DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
404 BNA Dr., Bldg. 200, Ste. 500 Nashville, TN 37217-2597 (615) 366-7801 Fax:(615) 366-7802 Industry Information: www.fda.gov/oc/industry	09/24/2013 - 10/02/2013* FEI NUMBER 3004034796

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Tommy T. Simpson, President

FIRM NAME	STREET ADDRESS
Delta Pharma, Inc.	114 W Mulberry St
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Ripley, MS 38663-1709	Producer of Sterile Drugs

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

Specifically,

a) Media fills or process simulations for injectable drug products have not been performed which simulate the entire production process including but not limited to: all process steps and manipulations; [redacted (b) (4)]; and aseptic filling of vials performed under a laminar flow hood (ISO 5 classified area). A review of your firm's records noted that a media transfer was last performed on 01/10/2006. Also, your firm has no written procedures which describe the frequency and acceptance specifications for media fills or process simulations.

b) Sterilization cycles using a [redacted (b) (4)] have not been validated for [redacted (b) (4)] sterilized finished drug products. Loading configurations, temperature mapping, and heat penetration have not been evaluated to ensure sterilization of finished drug products. The washing and sterilization processes for finished product closures (rubber stoppers) have not been validated. Bioburden, loading configurations, temperature mapping, and heat penetration have not been evaluated to ensure sterilization of finished product closures. The cleaning and sterilization processes for reused plastic tubing used in the aseptic processing and filling of injectable drug products have not been validated. Also there are no written procedures which describe the methods for cleaning and sterilizing reused plastic tubing.

c) The washing and depyrogenation processes for finished product containers (10 ml amber glass vials) have not been validated. Per your firm's procedures, SOP for Cleaning, Sterilizing and Depyrogenation of Vials, city water is used for washing vials instead of purified or sterile water. Depyrogenation processes using an [redacted (b) (4)] have not been validated. Endotoxin burden and challenges, loading configurations, temperature mapping, and heat penetration have not been evaluated to ensure depyrogenation of finished product containers.

d) You have not qualified the [redacted (b) (4)] for its intended use to demonstrate bacterial retentive and physical/chemical compatibility for each sterilized injectable drug product formulation made from non-sterile drug components.

e) [redacted (b) (4)] testing of the [redacted (b) (4)] is not performed according to

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the manufacturer's specification. According to the manufacturer the [redacted] (b) (4) test of this (b) (4) is (b) (4) using (b) (4) as the (b) (4) at (b) (4). The (b) (4) test performed by your firm uses (b) (4) as the (b) (4) with an acceptance value of (b) (4).

f) You have not qualified the [redacted] (b) (4) for its intended use to demonstrate bacterial retentive and physical/chemical compatibility with (b) (4) used in the production of injectable drug products. Integrity testing of the [redacted] (b) (4) is not performed.

The above is a repeat observation from previous FDA inspections ending on 09/17/2010, 10/17/2007, and 03/10/2004.

OBSERVATION 2

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

a) Smoke studies for qualification of the ISO 5 area where injectable drugs are processed were not conducted under dynamic conditions and were not documented with video evidence.

b) Surface monitoring of the ISO 5 environment is not conducted.

c) Non-viable particulate air monitoring of the ISO 5 environment is not conducted during production of sterile drug products.

d) Viable air and personnel monitoring is not conducted for every production of injectable drug products. Currently, you only conduct viable air and personnel monitoring every (b) (4).

OBSERVATION 3

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,

a) There is no equipment installed to measure pressure differentials between the ISO 6 (clean room) and adjacent unclassified areas. Pressure differentials in ISO 5 and ISO 6 areas are not monitored and documented.

b) Design and operation of the clean room used for processing sterile drug products is not adequate to prevent influx of lower quality air into the clean room (ISO 6 area). Specifically, the clean room door, separating the clean room from the gowning

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room, is equipped with an unfiltered vent and the supply air for the clean room is not continuously operated. Additionally, the air quality of the gowning room has not been qualified/classified.

c) Qualifications of the clean room (ISO 6) do not include documentation of filter integrity and leak testing of the HEPA filters for the room. Cleanroom Certification reports ENV0716131431RM and ENV1220120741BM performed on 11/21/2012 and 06/13/2013 respectively do not document the performance and results of HEPA leak tests for the clean room.

