Beyond bacterial culturing of platelets

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Medical Director
Vitalant
Agenda

- Overview of Cerus Intercept Blood System for platelets, reduction system
- Overview of Verax Platelet PGD point of release test
Pathogen Reduction
Psoralen/UVA Light Treatment
Key Benefits: INTERCEPT® Blood System for Platelets

- Only FDA-approved pathogen reduction system for platelets
- Proactive strategy towards potential infectious agents*
  - Bacteria
  - Viruses
  - Spirochetes
  - Protozoa
  - Leukocytes
- Authorized by the FDA and AABB Standards as an alternative to irradiation for prevention of TA-GVHD
- Replaces need for initial bacterial testing at blood center or subsequent point of issue testing at the hospital
- No need for CMV testing
- No patient population restrictions, no documented sensitivity to date
- Meets anticipated FDA guidance for 5-day platelets with no additional intervention needed

*There is no pathogen inactivation process that has been shown to eliminate all pathogens. Certain non-enveloped viruses (e.g., HAV, HEV, B19 and poliovirus) and *Bacillus cereus* spores have demonstrated resistance to the INTERCEPT process.
Mechanism of Action: Targeting DNA & RNA to Prevent Pathogen Proliferation

1. Intercalates into regions of DNA and RNA
2. Crosslinks upon UVA illumination
3. Blocks replication, transcription and translation

Psoralen/UVA Light Treatment for Pathogen Reduction: Key Processing Steps

1. Sterile connect the platelet or plasma product to a sterile processing set.
2. Gravity-transfer the platelets or plasma and psoralen into the illumination container and mix.
3. Illuminate the product.
4. Platelets: Transfer the platelets by gravity into the CAD bag. Incubate the platelet product with continuous agitation.
5. Plasma: On plasma sets, the CAD is a flow-through device. Gravity-transfer the plasma through the CAD.
6. Transfer the product by gravity into the final storage container(s) (1 or 2 platelet containers, 3 plasma containers).

*CAD: Compound Adsorption Device

Clinical indications = Conventional Platelets

- Apheresis Platelets collected on Amicus with PAS-3
- Apheresis Platelets collected in 100% plasma on Trima

5-day storage

No age or population restrictions

Replacement for primary and secondary bacterial culture screening

Approved alternative to gamma irradiation for the prevention of TA-GVHD

Reduces the risk of transfusion transmitted infections from established and emerging pathogens
There is no pathogen inactivation process that has been shown to eliminate all pathogens. Certain non-enveloped viruses (e.g., HAV, HEV, B19, and poliovirus) and Bacillus cereus spores exhibit resistance to inactivation by the psoralen/UVA light process.
How well does Psoralen/UVA light treatment inactivate pathogens?

### Viruses

<table>
<thead>
<tr>
<th>Virus</th>
<th>Log Reduction PAS-3/Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1, cell-associated</td>
<td>≥5.4/≥4.7</td>
</tr>
<tr>
<td>DHBV (model virus for HBV)</td>
<td>≥4.8/≥4.3</td>
</tr>
<tr>
<td>BVDV (model virus for HCV)</td>
<td>≥4.1/&gt;3.5</td>
</tr>
<tr>
<td>HTLV-I</td>
<td>4.7/b</td>
</tr>
<tr>
<td>HTLV-II</td>
<td>≥5.1/b</td>
</tr>
<tr>
<td>West Nile Virus</td>
<td>≥6.3/&gt;6.3</td>
</tr>
<tr>
<td>Chikungunya virus (CHIKV)</td>
<td>≥5.7/&gt;6.5</td>
</tr>
<tr>
<td>Dengue virus (DENV)</td>
<td>≥4.3/3.6</td>
</tr>
<tr>
<td>Cytomegalovirus (CMV), cell-associated</td>
<td>≥4.9/≥4.2 (PRV)</td>
</tr>
<tr>
<td>Influenza A virus</td>
<td>≥5.9/b</td>
</tr>
<tr>
<td>Bluetongue virus</td>
<td>5.2/4.4</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>≥4.9/&gt;5.3</td>
</tr>
</tbody>
</table>

### Bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Log Reduction PAS-3/Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>≥6.3/&gt;5.9</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>≥5.9/&gt;6.3</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>&gt;6.2/&gt;6.2</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>≥6.7c/&gt;7.1</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>≥6.4/&gt;6.5</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>≥6.6/&gt;6.5</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>≥6.8c/&gt;6.1</td>
</tr>
<tr>
<td>Bacillus cereus (vegetative)</td>
<td>≥5.5/&gt;5.6</td>
</tr>
<tr>
<td>Bacillus cereus (spore forming)</td>
<td>3.7c/b</td>
</tr>
<tr>
<td>Clostridium perfringens (vegetative)</td>
<td>≥6.5/&gt;6.0</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>≥6.5/&gt;6.7</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>≥6.4/a</td>
</tr>
<tr>
<td>Borrelia burgdorferi</td>
<td>≥6.8/a</td>
</tr>
</tbody>
</table>

### Protozoan Parasites

<table>
<thead>
<tr>
<th>Protozoan Parasites</th>
<th>Log Reduction PAS-3/Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmodium falciparum</td>
<td>≥6.6/d</td>
</tr>
<tr>
<td>Babesia microti</td>
<td>≥4.9/d</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>≥7.8/&gt;8.4</td>
</tr>
</tbody>
</table>

