

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

DISTRICT ADDRESS AND PHONE NUMBER 550 W. Jackson Blvd., Suite 1500 Chicago, IL 60661-4716 (312) 353-5863 Fax: (312) 596-4187	DATE(S) OF INSPECTION 3/12/2018-4/11/2018*
	FEI NUMBER 3005051736

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Jennifer M. Adams, SVP & President Clinical Product Solutions

FIRM NAME Pharmedium Services, LLC	STREET ADDRESS 150 N Field Dr Ste 350
CITY, STATE, ZIP CODE, COUNTRY Lake Forest, IL 60045-2506	TYPE ESTABLISHMENT INSPECTED 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 WE OBSERVED:
OBSERVATION 1**

Procedures are not established which are designed to assure that the responsible officials of the firm, if they are not personally involved in or immediately aware of such actions, are notified in writing of investigations conducted.

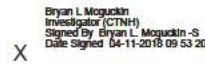
Specifically,

Per CPS-086, the Corporate VP of Quality is “responsible for all product dispositions associated with failure investigations” and the “administration of Quality programs to include: Nonconformance’s (NCR’s), Out of Specifications (OOS), Corrective Action/Preventative Action (CAPA) and complaints”.

Examples of product failures missing Corporate Quality Unit notification:

1. Investigation 17TN927 was initiated on 06/01/2017 as a suspected “sterility failure”.
2. CNC-17-401 was reported on 10/26/2017 as a confirmed OOS for “failed endotoxin”.
3. CNC-17-472 was reported on 12/07/2017 as a confirmed OOS for “failed endotoxin”.

Your firm has failed to provide documentation to ensure the Corporate Quality Unit was routinely informed and procedures followed from 01-01-2017 to 01/03/2018, of any ongoing product safety concerns generated as a NCR or OOS investigation.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Bryan L Mcguckin, Investigator (CTNH) Michele L Glendenning, Investigator	 Bryan L. Mcguckin Investigator (CTNH) Signed By: Bryan L. Mcguckin-S Date Signed: 04-11-2018 09:53:20	DATE ISSUED 4/11/2018

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OBSERVATION 2

The responsibilities and procedures applicable to the quality control unit are not fully followed. Electronic records are used, but they do not meet requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records.

Specifically,


The Corporate Quality/Compliance Unit has failed to follow written procedures, vital to maintaining overall Corporate Quality/Compliance oversight of your production facilities from 01/01/2017 to 01/03/2018.

Per CPS-086, "Quality Unit Responsibility" is directly assigned to the VP of Quality, Corporate HQ, Lake Forest, IL. This position is responsible for "all product dispositions associated with failure investigations" & "for the appropriate elevation to Corporate Management of any critical quality events".

Additionally, CPS-80 establishes that, at least (b) (4) Corporate Management is to attend a "Compliance Review/Management Review" to: "ensure that the quality system and subsystems are effectively established, implemented and maintained at all levels".

Review of this Quality System attribute found:

1. (b) (4) Compliance/Management Review was not conducted.
2. (b) (4) Compliance/Management Review consisted purportedly of quality data from (b) (4) (b) (4) (b) (4) period (approximately (b) (4)), however the summarized conclusion and meeting minutes and other data from the combined (b) (4) meeting are missing and purportedly cannot be found. Neither the Director of Compliance, VP Legal & Compliance or the VP of Quality at Corporate HQ, Lake Forest, IL could define how such data is ultimately stored, where it is stored, when it is stored and who has access.

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3. (b) (4) Compliance/Management Review meeting minutes were hand written, unsecured in the home of a Compliance Analyst when requested and did not contain the required minimum information per CPS-080.
4. (b) (4) Compliance/Management Review meeting minutes were written in Microsoft Word, stored on a Compliance Analyst's lap top and with no controls established to ensure data integrity.

Additionally, per CPS-80, at a minimum the Chief Compliance Officer “shall be given copies of all meeting minutes” for review. There is no indication this quality data was received or reviewed by the Chief Compliance Officer.

OBSERVATION 3

Written records of investigations into unexplained discrepancies do not include the conclusions and follow-up.

Specifically,

Your firm has approximately 630 confirmed OOS’s with associated investigations and no conclusion or follow up.

For example:

CNC-17-366 (0.2mg/ml Hydromorphone and 1 mg/ml Hydromorphone), reported on 10/12/2017 is approximately 157 days past due.

MNC-17-2012 (10mcg/mL Fentanyl Citrate), reported on 12/06/2017 is approximately 90 days past due.

CNC-18-064 (0.2 mg/ml Hydromorphone), reported on 02/13/2018 is approximately 30 days past due.

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MNC-17-2013 (Fentanyl Citrate/Bupivacaine), reported on 12/06/2017 is approximately 90 days past due.

Review of each facility and year the OOS was initiated demonstrates:

Memphis:

2017: approximately 267 open OOS's that are 420-60 days without resolution.

2018: approximately 51 open OOS's that are 90-30 days without resolution.

Cleveland, MS:

2017: approximately 47 open OOS's that are 165-70 days without resolution.

2018: approximately 31 open OOS's that are 78-30 days without resolution.

Sugar Land, TX:

2017: approximately 187 open OOS's that are 420-120 days without resolution.

2018: approximately 27 open OOS's that are 90-14 days without resolution.

Dayton, NJ:

2017: approximately 14 open OOS's that are 420-180 days without resolution.