OBSERVATION 4

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically,

a) The [redacted] (b) (4) with serial number [redacted] (b) (4) used for depyrogenation of finished sterile drug product containers and for the depryogentaion of glassware used in the production of sterile drug products has not been qualified.

b) The [redacted] (b) (4) with serial number [redacted] (b) (4) used in the [redacted] (b) (4) sterilization of finished injectable drug products and for the sterilization of closures, utensils, filters, hoses, and other process equipment has not been qualified.

c) The incubator with ID # [redacted] (b) (4) used for the incubation of environmental monitoring samples has not been qualified.

The above is a repeat observation from the previous FDA inspection ending on 10/17/2007.

OBSERVATION 5

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

Specifically,

a) On 09/24/2013 sterile gowning components including sterile gowns and gloves were observed to be stored on a shelf in the restroom equipped with a functioning toilet and sink. Also, there are no procedures for the sanitization of the outer packaging of gowning components prior to their use in the clean room.

b) On 09/24/2013 non-sterile gowning components including face masks, hair nets, shoe covers and dedicated under garments and shoes were observed to be stored uncovered on a shelf in the washroom equipped with a functioning sink.

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Also, non-sterile face masks which are not individually packaged are used in the production of sterile drug products.

OBSERVATION 6

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

a) The cleaning agents used to clean the ISO 5 area are not sterile.

b) Your procedure, "Environmental Control: SOP for Primary Cleaning of Clean Rooms" does not include or reference a list of approved cleaning agents, the rotation of disinfectants/sporicidal agents, and instructions for the dilution of disinfectants/sporicidal agents.

c) It is your firm's practice to dilute the sporicidial agent [redacted (b) (4)] at a rate of [redacted (b) (4)], however the manufacturer's directions for use does not state to dilute the activated solution. Also, you have not demonstrated the efficacy of the diluted sporicidial agent at the concentration in which it is used. Additionally, the stability and shelf life of the diluted sporicidial agent have not been evaluated by your firm.

d) Your firm lacks specific procedures for the disinfection and handling of equipment and materials before introduction into the ISO 5 area. Specifically, the exterior surfaces of equipment and material containers are not disinfected/sanitized before being introduced from unclassified areas into the ISO 5 area.

OBSERVATION 7

Routine calibration of equipment is not performed according to a written program designed to assure proper performance.

Specifically,

There are no written procedures or records which demonstrate the following equipment has been calibrated:

a) the pressure gauge used for the [redacted (b) (4)] testing of the [redacted (b) (4)].

b) the digital thermocouple model # [redacted (b) (4)] used in the depyrogenation oven.

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c) the dial thermometer used in the depyrogenation oven.

d) the glass thermometer in incubator with ID # (b) (4) which is used for the incubation of environmental monitoring samples.

The above is a repeat observation from the previous FDA inspection ending on 09/17/2010.

OBSERVATION 8

Reports of analysis from component suppliers are accepted in lieu of testing each component for conformity with all appropriate written specifications, without performing at least one specific identity test on each component and establishing the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

Specifically, you do not conduct any additional testing of raw materials used to produce sterile injectable drug products. In addition, you have not qualified your suppliers to verify the reliability of the Certificate of Analysis you receive for each raw material.

The above is a repeat observation from the previous FDA inspection ending on 09/17/2010.

OBSERVATION 9

Each lot of a component that is liable to microbiological contamination that is objectionable in view of its intended use is not subjected to microbiological tests before use.

Specifically,

Certificates of analysis for raw materials used for production of finished sterile injectable drug products do not include the results of microbiological analysis for every lot. Also, your firm does not conduct further testing of lots of raw materials before acceptance and use in production of finished sterile injectable drug products.

*** DATES OF INSPECTION:**
09/24/2013(Tue), 09/25/2013(Wed), 09/26/2013(Thu), 09/27/2013(Fri), 10/02/2013(Wed)

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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."