DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CBER/OCBQ/Division of Inspection and Surveillance/HFM-650 1401 Rockville Pike, Suite 200 North Rockville, MD 20852-1448 USA Tel: (301) 827-6220 Industry Information: www.fda.gov/oc/industry	6/12-21/12
	FEI NUMBER 3003153579

OCBQ/DIS 9/27/2012

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Gary C. Floyd, Chief Operating Officer

FIRM NAME	STREET ADDRESS
Cangene Corporation	155 Innovation Drive
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Winnipeg, MB, 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. The firm's investigation into (b)(4) process interruptions for VIGIV bulk lots (b)(4) was inadequate. For example:

A. The material leading to fouling of the (b)(4) was not identified.
The manufacturing process for VIGIV bulk lot (b)(4) was reinitiated after the process automation stopped the process due to a (b)(4) across the (b)(4) This resulted in the stripping of the fouling material from the (b)(4) and precluded identification of the fouling material.
The subsequent VIGIV bulk lot (b)(4) also demonstrated evidence of filter fouling. The manufacturing process was continued and no attempt was made to examine the (b)(4) to identify material retained on the (b)(4) (b)(4)

B. The corrective actions identified in CAPA 219683 as a result of investigations described in deviation 208223 and deviation 211915 failed to prevent (b)(4) fouling in VIGIV bulk lot (b)(4) Specifically, exclusion of specific (b)(4) lots of plasma did not preclude (b)(4) fouling.

2. There are no individual reject rates established for each defect category that is classified as (b)(4) The reject rate established is cumulative for all (b)(4) defects.
Change Control 219756 dated June 11, 2012 was implemented to change the cumulative reject rate for (b)(4) defects, such as (b)(4) associated with Microbial contamination" from (b)(4) to a cumulative reject rate of (b)(4) for the WinRho (liquid formulation), HepGamB (Liquid), and Vaccinia Immune Globulin (VIG) products.

A. (b)(4) are categorized as (b)(4) defects as opposed to (b)(4) "(b)(4) is categorized as a (b)(4) Defect.

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	Paula A. Trost Jacqueline Diaz Albertini	Paula A. Trost/Investigator Jacqueline Diaz-Albertini/Investigator Robert W. Fisher/Staff Fellow	06/21/2012

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B. There are no individual reject rates established for the (b)(4) and (b)(4) defect categories for the WinRho (liquid formulation), HepGamB (Liquid), and Vaccinia Immune Globulin (VIG). A cumulative reject rate of (b)(4) is applied for both categories of defect

3. Not all lots of product that fail the Acceptable Quality Limit (AQL) after the initial (b)(4) inspection is performed are reinspected under tightened limits for both the additional (b)(4) reinspection performed by production or the AQL performed by Quality. For example:
Deviation 212555 was initiated on May 29, 2012 for HepaGam B lot (b)(4) using 3mL Vial Lot (b)(4) having an atypical number of (b)(4) defects (classified as a (b)(4) defect), detected during the initial (b)(4) (b)(4) inspection process. The Acceptable Quality Limit for this inspection also failed the acceptance criteria as a vial with the (b)(4) defect was detected. The lot was 100% reinspected for this defect. There were no reject limits established for this 2nd reinspection and there was no AQL performed for this reinspection. This lot was reinspected a third time under a tightened limit of (b)(4) and failed to meet this criteria with additional (b)(4) defects being found.
Additional lots of product that were affected by this deviation were also reinspected and failed either the reinspection and/or the AQL for the (b)(4) defect of (b)(4) There are no procedures in place which address the criteria for the reinspection of lots that fail the initial (b)(4) nspection or an AQL. Additionally, there are no procedures in place which address the limit for the number of reinspections that can be performed on any given lot.

4. There is a lack of assurance that there is adequate control over critical documents including, but not limited to, Policies, Standard Operating Procedures (SOPs), Work Instructions (WIs) Forms, Electronic Templates (ETs) Drawings and Manuals. The firm's Record and Information Department (R&I) distributes controlled documents to a (b)(4)
(b)(4)
(b)(4)
(b)(4) in which documents are to be returned is not always effective in that numerous incidences were observed where obsolete documents have been used by operators and technicians and have resulted in deviation investigations. Examples include, but are not limited to:

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A. Deviation Report #122799, dated August 11, 2010, documents the most current revision of pH calibration document not being used in the QC Raw Materials laboratory. The investigation states that the (b)(4) (b)(4) did not replace the old document with a newer version of the procedure.

B. Deviation Report #197739, dated October 21, 1011, documents that an incorrect version of a form was being used for raw material testing in the QC Microbiology laboratory. The (b)(4) did not print the new revision on its appropriate effective date and the analyst did not check the revision prior to using it.

5. SOP 25.026.0002.01.00, (b)(4) defines a controlled document as (b)(4)
(b)(4)
(b)(4) The printing, and circulation of such documents are not always controlled:

A. The firm uses (b)(4) software as a system for maintenance of controlled documents. This allows for documents to be (b)(4) for use in various departments. There is a lack of assurance that there is adequate control over controlled documents available to operators on (b)(4) Users who have access to the system are allowed to print off any of the effective controlled forms and procedures without accountability for these documents.

6. The firm's deviation control system is inadequate in that it fails to adequately assess the classification of deviations that may affect product quality. Specifically, during manufacture of Liquid WinRho lot (b)(4) and HepaGam B lot (b)(4) the (b)(4) was exceeded. There is a lack of assurance that the product impact for these lots was adequately addressed in that these deviations were classified as (b)(4) Deviations" that are used (b)(4) Per SOP 10.060.0023.20.19, QA Batch Record Review, (b)(4) Deviations require (b)(4) (b)(4)

7. Deviation 109218 was initiated on June 7, 2010 for HepaGam B Finished Goods lot (b)(4) having been

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processed in Packaging using an incorrect process specification revision. This lot was reworked by being delabeled and relabeled into Finished Goods lot numbers 11006874 and 11006886. There is no approval in the license for routine rework. These lots have been distributed in the US and are within expiration dating.

8. Written procedures are not always followed. The (b)(4) treatment module of the batch record (Document number 24.5002.08, step 17, page 24 of 35) specifies a (b)(4) As described in deviation 211915, the (b)(4) was terminated early during manufacture of VIGIV lot (b)(4)

9. There is no defined change out period for product contact flexible hoses used in manufacturing.

10. The SOP for Growth Promotion of media used for environmental monitoring is incomplete in that it does not specify the length of time test articles should be incubated.

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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."