Inspections, Compliance, Enforcement, and Criminal Investigations

Puget Sound Blood Center and Program 4/16/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Seattle District
Pacific Region
22215 26th Avenue SE, Suite 210
Bothell, WA 98021

Telephone: 425-302-0340
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April 16, 2013

OVERNIGHT DELIVERY
SIGNATURE REQUIRED

In reply refer to Warning Letter SEA 13-16

James P. AuBuchon, MD, FCAP, FRCP(Edin)
President and CEO
Puget Sound Blood Center and Program
921 Terry Avenue
Seattle, Washington 98104-1256

WARNING LETTER

Dear Dr. AuBuchon:

The Food and Drug Administration conducted an inspection of your firm, Puget Sound Blood Center (PSBC), located at 921 Terry Avenue, Seattle, Washington, from January 14, 2013 - February 15, 2013. During the inspection, FDA investigators documented significant deviations from applicable current Good Manufacturing Practice (cGMP) regulations for blood and blood products, Title 21, Code of Federal Regulations (21 CFR), Parts 606, 610 and 640 and the cGMP regulations for finished pharmaceuticals, 21 CFR Part 211. These deviations cause your blood products to be adulterated within the meaning of Section 501(a)(2)(B) of the Food, Drug and Cosmetic Act (the Act). [21 U.S.C. 351(a)(2)(B)]. These deviations include but are not limited to the following:

1. Where an investigation under 21 CFR 211.192 is conducted, failure to include in the written record the findings of the investigation and follow up [21 CFR 211.198(b)(2)].

Your firm's complaint records are deficient in that they do not include the findings of an investigation and the follow-up. For example,

(a) A Red Blood Cell unit was returned from a hospital on January 14, 2013, with a complaint that it contained "small greenish clots." There was no documented investigation beyond a visual inspection of the unit on its return. The unit was redistributed on January 17, 2013.

(b) On August 27, 2012, a Red Blood Cell unit was recorded in BloodTrack as having a "Blood Unit Visual Inspection" alert. When a unit fails a visual inspection, BloodTrack generates an error message. According to your Reference Document: **BloodTrack Alert Table**, the error message is to be printed and the resolution documented on the printout. The resolution description for this unit states that "F/u documented on print screen – Confirm Occurrence Report Form (ORF) done." The print screen containing the follow-up could not be located and there was no other documented investigation of why the unit was marked as failing visual inspection or why it was returned to an available status. The unit was never returned to your firm and is presumed transfused.

2. Failure to take immediate corrective action and maintain a record of such action if the results of the quality control testing indicate that the product does not meet the prescribed requirements [21 CFR 640.25(b)(4)].

(a) Leukoreduced Platelet products have not met the standards established in your product quality control procedures. For example,

i. The standards listed in the **Component Quality Control (QC) Testing Frequency Chart for Platelets Leukocytes Reduced** (referred to as "Plt LR"), require a minimum yield of 5.5×10^{10} platelets in at least 75% of products tested each month. Your firm has tested at least four units each month and out of 30 months reviewed, the monthly QC target of 5.5×10^{10} platelets in at least 75% of products was only met in August 2011.

ii. According to the Frequency Chart, the standards for filtered platelets also require at least 85% platelet recovery after filtration in 100% of the products tested each month. [Your spreadsheet identifies a second standard of **(b)(4)**% recovery in **(b)(4)**% of tested products]. The most recent single unit that met the 85% recovery target was tested on July 16, 2010. The most recent month when sufficient units met the post-filtration monthly QC target was May 2010. Since August 2010, the % platelet recovery, post-filtration QC testing results, ranged from **(b)(4)**%-**(b)(4)**%.

(b) Occurrences were opened in 2009 and 2010 to address prior quality control failures and were closed in January 2010 and May 2010 despite the product continuing to fail to meet the established standards. Your firm distributed **(b)(4)** units of Platelets Leukocyte Reduced between August 2010 and January 2013. In August 2010, your firm began using a different filter for platelet leukoreduction. No investigation into the current failures has been conducted.

3. Failure to obtain approval for an exception or an alternative procedure in accordance with 21 CRF 640.120 prior to distributing products made using the exception or alternative procedure [21 CRF 640.120(a)]. Specifically,

Supplies and reagents were not used in a manner consistent with instructions provided by the manufacturer. For example, your transfusion service uses a filtration system for Platelets that is labeled for use in leukoreduction of pooled Platelets and single donor (apheresis) Platelets. There is no indication by the manufacturer of the filter that the system can be used for the leukoreduction of Platelets. Records indicate that you have been using the filters in this manner since August 2010, but you had not requested an alternative procedure to distribute the product prior to the closing date of the most current inspection.

4. Failure to establish and maintain written standard operating procedures which include all steps to be followed in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for transfusion, including procedures for investigating adverse donor and recipient reactions. [21 CFR 606.100(b)(9) and 21 CFR 606.100(b)].

Standard Operating Procedures (SOPs) were not consistently followed by your firm's collection and transfusion services staff. For example,

(a) BCS 2340 SOP requires the Blood Collection Service (BCS) nursing staff to contact donors who experienced loss of consciousness during or after the collection procedure and to document the follow-up on the **Donor Reaction/Complication Form**. On October 13, 2012, and October 30, 2012, donors experienced loss of consciousness while in the canteen after completing their donations. There was no documentation to show that either of the donors was contacted by a BCS RN to follow-up on their reaction.

