DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

| DISTRICT OFFICE ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| Director, Division of Inspections and Surveillance<br>FDA/CBER/Office of Compliance and Biologics Quality<br>10903 New Hampshire Avenue (WO71-5128)<br>Silver Spring, MD. 20993-0002 Tel:240-402-9159<br>Industry Information: www.fda.gov/oc/industry | 05/08 - 05/16/2017<br>FEI NUMBER<br>3003153579 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Jeffrey R. Broadfoot, Senior Director, Quality Assurance Bioscience Division

| FIRM NAME | STREET ADDRESS |
|---|---|
| Cangene Corporation dba Emergent Biosolutions | 155 Innovation Drive |
| CITY, STATE AND ZIP CODE | TYPE OF ESTABLISHMENT INSPECTED |
| Winnipeg, Canada R3T 5Y3 | 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 (I) (WE) OBSERVED:

1. Aseptic processing areas are deficient regarding air handling systems that maintain air quality. The firm has experienced recurring HEPA filter failures during the last three (3) (b) (4) Hepa filter certifications. Consequently, a BPDR was submitted was on July 18, 2016 relating to Quality Notification 310000740.

A. Quality Notification 3100000138 - The (b) (4) certification of the high efficiency particulate air (HEPA) filters in the (b) (4) and (b) (4) disclosed HEPA filter failures on November 26, 2015. (b) (4) exceeded the velocity action limits ( (b) (4) ) and (b) (4) failed the filter integrity test at 0.55% (Limit: (b) (4) ).

B. Quality Notification 3100001473 – The (b) (4) certification of the high efficiency particulate air (HEPA) filters in the (b) (4) and (b) (4) on December 05, 2016 disclosed HEPA filter failures. (b) (4) in the Grade (b) (4) area yielded results of 22 to 67 FPM (Limits: (b) (4) ).

C. Quality Notification 3100000740 - During the execution of the (b) (4) HEPA filter inspection (b) (4) (b) (4) on June 22, 2016, contractors identified two certification failures. Grade (b) (4) HEPA filter (b) (4) in (b) (4) (b) (4) exceeded the (b) (4) limit for average velocity. The average velocity measured was 48 FPM (Limits: (b) (4) . HEPA filter (b) (4) is located above the (b) (4) Grade (b) (4) HEPA filter (b) (4) in (b) (4) failed integrity testing with a leak (b) (4) of the challenge concentration. HEPA filter (b) (4) is located above the (b) (4)

2. (b) (4) controls to prevent the inclusion of foreign materials are deficient. Specifically, extrinsic particle investigations found animal hair and other particulates (i.e., metal, glass) during the visual inspection process.

A. (b) (4) - A single vial from (b) (4) Lot (b) (4) was found to contain a fiber like particulate identified as animal hair that has gone undergone some amount of (b) (4) degradation on June 5, 2015. Sample (b) (4)

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|---|---|---|---|
| | | Burnell M. Henry, Investigator<br>Prabhu P. Raju, Investigator | 05/16/2017 |

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(b) (4) from (b) (4) Lot (b) (4)); the defect was characterized by (b) (4) (b) (4) as a fine brownish hair, approximately 7.5 mm long. The analysis confirmed that characteristics of the hair are only seen in animal, not human hair.

B. Deviation 341430 – On March 3, 2015, three (3) vials were found to contain particulates that have been identified as glass. Vial (1): WinRho SDF 300µg Lot (b) (4) characterized as having flakes with the appearance of glass delamination. Vial (2): WinRho SDF 300µg Lot (b) (4) characterized as a glass chunk. Vial (3): WinRho SDF 300µg Lot (b) (4) characterized as having flakes with the appearance of glass delamination. (b) (4)

C. (b) (4) – On March 3, 2015, during the inspection of WinRho SDF 120µg Lot (b) (4) (b) (4) -filled Jan. 23, 2015), 27 vials were rejected for product related-particulates. Nineteen (19) were subjected to (b) (4) particulate matter identification. The particulates were identified as degraded organic material, stainless steel and steel corrosion.

3. SOP018351, PostMarketing Surveillance-Individual Case Safety Reports, dated 26May2016, requires a comparison of lots reported in post marketing cases received in the previous quarter, to a cumulative listing of all lots associated with post marketing cases within the PV Safety Database to identify if any Adverse Events (AEs) have been associated with the lots. Lots associated with the following are of particular interest for performing a trend analysis

- a death following the administration of an Emergent product,
- (b) (4) cases with serious or non-serious unexpected AEs following the administration of the same lot number,
- (b) (4) cases with serious or non-serious expected AEs following the administration of the same lot number.

