DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Customhouse, Rm 900 2nd & Chestnut St Philadelphia, PA 19106 (215) 597-4390 Fax:(215) 597-0875 Industry Information: www.fda.gov/oc/industry	03/18/2013 - 04/01/2013* FEI NUMBER 3006489293

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Joseph C. Cosgrove, Chairman and Chief Executive Officer

FIRM NAME	STREET ADDRESS
Pentec Health, Inc.	4 Creek Pkwy Ste A
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Boothwyn, PA 19061-3132	Producer of Injectable Drug Products

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:

The following deficiencies apply for all injectable drug products that are processed at your facility and intended for administration via intrathecal and intravenous injection:

OBSERVATION 1

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

Specifically,

A) SOPs for aseptic processing were not followed and aseptic techniques used during the processing of drug products are deficient as demonstrated by the following observations made on 3/18-19/13:

1) Personnel with exposed skin (face and neck) were observed leaning their head and torso inside and resting forearms on surfaces while processing injectables inside the ISO 5 Laminar Air Flow (LAF) hoods.

2) Personnel working inside an ISO 5 LAF hood Specialty Infusion (SI) #3 LAF hood was observed leaning into the hood, with her face positioned over an open container while drawing solution into a syringe.

3) An employee processing injectable drug products in an ISO 5 LAF hood was observed to have facial hair exposed.

4) During filling of an SI morphine syringe prescription, a plastic cup containing reconstituted morphine powder was taken out of the hood and reintroduced without first disinfecting it.

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5) A technician preparing to work in SI #2 did not disinfect equipment including packaged syringes, caps, vials, and mixing containers before placing them in the ISO 5 LAF hood.

6) The following observations were made about the surfaces inside the ISO 5 LAF hoods where injectable drug products were being processed:

a) Whitish residues were apparent on the (b) grating covering the HEPA filters in the back of the horizontal flow hoods and on the light covers inside the ISO 5 LAF hoods.

b) Dark, amber-colored stains were apparent on the HEPA filter of the horizontal flow ISO 5 LAF hood and in the crevice along the seam of the filter grate.

c) Dark splatters were apparent on the light fixtures above the critical work space inside a ISO 5 LAF hood.

7) Equipment and production supplies were placed in front of the HEPA filters in the horizontal flow ISO 5 LAF hoods in a manner that appeared to obstruct airflow to the critical workspace.

8) Dispensing of non-sterile morphine and bupivicaine powders was not confined within an ISO 5 LAF hood.

9) IV bags stored in an uncontrolled manner for examples, port facing near floor, bags on rack near floor, bags hanging halfway out of the ISO 5 area with ports exposed, and bags not spayed as required with (b) (4) .

B) Your firm aseptically (b) (4) the injectable Morphine IT, Morphine /Bupivacaine, Fentanyl/Bupivacaine, Fentanyl/Bupivacaine/Clonidine and stock solutions utilizing a (b) (4) (b) (4) . The following observations listed below were observed:

1) There were no validation records available for the (b) sterilization step.

2) According to testing procedures a (b) (4) is to be performed to assure the integrity of the (b) used. There were no records describing how the (b) (4) will be wetted, how much pressure will be applied and what the specifications for the (b) (4) value are.

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3) There were no instructions on how the (b) (4) value will be calculated and the specifications.
4) Procedures on how to use the sterile (b) unit were incomplete and did not describe how to fill the syringes, how to aseptically remove the (b) cover from package, how to attach the (b) and deliver the solution.
5) For 15 Morphine IT syringes orders, 8 Fentanyl / Bupivacaine orders and 15 Morphine /Bupivacaine orders no (b) (4) was documented to assure the integrity of the (b) sterilization step.

C) The media fills conducted 09/17/2012 through 03/19/2013 do not simulate the production of injectable drug products produced in your facility. The positive controls were performed for the media (b) (4) used in the media fill studies. The media used in the media fill have not been verified to support microbial growth. Additionally, the procedure 4.16 Process Verification was incomplete in that the SOP does not describe the steps for adding contents of the ampoule, sanitizing the work area and aseptically attaching the needle.

OBSERVATION 2

Clothing of personnel engaged in the of drug products is not appropriate for the duties they perform.

