DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
550 W. Jackson Blvd., Suite 1500 Chicago, IL 60661-4716 (312)353-5863 Fax:(312)596-4187	11/17/2015-1/4/2016* FEI NUMBER 3005051736

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Jennifer M. Adams , President

FIRM NAME	STREET ADDRESS
Pharmedium Services, LLC	150 N Field Dr Ste 350
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Lake Forest, IL 60045-2506	Outsourcing Facility Headquarters

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

Drug product containers or closures are reactive so as to alter the safety, identity, strength, quality, and purity of the drug beyond the official or established requirements.

Specifically, your firm failed to identify that (b) (4) resulted in the container no longer meeting the characteristics evaluated during initial stability testing for each of your applicable finished drug products. As a result, your firm formulated finished drug products into container/closures (b) (4) and approved the release of multiple batches from different drug products that subsequently failed to meet potency and/or purity limits.

Your firm has since attributed the following out-of-limit potency results for released drug product lots tested between July, 2014 and July, 2015 to this issue:

- Lot # 14192051M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 7.78mcg/mL (limits (b) (4))
- Lot # 14192247M, 20mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 15.26mcg/mL (limits (b) (4))
- Lot # 14191205M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 6.50mcg/mL (limits (b) (4))
- Lot # 14197159M, 20mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 15.26mcg/mL (limits (b) (4))
- Lot # 14198075M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 5.87mcg/mL (limits (b) (4))
- Lot # 14197305M, 20mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe,

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tested for potency at 12.58mcg/mL (limits (b) (4))

- Lot # 14199188M, 25mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 19.09mcg/mL (limits (b) (4))
- Lot # 14231147M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 30mL BD Syringe, tested for potency at 7.18mcg/mL (limits (b) (4))
- Lot # 15002077M, 5mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 3mL BD Syringe, tested for potency at 3.04mcg/mL (limits (b) (4))
- Lot # 15002250M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 3mL BD Syringe, tested for potency at 4.38mcg/mL (limits (b) (4)
- Lot # 15041045M, Methadone HCl 1mg per 1mL in 3mL BD Syringe, tested for potency at .08mg/mL (limits (b) (4)
- Lot # 15098067M, Methadone 10mg per 1mL in 3mL BD Syringe, tested for potency at 8.3mcg/mL (limits (b) (4)
- Lot # 15138061M, Atropine Sulfate 0.4mg/mL per 2.5mL in 3mL BD Syringe, tested for potency at 0.34mg/mL (limits (b) (4))
- Lot # 15149004M, 10mcg/mL Fentanyl Citrate in 0.9% Sodium Chloride in 3mL BD Syringe, tested for potency at 1.1mcg/mL (limits (b) (4))
- Lot # 1515107008C, Methadone HCl 10mg per 1mL in 3mL BD Syringe, tested for potency at 8.2mg/mL (limits (b) (4)

OBSERVATION 2

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, your firm has not established a procedure for release testing of finished drug products that ensures each batch conforms at a minimum to limits for potency for each active ingredient before the batch is approved and released by your quality unit.

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For example, your firm's Memphis, TN Center formulated a total of (b) (4) batches of Fentanyl Citrate drug products between August 20, 2014 and July 13, 2015. In accordance with your current monitoring procedure for Potency and Purity, your firm tested only (b) (4) out of (b) (4) batches.

OBSERVATION 3

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

Specifically, your firm has not implemented a procedure requiring for every batch of finished drug product purporting to be sterile that Sterility testing be performed, or initiated if applicable, prior to the release. Also, your firm has not implemented a procedure requiring that each batch of finished drug product purporting to be non-pyrogenic is tested to show conformance to bacterial endotoxin limits prior to release.

- Document number CPS-775, "On-Going Sterility Monitoring Program," effective AUG 04 2015, Version 10.0, section 5.2, establishes a sampling program for Sterility Monitoring that allows for a (b) (4) number of batches to be tested based on a (b) (4) It does not require Sterility testing for each individual batch.
- Bacterial endotoxin testing is not performed for any finished drug product batches.

OBSERVATION 4

Results of stability testing are not used in determining expiration dates .

Specifically, stability test results documenting a failure to meet product potency limits within the labeled product expiry date were not used to evaluate the appropriateness of current expiry dating for marketed drug products.

The following investigations of out-of-limit stability monitoring samples failed to include a documented evaluation of product expiry dating for all affected product lots represented in the study:

- HHE-15-017-R1 investigated the impact of a stability failure for 50mcg/mL Remifentanil in 0.9% Sodium Chloride 2mL in 3mL BD syringe, lot number 15132004C. The action limits at expiry were (b) (4) ; and your firm obtained results for the three samples tested of 0.9mcg/mL, 0.29mcg/mL, and 0.4mcg/mL. The report concluded that (b) (4) and the lot in question had expired on 6/8/2015.
- HHE-15-020 investigated the impact of a stability failure for 50mcg/mL Fentanyl Citrate Injection 100mL in 100mL Smiths Medical Cassette, lot number 150740034C. The action limits at expiry were (b) (4) , and your firm obtained results for two of the samples tested of 43.1mcg/mL and 42.9mcg/mL. The report concluded that (b) (4) and the batch in question had expired on 5/8/2015.
- HHE-15-023 investigated the impact of a stability failure for Methadone 10mg/mL HCl Injection 1mL in 3mL BD syringe, lot number 1515107008C. The limits at expiry were (b) (4) ; and your firm obtained results for the three samples tested of 8.3mg/mL, 8.2mg/mL, and 8.2mg/mL. The root cause was determined to be (b) (4) ; however, your firm did not evaluate the impact of a lack of stability data in support of those lots remaining in the field that were not involved in the recall of products (b) (4)

OBSERVATION 5

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

Specifically, your firm has not established your own specifications for all incoming materials used in the formulation of finished drug products. Incoming materials include all approved finished human drug products, all critical product-contact components used in the compounding of sterile drug products, and all container-closure systems into which the compounded drug products are packaged.

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Your firm has also not documented specifications for each of your formulated drug products purporting to be sterile to include at a minimum the identity and strength of each active ingredient, a limit for visible particles, sterility, and a limit for bacterial endotoxins.

OBSERVATION 6

Investigations of an unexplained discrepancy and a failure of a batch or any of its components to meet any of its specifications did not extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy .

Specifically, your firm's historical trend reviews and impact evaluations documented for each investigation are deficient.

- Your firm's complaint handling procedure, document CPS-009, Version 8.0, effective SEP 25 2015, "Incident / Complaint Handling Procedure," requires (b) (4) and does not extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy.
- Forty-four (44) Health Hazard Evaluations (HHE) were performed by your firm between January 12, 2015 and November 25, 2015 to investigate confirmed out-of-limit test results, out-of-limit stability results, container/closure defects, product quality defects, and labeling discrepancies for released product batches. Your firm's HHEs which result in field corrections to remove or destroy affected product do not adequately evaluate other batches of the same drug product and other drug products that may have been associated with the probable root cause conclusion of such investigations. Your firm's (b) (4)

*DATES OF INSPECTION

11/17/2015(Tue),11/18/2015(Wed),11/19/2015(Thu),11/20/2015(Fri),11/23/2015(Mon),11/24/2015(Tue),11/30/2015(Mon),12/01/2015(Tue),12/02/2015(Wed),1/04/2016(Mon)

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