Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

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Ms. Victoria Hurlbut
Biologic Products Specialist
Regulatory Operations and Regions Branch
Health Canada
Suite 1625, 16th Floor
1505 Barrington Street
Halifax, Nova Scotia
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Dear Ms. Hurlbut:

Re: Further to the Responses to the Health Canada Inspection of Dartmouth Operations 2019-05-13 to 2019-05-17

The following are the actions taken by Canadian Blood Services in response to the Health Canada email dated 2019-08-08, requesting additional information for observations to the Exit Notice for Health Canada's Inspection of Dartmouth Operations.

Section 94 – Quality Management System

3. **There is no process to ensure that the labeled volume of all blood components processed meet the specifications documented in the circular of information. For example, red blood cell unit C0511864878300F was released for distribution even though the labeled volume was 418 ml. The circular of information indicates the volume should be 293 +/- 26 ml. Additionally, procedures for performing end labeling and distribution do not require the labeled volume of blood components to be verified.**

The mean volume of a red cell unit for the time periods of July 2017 to June 2018 and July 2018 to May 2019 are 290 ± 24 ml (n = 7,749) and 289 ± 24 ml (n= 7,046), respectively. The unit noted in the observation is simply an outlier.

An upper volume limit of less than 390 ml verified during component production was implemented on 2018-10-22 (SOP 02 256.001, Preparation of Initial Components – Whole Blood Filter System and SOP 02 739.001, Review of Production Records). Any red cell unit above this volume is rejected. The unit noted above was collected on 2018-05-31, before the upper volume limit was introduced.

Health Canada Follow-up email dated 2019-08-08:

Although the response describes the processes involved and their implementation, it does not explain the discrepancy between the maximum volume of a red blood cell unit in the circular of information (319 ml) or the maximum mean volumes of a red blood cell unit (July 2017 to June 2018 of 314 ml; July 2018 to May 2019 of 313 ml) described in your response and the fact that production will accept red cell units that have a volume range of 320 to 389 ml which appear to be outside of the maximum mean volumes of a red cell unit. Please provide Health Canada with the rationale for determining the upper volume limit for discard at > or = to 390 ml.

During the inspection, it was explained that CC 16716 defines the process for visual verification of the weight of red blood cell units during production including an upper volume limit of > or = to 390 ml. It was also explained that IOQ-EXT-002 ver 5.0 was in process of being conducted at the St. John's Operations site that would include changes to the optic sensors of the MacoPress and was expected to eliminate this issue of red blood cell units being overweight. It was also indicated that with an acceptable qualification and successful monitoring period that this new process would be implemented at all production sites (no later than June 26, 2019). Once this was in place it was anticipated that the visual weight verification process would no longer be required and would be discontinued. Please provide Health Canada with an update on this qualification including a summary of the results and if the new process was implemented as expected. If this project is still ongoing please provide an update on its' progress.

In addition, during the inspection the inspector requested a list of any deviations associated with the new process using the Hettich centrifuges and MacoPress extractors. The list provided indicated fifteen occurrences where the red blood cell unit was > than or = to 390 ml between November 29, 2018 and April 18, 2019 at the Dartmouth Operations location. So although you have indicated this particular incident was an outlier, it appears this issue happens more frequently than suggested in your response.

Canadian Blood Services Response:

The circular of information does not state that the maximum volume of a red blood cell unit is 319 mL. It states that the volume of a red blood cell unit is 293 +/ - 26 mL, expressed as the mean volume +/- one (1) standard deviation. That implies that of that population 68.3 % of the red blood cell units are within one standard deviation or between 267 mL and 319 mL. Based on three (3) standard deviations, 99.7% of the population is expected to be below 371mL. The fifteen occurrences mentioned in the observation were identified through the visual weight verification and discarded. These represent 0.05% of the red cell production in Dartmouth in that time period and the 390 ml was simply chosen to exclude such outliers.

Regarding the execution of IOQ-EXT-002 ver 5.0 at the St. John's Operations site, which included changes to the optic sensors of the MacoPress. This did not eliminate larger red blood cells. As a result, Canadian Blood Services will maintain the visual weight verification process until such time ePROGESA can be updated to ensure there is an automatic rejection of red blood cell units ≥ 390mL.

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

Sincerely,

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

cc: Anita Mahadeo
A/Supervisor – Blood Tissues, Organs and Xenografts
Regulatory Operations and Regions Branch