Specifically,

A) Gowning apparel is not sterile and does not provide coverage of the eyes, exposed skin, and hair on the face and neck of the personnel who process injectable drug products inside the ISO 5 LAF hoods.

B) Gowning practices are deficient in that disposable lab coats are hung up in the ISO 8 anteroom and reused by personnel who are returning from lunch breaks to processing inside the ISO 5 LAF hoods.

OBSERVATION 3

Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable construction to facilitate cleaning, maintenance, and proper operations.

Specifically,

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A) On 3/18/13, the following deficiencies were observed in the design and maintenance of the cleanroom and ISO 5 LAF hoods that are used for the processing of injectable drug products:

1) Pre-filters installed on ISO 5 LAF hoods were not fitted inside the filter frames and were covered in dust.

2) Light covers above the work space inside an ISO 5 LAF hood were bowed so that openings were visible between the light bulbs and the cover.

3) (b) (4) inspection and cleaning, routine preventative maintenance, and periodic replacement of the pre-filters on the ISO 5 LAF hoods was not performed as required per the SOP for Laminar Flow Hood Maintenance.

4) Large gaps were present between the doors separating the ISO 8 and ISO 7 areas that support the ISO 5 hoods.

B) The (b) (4) ISO 5 LAF hood certifications performed by a third party vendor in June 2012 and Jan. 2013 were not adequate to demonstrate adequate control of air flow, performance of equipment responsible for assuring air quality, and the absence of microorganisms, in that:

1) Surface sampling was performed in only (b) (4) ISO 5 LAF hoods and samples were taken from the same (b) hoods in June 2012 and January 2013.

2) Smoke studies were not performed under dynamic conditions within the ISO 5 LAF hoods.

3) No criteria was established to measure acceptability and uniformity of air velocity across the HEPA filters inside the ISO 5 LAF hoods (aka clean air benches).

OBSERVATION 4

Equipment and utensils are not cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions and contamination that would alter the safety, identity, strength, quality or purity of the drug product.

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Cleaning validation studies were not conducted for the ISO 5 LAF hoods to establish clean, dirty, and sterile hold times, and determine the effectiveness of cleaning methods to remove product residues and microorganisms. Only (b) (4) are used (b) to clean and sanitize all surfaces inside the ISO 5 LAF hoods.

OBSERVATION 5

Sampling and testing plans for drug products are not described in written procedures which include the method of sampling and number of units per batch to be tested.

Specifically,

1. For Proplete IV (containing Prosol, Dextrose and Water for Injection) the testing plan described in the procedure End Product Testing 4.22 does not include sample size (number of IV bags to be pulled) or data to support the sample is representative. For example, the procedure reads products will be submitted on a (b) (4) basis but does not indicate how many samples will be pulled for testing. Additionally, the procedure End Product Testing 4.22 indicates the sample will be tested for sterility for a period of (b) (4) from date of production. Testing records provided document (b) (4) sterility. Also, no endotoxin studies are performed on the final product.

2. For the Stock Solutions Bupivacaine 30mg/ml, Morphine 50mg/ml, or Hydromorphone 100mg/ml the procedure is incomplete in that, it does not include the sample size or a description of the sampling plan. Procedure 6.4 Quality Assurance of Batched Compounds indicates to (b) (4) select representative samples of the drug batch but does not explain the numbers of samples that will be pulled or how the samples will be selected.

3. The SOPs concerning sterility and endotoxin testing for injectable drugs were not signed or approved by a qualified person.

4. Finished products were not incubated at (b) (4) °C per the (b) (4) test method. The end product test log for March 2013 indicated that IDPN and IPN injectable products were incubated at temperatures above 39 °C.

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OBSERVATION 6

There is no written testing program designed to assess the stability characteristics of drug products.

Specifically,

1. There is no written stability program in place or stability data available for preservative free Proplete (containing Prosol, Dextrose and Water for Injection) to support a 21 before use date. The final product is not sterilized by filtration or any other means.

2. There is no written stability program in place or stability data available for the preservative free Stock Solutions Bupivacaine 30mg/ml, Morphine 50mg/ml, or Hydromorphone 100mg/ml to support a 14 before use date. These Stock solutions are further processed with non-sterile powders such as Bupivacaine, Morphine, Hydromorphone or Fentanyl. The final preservative free injectable drug is sterile (b) (4) but not tested to assure sterility. The final drug is assigned a 3 before use date.

