DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA 4040 North Central Expressway #300 Dallas, TX 75204 (214) 253-5200	9/4-7; 10,12-13,17,19/07
	FEI NUMBER 3000717703

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Bruce W. Bagley, General Manager

FIRM NAME	STREET ADDRESS
Pharmedium Services LLC	12620 West Airport Blvd. #130
CITY, STATE AND ZIP CODE Sugar Land, TX 77478-6141	TYPE OF ESTABLISHMENT INSPECTED Sterile Drug Manufacturer

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

This document lists observations made by the FDA representatives 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 representatives 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.

OBSERVATION #1

The firm's sampling and testing plan for sterility and potency testing of manufactured lots of sterile drug products does not provide assurance that statistical criteria and specifications are met. Based on your firm's volume of production, your sampling of product is not representative of the total lots manufactured.

The firm utilizes a (b) (4) by which lots of manufactured, sterile drug products are sampled on a (b) (4) (b) (4) (b) (4) and tested for sterility and potency.

For sterility testing, a total of (b) (4)

For potency testing, the firm (b) (4)
(b) (4) (b) (4) (b) (4)

The firm manufactures approximately (b) (4) units, or about (b) (4) lots of sterile products annually which are distributed nationally.

Some examples of recent shipments for drug products which were not tested for sterility or potency consist of the following:

- Cefazolin 2 Grams (b) (4) 100 ml 5% Dextrose Injection USP, lot #100723400051, was manufactured on 8/22/07 (Expiration date: 9/21/07) and shipped on 8/27/07 to consignees.

- Oxytocin 20 Units (b) (4) 1000ml 0.9% Sodium Chloride Injection USP, lot

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#100723600016 , was manufactured on 8/24/07 (Expiration date: 10/8/07) and shipped to consignees on 8/28/07.

- Magnesium Sulfate (b) (4) 500 ml 5% Dextrose, lot #100724000048, was manufactured on 8/28/07 (Expiration date: 10/12/07) and shipped to consignees on 8/30/07.

OBSERVATION #2

The firm's procedure for sanitizing supplies and equipment used to manufacture lots of sterile drug products does not provide assurance that adequate sanitization with the secondary method of using (b) (4) is performed.

Specifically, review of SOP# CPS-310 entitled, "Sanitization of Vial Stoppers and Bag Injection Ports Including Preparation of Sanitization Solution" (Issue date: 5/16/06) revealed that the SOP did not include the following:

- The SOP addresses the use of (b) (4) in conjunction with the current method of using sterile (b) (4) as a sanitizing agent on the injection ports of recipient bags. However, the SOP does not address the suitability of the time of exposure for the (b) (4) (b) (4) for the destruction of spore forming mold and bacteria. Between 6/06 and the present, the firm's environmental monitoring program for viable particulates in the Class 100 Laminar Flow Hoods revealed in at least 10 different cases where settling and/or contact plates were contaminated with Bacillus spp. or mold during production.

- The SOP does not include an evaluation of the effectiveness of the (b) (4) (b) (4) which is used to sanitize the injection ports of up to (b) (4) recipient bags. The firm has not established that the (b) (4) (b) (4) at the end of the swabbing process are equivalent to the start of the process with less organic matter present in the (b) (4) (b) (4) .

OBSERVATION #3

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The firm has not evaluated the appropriateness of sanitizing the surfaces of (b) (4) bags of (b) (4) drug products (b) (4) . Between 1/06 and the present, the firm's environmental program for viable particulates in the Class 100 Laminar Flow Hoods revealed that settling plates and/or contact plates were contaminated with bacteria or mold on at least 80 different occasions (i.e. *Bacillus spp., Staphylococcus spp.* mold, and yeast) during manufacturing operations.

SOP #CPS519 entitled, (b) (4) Process" (Issue date: 3/23/07) documents, in part, that prior to entry into the (b) (4) . In addition, each unit or bag of (b) (4)/drug product (b) (4)

OBSERVATION #4

The firm's disinfectant effectiveness studies do not include microbial challenge (microbial recovery) studies to demonstrate that (b) (4) and (b) (4) are effective sanitizing agents in the interior of the (b) (4) Laminar Flow Hoods (Class 100) used in the production of sterile, drug products.

Between 1/06 and the present, the firm's environmental program for viable particulates in the Class 100 Laminar Flow Hoods revealed that settling plates and/or contact plates were contaminated with bacteria or mold on at least 80 different occasions (i.e. *Bacillus spp., Staphylococcus spp.* mold, and yeast).

OBSERVATION #5

The firm does not conduct on-going stability studies for any finished drug products which are manufactured and distributed to provide assurance that the established expiry dates of 15 days, 30 days, and 45 days remain valid. Some examples are included under observation #1.

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Additionally, contracts prepared by PharMEDium for providing services to hospital customers contain a statement reading, "Stability: PharMEDium will provide the most current and extended stability which is commercially reasonable for services, consistent with requirements of the US Food and Drug Administration ("FDA")."

OBSERVATION #6

The firm's procedures do not include requirements for analytical testing of incoming, commercially available drug products which are used in the production of sterile, finished drug products distributed to consignees. The firm receives the following products which are used in the production of finished drug products:

- Magnesium Sulfate for Injection USP (b) (4) (Vendor: (b) (4) (b) (4))
- Cefazolin for Injection USP (Mfd. By (b) (4))
- Oxytocin for Injection USP (Vendor: (b) (4))
- Sterile Vancomycin for Injection USP (Vendor (b) (4))

OBSERVATION #7

The firm does not maintain reserve samples for any sterile drug products manufactured and distributed.

Review of product complaints for the period between 1/06 and the present revealed at least 10 complaints for Oxytocin products involved lack of therapeutic response. In each case, there were no retention samples available for evaluation and/or analysis during the firm's investigation. The complaints consist of the following (See table on following page):

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COMPLAINT #	PRODUCT	LOT#	MFD. DATE
IR-SL-06-19	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100629700060	10/24/06
IR-SL-06-14	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100627700016	10/4/06
IR-SL-06-12	30 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100622100029	8/9/06
IR-SL-06-20	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100634200009	12/8/06
IR-SL-06-18	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100630000004	10/27/06
IR-SL-06-13	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100622100067	8/9/06
IR-SL-06-01	20 Units Oxytocin Added to Lactated Ringer's Inj USP	100600300025	1/3/06
IR-SL-07-13	30 Units Oxytocin Added to 5% Dextrose and Lactated Ringer's Inj. USP	100716600035	6/15/07
IR-SL-07-02	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	10070450035	2/9/07
IR-SL-07-01	20 Units Oxytocin Added to 0.9% Sodium Chloride Inj. USP	100633400059	11/30/06

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