Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

1800 Alta Vista Drive
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Canada

2019-05-17
CBS Control #: CBS6319
HPFB File #: C1892-100390
REF: H-1819-NF-W

Ms. Ann McAlduff
Senior Compliance Officer
GMP Inspection - Central
Regulatory Operations and Regions Branch
Health Canada
Suite 1625, 16th Floor
1505 Barrington Street
Halifax, Nova Scotia
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Dear Ms. McAlduff:

Re: Responses to Health Canada Inspection of Wholesale Activities at St. John's Operations 2019-03-27

The following are the actions undertaken by Canadian Blood Services in response to the observations contained in the Health Canada Exit Notice dated 2019-04-12.

C.02.015 - Quality control department

1. **The guidelines and/or procedures were inadequate in ensuring storage and/or transportation conditions would maintain the quality and safe distribution of the drug.**
   a) The qualification study for the 8 L size packing configuration shipped under refrigerated conditions (2 to 8 C) did not include a challenge of simulated full packing conditions. The study was only done on empty conditions.

   All packing configurations and various conditions representative of the different shipping routes in use by Canadian Blood Services were verified for the 8L PUR insulated shipping container. For products shipped under refrigerated conditions (2 to 8 °C) testing was conducted under two different ambient temperature profiles, warm (report # TR-CBS-16-006-1 Rev-A) and cold (report # TR-CBS-16-222-1 Rev-A). For testing under warm ambient temperature, testing was performed with minimum and maximum load conditions. For testing under cold ambient temperature, testing was only performed under an empty load condition as this represents the worst-case scenario in that any added refrigerated load to the insulated shipping container increases the thermal mass and improves the performance of the shipping container (i.e., provide additional protection against cold ambient extremes).

   b) A verification of the delivery time of the shipment was not being recorded. Therefore, there was a lack of documented evidence that cold chain shipments were delivered within their qualified timeframe. The time of receipt was being visually noted but not being recorded.

   As per 05 127, Managing Shipments Designated for Temperature Monitoring, shipments are designated for temperature monitoring in January and July. These shipments have temperature

monitoring devices included in each shipment. This monitoring process was established to provide an on-going mechanism to evaluate the current shipping process, and to demonstrate that required shipping temperatures and maximum shipping times are met. In addition, Canadian Blood Services works closely with our hospital customers when determining delivery times, routes and mode of transportation. Based on the agreed upon delivery times, Canadian Blood Services schedules our staff accordingly to ensure the shipments are not packed far in advance of the shipping times, keeping in mind the expected duration of the shipment.

In addition, as communicated to customers in Customer Letter 2018-21 "Qualification Information – New Insulated Shipping Containers for Hospital Deliveries" (2018-05-28), customers are asked to confirm upon receipt the packing time to time of receipt ≤ 27 hours.

We will consider the need for documented evidence that shipments are delivered within their qualified timeframe as part of future opportunities to improve this process.

c) Although mapping studies had been performed by Skelton on each of the trailer sizes used to transport drug products to the St. John's site, there was no evidence to demonstrate that:

i. CBS had reviewed the mapping studies as required by the Quality Agreement;

The approved carrier trailer and truck validation summaries will be reviewed by 2019-07-31.

ii. CBS had ensured that the vehicles were re-validated on a pre-determined scheduled as required by the Quality Agreement.

The Quality Agreement with the approved carrier will be amended to include the requirement to revalidate the equipment every 7 years. This will be completed by 2019-05-31.

iii. There was no assure that temperature monitoring devices were placed in the worst case locations based on the mapping study. Temperature monitoring devices were placed on the top row of pallets closest to the door or as far as the leading probe would permit.

The current placement of the temperature monitoring devices, on the top row of the pallets closest to the door or as far as the leading probe, is to monitor product temperature in the conditioned area and to provide assurance that temperature is maintained within specifications when the door is opened

All trailer mapping studies by the approved carrier will be reviewed for worst-case locations and the current placement of the temperature monitoring devices re-assessed by 2019-08-31.

2. The receiving procedure did not require the visual inspection of inbound packages and the condition of the transportation vehicle to be recorded.

Work instruction 12 204, Receiving Plasma Protein Products – Canadian Blood Services Sites will be updated by 2019-09-23 to include instructions for documenting the result of visual inspection of inbound packages.

The only other requirement related to the condition of the transportation vehicle that is required to be documented for each shipment is the temperature of the conditioned area during shipment. Vehicle sanitation is a requirement detailed in the Agreement between Canadian Blood Services and the approved carrier. These are verified for compliance during supplier audits.

C.02.024 - Records

3. **Change control # 15463, opened to manage the replacement of the temperature monitoring system (including hardware, software and vendor changes), was inadequate for the following reasons:**
   i. **It did not describe how temperature-monitoring records generated under the previous temperature monitoring system would be maintained for their required retention period.**

   Change Request 15463 was initiated for the replacement of the NDAS temperature monitoring system with the ViewLinc temperature monitoring system. The disposition of the temperature-monitoring data on the servers was addressed in an approved project document, CMS-DP-005 Decommissioning Plan. The decommissioning activities are still in process; the completed decommissioning documentation will be attached to CR 15463.

   The previous temperature monitoring system records were maintained in paper format (hard copy) which were signed, dated, and filed. These hard copy system records are retained until the end of their retention period of 5 years.

   The electronic temperature-monitoring data within the NDAS temperature monitoring system was considered to be 'transitory' and therefore was deleted with the decommissioning of the system. This is captured in a disposition authorization that was approved with the decommissioning of the system. No further actions are deemed necessary.

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,

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

cc: Ms. Joy Bregg
Regulatory Operations and Regions Branch