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	03/13/2012 - 03/29/2012* 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	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

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

Specifically,

i- Investigation into Deviation PR 2042, initiated in response to incorrect storage conditions (°F) printed on the 25 vial carton label for Pitocin 10 mL, did not address the sterility assurance of the container closure of distributed Pitocin vials that may have been stored incorrectly as a result of this deviation. As filed with the Agency in the Annual Report dated 11/01/10-10/31/11, Pitocin storage conditions should be labeled, "Store between 20° to 25°C (68° to 77°F)". Pitocin 10 mL lot 225867 ([(b)(4)] cartons) and part of Pitocin 10 mL lot 231423 ([(b)(4)] cartons) were packaged, released and distributed in a 25 count carton labeled, "Store between 20° to 25°C (28° to 77°F)". As of 3/26/2012, data had not been provided to support that the integrity of the Pitocin vial container closure system would not be compromised (with respect to sterility) if stored at the lower extreme of the temperature range as listed on the carton label.

ii- Open deviation investigation PR 2204, initiated 1/09/2012 had not documented an assessment of marketed lots of Coly-Mycin M, Injectable that may have been impacted by a failed stopper washer cycle requalification, at the time of this observation (3/22/2012). Specifically, the 2011 annual requalification of the stopper washer cycle [(b)(4)] for endotoxin control of incoming stoppers failed to meet the acceptance criteria of a [(b)(4)] reduction of endotoxin in 3 of 12 samples submitted for testing. The previous cycle [(b)(4)] requalification occurred 3/2010. Finished product utilizing stoppers processed under cycle [(b)(4)] from the time of the last successful requalification to present included 6 lots of Coly M

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Parenteral, ([b)(4) redacted] 237535F, [b)(4) redacted].

iii- Corrective Action to the July and August 2011 NVP Environmental Monitoring Deviations (PR 1479 and 1539: failure to initiate NVP monitoring prior to aseptic filling commencement) did not extend to all applicable production departments in that in November 2011 (11/16/11) deviation PR 1995 was initiated for the failure to initiate NVP monitoring prior to aseptic bulk operations for Media Fill lot [b)(4) redacted]

OBSERVATION 2

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically,

i-As of the time of this Observation, the duties and responsibilities of the Quality Unit were not clearly defined in written procedures. For example and pertaining to a "label error" with respect to Pitocin 10 mL cartoned product, lots 231423 and 225867 as reported to the Agency under Field Alert Report 12/07/2011:

a- Written procedure CQP-GEN-00020, Critical Action Committee, indicates that, "[(b)(4) redacted]". The Critical Action Committee met on 12/06/2011 to address the aforementioned label error and a decision was made to submit a Field Alert Report.

b- Written procedure SOP-QLA-MQA-03309-RO, Field Alert and Recall Procedure, indicates that "[(b)(4) redacted]". A Field Alert was filed on 12/07/2011 for the same aforementioned label error pertaining to Pitocin 10 mL cartons.

ii- Written procedure SOP-QLA-MQA-03437-RO, Deviation/Investigation Management, was not followed in that it states, "[(b)(4) redacted]". The following deviations were not initiated within one business day of event recognition, and no justification was documented:

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a- Deviation 2204 - (b)(4) Stopper Washer did not achieve Endotoxin (b)(4) Reduction during Requalification; date of recognition 12/22/11, date of deviation initiation 01/09/12. Coly Mycin M Lot (b)(4) was listed in this Deviation Investigation.
b- Deviation 2548 - Water leak discovered from ceiling in Bulk Formulation Room; date of recognition 02/25/12, date of deviation initiation 03/01/12. Thrombin lot 233859 was manufactured in this room on 2/27/2012.
c- Deviation 2566 - Water leak in Manufacturing Suite (b)(4) ceiling; date of recognition 02/27/12, date of deviation initiation 03/02/12. Dantrium lot (b)(4) was manufactured in Suite (b)(4) on 2/27/2012.

iii- There are no written specifications established for the receipt of goggles used as part of the gown donned by personnel entering the aseptic processing core. Use of these goggles was observed worn by aseptic core personnel during the manufacture and filling of Ketalar 100 mg/mL, 5mL, lot (b)(4) on 3/21/2012.
Though observed goggles, lot # (b)(4) were received with a Sterility Report and a Certificate of Processing, SOP-QLA-SQC-03389-RO, Incoming Quality Inspection for Components, section WI-QLA-SQC-03389.4-RO, MRO Components and Supplies does not list or require written specifications to compare the supplier provided reports and certificates against for this gown component.

