Coram®

CVS specialty infusion services

May 31, 3017

VIA EMAIL AND EXPRESS MAIL

Mr. Arthur O. Czabaniuk
District Director
Department of Health and Human Services
Food and Drug Administration
Detroit District Office
300 River Place, Suite 5900
Detroit, MI 48207
Art.Czabaniuk@fda.hhs.gov

Dear Mr. Czabauk:

On behalf of Coram Healthcare Corporation of Indiana ("Coram"), I authorize the United States Food and Drug Administration (FDA) to publicly disclose the information described below on FDA's web site. I understand that the information that is disclosed may contain confidential commercial or financial information or trade secrets within the meaning of 18 U.S.C. § 1905, 21 U.S.C. § 331, and 5 U.S.C. § 552(b)(4) that is exempt from public disclosure under those statutory provisions and/or relevant FDA regulations. I agree to hold FDA harmless for any injury caused by FDA's sharing the information with the public.

Information to be disclosed: Coram's letter dated 05/16/2017 excluding attachments/exhibits, which responds to FDA's Form 483 dated 04/26/2017.

Authorization is given to FDA to disclose the above-mentioned information which may include confidential commercial or financial or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of Coram and my full name, title, address, telephone number, and facsimile number is set out below for verification.

Respectfully yours,

Carol Harwood

Carol Harwood
Senior Manager Branch Operations – Infusion
1290 Arrowhead Court, Suite A
Crown Point Indiana, 46307
Telephone 219-661-0272
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Coram®
CVS specialty infusion services

May 16, 2017

VIA EMAIL AND EXPRESS MAIL

Mr. Arthur O. Czabaniuk
District Director
Department of Health and Human Services
Food and Drug Administration
Detroit District Office
300 River Place, Suite 5900
Detroit, MI 48207
Art.Czabaniuk@fda.hhs.gov

Re: Form FDA 483 Response by Coram Healthcare Corporation of Indiana, Crown Point Facility ("Coram Crown Point"); FEI No. 3004593468

Dear Mr. Czabaniuk:

Please accept this correspondence in response to the Form FDA 483 Observations ("Form 483") issued to Coram's Crown Point facility, located at 1290 Arrowhead Court, Crown Point, Indiana 46307, and dated April 26, 2017.[1]

Coram Crown Point hereby requests that the FDA publicly disclose this response, excluding the exhibits, on the FDA's website in the event that the Form 483 is posted. Coram Crown Point understands that this response may contain confidential commercial or financial information or trade secrets within the meaning of 18 U.S.C. § 1905, 21 U.S.C. § 331(y)(2) and 5 U.S.C. § 552(b)(4) that is exempt from public disclosure under those statutory provisions and/or relevant FDA regulations.

Coram Crown Point has a great deal of respect for the FDA investigators and the function they perform, and we take very seriously the FDA audit findings. Coram Crown Point is committed to continuous quality improvement and to evaluating our processes, and, as reflected by the corrective action plans outlined herein, we are committed to addressing each observation diligently and thoroughly.

[1] FDA's Form FDA 483 for the Coram Crown Point facility was addressed to "Bryan O'Neill, Director of Quality." Bryan O'Neill, however, is not a Coram Crown Point employee or manager. Consistent with FDA's practice, the Form 483 should have been addressed to Carol Harwood, Branch Manager of the Coram Crown Point facility under inspection.

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If you have any questions about the content of this letter, please do not hesitate to contact me.

Respectfully yours,

Carol Harwood

Carol Harwood
Senior Manager Branch Operations - Infusion
Carol.Harwood@coramhc.com

CC: Bill Bolgar, CVS Caremark, Vice President, Clinical Operations
Wanda Rogers, CVS Caremark, Director, Pharmacy
Florence Crisp, CVS Health Vice President and Senior Legal Counsel, Litigation and Regulatory
Emilie E. Kahn, U.S. Food & Drug Administration Investigator
Sarah E. Rhoades, U.S. Food & Drug Administration Investigator

Observation 1

Equipment, materials, and/or supplies are not disinfected prior to entering the aseptic processing areas.

Specifically, inadequate aseptic practices were observed while transferring materials on 4/18/2017 during the aseptic processing of 7 units of Ertapenem 1 gm/100ml Rx (b) (6), (b) (7)(C), including the following:

-Pharmacy technicians wiped down IV bags with sterile IPA but without gloves prior to putting bags in prep room (ISO-8) and then directly moving bags from the prep room (ISO-8) into the hood (ISO-5) without disinfecting the bags;
-Vials of sterile drug products were removed from product boxes and were not cleaned. These vials were subsequently placed directly under the hood (ISO-5) without being disinfected;

Additionally, while bins that are used for transferring all of the components and ingredients for sterile drug production are wiped down on the inside; these bins are routinely stacked on top of each other with the components such as vials inside. Therefore, vials of active ingredients are touching the bottom of a bin while being transferred from the prep room (ISO-8) to the compounding room (ISO-7) and these vials are subsequently placed directly under the hood (ISO-5) without being disinfected.

