Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

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Lydia Paparistotelis
Regional Regulatory Compliance & Enforcement Specialist
Biological Product Compliance Program
Regulatory Operations and Enforcement Branch
Health Canada
2301 Midland Ave
Scarborough, ON M1P 4R7

Dear Lydia:

Re: Responses to the Health Canada Inspection of the Ottawa Cord Blood Bank 2024-02-13 to 2024-02-20

The following are the actions undertaken by Canadian Blood Services in response to the observations contained in the Health Canada Exit Notice dated 2024-03-15.

Section 55 - Records

1. The establishment's records were not always complete.

a. Deviation reports did not always document or include all relevant follow-up actions taken to completion. For example:
i. DEV-21-008325 outlined follow-up measures to be taken for on-demand equipment maintenance for the controlled rate freezer due to an unacceptable freeze curve, but the completion of the maintenance or outcome thereof was not included as part of the report.

DEV-24-002839 was initiated on 2024-03-19.

During the inspection, the missing documentation was located and added to DEV-21-008325. A review of this event for awareness and the requirement to ensure completeness of documentation as per Work Instruction WI-00519 Deviation / Minor Quality Event - Operational Review was completed with both Operational and Quality Assurance staff by 2024-03-27.

ii. DEV-22-001196 outlined that 3 cord blood units were accidentally released into inventory on February 10, 2022, however, no follow-up was documented to have been taken with the responsible individual to advise them of this event. It is acknowledged that the 'released' units were not searchable by stem cell registries and moved back to quarantine status on the following day and that WI-00519 Deviation/Minor Quality Event - Operational Review was updated on March 28,

2022 to indicate that staff involved are to be made aware of the associated deviation(s)/quality events as part of operational review.

The investigation revealed that there is documented evidence from 2022-02-11 of a follow-up with the responsible individual to advise them of the event. The evidence was added to the deviation on 2024-04-08. As noted in the observation, WI-00519 Deviation / Minor Quality Event - Operational Review, implemented on 2022-03-28, was updated to require that follow-up be done with staff to provide awareness and to document such action in the deviation. All Canadian Blood Services staff having a role in the Quality Event Management process were trained to this new requirement at that time.

b. Not all the documentation that accompanied the cord blood unit (CBU) shipment to the transplant establishment were retained as part of the donor files and in accordance with Form F800531 Cord Blood Distribution Record instructions (e.g., final distribution label for C064320000981 and final distribution label and second page of package insert for C064321000510).

Furthermore, the step of scanning all documents into the Stem Cells National Solutions System (SCNSS) was not checked off, initialed and dated as completed on the Cord Blood Distribution Record for both CBU C064320000981 and C064321000510

DEV-24-002861 was initiated on 2024-03-20.

Awareness of this event will be provided to the Lab Assistants who perform these functions, and re-training to WI-01993 Cord Blood Distribution will be completed by 2024-04-30.

Section 64.02 - Personnel

2. Personnel training records were not always complete.

There was no documentation to demonstrate that a back-up medical director was trained on the curriculum training matrix for Cord Blood Manufacturing: Release to Inventory and Distribution – Awareness- Director (curriculum ID 1256), even though he was granted access in the system (SCNSS) to perform the release to inventory and distribution functions.

It was determined after the inspection that access had been granted to the Stem Cells National Systems Solution (SCNSS) for a back-up medical director on 2023-02-28, with a training date of 2023-03-03. In order for process training to be completed in full, access to the system must be granted, which is the reason that the access date precedes the training date.
As per Canadian Blood Services policy and practice, staff are not to perform tasks until they are fully trained to the applicable process/work instructions. Review of the situation confirmed that the back-up medical director had never performed any related tasks.

Section 66 - Equipment and Supplies

3. Not all of the equipment was adequately cleaned and maintained.

There was no documentation that any follow up action was taken for the STEMvision colony counter (RAM #R000001509) as a result of the service provider's June 2023 maintenance report, which indicated the heater system was not working and also recommended that the computer associated with the analyser be replaced. Additionally, the step in the report for the technician to include the type of assay installed on the equipment was not completed.

