QUALITY IMPLICATIONS OF CRYOPRESERVATION: BUILDING A SMALL-SCALE MODEL TO DETERMINE THE SHELF-LIFE OF CRYOPRESERVED BLOOD PRODUCTS FOR DRUG PRODUCT MANUFACTURING

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Cryopreservation of mobilized apheresis products could prove to be very important in the manufacture of scalable and more globally accessible cell-based gene therapies. However, it introduces a new challenge of how to assess the stability and shelf-life of these products in the context of advanced cell therapy products. The stability of cryopreserved mobilized apheresis products for direct transplantation has been established, but the challenges of separating and recovering the rare CD34+ hematopoietic stem and progenitor cell (HSPCs) population from other cells in the blood products after cryopreservation suggest that further work to assess stability is needed to understand the impact of storage on further cell processing. Typically, a stability study involves the generation of material using an at-scale manufacturing process that mirrors the clinical manufacturing process, storing the material and testing it at predetermined timepoints. As mobilized apheresis products are small, expensive and limited, it is not feasible to generate and test material at-scale. Therefore, a small-scale model was developed to inform the design of a stability study for cryopreserved apheresis products.

First, we assessed two types of container closures, a rigid cryovial and flexible cryopreservation bag, that are similar to what is used clinically. Once the target vessel was determined, we identified the number of vessels that would be needed to complete characterization testing of the thawed apheresis and generate a representative drug product to assess process performance. Second, we assessed the cryopreservation configuration to ensure that all of the vessels had similar cryopreservation profiles as material during at-scale processing. Finally, healthy donor material was cryopreserved in several bags with our small-scale model, stored in vapor phase of liquid nitrogen, and then thawed at various intervals over a one-year period.
We assessed multiple stability indicating parameters at thaw, including cell health and CD34+ cell recovery. The thawed apheresis product was forward processed through CD34+ cell enrichment and transduction to generate a representative drug product for further characterization, including cell health, CD34+ cell recovery, transgene expression and vector copy number. The results from these studies are reported herein and will inform the study design, including the cryopreservation process and best measures of stability, of a larger quality-controlled study performed at the manufacturing site.