ASFA Annual Meeting
May 7, 2015
Margaret Hannan LPN, AT (ASCP)
Our Journey

• What is Intersol
• Why InterSol
• Educating the Hospitals
• PAS Implementation
• PRBI Variance Approval
• Licensure - PAS Platelets
• cPlasma Benefits
• Post Implementation Review
Risk Reduction for Patient Safety
Progression to PAS

1950: Whole blood

1960: Blood components: RBCs, plasma and platelets

1970: Plasma fractionation – albumin, Factor VIII, IgG, etc.

1980: RBC additive solution replaced most plasma in RBCs, with 42 day dating

1990: Leukoreduction

2000: PAS

2010: PAS
Additive solutions are balanced isotonic electrolyte solutions designed to sustain platelets in storage

- Energy source: glucose or acetate
- Buffer to maintain pH: phosphate and bicarbonate
- Electrolyte: sodium, potassium, magnesium
PAS History

- 1991 first PAS solution launched in Sweden
- 1991 – 2009 multiple forms of PAS developed and used worldwide
- 2007 PAS 3 approved for use in Europe
- 2010 PAS 3 became first FDA approved additive solution
A comparison of adverse reaction rates for PAS C versus plasma platelet units

Claudia S. Cohn,¹ James Stubbs,² Joseph Schwartz,³ Richard Francis,³ Cheryl Goss,⁴ Melissa Cushing,⁴ Beth Shaz,⁵ David Mair,⁶ Barbara Brantigan,⁷ and W. Andrew Heaton⁸

<table>
<thead>
<tr>
<th></th>
<th>InterSol Platelets</th>
<th>Plasma Platelets</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusions</td>
<td>4160</td>
<td>9845</td>
<td>14,005</td>
</tr>
<tr>
<td>Patients transfused</td>
<td>1444</td>
<td>2202</td>
<td>2605</td>
</tr>
</tbody>
</table>
## Reaction Rates

<table>
<thead>
<tr>
<th></th>
<th>InterSol (N=4160) n (%)</th>
<th>Plasma (N=9845) n (%)</th>
<th>Relative Risk (PAS C/Plasma)</th>
<th>Upper Confidence Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusions That Led to Reactions</td>
<td>23</td>
<td>135</td>
<td>0.403</td>
<td>0.663</td>
</tr>
<tr>
<td>Reaction Rate</td>
<td>0.006 (0.55%)</td>
<td>0.014 (1.37%)</td>
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</tr>
</tbody>
</table>
# Reactions by Type

<table>
<thead>
<tr>
<th>Adverse Reaction Type</th>
<th>InterSol (N=4160)</th>
<th>Plasma (N=9845)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trx n (%)</td>
<td>Rxn n (%)</td>
</tr>
<tr>
<td>Allergic</td>
<td>12 (0.29)</td>
<td>81 (0.82)</td>
</tr>
<tr>
<td>Febrile Non-Hemolytic Transfusion Reaction</td>
<td>7 (0.17)</td>
<td>49 (0.50)</td>
</tr>
<tr>
<td>Hypotensive Transfusion Reaction</td>
<td>1 (0.02)</td>
<td>2 (0.02)</td>
</tr>
<tr>
<td>TACO</td>
<td>2 (0.05)</td>
<td>6 (0.06)</td>
</tr>
<tr>
<td>Transfusion Associated Dyspnea (TAD)</td>
<td>0 (0.00)</td>
<td>2 (0.02)</td>
</tr>
<tr>
<td>TRALI</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.02)</td>
<td>2 (0.02)</td>
</tr>
<tr>
<td>Overall</td>
<td>23 (0.55)</td>
<td>135 (1.37)</td>
</tr>
</tbody>
</table>

Be Someone’s Hero. **Give Blood.**
Benefits of InterSol

• Reduced transfusion reaction rate with PAS C compared to platelets stored in plasma
  – Overall population
  – Allergic Transfusion Reactions
  – Febrile Non-hemolytic Transfusion Reactions
• Opportunity with pathogen inactivation/reduction (Intercept) – In February BBD signed a purchase agreement with Cerus for the INTERCEPT Blood System for platelets and plasma

- Reduces the risk of transfusion-transmitted infections such as Hepatitis B and C, HIV, West Nile Virus and malaria that could be present in donated blood
- Blocks the replication of pathogens such as viruses, bacteria and parasites, making them inactive
Additional benefit for blood centers:

Increase amount of plasma collected concurrently with platelet donation
InterSol

• Used with AMICUS Blood Cell Separator
• PAS apheresis platelets: 65% PAS and 35% plasma
• Stored up to 5 days at 20-24 C with continuous agitation
• Validated for use with BacT/ALERT
• PAS code was added to ISBT product codes
InterSol

PAS 3 Replaces 65% Plasma

Platelets in InterSol

~65% InterSol

~35% Plasma

Platelets in 100% Plasma

100% Plasma

Plasma transfused is decreased by 65%
Why InterSol?