OBSERVATION 7

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A) On 12/06/2012 Bupivacaine 30mg/mL was OOS with a result of 111.52% concentration of 33.46 mg/mL. The specification for potency/purity is (b) (4) No investigation into the root cause was performed. Additionally, there was no laboratory investigation conducted to determine if the sample was prepared correctly, expiration dates for materials, and if the method was validated.

B) Recurring organisms found in the ISO 7 and ISO 8 classified support areas were not thoroughly investigated and trended, including *Pasteurella spp.*, and no product impact assessment was made.

OBSERVATION 8

The control systems necessary to prevent contamination or mix-ups are deficient.

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1) Personnel and environmental monitoring of surfaces and active air sampling is not performed on each day that injectable drug products are processed inside the ISO 5 LAF hoods

2) Personnel monitoring does not include sampling of employees' foreheads, labcoats, or sleeve cuffs.

3) ISO 5 LAF hood environmental and personnel monitoring samples are not incubated according to the prescribed test procedure.

4) Testing of ISO 5 LAF hood environmental and personnel monitoring samples is not adequate to detect all objectionable organisms that may be present, including yeast and mold.

5) (b) (4) [redacted] paddles that are used for environmental and personnel monitoring are not qualified or challenged before use to assure they are capable of microbial growth.

6) The incubators are not qualified or subjected to a periodic preventative maintenance program.

OBSERVATION 9

Written procedures are lacking which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, drug product containers, and closures.

Specifically,

Component vendors have not been qualified and verification of the identity and potency of drug components, and verification of the sterility and depyrogenicity of drug components, processing equipment, and packaging components is not performed.

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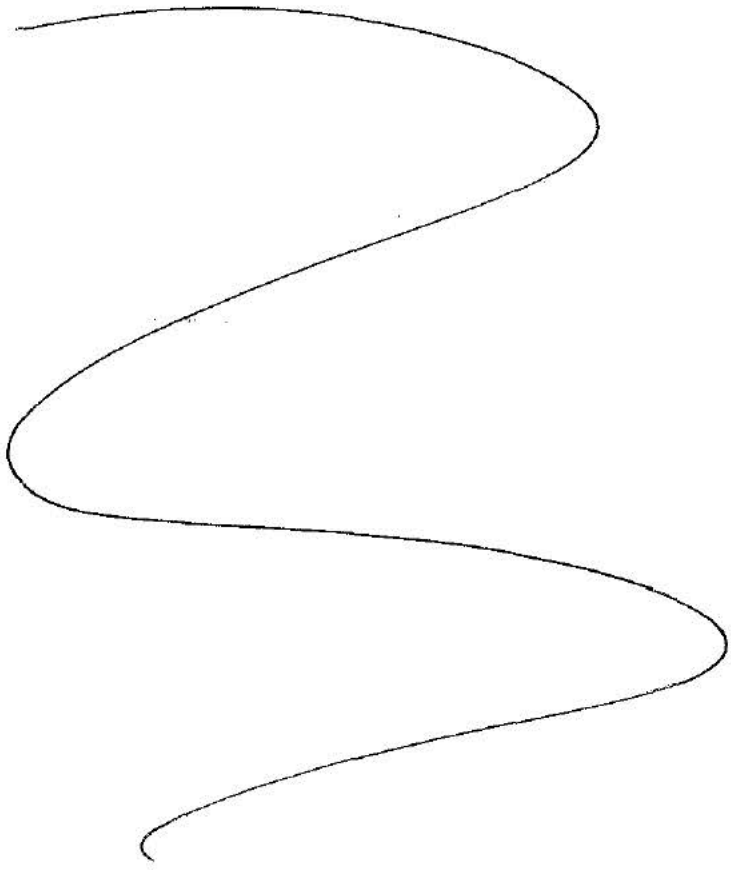
*** DATES OF INSPECTION:**
03/18/2013(Mon), 03/19/2013(Tue), 03/20/2013(Wed), 03/21/2013(Thu), 03/26/2013(Tue), 03/27/2013(Wed), 04/01/2013(Mon)



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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."