Implementation of 7 Day Platelets in a Hospital Transfusion Service

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Disclosure

Member of the Medical Advisory Committee for Verax Biomedical, the makers of the PGD rapid test which is FDA cleared to allow extension of platelet outdate to day 7.
The Journey Begins…
Learning Objectives

• Describe the use of rapid testing to enhance the safety of platelet transfusion.
• Review steps necessary for implementation of 7 day platelets using an FDA cleared rapid test.
• Summarize data illustrating the impact of implementation of 7 day platelets on platelet transfusion patterns and outdate rates.
Background: A bit about us....
Dartmouth-Hitchcock Medical Center

- 400 bed Academic Medical Center
  - Level 1 Trauma, Neonatal ICU, Stem Cell Transplant
- Transfuse ≈ 2500 PLT/year
- 100% Leukoreduced Irradiated Apheresis Platelets
“Local” Apheresis Platelet Suppliers

A. DHMC Blood Donor Program
   ≈ 40% of our inventory

B. American Red Cross
   • 97-114 miles away
   • 1 ½ to 2 HOURS

C. Rhode Island Blood Center
   • 174 miles away
   • 3 HOURS

D. New York Blood Center
   • 273 miles away
   • 4 ½ HOURS
Part 1: Describe the use of rapid testing to enhance the safety of platelet transfusion.
Routine bacterial screening of apheresis platelets on Day 4 using a rapid test: a 4-year single-center experience

Nancy M. Dunbar,* Justin D. Kreuter,* Cynthia R. Marx-Wood, Larry J. Dumont, and Zbigniew M. Szczepiorkowski

Apheresis platelet is inspected, irradiated, and entered into inventory.

Day 3

Day 4 platelets batch tested by Rapid Test (RT) at ≈10PM

Day 4

Day 5

OUTDATE

Day 6 or 7 use requires MD approval

- Report identifies all Day 4 platelets that require testing
- Outdated platelets are manually quarantined
- Computer alert prevents dispense of outdated units
DHMC Platelet Labeling

- 100% APHERESIS PLATELETS
- Platelets are inspected upon arrival
- Platelets are labeled:

  * ISBT Code E3077
  * Apheresis Platelet Leukoreduced
  * (5 day outdate)
DHMC Platelet Labeling

- Platelets are irradiated immediately upon entry into inventory
- Laboratory Information System (LIS) will only allow dispense of irradiated platelets
- FDA registered facility
- Platelets are modified and re-labeled: ISBT Code E3046
  Apheresis Platelet Leukoreduced Irradiated (5 day outdate)
DHMC Platelet Labeling

- Day 6 and Day 7 PLTS used with physician approval
- Outdate manually changed on unit and in computer system prior to dispense

ISBT Code E3046
Apheresis Platelet Leukoreduced Irradiated
(7 day outdate)
DHMC Experience with Day 4 RT

- July 2008 – October 2015

- 0.5% positive test rate
- 0.05% false positive discard rate
DHMC Experience with Day 4 RT

- July 2008 – October 2015

- 11% outdate rate decreased to 5%
- No test conversions identified
Part 2: Review steps necessary for implementation of 7 day platelets using an FDA cleared rapid test.
Bacterial Detection Testing by Blood and Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
December 2014

DRAFT GUIDANCE FOR INDUSTRY
III. CONSIDERATIONS FOR THE EXTENSION OF APHERESIS PLATELETS DATING FOR UP TO 7 DAYS

Dating may be extended if:

• 1) the platelets are collected in FDA-cleared or approved 7-day platelet storage containers with labeling that requires testing every product with bacterial detection device cleared by FDA and labeled for use as a “safety measure;”

• 2) the platelets are subsequently individually tested for bacterial detection using such a device, consistent with its instructions for use.
A. Extension of Dating Based on Additional Rapid Testing

- The use of an FDA-cleared rapid bacterial detection device labeled as a “safety measure,” one-time, could support a dating extension of up to 24 hours following the time of the test, and not exceeding the 7-day expiration date of leukocyte reduced apheresis platelets that had tested negative by early culture…and were stored in FDA-cleared or approved 7-day platelet storage containers, thereby extending the dating period through day 6 or day 7.
A. Additional Considerations for Transfusion Services

In addition to implementing inventory management to minimize the proportion of day 4 and day 5 platelets issued for transfusion (section VI of this document), we suggest that transfusion services consider the following:

1. Implement secondary testing of apheresis platelets and pre-storage pooled platelets to enhance safety through day 5 storage as described below:

   a. On the day of transfusion, perform rapid testing on day 4 or day 5 platelets using a device cleared by FDA. Consistent with the instructions for use of the FDA-cleared device, rapid testing of apheresis platelets is conducted within 24 hours prior to transfusion;

   or,

   b. Culture on day 4, using a device cleared by FDA, for issuance 24 hours after the time of sampling on day 4, provided a negative result obtained.

