Canadian Blood Services
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2018-09-27
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REF: H-1819-HO

Ms. Victoria Hurlbut
Compliance Specialist
Regulatory Operations and Regions Branch
Health Canada
180 Queen Street West, 10th Floor
Toronto, ON M5V 3L7

Dear Ms. Hurlbut:

Re: Further to the Responses to Health Canada Inspection of Head Office 2018-07-09 to 2018-07-13

The following are the actions undertaken by Canadian Blood Services in response to the Health Canada email dated 2018-09-11 requesting additional information for observations to the Exit Notice dated 2018-08-08.

Section 52 – Testing

1. **During the review of records associated with the subculture of BacT/ ALERT Positive Bottles (BPA-BT-18015) for apheresis platelet unit C055618271200201, it was noted that the subculture QC plates and Test plates (BA, ChA, CDC) were only incubated for 3 days and then reported as no growth. Procedure 11 012 TCC00110 Follow-up of Positive Bacterial Cultures and/or Blood Components, steps 4.1.1 to 4.1.3 require subculture plates to be incubated for at least 5 days before reporting as no growth. As a consequence of this testing, an apheresis plasma unit collected concurrently with the apheresis platelet unit was removed from quarantine, released, and distributed as safe for transfusion.**

   QER # 135-18-103017 and CAPA # 135-18-103017 were initiated on 2018-07-19.

   Repeat testing of bottle BPA-BT-18015 was performed showing negative growth on the plates after 5 days of incubation. Staff will re-train to procedure 11 012 TCC00110 Follow-up of Positive Bacterial Cultures and/or Blood Components by 2018-09-30.

Health Canada Follow-up email dated 2018-09-11:

Please clarify the following:

1. **What actions were taken with the apheresis plasma unit that was released as a consequence of the testing being considered a false positive result after only 3 days of incubation?**

   Canadian Blood Services Response:

   QER 135-18-103017 initiated on 2018-07-19 included the retrieval of all associated components to donation ID C055618271200201. Only one associated component, an ACD FFPA, was manufactured, quarantined and then released following the BacT testing confirmed false positive of the associated platelet product. The unit was destroyed by the hospital on 2018-07-12 due to not following their own procedures.

2. **Can you confirm that all other testing records performed for subculture of BacT/ALERT positive bottles were reviewed and whether there were any testing results released inappropriately and other blood components released as a consequence of this testing?**

   Canadian Blood Services Response:

   All records since the date of implementation of March 5th, 2018, have been reviewed. There have been no other cases where culture plates were removed before 5 days of incubation for false positive results and therefore no other blood components have been inappropriately released.

3. **Were there any further actions identified as a consequence of CAPA# 135-18-103017 and if so what are they and when do you anticipate their implementation?**

   Canadian Blood Services Response:

   CAPA#135-18-103017 was approved by the Business Owner and Quality Assurance on2018-09-19 and the following corrective actions have been taken:

   a. *Staff were reminded of the safety implications of this observation as associated components to platelet units with false positive results can be issued and transfused. Weekly staff meetings are held to monitor any errors and improvements of the process.*

   b. *A project lead has been assigned to work with the laboratory to revise Procedure 11 012 TCC00110, along with the associated forms to streamline the work instructions and facilitate the documentation of results. Target date of implementation is Q2 of fiscal year 2019/2020.*

   c. *A supervisory review of all reports has been implemented.*

Section 94 – Quality Management System

2. **The processes for performing bacteriological culturing and identification testing did not ensure procedure 11 012 TCC00110 Follow-up of Positive Bacterial Cultures and/or Blood Components is performed consistently and as it was intended to be performed in order to produce predictable outputs. For example,**
   a) **Numerous records of Identification of Gram Positive Cocci from BPA Bottles (F800947) did not document the results for the positive and negative control organisms for catalase and coagulase testing.**
   b) **Numerous records of Identification of Gram Positive Cocci from BPA Bottles (F800947) did not document the coagulase and lyostaphin results for the test organism to be identified.**
   c) **The positive control result (Staphylococcus aureus) for catalase testing was documented as negative instead of the expected positive result. This documentation invalids the testing performed on the bacterial isolate from BPN-BT-18091.**
   d) **The coagulase test result for the BPN-BT -18091 bacterial isolate was not documented.**
   e) **The Bacterial Identification-BacT/ALERT Positive Bottles (F800946) did not document growth for the BA agar plate for BPN-BT-18027.**
   f) **The Bacterial Identification-BacT/ALERT Positive Bottles did not document the expiry date check for the gram stain reagents for testing performed 2018-03-13.**
   g) **A number of records for the Identification of Gram Positive Cocci from BPA Bottles (F800947) did not document the performed by section for Catalase control strain testing.**
   h) **Records were reviewed and signed off as complete and accurate even though numerous documentation errors and omissions were noted.**

   Combined response for 2a to 2h:

   QER 135-18-103020 was initiated on 2018-08-10.

