

AWARD NUMBER: W81XWH-13-2-0089

TITLE: Extended Storage of Pathogen-Reduced Platelet Concentrates (PRECON)

PRINCIPAL INVESTIGATOR: Sherrill J. Slichter, MD

CONTRACTING ORGANIZATION: Puget Sound Blood Center

Seattle, WA 98104

REPORT DATE: OCT 2014

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

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| 1. REPORT DATE<br>OCT 2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                             | 2. REPORT TYPE<br>Annual     |                                                | 3. DATES COVERED<br>26-SEP-13 to 25-SEP-14 |                                            |
| 4. TITLE AND SUBTITLE<br>Extended Storage of Pathogen-Reduced Platelet Concentrates                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                             |                              |                                                | 5a. CONTRACT NUMBER                        |                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              |                                                | 5b. GRANT NUMBER<br>W81XWH-13-2-0089       |                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              |                                                | 5c. PROGRAM ELEMENT NUMBER                 |                                            |
| 6. AUTHOR(S)<br>Sherrill J. Slichter, MD<br><br>E-Mail:sherrills@psbc.org                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                             |                              |                                                | 5d. PROJECT NUMBER                         |                                            |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              |                                                | 5f. WORK UNIT NUMBER                       |                                            |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)<br>Puget Sound Blood Center<br>921 Terry Ave<br>Seattle, WA 98104                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                             |                              |                                                | 8. PERFORMING ORGANIZATION REPORT NUMBER   |                                            |
| 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)<br><br>U.S. Army Medical Research and Materiel Command<br>Fort Detrick, Maryland 21702-5012                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                             |                              |                                                | 10. SPONSOR/MONITOR'S ACRONYM(S)           |                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              |                                                | 11. SPONSOR/MONITOR'S REPORT NUMBER(S)     |                                            |
| 12. DISTRIBUTION / AVAILABILITY STATEMENT<br><br>Approved for Public Release; Distribution Unlimited                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                             |                              |                                                |                                            |                                            |
| 13. SUPPLEMENTARY NOTES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                             |                              |                                                |                                            |                                            |
| 14. ABSTRACT<br>This grant pertains to increasing the availability and safety of platelets for transfusion. Ultimately our project proposes to determine the efficacy of using a pathogen inactivation technique (Mirasol) coupled with a Platelet Additive Solution (PAS) to extend the life of platelet concentrates. Preliminary steps to this ultimate goal are to determine the best storage bag and the optimum PAS to plasma ratio to utilize in our Mirasol experiments. Once we have established the optimum storage bag and PAS concentration we will evaluate the effects of Mirasol treatment on extended storage of PAS-stored platelet concentrates prepared from treated WB. These studies will be conducted using healthy donor autologous radiolabeled stored versus fresh platelet recovery and survival measurements to identify storage conditions that meet FDA post-storage platelet viability criteria. Thereafter, we will determine the post-transfusion recovery and survival of pre-storage pooled extended stored platelet concentrates prepared from Mirasol-treated WB given to thrombocytopenic patients. |                             |                              |                                                |                                            |                                            |
| 15. SUBJECT TERMS<br>bleeding, extended storage, hemorrhage, hemostasis, InterSol, Mirasol, pathogen inactivation, pathogen reduction technology, platelet additive solution, platelet recovery and survival, platelet storage, platelet storage solution, platelets, thrombocytopenia, transfusion, whole blood                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                             |                              |                                                |                                            |                                            |
| 16. SECURITY CLASSIFICATION OF:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                             |                              | 17. LIMITATION OF ABSTRACT<br><br>Unclassified | 18. NUMBER OF PAGES<br><br>6               | 19a. NAME OF RESPONSIBLE PERSON<br>USAMRMC |
| a. REPORT<br>Unclassified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | b. ABSTRACT<br>Unclassified | c. THIS PAGE<br>Unclassified |                                                |                                            | 19b. TELEPHONE NUMBER (include area code)  |

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Extended Storage of Pathogen-Reduced Platelet Concentrates (PRECON)

Grant Number 13335012

Annual Report

26-SEP-13 to 25-SEP-14

**INTRODUCTION:** The purpose of this project is to find better ways to store platelets for patients that need platelet transfusions. In this research study, we are interested in evaluating storage and pathogen reduction of platelet concentrates.

**KEY WORDS:** bleeding, extended storage, hemorrhage, hemostasis, InterSol, Mirasol, pathogen inactivation, pathogen reduction technology, platelet additive solution, platelet recovery and survival, platelet storage, platelet storage solution, platelets, thrombocytopenia, transfusion, whole blood

**OVERALL PROJECT SUMMARY:** The following specific aims were described in the original statement of work, Extended Storage of Pathogen-Reduced Platelet Concentrates (PRECON).

1. Determine the optimum conditions for extended storage of autologous platelet concentrates in a platelet additive solution (PAS).
2. Evaluate the effects of Mirasol treatment of autologous whole blood (WB) on extended storage of PAS-stored platelet concentrates prepared from treated WB.
3. Determine the post-transfusion recovery and survival of pre-storage pooled extended stored platelet concentrates prepared from Mirasol-treated WB given to thrombocytopenic patients.

As a first step we will identify an acceptable storage bag and determine the best PAS-to-plasma ratio for platelet storage.

We do not, as yet, have approval to begin this study from our local IRB, our local radiation safety committee, TATRC or HRPO. A study that evaluates apheresis platelets but is otherwise the same as this study is currently under review by our local IRB. Once the apheresis platelet study has been approved we will modify the approved protocol/consent etc. to reflect evaluation of platelet concentrates instead of apheresis platelets and submit it to the various regulatory oversight bodies with the expectation of an expedited review. HPRO and TATRC are aware of this plan.

