



## DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Center for Biologics Evaluation and Research  
Office of Compliance and Biologics Quality  
Division of Manufacturing and Product Quality

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**To:** NDA BN110059/0, HEMERUS LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive

**From:** Ellen Huang, CSO, OCBQ/DMPQ/MRB II, HFM-676

**Through:** Marion Michaelis, Branch Chief, OCBQ/DMPQ/MRB II, HFM-676

**Cc:** Sondag Kelly, RPM, OBRR/DBA/RPMB, HFM-380  
Jennifer Schmidt, Consult Reviewer, OCBQ/DMPQ/MRB I, HFM-675

**Subject:** **Complete Response Review Memo:** Review of the Complete Responses submitted to CBER February 27, 2013 and associated with NDA submitted by Hemerus Medical, LLC, for HEMERUS LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive.

**Due Date:** April 28, 2013

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### REVIEW RECOMMENDATIONS

Based on the review of the firm's response, approval is recommended.

### REVIEW SUMMARY

Hemerus Medical, LLC (Hemerus) submitted a NDA for HEMERUS LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive. Hemerus is manufacturing the Leukocyte reduction filter and using JMS Singapore PTE LTD (JMSS) as a contract manufacturer for CPD and SOLX® solutions, SOLX® System device assembly, packaging, labeling, and sterilization. The system is terminally sterilized by using a -----  
------(b)(4)-----.

CBER issued a complete response (CR) letter on August 31, 2012. Please refer to my review memo dated August 10, 2012 for a complete review of the original NDA submission.

Hemerus submitted a complete response to the CR letter on February 27, 2013. Please refer to the review memo below for a review of the firm's response to the CR letter for CR Issues 5-7. All responses were found acceptable.