The following quarterly Product Safety Committee Meetings did not include any recommendation for a trend analysis by the Pharmacovigilance Specialist. BAT® [Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)-Equine] Lot 11300324, (b) (4)

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a. The April 21, 2017 Product Safety Committee Meeting, did not include a request for a trend analysis and Lot Review for BAT® Lot # 11300324. The following three cases with serious or non-serious unexpected AEs, were noted from the previous quarter, following administration with BAT® Lot # 11300324:

i. Case 17BA00023SP, dated 20Mar2017, Serious Unlisted
ii. Case 17BA00021SP, dated 1Mar2017, Non Serious Unlisted
iii. Case 17BA00008SP, dated 11Jan2017, Serious Unlisted

b. The January 26, 2017 Product Safety Committee Meeting did not include a request for a trend analysis and Lot Review for BAT® Lot # 11300324. The following case reported a death from the previous quarter, following administration with BAT® Lot # 11300324:

i. Case 16BA00140SP, dated 20Jan 2017

c. The November 10, 2016, Product Safety Committee Meeting, did not include a request for a trend analysis and Lot Review for BAT® Lot # 11300324. The following three cases, with serious or non-serious unexpected AEs, were noted from the previous quarter, following administration with BAT® Lot #11300324:

i. Case 16BA00134SP, dated 21Oct2016, Serious Unlisted
ii. Case 16BA00145SP, dated 28Sep2016, Serious Unlisted
ii. Case 16BA00119SP, dated 5Sep2016, Non Serious, Unlisted

d. The August 10, 2016, Product Safety Committee Meeting, did not include a request for a trend analysis and Lot Review for BAT® Lot #11300324. The following three cases with serious or non-serious unexpected AEs, were noted from the previous quarter, following administration with BAT® Lot #11300324:

i. Case 16BA00090SP, dated 11Jul2016, Serious, Unlisted
ii. Case 16BA00098SP, dated 24Jun2016, Non Serious, Unlisted
iii. Case 16BA00099SP, dated 18Jul2016, Non Serious, Unlisted

4. Specifications established during process validations are inadequate for (b) (4) steps.

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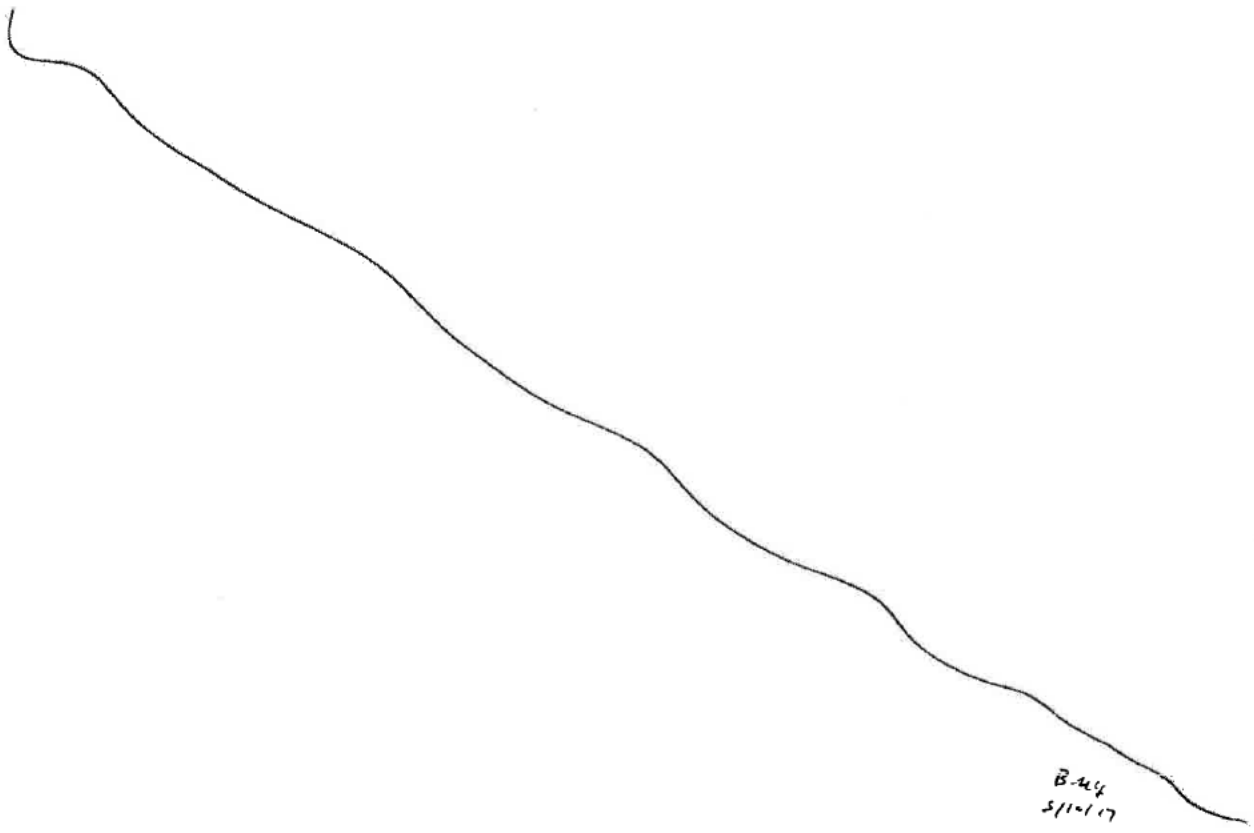
Specifically, microbial data obtained from the (b) (4) process validation reports are inconsistent with established Bioburden (Action limit: (b) (4) ) and Endotoxin (Action Limit: (b) (4) ) process capabilities. The microbial data disclosed that the preceding action limits are set (b) (4) for the preceding (b) (4) steps. Per process validation report, "PV_0234_rep_v1", the limits are based on (b) (4) used by Cangene Corporation, and on (b) (4) (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."