Coram Crown Point Response to Observation 1

The pharmacy technician observed on 04/18/2017 did not comply with Coram policies. The appropriate process used to disinfect material is repeated in multiple policies, all of which emphasize to staff the importance of disinfecting material before transferring to a lower ISO classification. The disinfection of material is documented in the following policies:

- INFPH-048133: GUIDELINES FOR ASEPTIC TECHNIQUE (I305-018) (Exhibit 1)
- INFPH-00500: CLEANROOM STANDARDS OF BEHAVIOR (I305-005) (Exhibit 2)
- INFPH-00506: GENERAL COMPOUNDING GUIDELINES (I305-020) (Exhibit 3)

Corrective Action for Observation 1:

1. An aseptic processing trainer will be on site to retrain the Coram Crown Point staff on all aspects of cleanroom and aseptic processing policies and procedures. To ensure continued compliance, the staff will be observed on a weekly basis for three (3) months. Retraining by the aseptic process trainer will be completed by May 30, 2017. Coram Crown Point will provide FDA a copy of the training documentation upon request. The Coram Crown Point staff will continue to be monitored per our existing semiannual personnel validation procedure.

Observation 2
The use of sporicidal agents in the cleanroom and/or the ISO 5 area is inadequate.

Specifically, the adequacy of cleaning frequency has not been appropriately assessed to ensure potential contaminants are removed from the surfaces in the ISO-5 classified area. For example, sporicidal agents that are used on a monthly basis are insufficient to assure the prevention of spores when, on a daily basis, intake materials are not disinfected prior to being placed under the ISO-5 hood. In addition, your firm does not have data to support that the current established contact time of 10 minutes is sufficient to remove sporicidal activity.

Coram Crown Point Response to Observation 2

Neither section 503A of the FD&C Act nor USP<797>, *Pharmaceutical Compounding – Sterile Preparations*, dictates or specifically addresses the frequency of disinfection with a sporicidal agent. USP<1072>, *Disinfectants and Antiseptics*, recommends the rotation of an effective sporicidal agent either weekly or monthly. Similarly, disinfectant dwell time studies are not required under section 503A of the FD&C Act or USP<797>, *Pharmaceutical Compounding – Sterile Preparations*. The draft guidance for industry, issued August 2016, *Insanitary Conditions at Compounding Facilities*, recommends a sufficient disinfectant contact time be utilized. Notwithstanding that the guidance is currently in draft form and expressly notes that it "contains non-binding recommendations" and is "not for implementation," Coram Crown Point will voluntarily and proactively follow FDA's recommendations regarding the use of a sufficient disinfectant contact time.

Corrective Action for Observation 2:

1. Coram Crown Point will increase cleaning with sporicidal agent in the ISO 5 area from monthly to weekly. We intend to complete the revisions to our current cleanroom cleaning policy reflecting this change by May 20, 2017, and will provide a copy of the revised policy to FDA upon request. Coram Crown Point will train its employees on the revised policy upon implementation, and will provide FDA documentation of that training upon request.

2. Coram Crown Point will engage the services of a 3rd party analytical microbiology laboratory to perform testing to ensure contact time is adequate. The cleaning and disinfecting program at the Crown Point facility will be modified, if necessary, based upon testing results. Coram Crown Point will provide FDA a copy of the revised procedures, if any, upon request.

Observation 3
Beta-lactam drugs are produced without adequate cleaning procedures to prevent cross contamination. Your firm's cleaning procedures are limited to use of sterile water and IPA (70%). There is no dedicated area for processing Beta-lactam products. Your firm has two ISO-5 hoods and beta-lactam products are processed in both. For example, 7 units of Ertapenem 1gm/100ml Rx (b) (6), (b) (7)(C) and 21 units of Vancomycin 1.5 gm/250ml Rx (b) (6), (b) (7)(C) were both processed under the same hood on 4/18/2017.

This is a repeat observation.

Coram Crown Point Response to Observation 3

Neither section 503A of the FD&C Act nor USP<797>, *Pharmaceutical Compounding – Sterile Preparations*, specifies cleaning or segregation requirements specific to beta-lactam products. The current cleaning policy was developed per USP<797> in order to minimize risk of microbial contamination and cross-contamination of compounded sterile preparations. In August 2016, (and over 18 months *after* the FDA's initial inspection of the Crown Point facility, which resulted in a similar Form 483 observation), the FDA issued draft guidance for the industry, *Insanitary Conditions at Compounding Facilities*. The draft guidance notes FDA's concern of cross-contamination of beta-lactam products with non-beta-lactam products.

Notwithstanding that the guidance is currently in draft form and expressly notes that it "contains non-binding recommendations" and is "not for implementation," Coram Crown Point will voluntarily and proactively implement the corrective action below consistent with the draft guidance for industry, *Insanitary Conditions at Compounding Facilities.*

Corrective Action for Observation 3:

1. Coram Crown Point has dedicated a laminar flow hood in the ISO 5 cleanroom for beta-lactam production.

Observation 4
Aseptic environmental conditions are not assured by current monitoring practices.

Specifically,

The dynamic smoke study video that we viewed demonstrated an operator standing at the hood making manipulations with one IV bag at the top of the hood. This was not representative of aseptic processing operations observed from 04/17-19/2017. We observed your staff aseptically processing on the bench, with components, equipment (such as the TPN mixer or the repeater pump), and other items which can affect laminar air flow.

Coram Crown Point Response to Observation 4

Corrective Action for Observation 4:

1. Coram Crown Point will complete a new smoke study under dynamic conditions. The dynamic conditions will be representative of production processes. This will be completed by June 30, 2017. Coram Crown Point will provide FDA the results of the smoke study upon request.