2. Perform secondary testing of apheresis platelets or single units of WBD platelets, using a device cleared by FDA, to extend the dating period beyond day 5 and through day 6 or day 7, after registering as a manufacturer as described in section XI of this document.
IMPORTANT NOTE

Currently, appropriately labeled bacterial detection devices and platelet storage containers for the extension of dating beyond day 5 are not available. The additional considerations to extend platelet dating beyond day 5 (section VII.A.2 of this document) may not be implemented until the availability of both:

1) Bacterial detection devices cleared by FDA and labeled as a “safety measure,” and

2) Platelet storage containers cleared or approved by FDA for 7-day platelet storage and labeled with a requirement to test every product with a bacterial detection device cleared by FDA and labeled as a “safety measure.”
The storage conditions of the Trima Platelet bag (ELP bag) have been verified for storage up to 7 days post-collection in 100% Plasma and up to 5 days in Isoplate Solution (PAS-F). Additionally, for storage up to 7 days, every product must be tested with a bacterial detection device cleared by FDA and labeled as a “safety measure.”
Platelet Storage Container Labeling

Fresenius Kabi USA LLC.
BK150242 Amicus Separator System
July 20, 2015

In the United States, blood centers that wish to store Platelets Apheresis Leukocytes Reduced in 100% plasma for 7 days must label every product with a statement that the product must be tested with a bacterial detection device cleared by FDA and labeled as a “safety measure”. The PL2410 plastic container was previously cleared for storage of platelets for up to 7 days under BK04005 (09/24/04). The labeling modification is only to revise the current statement for the 7-day platelet storage and bacterial testing requirement in the AMICUS Operator’s Manual and the Apheresis Kits Instructions for Use.
VERAX:

INDICATIONS FOR USE

The Platelet PGD Test is a rapid, qualitative immunoassay for the detection of aerobic and anaerobic Gram-positive and Gram-negative bacteria in leukocyte reduced apheresis platelets (LRAP) suspended in plasma, LRAP suspended in Platelet Additive Solution C (PAS-C) and plasma, and pre-storage pools of up to six (6) leukocyte reduced whole blood derived platelets suspended in plasma, within 24 hours prior to platelet transfusion as a safety measure following testing with a growth-based quality control test cleared by the FDA for platelet components and pools of up to six (6) units of leukocyte reduced and non-leukocyte reduced whole blood derived platelets suspended in plasma that are pooled within four (4) hours of transfusion.
Enter all changes in red ink and circle.

4. Legal name and location (Include legal name, number and street, city, state, country, and post office code)
   Dartmouth-Hitchcock Medical Center
   Transfusion Medicine Service
   Dept of Pathology, Borwell Building
   One Med. Ctr. Drive
   Lebanon, NH 03756
   4.1 Phone 603-650-7171

5. Other names used at this location (Include trade name, doing-business-as, previous names, and other firms co-located. If applicable, include registration number.)

6. Mailing address of reporting official (Include institution name if applicable, number and street, city, state, country, and post office code)
   Dartmouth-Hitchcock Medical Center
   ATTN: Zbigniew M. Szczepankowski
   One Medical Center Dr
   Lebanon, NH 03756

7. U.S. Agent (Include name, institution name if applicable, number and street, city, state, and zip code)

8. Reporting official's signature

11. Products

<table>
<thead>
<tr>
<th></th>
<th>COLLECT</th>
<th>MANUALLY</th>
<th>AUTOMATION</th>
<th>DIRECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Blood</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red Blood Cells (RBC)</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>RBC Frozen</td>
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<tr>
<td>RBC Deionized</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBC Rejuvenated</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBC Rejuvenated Frozen</td>
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<td></td>
</tr>
<tr>
<td>Cryoprecipitated Apheres</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

|                         | X       | X        | X          | X        | X        | X          | X          | X          |
| Leukocytesgranulocytes  |         |          |            |          |          |            |            |            |
| Plasma                  |         |          |            |          |          |            |            |            |
| Plasma Cryoprecipitated Reduced |          |          |            |          |          |            |            |            |
| Fresh Frozen Plasma     |         |          |            |          |          |            |            |            |
| Liquid Plasma           |         |          |            |          |          |            |            |            |
| Therapeutic Exchange Plasma |          |          |            |          |          |            |            |            |
| Source Leukocytes       |         |          |            |          |          |            |            |            |
| Source Plasma           |         |          |            |          |          |            |            |            |
| Recovered Plasma        |         |          |            |          |          |            |            |            |
| Blood Products for Diagnostic Use |          |          |            |          |          |            |            |            |
| Blood Bank Reagents     |         |          |            |          |          |            |            |            |
| Other                   |         |          |            |          |          |            |            |            |
Apheresis platelets collected on devices approved for 7 day storage as per manufacturer instructions, tested by culture based methods by supplier, received into Blood Bank inventory and irradiated, modified and relabeled.
# Product Labeling