MQE-24-000795 was initiated on 2024-02-22.

Although the service report indicated the heater was not functioning properly and recommended the computer be replaced, it also indicated that the annual PM routine was completed successfully. The heater is only necessary to emulate the incubator temperature, and it does not have any impact on the imaging system or the analyzer, which is what this instrument is used for. There is therefore no impact on any CFU test results. At the time, management discussed the CPU concerns and decided that a replacement was not required but would be monitored further as there had not been any issues during day-to-day operations. This discussion was, however, not documented. The MQE referenced above was created to capture the decision not to proceed with the replacement of the computer, and this number has been referenced on the service report.

Section 72 – Quality Assurance System Standard Operating Procedures

4. Some operating procedures were not always followed as written.

a. Contrary to WI-00665 Premises Cleaning (revision 1; reissue #2; 2023-09-05), the cleaning communication log book for the Stem Cell Laboratory was not reviewed daily by Facilities Operations. For example, the reviews were only documented as completed by Facilities (or service provider) on October 3, 16, 17 and 31 and November 14 and 28 for the months of October and November 2023, respectively.

DEV-24-003194 was initiated on 2024-03-28.

A review was completed of the Cleaning Communication Logbook and other supporting documentation (including Premises Monthly Cleaning Inspections, Stem Cell Laboratory Cleaning Checklists and the Facilities work order system) for the dates on which the daily reviews did not take place and did not identify any deficiences.

Building Systems Technicians were retrained to the requirements of WI-00665, Premises Cleaning on 2024-02-27. In addition, outsourced cleaning staff were advised of the requirement to review the log book daily, on 2024-02-27.

b. Regarding the quarterly cleaning of the Stem Cell Laboratory:
i. The quarterly cleaning as per the Stem Cell Laboratory Cleaning Checklist (F800590 revision 1) that was due in October 2023 was not completed until December 31, 2023.

ii. Additionally from the Stem Cell Laboratory Cleaning Checklists completed for the months of August - November 2023, it was unclear when the quarterly cleaning was required to be done, as all the checklists were filled out to indicate the cleaning was due in December 2023

Combined response 4bi and 4bii:

DEV-24-003196 was initiated on 2024-03-28.

Building Systems Technicians were retrained to WI-00665 Premises Cleaning on 2024-02-27. This included providing clarification that quarterly inspections are due every three months.

In addition, the Stem Cell Laboratory Cleaning Checklist will be updated to add clarity as to when quarterly cleaning inspections were last performed and when the next ones are scheduled. Target date for implementation is 2024-12-31.

Section 73 – Quality Assurance System Standard Operating Procedures

5. Some operating procedures were not kept up to date.

a. The Cord Blood Medical Health History/Health Assessment Questionnaire (F800490 (revision 2); 2023-05-28) and associated standard operating procedures (e.g., Medical Conditions Chart CO-00099) did not clearly outline the exclusion criteria stipulated in clause 13.1.3(n) of the lymphohematopoietic standard (CAN/CSA-Z900.2.5:22) for persons with melanoma. It is acknowledged that CO-00099 Section C (revision 1; 2023-05-28) listed skin cancer as an exclusion criteria for the baby's mother and father, however, there was no reference to melanoma.

DEV-24-001895 was initiated on 2024-02-21.

The Cord Blood Bank Medical Conditions Chart will be revised to add melanoma as an exclusion criteria for the baby's mother. In addition, the Cord Blood Medical History/Health Assessment Questionnaire (MHHAQ) question #17, "Have you ever had any type of cancer, including leukemia or lymphoma" will be revised to include melanoma.

Target date for implementation of these revised documents is 2024-10-31.

b. There was no documentation to show that WI-01213 Cord Blood Recall/Withdrawal (rev. 3.3; 2020-03-30) had its periodic review conducted to-date, nor was a quality event initiated for this delay.

Periodic review RR-02398 of WI-01213 Cord Blood Recall/Withdrawal was completed on 2024-03-01. The review identified some editorial changes to be made to the document. Target date for implementation is 2024-04-30.

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