DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
22215 26th Ave SE Suite 210 Bothell, WA 98021 (425) 302-0340 Fax:(425) 302-0404 Industry Information: www.fda.gov/oc/industry	11/03/2014 - 12/02/2014 FEI NUMBER 3010477

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Rajesh (nmi) Kapoor, Ph.D., Global Head, Quality and Senior Vice President

FIRM NAME	STREET ADDRESS
Jubilant HollisterStier, LLC	3525 N Regal St
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Spokane, WA 99207-5788	Sterile Drug Manufacturer

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 are not established and followed.

Specifically,

A. Filling Line 2 has a (b) (4) located inside the ISO 5 enclosure that connects with the (b) (4) to transfer partially stoppered vials from the filling line to the (b) (4) This (b) (4) must be partially moved into ISO 6 conditions during routine operations to allow movement of operators through the ISO 5 area to the back of the room to conduct operations such as (b) (4), aseptic (b) (4) (b) (4)), placement and removal of settling plates, line adjustments, etc. On 11/03/14, while observing set up of the Filling Line 2 in preparation for a (b) (4) media fill, we observed operators crossing multiple times through the ISO 5 enclosure to perform the operations described above. Due to the limited space, we observed that, every single time the operators crossed through the ISO 5 enclosure, they brushed the lower part of their gowns against the (b) (4) Although the operators were observed to wipe the doors of the enclosure with (b) (4) soaked wipes every time they moved through the enclosure, the first shift operators were never observed to wipe the (b) (4). Additionally, there are no written procedures governing this operation.

B. On 11/06/14 during the setup of and filling for Yellow Jacket Venom batch A1400084 in the SLM area on the (b) (4) filling line, the following was observed:
   i. In the SLM manufacturing area, the vessel containing Yellow Jacket Venom batch A1400084 was pushed from the (b) (4) into the ISO 7 portion of room (b) (4) on

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a cart. Shortly thereafter, an operator picked up the vessel and placed it inside the (b) (4) filler. No disinfection of the vessel was observed prior to its placement within the aseptic filling line.

ii. During both set up and filling operations, an operator was observed to remove a tray of vials from the cart stored within the ISO 7 area of room (b) (4) and placed the tray on the (b) (4) . No disinfection of the tray was observed. The vial trays are not monitored as part of the environmental monitoring program.

iii. There is a plastic hanging curtain in room (b) (4) which separates the ISO 7 area of the room from the ISO 5 fill room. An operator was observed to touch the curtain with one or both hands and many of the times she did this with her finger tips as she moved between the two areas of the room. During setup, this was observed to occur 10 times and five of the times she touched the curtain with both hands. During the filling of the vials, this was observed to occur another 10 times and 3 of the times she touched the curtain with both hands.

C. The control over Cold Room (b) (4) (ISO 7) within the SLM is inadequate in that:

i. The Interim and Final Acceptance Reports which were generated for the Environmental Monitoring Performance Qualification (EMPQ) that was performed between April and May 2014 for SLM, failed to address the fungal isolates recovered during the study. Both of these reports were approved by the Quality Unit.

ii. Due to its design, Cold Room (b) (4) (where (b) (4) allergenic extract bulk products (WIP) are stored) cannot be adequately cleaned. Additionally, fungal isolates have been recovered from this room.

D. Two different types of goggles were observed on employees working in the ISO 5 fill room inside the Small Lot Manufacturing area (SLM). One of the goggles (b) (4) is similar to a ski goggle with two ½ by 1 inch openings in the top of the goggles and a 1+ inch thick cloth-like elastic strap. The other goggle has smaller openings at the top which have a covering over them with a ½ inch elastic strap. The goggles are sanitized with (b) (4) before and after each use which is not documented. The goggles are not sterile and there is no defined use period. The firm has not evaluated the risk of contamination to the aseptic area from the openings on the tops of the goggles.

E. On 11/06/14, operators in the ISO 5 SLM manufacturing room were observed using pens to write on the labels of the active and passive (b) (4) plates that were then placed inside the (b) (4) fill line.

