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	12/01/2014 - 12/16/2014* FEI NUMBER 3004593468

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carol D. Harwood, Branch Manager

FIRM NAME	STREET ADDRESS
Coram Healthcare Corp. of Indiana	1290 Arrowhead Ct, Ste A
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Crown Point, IN 46307-7766	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

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

Specifically,

During qualification of the firm's cleanrooms ("ISO 7/ISO 8") and 2 laminar flow hoods ("ISO 5"), performed on 9/08-10/2014, the firm failed to complete an investigation for an OOS result obtained during viable air particle testing of the ("ISO 7") Processing room on 9/10/2014 (result=11cfu/m^3; specification: (b) (4)). Additionally, an investigation into another OOS result during viable air particle testing of the "ISO 8" Ante room was inadequate, in that (b) (4) surface sample testing was used to evaluate cleaning effectiveness over (b) (4) rather than using the same viable air particle test method (result=32cfu/m^3; internal specification: (b) (4)).

OBSERVATION 2

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

Specifically,

i. Environmental monitoring is not performed (b) (4) during production in the processing areas, to evaluate the quality of the aseptic processing environment and assess whether aseptic conditions are maintained.
   a. Non-viable particulate monitoring is performed in the classified cleanrooms [Prep room ("ISO 8"), Ante room ("ISO 8"), Processing room ("ISO 7")] and (b) (4) laminar flow hoods ("ISO 5") once every (b) (4)
   b. Viable air monitoring is performed in each of the (b) (4) laminar flow hoods ("ISO 5") once every (b) (4)
   c. Viable surface monitoring is performed in the classified cleanrooms [Prep room ("ISO 8"), Ante room ("ISO 8"), Processing room ("ISO 7")] and (b) (4) laminar flow hoods ("ISO 5") once (b) (4)
   d. Personnel fingertip monitoring is performed initially for each qualified operator and once every (b) (4) thereafter.

ii. "In Situ" smoke studies, during dynamic conditions, were not performed to evaluate unidirectional air flow patterns over product in the firm's (b) (4) laminar flow hoods ("ISO 5") which were certified on 9/08-10/2014.

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iii. Growth promotion testing for environmental monitoring growth media (TSA and TSB) has never been performed, so as to ensure that it promotes growth of gram positive/negative bacteria, yeast, and molds.

For example: Vancomycin750mg/250ml NS IV, Rx #(b) (6), (b) (4) processed on 11/12/2014 and Cefazolin 2gm/20ml SWFI IV, Rx #(b) (6), (b) (4) processed on 11/21/2014.

OBSERVATION 3

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

Specifically,

i. Adequate validation of aseptic processing operations, specifically, process simulations (media fills) have not been performed under representative worst-case aseptic processing conditions to assure the sterility of drug products. Currently, procedure I305-015 *Aseptic Technique Process Validation*, requires the preparation of (b) (4) for initial personnel competency in aseptic technique and (b) (4) thereafter on just (b) (4). While the media fill procedure includes the use of both, (b) (4), it is not performed on a representative worst-case lot size. For example: (b) (4) units of Piperacillin/Tazobactam 3.375gm/100ml NS MB+ IV/Rx (b) (6), (b) (4) aseptically filled on 12/02/2014 and (b) (4) units of Meropenem 2gm/100ml NS HomePump aseptically filled on 12/03/2014.

ii. Inadequate aseptic practices and techniques performed at your facility that were observed on 12/02/2014 during aseptic processing of Piperacillin/Tazobactam 3.375gm/100ml NS MB+ IV/Rx (b) (6), (b) (4) include the following:
- Occurrences were observed where the operator's gloves were not always appropriately sanitized with "sterile" (b) (4) after drug product materials were transferred from the plastic tote container in the "ISO 7" Processing room to the "ISO 5" laminar flow hood. Additionally, outer wrapping of drug product and/or supplies, like vial caps and needle covers, were left on the workbench surface in the "ISO 5" laminar flow hood, after which were then gathered and transferred to the operator's gown pocket, followed by immediate reentry of gloved hands into the laminar flow hood without sanitization being performed.
- The operator was observed to rest their gloved hand(s) on the workbench surface of the "ISO 5" laminar hood at times.
- The operator was observed to recross-over the demarcation line in the ante room ("ISO 8") while gowning prior to entry into the Processing room ("ISO 7").
- The vent grill cover in the aseptic Processing room ("ISO 7") was observed to be obstructed with a chair and cart placed in front of it.

