

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 19701 Fairchild Irvine, CA 92612 (949) 608-2900 Fax: (949) 608-4417 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 05/06/2013 - 05/17/2013*
	FEI NUMBER 3003542383

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Micheal R. Blaire, CEO / Pharmacist in Charge

FIRM NAME Diamondback Drugs of Delaware, LLC	STREET ADDRESS 7631 E Indian School Rd
CITY, STATE, ZIP CODE, COUNTRY Scottsdale, AZ 85251-3607	TYPE ESTABLISHMENT INSPECTED 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 I OBSERVED:

PRODUCTION SYSTEM

OBSERVATION 1

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

Specifically,
Environmental Monitoring of the firm's ISO 5 Hood environments and ISO 7 Cleanroom Environments used to produce sterile drug products does not represent actual production, for example:

- a) Lack of active viable particulate air monitoring - ISO 5 and ISO 7. There is no active monitoring of the viable air particulates during aseptic processing of drug products in the ISO 5 or ISO 7 environments. There is only (b) (4) viable air particulate monitoring conducted at static room condition by an outside contractor.
- b) Lack of active non-viable particulate air monitoring - ISO 5 and ISO 7. There is no active monitoring of the non-viable air particulates during aseptic processing of drug products in the ISO 5 or ISO 7 environments. There is only (b) (4) non-viable air particulate monitoring conducted at static condition by an outside contractor.
- c) Lack of active monitoring of differential pressures. There is no monitoring of the cleanroom pressure differentials during aseptic processing of drug products. There are no gauges to measure pressure differentials between the cleanroom and unclassified areas. There is one pressure gauge located on one of the firm's hoods; however, there is no reading of this gauge by the firm. Pressure differentials are only measured by the firm's outside contractor every (b) (4).
- d) Lack of personnel monitoring. There is no monitoring of personnel gloves or arms post shift of aseptic processing of drug products in the ISO 5 hoods.
- e) Insufficient frequency of environmental monitoring of the ISO 5 hood (work surfaces) and Cleanroom ISO 7 (surfaces, walls, ceilings, floors). Environmental monitoring is only conducted every (b) (4) by an outside contractor.

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OBSERVATION 2

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

Specifically,

- a) Media fills conducted by the firm within the ISO 5 environment do not adequately represent actual production in that,
- i. Media fills by the firm are performed within approximately (b) (4) minutes, however actual production of drug products such as Buprenorphine HCl vials are produced in batches filled over an hour period or more.
 - ii. Media fills by the firm result in a total of approximately vials filled (including control vials) however, actual production of drug products such as Buprenorphine HCl vials result in a batch size of (b) (4) vials.
 - iii. The media fill record does not include sufficient detail to establish that conditions mimic those that occur during routine production, such as, number of individuals in the room, equipment placement, doors opening and closing, etc.

Furthermore, there is no documentation made of which ISO 5 Environment or room was used to conduct each media fill.

- b) In October 2012, certification conducted by an outside contractor for the firm's cleanroom environments used to aseptically process drug products yielded an out of specification result in one location of the firm's ante-room for non-viable particulate air. The ante-room is separated from the ISO 7 cleanroom by a plastic flexible curtain. The following result was reported:

Sampling Location	5.0µ per m ³ - Result (Specification ≤ (b) (4))
Ante-room, Location 1	4,750 particulates

There was no re-sampling of the location performed. Although the location exceeded the specification at the static condition, the room was still certified.

- c) Certification conducted by an outside contractor for the firm's ISO 5 environments used to aseptically process drug products includes performing airflow pattern studies (smoke studies) to demonstrate the flow of HEPA filtered air within the Laminar air flow hoods. There is no recording made of the smoke study to confirm that the airflow is smooth, laminar, and without turbulence. Furthermore, there is no smoke studies performed within the ISO 7 cleanrooms.

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OBSERVATION 3

Protective apparel is not worn as necessary to protect drug products from contamination.

Specifically,

During sterile drug production, a technician was observed wearing non-sterile gowning with exposed skin within the cleanroom environment. The firm's gowning components for entry in the cleanroom includes: shoe covers, head and facial hair covers, face mask, lab coat, and gloves. The gowning components are non-sterile. There is no provision to cover or protect the areas of the face around the eyes and area around the neck. During the walkthrough of the facility on 05/06/13, an operator was observed with exposed skin around the eyes and neck area in the cleanroom ISO 7 environment in which the ISO 5 Vertical Laminar air flow hoods are located. In addition, although the non-sterile gloves are wiped with (b) (4) periodically, the operator was observed contacting sterilized rubber stoppers directly with his gloved hands, there is no use of forceps.

During the inspection, the firm ordered sterilized gloves and sterile sleeves and implemented its use within the cleanroom for aseptic processing.