<table>
<thead>
<tr>
<th>E-code</th>
<th>Description</th>
<th>Product name</th>
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<tbody>
<tr>
<td>E3077</td>
<td>Apheresis PLATELETSiACD-A/XX/ 20-24CIResLeu: &lt; 5E6</td>
<td>Apheresis PLTs leukoreduced</td>
</tr>
<tr>
<td><strong>PLTs irradiated, modified, and relabeled</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E3046</td>
<td>Apheresis PLATELETSiACD-A/XX/ 20-24CIrradiatedResLeu: &lt; 5E6</td>
<td>Apheresis PLTs leukoreduced irradiated</td>
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<tr>
<td><strong>Negative RT just after midnight on Day 6, modified and relabeled</strong></td>
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<tr>
<td>E8598</td>
<td>Apheresis PLATELETSiACD-A/XX/ 20-24CIrradiatedResLeu: &lt; 5E6</td>
<td>Apheresis PLTs leukoreduced irradiated Day 6</td>
</tr>
<tr>
<td><strong>Negative RT just after midnight on Day 7, modified and relabeled</strong></td>
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</tr>
<tr>
<td>E8644</td>
<td>Apheresis PLATELETSiACD-A/XX/ 20-24CIrradiatedResLeu: &lt; 5E6Approx 300 E9 pltslBacterial test</td>
<td>Apheresis PLTs leukoreduced irradiated Day 7</td>
</tr>
</tbody>
</table>

* Additional E-codes with similar attributes exist for Part 1, Part 2, and Part 3 products.
Key requirements and activities necessary to implement 7-day outdated

- Implement use of FDA-cleared “safety measure” bacterial test
- Verify supplier uses FDA-cleared 7 day platelet storage containers with “safety measure” test labeling
- Update facility FDA registration and blood product listing
- Modify contractual agreements with outside suppliers to assure platelets are supplied only in the cleared storage containers and collected according to manufacturer instructions for 7 day storage
- Structure blood bank testing and labeling work flow to accommodate RT of platelets every 24 hours as per manufacturer instructions
- Procure appropriate E-codes (iccbba.com) to enable accurate product labeling
- Configure laboratory information system to enable product modification and re-labeling using new E-codes after testing is completed
- Update institution specific circular of information to include Day 6 and Day 7 platelets
MOOSE MOUNTAIN
SOUTH PEAK
ELEVATION 2,222 ft.
Nancy Dunbar – Run

Morning Run

9:33 AM on Sunday, August 28, 2016

16.1 mi 4:48:04 17:53/mi

Distance Moving Time Pace

Elevation 4,065 ft Calories 2,477

Elapsed Time 5:16:42

© Mapbox © OpenStreetMap Improve this map
How do we implement Day 6 and Day 7 platelets at a hospital-based transfusion service?

Nancy M. Dunbar,1,2,4 Larry J. Dumont,1,3,4 and Zbigniew M. Szczepiorkowski1,4

TRANSFUSION 2016;56;1262–1266
Part 3: Summarize data illustrating the impact of implementation of 7 day platelets on platelet transfusion patterns and outdate rates.
DHMC Experience with Day 5/6/7 RT

- November 2016 – January 2017

0.6% initial test positive rate
- 0.02% false positive discard rate

- CULTURED AP N = 2963
- REQUESTED PRIOR TO DAY 4 or 5 PGD TEST
- RELEASE
- TRANSFUSE N = 1476 (50%)
- 5 RT POSITIVE x 3 CULTURE NEGATIVE
- 4 RT NEGATIVE x 3

TESTED AND AVAILABLE, N = 1482 (50%)
DHMC Experience with Day 5/6/7 RT

- November 2016 – January 2017

- 24% outdate rate decreased to 3%
- No true test conversions identified
Before and After Comparison

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>RT on Day 4 Only</th>
<th>RT on Days 5, 6, 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Inventory Transfused w/o Test</td>
<td>61%</td>
<td>50%</td>
</tr>
<tr>
<td>% Inventory Tested</td>
<td>39%</td>
<td>50%</td>
</tr>
<tr>
<td>Outdate Rate</td>
<td>11%</td>
<td>3%</td>
</tr>
</tbody>
</table>

- Increased RT volume/cost offset by decreased platelet wastage due to outdate
February 2016 - January 2017 compared to October 2014 - September 2015

• % Transfused units tested at least once by RT increased from 33% to 54%
• Outdate rate decreased from 5.1% to 2.2%
• Ad Hoc rate decreased from 21% → 9%
• Number of platelets transfused per patient is unchanged (3.16 vs. 3.12)
Opportunities for Improvement

- Test volume could be decreased by selective testing based on anticipated need
- Amicus package insert could be modified to allow for routine day 7 outdate for all units
- RT package insert could be modified to allow for single time testing on Day 4 or 5 to allow outdating to Day 7
Conclusions

- Pathway for use of Day 6 and Day 7 platelets available
- Increased cost associated with repeat testing may be offset by decreased waste
- Use of RT as an additional safety measure along with outdate extension to day 7 results in more patients receiving tested units without increased transfusion rates
Acknowledgements

- Zbigniew (Ziggy) Szczepiorkowski
- Larry Dumont
- Pat Distler
- Kathy Grindle
- Jody Barna
- Don Ulinski
- DHMC Blood Bank and Blood Donor Room
Any Questions?