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The pens are not sterile.

F. The smoke studies performed in the ISO 5 (b) (4) area of SVP Line 1 are inadequate in that there is insufficient smoke to clearly show unidirectional air flow, the dynamic portion of the smoke study at the (b) (4) included an operator who did not move, and the study did not include smoke near the window on the back side of the (b) (4) area which has two 2-3 inch holes that were open to the ISO 8 room in order to perform (b) (4)

G. For personnel monitoring, on 11/04/14, during the setup for the filling of Albumin Saline with Phenol batch C1400228 in SVP-1, after making an aseptic (b) (4) an operator was observed to spray his hands with (b) (4) and rub them, and used wipes saturated with (b) (4) to disinfect the inside of the doors. The operator then had his fingertips plated. At the time of the fingertip monitoring, his gloves were shiny and appeared wet from the (b) (4)

H. The corrective action to Observation 2A from the Form FDA 483 issued on 12/14/12 is inadequate. SOP 605.27 R-16 entitled "Set Up and Operation of the (b) (4) Filler" does not reflect current practice in that as per the procedure (b) (4) used on the (b) (4) Filler are to be stored in bottles containing (b) (4) when not in use. In practice the (b) (4) are stored in empty bottles after being wiped with a wipe saturated with (b) (4)

I. The following was observed in the (b) (4) Filler area (where venom allergenic extract products are aseptically filled):

   i. A gap between a light cover and its housing for a light located in the ISO5 area above and in the vicinity of the location where open empty vials are loaded onto the filler.

   ii. Tape-like material on a rigid barrier located on the filler within the ISO5 area.

OBSERVATION 2

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

Specifically, on June 11, 2013, the firm opened incident 2013-0209 to investigate black residue which was observed on the (b) (4) for (b) (4) after the filling of Albumin Saline with Phenol batch C1300170 in SVP-1. There is no grease or lubricant used on the

equipment or (b) (4) The (b) (4) are single use and are inspected along with the clean equipment prior to the equipment being setup for (b) (4) sterilization. The firm did not perform any microbial or chemical testing on the black residue to determine its identity. No root cause was confirmed but the likely cause was documented as being "due to the (b) (4) rubbing on the (b) (4) during the run". The investigation closed with the following: "The investigations were found to be thorough and complete in identifying the root cause, corrective action, and potential impact of the excursion. There is no quality impact to the JHS facility, processes, or the manufacture of any other product at JHS...." This investigation was approved by QA on 8/30/13. For Albumin Saline with Phenol batch C1300170, (b) (4) vials, were released by QA for distribution on 11/04/13.

OBSERVATION 3

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Specifically, the procedure: Reporting Potential Adverse Information on Product Quality and Safety, SOP 101.4, states if (b) (4) complaints are received for the same batch and category that this would be a trend and that the Director of Regulatory Affairs, Director of the Quality Unit, President of ABU, and Manager QA Compliance are to be notified and that additional actions such as retain sample testing may occur. The following files were deficient in that no trends were identified and there was no documentation that management was notified or if additional actions were taken:

i. On 4/15/13, complaint (T2013-151) of a broken vial for Albumin Saline with Phenol for batch C1200281. The database query documented two other complaints for broken vials for this same batch.
ii. On 8/14/14, complaint (M2014-009) for 4 patients who all had adverse events after receiving Candida Albicans batch E1401692. The database query documented one other adverse event from the same batch.
iii. On 9/10/14, complaint (M2014-011) for 3 patients who all had adverse events after receiving AP Dog Hair and Dander batch E1303255.
iv. On 9/23/14, complaint (M2014-013) for 3 patients who all had adverse events after receiving AP Dog Hair and Dander batch E1400648. Two additional adverse events for the same batch were received following this report.

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OBSERVATION 4

Batch production and control records do not include complete information relating to the production and control of each batch.

Specifically, actual (b) (4) are not documented in allergenic extract batch records. As per SOP 901.1 entitled "Sterile (b) (4) of Extracts and Diluents" the maximum (b) (4) allowed during (b) (4)

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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."