OBSERVATION 4

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

Specifically,

- a) The firm does not conduct any (b) (4) testing of the (b) (4) used as the sterilizing step for drug products produced such as Buprenorphine HCl. The firm does not have any written procedure or equipment to conduct (b) (4) testing. Buprenorphine HCl is aseptically processed and there is no terminal sterilization of the finished drug product.
- b) The firm prepares components (vials and stoppers) via moist heat sterilization utilizing either of the firm's (b) (4) (b) (4) Autoclave, both located in the ISO 7 cleanroom. There is no data to demonstrate that the firm's practice of autoclaving glass vials and rubber stoppers used in (b) (4) operations renders them clean, sterile, and pyrogen free. There is no rinsing or washing of the vials and stoppers conducted prior to the autoclave sterilization run. Load patterns have not been established and the cycles have not been adequately validated.
- c) The firm runs Biological indicators on a (b) (4) basis within the autoclaves to monitor the equipment's sterilization capability. However, the firm conducts the biological indicator runs on an (b) (4) and there is no runs performed with the autoclave chamber filled with (b) (4). In addition, the firm does not record which program cycle was run.
- d) There is no clear instruction outlining which of the six (6) pre-programmed cycles to use for vials and/or stoppers.

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Although there is a written procedure, there is not enough detail instructing personnel on which autoclave programmed cycles to use. In addition, the written procedure is not followed regarding the scheduled maintenance of the equipment. It was explained that operators are trained through on-the-job training, however there are no records documenting the training.

OBSERVATION 5

The separate or defined areas necessary to prevent contamination or mix-ups are deficient.

Specifically,

The firm's two (2) ISO 5 laminar flow hoods are located in the ISO 7 cleanroom #1. Adjacent to each hood are the firm's (b) (4). The autoclave doors when opened after a sterilization cycle generates steam that is introduced into the ISO 7 room and may be introduced into the ISO 5 laminar flow hoods. There is no separate venting for the autoclaves exhaust.

OBSERVATION 6

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

Specifically,

The firm labels Preservative-free Buprenorphine HCl, Injectable vials with a "Discard after" date which is 6 months from the date of formulation. However, the firm has not established this use-by date with real-time product testing to assure the products safety, its identity, strength, and that it meets the quality and purity characteristics which it purports or is represented to possess. The firm provided documentation for a time-point realtime study of Buprenorphine HCl PF (C) 0.3mg/ml lot 100826:94@106 that was tested for Sterility per USP up to a 4 month time point. However, there was no potency testing performed on the samples.

In addition, the firm's formulation worksheet for Buprenorphine, Preservative Free, 0.6mg/ml Injectable, Lot# 121119:71@9 states the following, "CONTAINS NO PRESERVATIVE. NOT FOR MULTIPLE DOSE USE. FILL 1ML SYRINGES". However, the firm fills the bulk into 10mL amber glass vials, and there is no instruction provided to the end user indicating that the product is "NOT FOR MULTIPLE DOSE USE".

OBSERVATION 7

Batch production and control records do not include the specific identification of each batch of component used for each batch of drug product produced.

Specifically,

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Formula worksheets did not include lot information for the following items used in the production of sterile products:

- a) 10mL vials and rubber stoppers used in the production of Buprenorphine, Lot# 121119:71@9 which are sterilized (b) (4).
- b) (b) (4) used in the production of Buprenorphine, Lot# 121119:71@9 at the sterilizing step of the bulk product.

Furthermore, the formula worksheets do not include the final number of vials that were filled.

OBSERVATION 8

Individual equipment logs do not show time, date, product, and lot number of each batch processed.

Specifically,

The firm does not maintain a use log for each of the (b) (4) ISO 5 hoods used to produce sterile drug products. The firm's laminar air flow hoods are not dedicated. There is no documentation to show what products were produced within the units and the equipment is not recorded on the individual product formulation sheets.

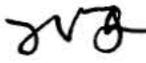
QUALITY SYSTEM

OBSERVATION 9

Written records are not always made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications.

Specifically,

- a) During the walkthrough of the facility on 05/06/13, an agar media plate with visible microbiological colony growth was observed in the firm's cleanroom suite, on a counter in the ante-room in plain view. It was later determined that the agar plate was left by an outside contractor on or about 04/29/13. Even after multiple room entries to include daily cleaning of the rooms, the agar plate was not questioned by firm personnel or cleaning staff. There was no written investigation conducted in response to the discovery of the agar plate with microbiological growth located in the firm's cleanroom suite.
- b) Product testing conducted in response to complaint #030413:A for Buprenorphine HCl, Lot# 121119:71@9 yielded out of specification results for potency (Result= 81.5% and 83.8%, Specification = 90-110%). There was no investigation conducted in response to these out of specification results.

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05/06/2013(Mon), 05/07/2013(Tue), 05/09/2013(Thu), 05/16/2013(Thu), 05/17/2013(Fri)

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