• Reduce platelet transfusion reactions
• Help meet the increased demand for plasma in the marketplace
  ➢ Optimize plasma collections by implementing InterSol Platelet Additive Solution on Amicus
  ➢ When using InterSol, 65% of the plasma collected for storage of platelets is replaced by InterSol solution. This plasma can be repurposed!
• Collect more plasma from every donor
How Our Journey Began

• Largest hospital customer: 2 significant patient reactions to non-ABO compatible platelet transfusions
• Subsequent investigation revealed increased titer of ABO antibodies
• Planned to implement policy change to ABO compatible platelets only
• Hospital Lab Manager and transfusion service Medical Director contacted BBD
How Our Journey Began

Our Response

• Director of Laboratory and Product Management offered PAS (InterSol) platelets as an alternate solution (*literally*)

• Rationale: If platelets contained less plasma, there should be fewer antibodies to cause a transfusion reaction

• Hospital response was favorable **BUT** they wanted a quick implementation
How Our Journey Began

• BBD was receptive to timeline
• Hospital customer refrained from implementing policy requiring ABO compatibility for platelet transfusions
• Viewed Intersol as a possible TRALI strategy and could eliminate the need for HLA matched platelets in some situations
Educating the Hospitals

• Director of Laboratory and Product Management led hospital communications
• Communicated through monthly meetings with hospital supervisors
• Provided package insert and new product codes
• Updated Circular of Information
• Encouraged to share internally with medical directors, blood utilization committees, etc.
Educating the Hospitals

- Response from hospitals was positive
- Two main concerns:
  - What is in PAS solution (a children’s hospital)
  - Will we charge more for PAS products
- Initiating hospital customer wanted as many as we could provide
- Out of state customers wanted them but we could not ship since product was not licensed
PAS Implementation

• Two Phases

➤ PAS Platelet collection with Increased volume of cPlasma products (InterSol replaces 65% of storage fluid volume)

➤ Collection of PRBI (Plasma Replaced by Intersol) at frequency <28 days

• Implemented PAS platelet collections within a few months from time of request
PAS Implementation

PAS Platelets

• SOP Perspective
  ➢ Collections: Minimal SOP changes
  ➢ Lab: New label was the only change for lab

• Staff Perspective
  ➢ InterSol is automatically metered into platelet during product transfer
  ➢ Most staff very comfortable in just a few days
PAS Implementation

PAS Platelets

- Training Perspective
  - About an hour (both phases)
  - Excerpts from Operator’s Manual
  - In-house student handout
  - Direct Observation
  - Study Guide (Quiz)

- The donor perspective
  - Looks the same from donor perspective
  - All other procedure parameters the same
  - Donation time not impacted
PAS and ‘PRBI’

PRBI? Don’t you mean RBI? Are they the same thing?
‘PRBI’ Benefits

**PRBI - Plasma Replaced by InterSol®**

*Or ~ Plasma ‘Run Batted In’*

- The plasma volume intended for platelet storage that is replaced by InterSol solution (65%)
- May be used as plasma product while still classifying the donor as a plateletpheresis donor for deferral purposes
- Total plasma for all products is calculated to manage the maximum per-procedure and annual plasma loss
- The absolute plasma product volume (plasma product volume minus ACD) cannot exceed the absolute volume replaced by InterSol by more than 5 mls
‘PRBI’ Benefits

Donor Scenario

• Last donation 14 days ago with cPlasma collected
  • Double Platelet Product
  • Storage Fluid = 600 mls
    • 65% (PRBI) = 390 mls
  • 90% of 390mls = **351mls** PRBI can be collected