2018: approximately 8 open OOS's that are 90-30 days without resolution.

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OBSERVATION 4

Batch production and control records do not include the results of any investigation made into any unexplained discrepancy, whether or not the batch of drug product had already been distributed. Electronic records are used, but they do not meet requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records.

Specifically,

A) Lot/batch numbers: 170320090S, 170320098S, 172120168S & 172280034S produced at your Sugar Land, TX facility all failed sterility testing.

Review of the following batch records demonstrated:

170320090S (0.2% Ropivacaine HCL in 0.9% Sodium Chloride Injection) batch record is incomplete.

- 1) F-728-4a has not been completed; the Investigation #/NCR# associated with a confirmed OOS has not been indicated. Form has not been signed as having been reviewed or is missing.
- 2) F-728-5c has not been completed or reviewed.
- 3) F-792-001 has been partially completed indicating a failed sterility test.
- 4) F-611-002 (Quarantine Report) is missing.

170320098S (0.2% Ropivacaine HCL in 0.9% Sodium Chloride Injection) batch record is incomplete.

- 1) F-728-4a has not been completed; the Investigation #/NCR# associated with a confirmed OOS has not been indicated. Form has not been signed as having been reviewed or is missing
- 2) F-728-5c has not been completed or reviewed.
- 3) F-792-001 has been partially completed indicating a failed sterility test.

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4) F-611-002 (Quarantine Report) is missing.

172120168S (0.2% Ropivacaine HCL in 0.9% Sodium Chloride Injection) batch record is incomplete.

- 1) F-728-4a has been partially completed; Investigation#/NCR# associated with a confirmed OOS has not been indicated. The form indicates it was reviewed without exceptions and marked "N/A (no exceptions occurred with this batch).
- 2) F-728-5c has been partially completed indicating Sterility and Endotoxin testing are still outstanding. "N/A" (no exceptions occurred with this batch) is marked and the form has been signed and dated indicating no anomalies.
- 3) F-611-002 (Quarantine Report) is attached but is incomplete, having not been reviewed by a second person.

172280034S (Vancomycin HCL 0.1 g/mL) batch record is incomplete.

- 1) F-728-4a has not been completed; the Investigation #/NCR# associated with a confirmed OOS has not been indicated. Form has not been signed as having been reviewed or is missing
- 2) F-728-5d has not been completed.
- 3) F-792-001 has not been followed.
- 4) F-611-002 (Quarantine Report) is missing.

B) Furthermore, per CPS-799, 5.0 "There must be prompt and timely communication to Supervision, Center Quality Management and Senior Quality Management of the potential of any out of specification results". When questioned about communications between Center Management and Senior Quality Management/Corporate Quality, defined per CPS-007 as individuals that have "the ultimate responsibility to ensure an effective Quality System is in place to achieve the quality objectives of PharMEDium", no said documented communication could be provided. Furthermore, per CPS 799 "the

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laboratory supervisor (or designee) will initiate a laboratory investigation and request a tracking number from Lake Forest Documentation Control”.

Neither the VP of Legal & Compliance nor the VP of Quality could speak to any documented procedure or communications resulting from any OOS generated prior to 01/03/2018.

C) Additionally, your firm is using (b) (4) a supply chain tracking software. Your firm upgraded from Version (b) (4) on approximately (b) (4)

CNC-18-056 generated by a customer complaint, indicates that Lot#: 173520071C, 50mcg/mL Fentanyl was expired and allowed to ship. An investigation was only initiated following a complaint issued by the receiving customer. The investigation identified “the Shipping Supervisor was unaware that the current (b) (4) system allowed the picking of expired product with (b) (4)”. The investigation is ongoing. It is unknown if any other expired product has inadvertently been shipped prior to discovering this system shortcoming.

OBSERVATION 5

Suitable reader or photocopying equipment was not made readily available for drug product records maintained using reduction techniques. Electronic records are used, but they do not meet systems validation requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records.

Specifically,

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The Corporate Quality Unit has been aware of and approved the use of (b) (4) document storage system provided by (b) (4) for the storage of production records since at least 08/2017 at all production facilities. There are currently no standardized operating procedures for its use. There is no indication this system has been validated and no documentation was provided to establish said validation, Per CPS-017. Use of this system during the establishment of formal procedures for its use is ongoing.

Furthermore, much of the documentation/forms used by your firm are currently in a Word File format, utilizing a combination of data entry, hand writing or both. Such modalities could subject your records to potential manipulation. Regular audit trails are not conducted on any system.

OBSERVATION 6

Individuals responsible for supervising the manufacture and processing of a drug product lack the training to perform their assigned functions in such a manner as to assure the drug product has the safety, identity, strength, quality and purity that it purports or is represented to possess.

Specifically,

Your firms training program qualification is not fully established.

Per CPS-0003 "New Course Design and Training Implementation Model", Trainers are to have had training provided by (b) (4) to conduct (b) (4) training. No (b) (4) or (b) (4) has been identified as having provided any such Aseptic Processing training to (b) (4)

***DATES OF INSPECTION**

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3/12/2018(Mon), 3/13/2018(Tue), 3/14/2018(Wed), 3/16/2018(Fri), 3/19/2018(Mon), 3/20/2018(Tue), 3/22/2018(Thu), 3/23/2018(Fri), 3/29/2018(Thu), 3/30/2018(Fri), 4/02/2018(Mon), 4/03/2018(Tue), 4/11/2018(Wed)

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