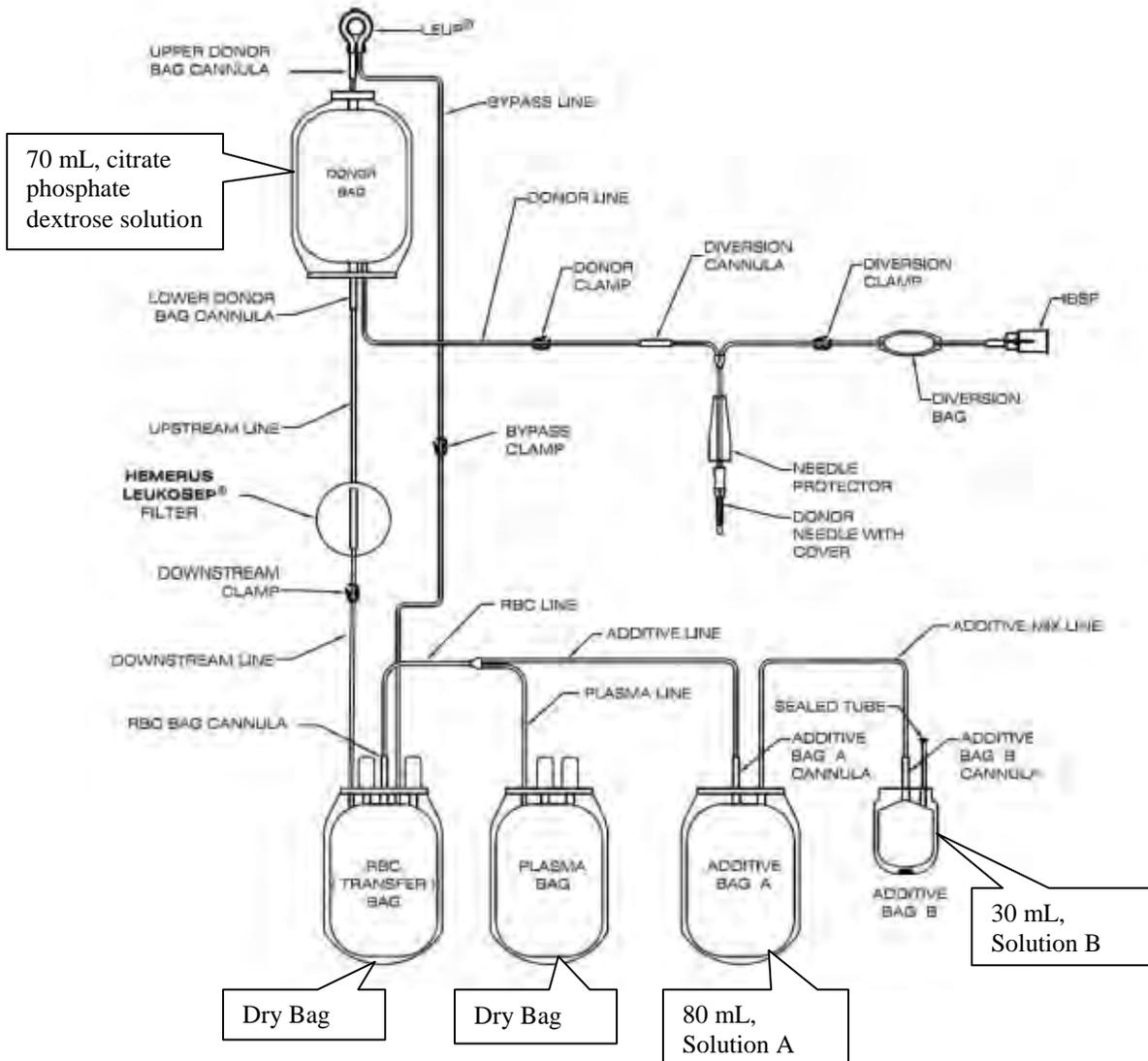
**NARRATIVE REVIEW**

**Items Reviewed**

- Items related to sterilization and transportation in NDA BN110059/0 (CR Questions 5-7, excluding the chemical analysis for sterilization and the label peel test)
- Teleconference on March 22, 2013

**Background**

The HEMERUS LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive is a whole blood collection system containing CPD anticoagulant and SOLX® Red Blood Cell additive solution. It is designed with a donor needle, blood diversion bag with integrated blood sampling port, whole blood collection bag, LEUKOSEP® leukoreduction filter, red blood cell storage bag, plasma storage bag and SOLX® additive solution bags. A schematic of the product is below:







[(b)(4)]

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----- (b)(4) -----  
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Other tests performed as part of the PQ included -----  
----- (b)(4) -----  
----- . Additionally, the units  
were inspected for ----- (b)(4) -----  
----- . All results passed these tests.

**Reviewer’s Comments:**

**I reviewed the firm’s response and validation protocol and report. The response and validation appears acceptable. The firm fulfilled this CR question by performing additional sterilization runs using a sufficiently resistant BI in comparison to their facility bioburden. Refer to CR Question 6 below for a comparison of the BI and facility bioburden.**

**I defer to the product office regarding the chemical tests performed by the firm. Xuan Chi from the product office reviewed the chemical analysis and found no issues.**

**Of note, while reviewing the attachments for sterilization, I noticed that JMSS was not following good documentation practices on some of the documents. On March 22, 2013 I informed Hemerus. Hemerus stated that they would communicate this observation to JMSS and would include it in their audit report.**

- 6. *For the heat shock studies used to evaluate the resistance of organisms at your facility, it is not clear how your study correlates to actual production sterilization conditions. Specifically, the heat shock conditions ----- (b)(4) ----- than the actual sterilization production cycle for all of the spore formers and mold found in the facility. It is not clear if the heat shock condition or the sterilization production cycle is actually the worst case.*

*Please perform additional studies to compare the resistance of spore formers and mold in your facility using test conditions that can be correlated with your sterilization production cycle. To facilitate comparison to your chosen validation biological indicator, we recommend that your thermal studies also include the biological indicator as a control.*



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A summary comparison of the previous shipping carton design and the most recent tested design is given in the table below.

[(b)(4)]

The complete protocol and report describing testing of the modified cartons and packaging are in Appendices 7 and 8 (PC412992 and FR412992). The modified packaging configuration met all performance criteria after simulated environmental conditioning performed according to ISTA 2A and transportation testing conducted according to ASTM D4169-09.

Inspection of ---(b)(4)---- ensured (b)(4) confidence and (b)(4) reliability that SOLX® System packaging is capable of withstanding extreme environmental conditioning and distribution simulation. A summary of the testing results in the Table below.

[(b)(4)]

According to protocol and final report PC412992 and FR412992 (Environmental Conditioning and Transportation Simulation Validation of Proposed SOLX System Packaging), the firm changed the shipping carton and packaging configuration again. Per ISTA 2A (2011), the cartons were subjected to the following environmental conditions: -----

----- (b)(4) -----

For the distribution simulation the cartons were subjected to all testing required per -----

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----- (b)(4) -----

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The firm concluded the proposed redesigned packaging effectively protected the contents throughout the simulated environmental conditioning and distribution testing.

The firm also provided information regarding the label peel test for CR Question 7.

**Reviewer's Comments:**

**I reviewed the firm's response and protocol and final report. I found the response and reports acceptable. The firm completed additional transportation studies with current shipping configuration using simulated shipping conditions.**

**I defer to the product office to review the label peel testing.**

----- (b)(4) -----