(b) TS 300-2 SOP **Irradiation of Blood Components** states that Red Cell components must not be left out of a monitored refrigerator for more than 30 minutes. In order to verify that units are maintained at the appropriate temperatures, the time when a unit is removed from and placed back into monitored storage must be documented. Your **Irradiation Time Log** for September 29, 2011, indicates that three Red Blood components were out of monitored storage for 54 minutes. The irradiated products were distributed on October 2, 2011, and September 29, 2011.

5. Failure of distribution and receipt procedures to include a system by which the distribution or receipt of each unit can be readily determined to facilitate its recall. [21 CFR 606.165(a)]. For example,

(a) A query of your firm's computer system for expired products which are not in quarantine and not previously shipped, identified seven units of Red Blood Cells, Fresh Frozen Plasma or Platelet pools. Your firm cannot determine if the units have been transfused or distributed since they are electronically still in inventory but cannot be physically located.

(b) Your firm identified instances where a final disposition could not be determined. Your firm calls these "discrepant discard" for tracking purposes, though the term "discard" is only used for the electronic discard and there is no evidence that the product was physically discarded. For example:

i. ORF-000053766 was created on July 8, 2012, for a unit of Platelets listed as present at the University District Laboratory. However, the unit could not be located. Your firm's attempts to find the unit were unsuccessful and it was electrically discarded as a discrepant discard and the investigation closed on July 10, 2012.

ii. ORF-000054674 was created on August 1, 2012, for a unit of Platelets and ORF-000052646 was created on June 6, 2012, for two units of thawed Fresh Frozen Plasma when the units could not be located at expiration. The "Investigation" and "Corrective Action" sections of both ORFs are blank. ORF-000054674 was closed on August 2, 2012, and ORF-000052646 was closed on June 11, 2012.

iii. ORF-000057006 was created on October 4, 2012, for the failure to initiate a missing unit investigation for a unit of Platelets. It was discovered that the unit was missing on October 3, 2012, but the unit had been appearing on the expiring unit report since August 28, 2012. The corrective action did not address the missing product; it only covered the failure to generate an investigation. The ORF was closed on October 4, 2012.

iv. ORF-000059424 was created on December 12, 2012, for an aliquot of Fresh

Frozen Plasma and Platelets that could not be located at expiration and no corrective action was taken beyond electronically discarding the units. The ORF was closed on December 14, 2012.

v. ORF-000059680 was created on December 19, 2012, for a returned unit of irradiated apheresis platelets that could not be located. The **Missing Unit Investigation** forms from the Inventory Management department and Bellevue laboratory (Eastside Lab) do not indicate that any locations were searched. The ORF was closed on January 14, 2013.

(c) During our inspection, a Red Blood Cell component was identified as being in quarantine according to an electronic inventory inquiry on January 30, 2013. However, the component could not be located in the expected physical quarantine location. After the discrepancy was identified by our investigators, a search was initiated and the component was found in the discard bin. The component had been physically discarded without maintaining a record of the discard as required by TS 500-2, **Final Disposition of Blood Components**.

6. Failure to check input to and output from the computer or related system of formulas or other records or data for accuracy [21 CFR 211.68(b)]. For example,

(a) On June 3, 2012, you identified that donor and patient identification numbers are carried forward from previous override functions when an override is performed by the same user. This causes the patient and donor numbers to be replaced with incorrect identification numbers on laboratory override reports. On June 8, 2012, this issue was reported to the computer software manufacturer, however, you failed to implement the computer system workaround identified by them. For example, on January 6, 8, and 10, 2013, at least three units were missing the Patient number and Order number from the PSBC Transfusion Service Laboratory Override Report.

(b) ORF-000055354 documents a problem where demographic changes, including blood type, CMV status and name changes can be lost if a different user is updating the record in another session. On September 4, 2012, this issue was reported to the computer software manufacturer, however, you failed to implement the computer system workaround that the manufacturer identified. During the inspection, your software was tested by BCS staff who confirmed that this event continues to occur when demographic changes are made by different users.

We acknowledge receipt of your written response, dated March 7, 2013, which addresses the inspectional findings on the Form FDA 483 issued on February 15, 2013. We have reviewed your response and find it generally adequate in terms of the corrective actions planned. However, we note the following:

1) The adequacy of your response cannot be fully determined at this time because many of your corrective actions to prevent the recurrence of the violations have not been completed.

2) You failed to provide a date or timeframe in which you plan to complete several of your corrective actions.

3) The draft procedure **Reporting Problems to Vendors and Completion of Follow-Up** provided in your response to Observation 8 is incomplete and several sections have been left blank.

4) You submitted a request for an exception or alternate procedure to CBER on March 1, 2013, regarding use of the **(b)(4)** System for leukocyte reduction of Platelets. Please be advised that product cannot be distributed until the supplement has been approved.

The above identified deviations are not intended to be an all-inclusive list of deficiencies at your

facility. It is your responsibility to ensure that your establishment is in compliance with all applicable requirements of the federal regulations. You should take prompt action to correct the violations cited in this letter. Failure to do so may result in administrative and/or regulatory action by FDA without further notice including, but not limited to, license suspension and/or revocation, seizure and/or injunction.

Please notify this office in writing, within fifteen working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including any documentation of the corrective actions you have taken and an explanation of how you will prevent their recurrence. If all corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your firm's response should be sent to Brenda L. Reihing, Compliance Officer, U.S. Food and Drug Administration, Seattle District Office, 22215 26th Avenue SE, Suite 210, Bothell, Washington 98021. If you have any questions about the contents of this letter, please contact Compliance Officer Brenda Reihing at 425-302-0429.

Sincerely,
/S/
Charles M. Breen
District Director

Page Last Updated: 04/23/2013
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.