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OBSERVATION 4

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

The monitoring frequency of pressure differentials between aseptic processing areas and surrounding areas of lower air quality is only recorded once "(b) (4) as per procedure, I305-016 *Cleanroom Specifications, Certification and Maintenance*, and not during all times when processing occurs. Assurance was not provided to support that a temporary loss in differential pressure during filling operations would be detected and appropriately handled. For example: Vancomycin750mg/250ml NS IV, Rx (b) (6), (b) (4) processed on 11/12/2014 and Cefazolin 2gm/20ml SWFI IV, Rx (b) (6), (b) (4) processed on 11/21/2014.

OBSERVATION 5

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

Specifically,

Gowning of personnel performing aseptic operations in the "ISO 5" laminar flow hoods is inadequate in that protective gowns, facemasks, and hair nets worn during aseptic processing are not sterile. Additionally, the current gowning method leaves facial skin (eyes and forehead) and tops of shoes/shoelaces exposed. Personnel shoes are not facility-dedicated and are also worn in non-classified areas. For example, gowning worn was observed during the aseptic processing of Piperacillin/Tazobactam 3.375gm/100ml NS MB+ IV/Rx # (b) (6), (b) (4) on 12/02/2014.

OBSERVATION 6

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

Specifically,

The suitability, efficacy, and limitations of cleaning equipment and disinfecting agents have not been appropriately assessed to ensure potential contaminants are adequately removed from surfaces in the ISO classified areas.

i. Procedures for cleaning do not include the use of sporicidal agents in the laminar flow hoods ("ISO 5").

ii. Beta lactam controls do not include data to support that the spill procedure clean up including use of (b) (4)

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(b) (4) would be effective in mitigating potential beta lactam residues if present. Several beta-lactam products, such as Cefepime, Cefazolin, and Ceftiaxone, are routinely aseptically processed in the laminar flow hoods ("ISO 5") that are also used for non-beta-lactam products. For example, Cefepime 2g/20ml SWFI IV Push, Rx #31677, and Vancomycin 1g/250ml NS V Eclipse, Rx #31676, were both aseptically processed on the same day, 11/20/2014.

iii. Non-sterile disposable lint-free wipes are used to wipe surfaces in the laminar flow hoods ("ISO 5") with "sterile" (b) (4) [redacted]. For example, such wipes were used for cleaning the "ISO 5" laminar flow hood prior to the aseptic processing of Piperacillin/Tazobactam 3.375gm/100ml NS MB+ IV/Rx #31756-0 on 12/02/2014 and Meropenem 2gm/100ml NS HomePump/Rx #31689-4 on 12/03/2014.

OBSERVATION 7

The written stability testing program is not followed.

Specifically,

According to procedure, I305-030 *Beyond Use Dating*, the firm is required to perform sterility testing over the labeled shelf life in representative container closure systems: "In order to provide the optimal BUD for CSPs ("compounded sterile preparations"), each company infusion pharmacy shall send a sample of CSPs, such as Parenteral Nutrition, solutions to an independent certified laboratory. The laboratory shall test the sterility of each solution to allow Coram Specialty Infusion Services,..., to provide extended BUD based on the results of this testing. The BUD determination will consist of an initial and ongoing test."

Currently, the firm has not performed sterility testing for any of the "sterile" drug products prepared at the facility in support of assigned BUDs. Examples include:
-Vancomycin750mg/250ml NS IV dial-a-flow, beyond use date of 21 days refrigerated (Rx (b) (4), (b) (6))
-Cefazolin 2gm/20ml SWFI IV Push, beyond use date of 21 days refrigerated (Rx (b) (4), (b) (6))
-Meropenem 2gm/100ml NS HomePump, beyond use date of 8 days refrigerated (Rx # (b) (4), (b) (6))

OBSERVATION 8

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

Specifically, aseptically processed "sterile" injectable drug products by the firm are released and distributed without having been tested for sterility and endotoxins. For example: Vancomycin750mg/250ml NS IV, Rx # (b) (4), (b) (6) shipped on 11/13/2014 and Cefazolin 2gm/20ml SWFI IV, Rx (b) (4), (b) (6) shipped on 11/23/2014.

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OBSERVATION 9

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

Specifically, aseptically processed "sterile" injectable drug products by the firm are released and distributed without having been tested for potency. For example: Vancomycin750mg/250ml NS IV, Rx #[redacted] shipped on 11/13/2014 and Cefazolin 2gm/20ml SWFI IV, Rx [redacted] shipped on 11/23/2014.

*** DATES OF INSPECTION:**
12/01/2014(Mon), 12/02/2014(Tue), 12/03/2014(Wed), 12/04/2014(Thu), 12/05/2014(Fri), 12/16/2014(Tue)

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