FACILITIES & EQUIPMENT SYSTEM

OBSERVATION 3

Written procedures are not established and followed for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically,

i- Filter integrity testing of the HEPA filters in the (b)(4) of the Line (b)(4) Depyrogenation Tunnel is not performed as specified under SOP-ENG-MNT-03137-RO, V.12.0, Test, Repair & Replacement of Environmental Air & Laminar Filters. Specifically, no Filter Integrity Testing is performed for these specific (b)(4) HEPA filters. Records indicated the subject HEPA filter within a bank of (b)(4) HEPA filters in this (b)(4) had been installed in July of 2006. The scientific rationale for not performing the Filter Integrity Testing was not supported when a single filter from this same Line (b)(4) Depyrogenation

tunnel (b)(4) was found damaged and pulled away from the underside of the HEPA frame during non-routine maintenance to the line on 1/03/2012. The point in time at which the damage occurred could not be specifically pinpointed with data from current filter monitoring including (b)(4) NVP testing.

(b)(4) ots are listed as potentially impacted under the damaged HEPA investigation with scope listed as all commercially distributed products manufactured on Line (b)(4) since 11/2010, including:

Brevital 500 mg, injectable, lot 190031 exp. 11/14
Coly Mycin M, injectable, lot 224668 exp. 05/14
Ketalar 100 mg/mL, 5mL, injectable, lot 220961 exp. 07/14
Pitocin 10 mL, injectable, lot 231423 exp. 02/13
Tigan 100mg/mL, 20 mL, injectable, lot 148665 exp. 12/13

ii-Written procedure SOP-ENG-MNT-03097-RO, Maintenance of Critical Equipment, section 6.3.8 requires that "(b)(4) (b)(4) (b)(4) ". This procedure was not followed on the following occasions pertaining to overdue Preventative Maintenance for "Critical" HEPA filters located in the Grade (b)(4) space:

a- Suite (b)(4) HEPA- (b)(4) PM due 7/08/2011 completed 8/14/2011 resulting in detection of a leak during Filter Integrity Testing, documented under Deviation 1580. Exception Report approved by QA on 8/16/2011
b- Suite (b)(4) HEPA- (b)(4) PM due 7/08/2011 completed 8/14/2011 resulting in detection of a leak during Filter Integrity Testing, documented under Deviation 1581. Exception Report approved by QA on 8/16/2011
c- Suite (b)(4) HEPA- (b)(4) PM due 7/08/2011 completed 8/14/2011 resulting in low air volumes during Filter Integrity Testing, documented under Deviation 1583. Exception Report approved by QA on 8/16/2011
d- Suite (b)(4) HEPA (b)(4) PM due 7/08/2011 completed 8/14/2011 resulting in detection of a leak during Filter Integrity Testing, documented under Deviation 1584. Exception Report approved by QA on 8/16/2011

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(b)(4) lots were manufactured in Suite (b)(4) during the time frame between the due date (7/08/2011) and the completed testing date (8/14/2011) including:

(b)(4) released by QA on 8/04/2011 and shipped on 8/26/2011.
Dantrium lot (b)(4) released by QA on 8/26/2011 and shipped on 9/16/2011.
(b)(4) released by QA on 9/13/2011 and shipped on 9/16/2011.

Additionally, the following 2 more recent Filter Integrity Testing deviation investigations pertaining to leaks detected in the HEPA filters in the Grade (b)(4) space of Suite (b)(4) were also found overdue and without supporting QA Exception Reports filed:

e- Suite (b)(4) HEPA - (b)(4) PM due 1/15/2012 performed 2/10/2012 resulting in detection of a leak during Filter Integrity Testing, documented under Deviation 2501. Exception Report approved by QA on 3/19/2012
f- Suite (b)(4) HEPA - (b)(4) PM due 1/15/2012 performed 2/11/2012 resulting in detection of a leak during Filter Integrity Testing, documented under Deviation 2500. Exception Report approved by QA on 3/19/2012

Product impacted under the above late deviations include Brevital lot #182060F, released and shipped for distribution on 3/9/2012.

iii-According to SOP-MAN-PRP-03270-RO, Cleaning of Bulk Manufacturing and Filling Equipment, Building 100, "(b)(4) (b)(4) ", though on 3/13/2012, a drum of "Interest" detergent lot (b)(4) was observed labeled as beyond expiration (exp. 2/19/12) yet connected to the (b)(4) parts washer located in the Suite (b)(4) Production Core of Building (b)(4) .This parts washer had been used on the day observed (3/13/2012) in washing of (b)(4) containers used for (b)(4) lot (b)(4) and (b)(4) lot (b)(4)

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*** DATES OF INSPECTION:**
03/13/2012(Tue), 03/14/2012(Wed), 03/15/2012(Thu), 03/16/2012(Fri), 03/19/2012(Mon), 03/20/2012(Tue), 03/21/2012(Wed), 03/22/2012(Thu), 03/27/2012(Tue), 03/29/2012(Thu)

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