From a donor not eligible for cPlasma donation!
Concurrent Plasma Benefit

Before PAS / PRBI

• Very strong cPlasma collection program
• cPlasma collected from male donors only
• In 2010 targeted cPlasma from 53% of all platelet procedures
• October 2013 implemented cPlasma collection from AB females
Concurrent Plasma Benefits

• PAS / PRBI Plasma
  – Additional plasma products: 65% increase, from 0.80 to 1.32 concurrent plasma products per procedure
  – Improved inventory of AB FFP
  – Divert more WB plasma to recovered: 4000-5000 units
  – $150k to $200k revenue
Lessons Learned

• Variance submission – send statement of process rather than SOP’s (discuss with your CSO)
• Overlap of variance submission and licensure submission caused some confusion & delays
• Submit sooner!
• Don’t submit during a government shutdown or office relocation!
• No regrets....
PAS and ‘PRBI’

• Determine volumes (the most challenging aspect)
  ➢ Platelet storage
  ➢ cPlasma
  ➢ PRBI

• Modify SOP’s

• Apply for FDA variance for alternate procedure

• Train staff for PRBI
  ➢ Understanding the PRBI concept was the most challenging aspect
Recommendations

• Use fixed platelet storage volumes and PRBI collection volumes (especially if using MPV to drive volume)
  - Easier for staff
  - Less risk of exceeding plasma loss limits
• Implemented initially at one (small) site to help manage licensed / non-licensed inventory
• Connect InterSol at product transfer step (cost savings in the event of an incomplete procedure)
PRBI Variance

• Donation interval for cPlasma and Platelet collection is 28 days
• FDA variance is needed to collect PRBI from frequent donors without changing donation interval to 28 days
• June 26, 2012 - applied for alternate procedure approval to collect the plasma replaced by InterSol (PRBI)
• Received FDA approval for the alternate procedure on June 17, 2013
PRBI Variance Submission Process

• Conference calls with FDA CSO – planning and ensuring understanding of FDA expectations

• Submission:
  - Cover letter
  - Form FDA 356h
  - Applicable SOP’s (“statement” of process may have been sufficient)
Licensure Submission

- Cover letter
- Form FDA 356h
- Submit CBE-30 supplement for other locations
- Labels
- SOP’s
- Validation data
- 2 months of QC data
- Submitted March 1, 2013
- Licensure received September 18, 2014.

BBD was the first blood center in the US licensed for Intersol!
Recommended Process Flow

• Submit for PRBI variance
• Begin PAS Platlet collections (higher volume cPlasma allowed because of 65% InterSol)
• Submit for licensure for PAS platelets with Comparability Protcol
• Begin PRBI collection when variance approved
• Submit CBE-30 for other sites once licensure received
Hospital Perspective

• Readily accepted as a favored product
• Felt it would reduce transfusion reactions in general
• Mixed PAS / non-PAS inventory policy:
  1 ABO incompatible unit within 24 hours until licensed / converted to 100% PAS inventory
Post Licensure Steps

• Hospitals: When can we have 100% PAS inventory?
  ➢ No ABO incompatibility transfusion restrictions

• Add license information to label & ship out of state

• Submit CBE-30
  ➢ submitted November 25th 2014
  ➢ approved December 12th 2014
Post Implementation Review

What’s next?

• TRALI mitigation?
• Will this change HLA matching needs?
• Future opportunity with Cerus INTERCEPT
Closing

• Hospital Education is easy ("WIIFM")
• PAS Implementation is not hard & can be done quickly
• PRBI Variance submission is easy; applying just makes sense!
• Licensure process can be painful but worth it!
• Plasma Collection Results
  ➢ Significant increase in cPlasma opportunities
  ➢ Ensures adequate FFP inventory (AB!)
  ➢ Increased revenue from recovered plasma
Why InterSol?

In Conclusion

• Platelets stored in additive solution bring many benefits
  – Increased patient safety
  – Increased versatility for transfusion service
  – Increased plasma for blood centers
Do it!

Launch a PAS Platelet and RBI collection program now!
I gratefully acknowledge Dr. Claudia Cohn, University of Minnesota for her contributions to this presentation

cscohn@umn.edu
Contact Information

Margaret Hannan
mhannan@bbd.org
(302) 737-8405 x 719

Blood Bank of Delmarva
100 Hygeia Drive
Newark, DE 19713

Telephone: (302) 737-8405
Toll Free: (800) 548-4009
Fax: (302) 737-8233

www.DelmarvaBlood.org

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