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	02/04/2014 - 03/21/2014* FEI NUMBER 1000391015

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: John W. Hollis, President & Owner

FIRM NAME	STREET ADDRESS
John W Hollis Inc dba John Hollis Pharmacy	110 20th Avenue North
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Nashville, TN 37203-2316	Producer of Sterile 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:

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) The [redacted] (b) (4) used for [redacted] (b) (4) sterilization of pellets intended for implantation has no data to support its ability to sterilize products under its conditions of use. [redacted] have not been evaluated to ensure sterilization of finished drug products. No documentation is maintained for [redacted] (b) (4) such as [redacted] (b) (4) [redacted].

b) The autoclave used for the sterilization of finished product containers, closures, and equipment for injectable drug products has no data to support its ability to sterilize containers, closures, and equipment under its condition of use. Endotoxin burden and challenges, load configurations, temperature mapping, and heat penetration have not been evaluated to ensure sterilization of finished product containers and closures. No documentation is maintained for critical process parameters, such as time, temperature, and pressure. Autoclaved containers, closures, and equipment are stored in the autoclave bags in which they are processed. No data exists to assure sterility of these items through the time of their use, which was estimated to be a month.

c) The [redacted] (b) (4) used during [redacted] (b) (4) sterilization of injectable drug products have not been qualified to demonstrate [redacted] (b) (4) and physical and chemical compatibility for each injectable drug product formulation made from non-sterile drug components. On 2/4/14, I observed the components for an injectable drug product mixed in the preparation room without any type of environmental controls in place. Per management, this practice is performed each time an injectable drug product is made prior to [redacted] (b) (4) sterilization. No studies have been conducted to analyze the bioburden load of products and the ability of [redacted] (b) (4) to remove this increased load.

d) [redacted] (b) (4) testing is not performed each time an injectable drug product is [redacted] (b) (4) sterilized. No record of testing is documented when [redacted] (b) (4) testing is performed.

e) Smoke studies have not been performed and documented for static or dynamic conditions in the laminar air flow hood

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(LAFH), which is used in the processing of drug products intended to be sterile.

f) The incubator used for final product sterility testing has no continuous temperature monitoring. No positive and negative controls are used during testing to confirm results.

g) Your firm has not established that the media fill procedure is representative of the most challenging aseptic process performed at your establishment. The media fill procedure currently in place is representative of filling up to (b) (4) vials, while your firm occassionally fills batches with up to (b) vials. Your firm performs media fills (b) (4), with the first one beginning in November 2013.

OBSERVATION 2

Drug product containers and closures were not sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use.

Specifically, drug product containers and closures do not undergo a depyrogenation process prior to their use for injectable drug products. No endotoxin testing has been performed on containers and closures.

OBSERVATION 3

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

Specifically, personnel involved in the production of sterile drug products don a non-sterile gown, mask, shoe covers, and hair net. The non-sterile gowns are saved and re-used up to (b) (4) and the mask does not fully cover the face and neck of the operator. Sterile gloves are donned, but gloves are never sanitized during wear. On 2/4/2014, I observed an employee don sterile gloves, then proceed to touch a spray bottle containing (b) (4) and the exterior of a container of sterile wipes before proceeding with aseptic manipulations. The employee was not observed to sanitize his gloves between touching non-sterile surfaces and aseptic processing.

OBSERVATION 4

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

Specifically, plastic strip curtains are in the doorways between the sterile product compounding room, ante room, and preparation room. The strip curtains are not routinely cleaned. Garbed personnel walk through the strip curtains from the ante room into the sterile product compounding room and then back into the ante room. Gowns, which are re-used for up to (b)

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(b) (4) and any components, containers, closures, and equipment that come into contact with the curtains are potentially exposed to increased bioburden.

OBSERVATION 5

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

Specifically,

a) Non-viable air monitoring is not performed by your firm.

b) Viable air monitoring is not performed each time a drug product intended to be sterile is produced. Your firm currently performs viable air monitoring (b) (4) and has no established alert or action limits.

c) Personnel monitoring is not performed each time a drug product intended to be sterile is produced and sampling is not representative of the conditions following production. Your firm currently performs personnel fingertip testing (b) (4) immediately after gowning and has no established alert or action limits.

d) Touch-plates used to monitor the LAFH work surface are used immediately following cleaning and sanitizing and sampling is not representative of the conditions following production. Your firm currently monitors the LAFH work surface (b) (4) and uses the same touch-plate for mulitple locations on the work surface. No mapping of sampling sites is documented and your firm has no established alert or action limits.

OBSERVATION 6

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

Specifically, the air supply to the sterile product compounding room, ante room, and preparation room does not undergo any type of filtration and no pressure differentials exist between rooms; none of these areas are classified. Additionally, the LAFH located in the sterile compounding room has not undergone any type of non-viable air monitoring, which indicates it has not been qualified as an ISO 5 environment. The LAFH is used in the processing of drug products intended to be sterile.

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OBSERVATION 7

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically, your firm does not perform sterility or endotoxin testing on each batch of drug product intended to be sterile. No endotoxin testing has been performed and only one product intended to be sterile is tested [redacted] (b) (4) for sterility. Between 12/10/13 and 3/10/14, approximately (b) (4) batches of drug products intended to be sterile were produced. Since June 2013, approximately 27 sterility tests have been performed for finished drug products intended to be sterile.

OBSERVATION 8

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications and identity and strength of each active ingredient prior to release.

Specifically, your firm does not test each batch of drug product for potency prior to its release and distribution. Your firm has contract tested two batches of products for potency testing since January 2012; approximately (b) (4) batches were produced between 12/10/2013 and 3/10/2014.

OBSERVATION 9

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

Specifically, no stability program exists to scientifically justify assigned expiration dates for each drug product made by your firm. All pellets for implantation receive a 1 year expiration, most injectable drug products receive a 6 month expiration, and injectable drug products held under refrigeration receive a 90 day expiration.

OBSERVATION 10

Each lot of components, drug product containers, and closures is not withheld from use until the lot has been sampled, tested, examined, and released by the quality control unit.

Specifically, drug components are accepted based on the manufacturer's certificate of anaylsis (CoA). Supplier's have not been qualified and no testing has been conducted to verify the reliability of the CoA.

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OBSERVATION 11

Procedures describing the calibration of instruments, apparatus, gauges and recording devices are not written or followed.

Specifically, your firm does not routinely calibrate equipment or have a procedure in place for equipment calibration. Equipment includes the (b) (4) (b) (4) used for product and equipment sterilization, thermocouples in all refrigerators used for the storage of raw and finished drug products, the pressure gauge used for (b) (4) testing, and the thermometer in the incubator used for all environmental samples and in-house finished product sterility testing.

*** DATES OF INSPECTION:**
02/04/2014(Tue), 03/10/2014(Mon), 03/11/2014(Tue), 03/12/2014(Wed), 03/13/2014(Thu), 03/21/2014(Fri)

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