   Staff will re-train to procedure 11 012 TCC00110 Follow-up of Positive Bacterial Cultures and/or Blood Components by 2018-09-30. Also, a re-training session on Good Documentation Practices will

be delivered to Micro Lab staff by Quality Assurance the week of September 10th, 2018.

Health Canada Follow-up email dated 2018-09-11:

Please clarify the following:

1. **How are the missing test results for bacterial cultures isolated from blood components (b)(d)(e) going to be reconciled?**

   Canadian Blood Services Response 2b and 2d:

   The lysostaphin test is one of the test of the API STAPH strip and as such results are part of the API test records (See Attachment 1) for each of the isolates. Therefore, for lysostaphin, reconciliation is not an issue.

   The coagulase results, however, can no longer be reconciled. This has no impact on the identification of the isolates given the high probability of the identification obtained with the API strips.

   Canadian Blood Services Response 2e:

   As identified on page 1 of 4 of form F800946 in Attachment 2 for test case BPA-BT-18027, there was no colony morphology for the BA test plates which indicates there was no growth and therefore no Gram stain required. Page 4 of 4 of form F800946 (Attachment 2) shows Gram staining performed from Chocolate and CDC plates, the only plates for which growth was obtained.

2. **Without results of QC test organisms for catalase and coagulase testing (a), how is the accuracy of the results of catalase and coagulase testing of bacterial isolates being confirmed?**

3. **How was catalase testing of BPN-BT-18091 (c) validated considering the QC testing results indicates reagent failure?**

   Combined Canadian Blood Services Response for 2 and 3:

   There is no evidence that allows us to confirm the catalase and coagulase results. This has no impact on the identification of the isolates given the high probability of the identification obtained with the API strips. It also has no impact on product safety as all companion products were discarded since platelet products were deemed to be contaminated.

3. **The Quality Event Management system is not followed consistently by staff to ensure errors and accidents are thoroughly investigated. For example,**
   a) **The defined criteria for determining the scope of an investigation are not consistently followed:**
      i. **To ensure all processes, equipment, supplies, personnel, etc. are identified, assessed and evaluated.**
      ii. **To evaluate whether the issue applies locally or nationally.**
      iii. **To ascertain whether the point of discovery (i.e. prior to release or after distribution) signifies potential risk to control of processes.**

   b) **The criteria for assessing the categories used to perform the Risk Assessment of an issue were not sufficiently defined to ensure consistent assessment.**

   Combined Response for 3a and 3b:

   An evaluation of quality event reports will be conducted to assess the extent of the inconsistency. Based upon the assessment, appropriate corrective actions will be identified by 2018-12-07.

   In the interim, consistent application of the Quality Event Management (QEM) process will be reinforced by 2018-09-28 with the quality assurance management team as all quality events are reviewed by quality assurance for appropriateness of actions and completeness of documentation.

c) Low risk Quality Event Reports are not assessed for Corrective Action Preventative Action (CAPA).

SOP 08 812, Quality Event Management – Quality Assurance Assessment and Review requires the quality assurance reviewer to perform a risk assessment for every quality event. The risk assessment includes an evaluation of the probability of occurrence, detectability, and severity of impact of product and patient/donor. The outcome of the risk assessment is documented on the quality event report.

Every quality event classified as medium or high risk results in the initiation of a CAPA. The CAPA, managed per SOP 08 175, CAPA Management, will investigate the event to identify the root cause(s) and address them with appropriate corrective/preventive actions.

Low risk quality events are defined as those which do not present a risk to patient, donors or staff. At this time, Canadian Blood Services has chosen to focus its corrective and preventive action resources on events that are more potentially impactful (i.e. medium and high risk).

Health Canada Follow-up email dated 2018-09-11:

Comment:
The current process for performing risk assessment of a quality event is contingent on the thoroughness of the investigation and its documentation of the incident to include all processes, equipment, supplies, personnel, etc. This appears to be a weakness in your current system which may contribute to events being risk rated at a lower level. In addition, the process is highly subjective without clear criteria for performing the risk assessment to ensure consistency.

The comment has been acknowledged and will be considered in our efforts to continuously improve this process.

If you require clarification or further information, please do not hesitate to contact the undersigned. **Please reference the above CBS control number in any correspondence.**

Sincerely,

Christian Choquet

Dr. Christian Choquet
Vice-President
Quality & Regulatory Affairs
Fax Number: 613-739-2505

cc: Shelley Smyth
A/Supervisor – Blood Tissues, Organs and Xenografts
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