DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
300 River Place, Suite 5900 Detroit, MI 48207 (313) 393-8100 Fax: (313) 393-8139 Industry Information: www.fda.gov/oc/industry	12/12/2012 - 12/28/2012* FEI NUMBER 1818977

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: J. Donald Ferry Jr., General Manager

FIRM NAME	STREET ADDRESS
JHP Pharmaceuticals, LLC	870 Parkdale Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Rochester, MI 48307-1740	Drug Manufacturer

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:

QUALITY SYSTEM

OBSERVATION 1

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

Specifically, investigations into glass particles found in or on vials of drug products purported to be sterile do not always include a thorough impact assessment and root cause analysis. For example, for closed events PR 4940 (opened 11/05/12), PR 4649 (opened 10/12/12), and PR 4380 (opened 9/27/12), pertaining to broken glass vials found during (b) (4) operations for Thrombin lot 594671F, Thrombin lot 594667F, and (b) (4) respectively, the rationale used to determine which vials in these lots were not impacted is not fully supported by scientific evidence and a thorough review of all associated records and data. Moreover, no investigation into the root cause was performed for event 4940. These lots were released on 11/28/12 and 12/15/12. A recall of (b) (4) manufactured 11/01/11 was initiated on or about 9/04/12 after receiving several complaints that revealed glass particles in or on vials or vial damage, which was attributed to glass breakage events during (b) (4) operations.

PRODUCTION SYSTEM

OBSERVATION 2

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

Specifically,
i. a. The 2012 Aseptic Process Simulation Master Plan states, "(b) (4) (b) (4) (b) (4) " There is no documented scientific rationale to support why these requirements are sufficient to represent routine commercial filling operations. According to Sterility Assurance, a Production Machine Operator can remain in the filling area for up to (b) (4) hours and may perform multiple interventions before a break and then return to the filling area at a later time during the same shift, however, there is no documentation of how long

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Michele L. Forster, Investigator Michele L. Forster Rebecca E. Dombrowski, Investigator Emily J. Orban, Investigator Emily J. Orban	12/28/2012

personnel participated in a media or production fill.

b. The 2012 Aseptic Process Simulation Master Plan states, "(b) (4) (b) (4) However, there is no written specification for the number of vials/bottles or length of time required to challenge the slowest and fastest line speeds. Media Fill batch #590384 challenged the slowest filling speed for approximately (b) (4) vials and the fastest filling speed for approximately (b) (4) vials on Line (b) out of (b) (4) vials. Media Fill batch #603801 challenged filling at the fastest line speed of (b) vpm on Line (b) for approximately (b) (4) bottles out of (b) (4) There is no documented scientific rationale that these run sizes mimic commercial batch sizes.

In addition, Line (b) (4) was not challenged in 2012 at the fastest fill speed of (b) (4) vpm. The fastest speed challenged was vpm during Media Fill batch #308825. The following production batches were filled at a speed greater than vpm: batch filled on 6/20/12 at vpm, batch filled on 7/6/12 at vpm, and Cytovene batch #488392F filled on 9/6/12 at vpm.

c. The 2012 Process Simulation Master Plan does not specify how many times to perform each routine intervention, only that each intervention must be performed during each media fill batch. Moreover, no data was provided to support that the frequency of interventions performed during media fill batches accurately simulates production activities.

ii. There is no data to support the determination that the "pack-off" area of line (b) where personnel pack partially stoppered vials of drug products purported to be sterile into trays and transfer the trays by hand into a HEPA filtered cart does not require routine monitoring for microbial contamination during filling operations. As an example, was manufactured on 9/19/12 and filled on line

Your firm routinely manufactures drug products purported to be sterile, for example, Thrombin lot 594671 released on 12/15/12 and shipped on 12/20/12, Coly Mycin S lot 592958 filled on or about 12/18/12, and (b) (4) of released on 11/28/12 and shipped on 12/04/12.

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."