowstop in Sodium Chloride 0.9%
- Succinylcholine 20 mg per mL (140 mg per 7 mL)
- Ketamine 10 mg per mL (50 mg per 5 mL) in 0.9% Sodium Chloride
- Fentanyl Citrate Injection 50 mcg per mL (250 mcg per 5 mL)
- Rocuronium Bromide 10 mg per mL (50 mg per 5 mL)
- Metoprolol Tartrate 1 mg per mL (5 mg per 5 mL)

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

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Claire M. Minden, Investigator <i>Cmm</i>	07/16/2015

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: www.fda.gov/oc/industry		DATE(S) OF INSPECTION 07/06/2015 - 07/16/2015*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Brenda L. Womak, Plant Manager		FEI NUMBER 3004153061
FIRM NAME PharMEDium Services, LLC.	STREET ADDRESS 913 N. Davis Ave	
CITY, STATE, ZIP CODE, COUNTRY Cleveland, MS 38732-2106	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility	

*** DATES OF INSPECTION:**
07/06/2015(Mon), 07/07/2015(Tue), 07/08/2015(Wed), 07/09/2015(Thu), 07/16/2015(Thu)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Claire M. Minden, Investigator <i>Claire M Minden</i>	DATE ISSUED 07/16/2015
-----------------------------	--	---------------------------