



**FOOD AND DRUG ADMINISTRATION**  
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

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MEMORANDUM

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**INTERNAL MEMORANDUM**

DATE: August 17, 2012

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SUBJECT: NDA BN110059 (The LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive also called "SOLX® System").

**Indications for Use:**

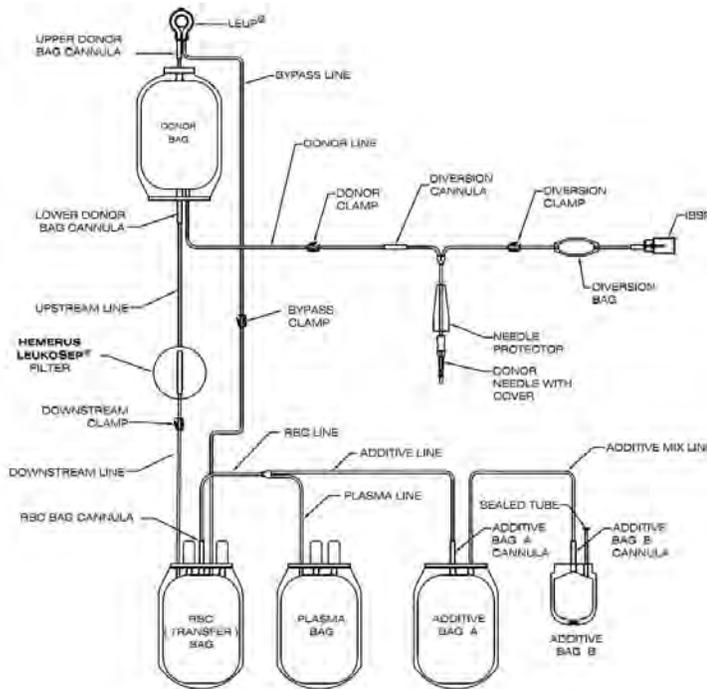
The LEUKOSEP® HWB-600-XL Leukocyte Reduction Filtration System for Whole Blood with CPD Anticoagulant and SOLX® Additive also called "SOLX® System" is intended for the manufacture of:

- CPD/AS-7 Red Blood Cells (RBC), Leukocytes Reduced prepared at ambient temperature and placed at 1 to 6° C within 8 hours of collection. CPD/AS-7 Red Blood Cells, Leukocytes Reduced may be stored at 1 to 6° C for up to 42 days after collection.

• Fresh Frozen Plasma (FFP), Leukocytes Reduced prepared and placed in a freezer at -18° C or colder within 8 hours of collection. Fresh Frozen Plasma (FFP), Leukocytes Reduced may be stored at -18° C or colder for up to one year after collection.

**Summary:**

HEMERUS Medical, LLC submitted an original NDA for the HEMERUS LEUKOSEP HWB-600-XL Leukocyte Reduction Filtration System for the Whole Blood with CPD anticoagulant and SOLX additive solutions (also called SOLX System). It is designed with an Integrated 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. SOLX additive solution is a new red blood cell additive solution.



1. **Clinical studies:** *In vitro* feasibility testing of SOLX system was performed initially (PC387970, PC396220) followed by *in vivo* testing conducted under IND 14199.

1). IND 14199 was conducted at three U.S. investigational sites (Hoxworth Blood Center University of Cincinnati, Dartmouth Hitchcock Medical Center and American Red Cross Mid-Atlantic Research Facility;

2). Three processing groups were studied under different filtration and processing times:

- Group 1 (FFP8hrRT-WB2hr): Up to two hour room temperature hold prior to whole blood filtration and processing at room temperature (60 test units). RBCs refrigerated and plasma frozen within 8 hours.
- Group 2 (FFP8hrRT- WB6hr): Greater than six hour room temperature hold prior to whole blood filtration and processing at room temperature within eight hours (60 test and 60 control units). RBCs refrigerated and plasma frozen within 8 hours.

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- 3). Results of 6 week RBC studies and plasma characterization and stability are the subject of this NDA submission.
- 4). Primary endpoints for RBC studies and results

Criteria	Result
A one-sided 95% lower confidence limit for the true proportion of units with a filtration recovery of red blood cell mass of at least 85% is greater than 95%.	Each Test Group processed with the SOLX System met the endpoint criteria for RBC mass recovery (60/60 successful).
A one-sided 95% lower confidence limit for the true proportion of units with residual leukocyte content of less than $5 \times 10^6$ per unit is greater than 95%.	All SOLX® RBC units from each processing group met study endpoint criteria for RBC, Leukocytes Reduced ( $<5 \times 10^6$ residual WBC/Unit). ----- ----- ----- ----- -----
A one-sided 95% lower confidence limit for the true proportion of units with hemolysis at end of storage of less than 1% is greater than 95%.	Each Test Group processed with the SOLX® System met the study endpoint criteria for hemolysis. 60/60 (# Units $<1.0\%$ / Total Units) for each testing group.
Mean 24-hour, post transfusion, <i>in vivo</i> red cell recovery at end of storage of at least 75% with standard deviation of at most 9%, and the lower limit of a one sided 95% confidence interval for the population proportion of successes is 70% or greater.	RBCs processed under each study condition and stored in SOLX® additive solution for up to 42 Days met acceptance criteria for <i>in vivo</i> 24-hour red blood cell recovery. The study endpoint for 24-hour <i>in vivo</i> red cell recovery was met for each processing group.

- 5). Primary endpoints for plasma testings and results
  - No primary endpoints for plasma testings were specified.
  - Residual WBC content per plasma unit is less than  $5 \times 10^6$ .
  - FFP conclusions: Fresh frozen plasma (FFP) prepared with the SOLX® System and placed at  $-18^\circ \text{C}$  or below within 8 hours of collection demonstrated comparable levels of plasma proteins (within 20% as compared to control FFP) including: coagulation factors (V, VII, VIII, IX, X, XI and XII), fibrinogen, IgG, Protein C, Protein S, von Willebrand Factor (vWF/Rco) and ADAMTS 13; For data collected to date using  $\pm 20\%$  criteria, SOLX® System FFP demonstrated lower Fibrinopeptide A and TAT Complex at all testing time points and lower C3a and C5a postfiltration as compared to the control FFP.



stability specification, you should change the shelf life claim accordingly. You can request a shorter shelf life if it is supported by available data to prevent a delay in approval. When the ---(b)(4)--- storage study data become available you can then request an extension of the shelf life.

2. The 14-Day Repeat Dose Intravenous Toxicity Study (Module 4, Appendix 4-5):
  - a. As shown by Table 2, there were 3 blood clotting events in test groups (2 specimens in female test group and 1 specimen in male test group) and 0 clotting event in control specimens.
  - b. Both male and female test animals were observed to have significantly lower platelet counts ( $p=0.0033$  and  $p=0.0440$  respectively) when compared to controls. The presence of clots within 2 specimens from female mice contributed to the decrease observed in female test group, but in the male test group, the specimen with clots was already excluded from the platelet count.

In your response to the advice letter, the lower platelet count in test animals was speculated to result from *in vitro*, spontaneous platelet aggregation. We think this response is not acceptable. We recommend that you provide a risk assessment based on results from the previous extraction study (# 06-5803-N2) conducted according to procedures described in ISO 3826.

**Labeling:**

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