For Aims 2 and 3 (above), an IDE will be needed to permit Mirasol treatment of WB. This IDE will be submitted by Terumo BCT.

**KEY RESEARCH ACCOMPLISHMENTS:** The following are the key research accomplishments to date.

- Protocol and other regulatory document developed

**CONCLUSION:** We anticipate regulatory approval to initiate enrollment into the first aim of the study in the next reporting period.

**PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:** None

INVENTIONS, PATENTS AND LICENSES: None

REPORTABLE OUTCOMES: None

OTHER ACHIEVEMENTS: None

REFERENCES: None

APPENDICES: None

- Statement of Work: Extended Storage of Pathogen-Reduced Platelet Concentrates (PRECON)

Date: 07-21-2014

Project Title: Extended Storage of Pathogen-Reduced Platelet Concentrates (PRECON)

Project Contract: W81XWH-13-2-0089

Effective date: 26SEP2013

PI: Sherrill J. Slichter, MD

## STATEMENT OF WORK:

### Specific Aims/Study Design:

Whole blood (WB) will be held for  $22 \pm 2$  hours at  $22^{\circ}\text{C}$  before preparing a platelet (plt) concentrate for all aims. For Specific Aims 1 and 2, up to 12 normal subjects will be evaluated for each storage condition using autologous radiolabeled stored *versus* fresh plt recovery and survival measurements to identify the best Platelet Additive Solution (PAS) storage conditions that meet FDA post-storage plt viability criteria.

For all Specific Aims, we will need both local IRB and HRPO approvals. For Specific Aims 2 and 3, an IDE will be needed to permit Mirasol treatment of WB, and this IDE will be submitted by Terumo BCT.

Specific Aim 1: Determine the optimum conditions for extended storage of autologous plt concentrates in PAS.

| Subjects<br>(#) | Timeline<br>(Weeks) |
|-----------------|---------------------|
| 162             | 104                 |

- 1a) Identify an acceptable storage bag.

Plt concentrates can be stored for 6 days in either plasma or 65% PAS/35% plasma in our standard Terumo plt storage bag (PVC plastic). However, Haemonetics apheresis plts can be stored for 13 days in Haemonetics bags (CLX plastic).

Plt concentrates will first be stored for 6 days in 65% PAS/35% plasma using our standard Terumo plt storage bag (PVC plastic). If FDA criteria are met, we will progressively increase the storage times in 1-day increments until the criteria are not met. If the FDA criteria are met for  $\geq 9$  days of storage, we will go to Aim 1b. If  $\geq 9$  day storage is not achieved, we will utilize the Pall CLX HP (high permeability) plt concentrate storage bags that should be similar to the Haemonetics CLX apheresis bag. We will repeat the same testing sequence with the Pall CLX bag as with the Terumo bag described above. If  $\geq 9$  day storage is not achieved, we will seal off the bottom half of a 1000 ml Fenwal polyolefin bag (PL2410) to reproduce the 500 ml volume of a plt concentrate storage bag. In prior studies using PAS, we have demonstrated that this bag gives the same apheresis 13-day storage results as the Haemonetics CLX bag which is no longer available. Plts will be stored in the Fenwal bag for as long as they could be stored in the Pall bag, and the storage time will be increased in 1-day increments until FDA acceptance criteria are not met.

- 1b) Determine the best PAS-to-plasma ratio for plt storage.

Using the optimum storage bag identified in Aim 1a and starting with a 65% PAS concentration at the maximum storage time identified above, the PAS concentration will be increased in 5% increments until FDA criteria are not met. If storage times cannot be improved, we will decrease the PAS concentration in 5% decrements from the 65% to determine if storage times can be increased. Continuing this iterative process of changing the PAS concentration and storage times will determine the maximum storage duration achievable and at what PAS concentration this occurred.

Specific Aim 2: Evaluate the effects of Mirasol treatment of autologous WB on extended storage of PAS-stored plt concentrates prepared from treated WB.

| Subjects<br>(#) | Timeline<br>(Weeks) |
|-----------------|---------------------|
| 20              | 8                   |

Once we have optimized the storage conditions in Aim 1, we will Mirasol treat the WB, a plt concentrate will be prepared and stored using the optimum storage conditions. The storage time will be decreased by one-day intervals, if needed, to meet FDA acceptance criteria.

Specific Aim 3: Determine the post-transfusion recovery and survival of pre-storage pooled extended stored plt concentrates prepared from Mirasol-treated WB given to thrombocytopenic patients.

| Patients<br>(#) | Timeline<br>(Weeks) |
|-----------------|---------------------|
| 40              | 52                  |

Four plt concentrates prepared as in Aim 2 (test plts) will be pre-storage pooled and added to Fenwal's 1000 ml PL2410 storage bag. After storage, a small aliquot of the pooled plts will be removed, radiolabeled, and transfused along with the remaining unlabeled plts into a thrombocytopenic patient. Post-transfusion plt recoveries and survivals will be determined by radioactivity as well as by plt counts to determine the comparability of plt viability results from these two methods. As a control, a small aliquot of plts obtained from a standard 5-day stored plt concentrate will be radiolabeled with another isotope and transfused concurrently with the test plts to determine the relative viability of the test and control plts. We will also document hemostatic efficacy and any adverse events associated with the pooled test transfusion.