### Leukocytes

<table>
<thead>
<tr>
<th>Leukocytes</th>
<th>Log Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human T-Cells</td>
<td>&gt;4.0</td>
</tr>
</tbody>
</table>

** There is no pathogen inactivation process that has been shown to eliminate all pathogens.
- INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; July 17, 2018

\( ^a \) = In clinical trial
\( ^b \) = Not tested
\( ^c \) = Based on culture of full platelet unit (300mL)
\( ^d \) = Study in progress
Mitigation Options for Zika Virus: 
Zika Testing or Pathogen Reduction

IV. RECOMMENDATIONS

The following recommendations are intended to reduce the risk of ZIKV transmission by blood and blood components. The recommendations apply to the collection of all Whole Blood and blood components in the United States and its territories. If, based upon the available scientific evidence, the risk of ZIKV transmission by blood and blood components significantly changes, FDA may update these recommendations as warranted. In making this determination, FDA will consider available epidemiologic and other scientific evidence.

A. Testing and Pathogen Reduction

We recommend the following:

1. Test all donations collected in the U.S. and its territories with an investigational individual donor nucleic acid test (ID-NAT) for ZIKV under an investigational new drug application (IND), or when available, a licensed test, or

2. Implement pathogen reduction technology for platelets and plasma using an FDA-approved pathogen reduction device as specified in the Instructions for Use of the device. If an FDA-approved pathogen reduction device becomes available for Whole Blood or red blood cells, you may implement pathogen reduction technology for such products rather than testing the donations as described in section IV.A.1.

CMV-Negative, CMV-Safe or CMV-Reduced

- Units that are either leuko-reduced or CMV-seronegative are often referred to as “CMV-safe” by blood banks
- Leukocyte reduction results in \(< 2 \log_{10}\) CMV clearance\(^{25}\)
- “CMV-safe” units still carry a 1-6.5% risk of CMV transmission\(^{26}\)
- Bone Marrow Transplant (BMT), pediatric, and neonate patients are most susceptible
- 15-20% mortality rate among BMT patients that get CMV.\(^{27}\)
- CMV pneumonia is associated with mortality rate of 80-90%.\(^{27}\)

Psoralen/UVA treatment results in a \(\geq 4.2-4.9\) log reduction in CMV\(^{23}\)

23. psoralen treated Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; July 17, 2018
Clinical Trials Using Psoralen/UVA Light Treatment Pathogen Reduction for Platelets

Over 800 subjects evaluated in several trials

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Patients</th>
<th>Design</th>
<th>Primary Endpoint</th>
<th>Primary Endpoint Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viability of test platelets, clearance of amotosalen, healthy patients(^\text{17})</td>
<td>65</td>
<td>Randomized, single-blind, cross-over</td>
<td>Recovery/survival, clearance of amotosalen</td>
<td>✓</td>
</tr>
<tr>
<td>Safety/efficacy of test platelets, thrombocytopenic patients(^\text{18})</td>
<td>645</td>
<td>Randomized, double-blind, parallel</td>
<td>WHO Grade 2 bleeding</td>
<td>✓</td>
</tr>
<tr>
<td>Safety/efficacy of test platelets, thrombocytopenic patients(^\text{19})</td>
<td>43</td>
<td>Randomized, double-blind, parallel</td>
<td>1 hour CCI</td>
<td>✓</td>
</tr>
<tr>
<td>Safety/efficacy of test platelets, thrombocytopenic patients(^\text{20})</td>
<td>32</td>
<td>Randomized, double-blind, cross-over</td>
<td>Bleeding time</td>
<td>✓</td>
</tr>
<tr>
<td>Safety of test Routine setting(^\text{21})</td>
<td>51</td>
<td>Single-arm, open label</td>
<td>Frequency of acute transfusion reactions was 1.6%</td>
<td></td>
</tr>
<tr>
<td>Safety of test Routine setting(^\text{22})</td>
<td>46</td>
<td>Single-arm, open label</td>
<td>Frequency of acute transfusion reactions was 2%</td>
<td></td>
</tr>
</tbody>
</table>

Prevention of TA-GVHD
Replacing Irradiation with Psoralen/UVA Light Treatment

- High DNA modification densities help ensure inactivation of most genes:

**Gamma irradiation** 1:37,000 strand-break:base pair

**Psoralen/UVA Light-Treated Platelets**
1:83 amotosalen adduct formed:base pair

In Vitro: Cytokine Production in Platelets: Psoralen/UVA Light Treatment vs. Gamma Irradiation

- Leukocytes in untreated controls produced high levels of IL-8 & IL-1β during storage of random donor platelet concentrates
  - Gamma irradiation partially inhibited cytokine synthesis
- Psoralen/UVA light treatment blocked production of IL-8 & IL-1β

American Association of Blood Banks (AABB) Revised Standards

- The AABB Blood Bank Transfusion Services (BBTS) Standards Program Unit (SPU) oversees the standards for irradiation of blood products.

- AABB has issued approval for the use of *apheresis platelets, leukocytes reduced, psoralen-treated* products as equivalent to irradiated platelets for patients at risk for transfusion-associated graft-vs-host disease (TA-GVHD) as follows:

<table>
<thead>
<tr>
<th>Standard Number</th>
<th>Standard Language</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.19.3.1</td>
<td>Methods known to prevent transfusion-associated graft-vs-host disease shall be used, and include either irradiation or the use of a pathogen reduction technology that is known to inactivate residual leukocytes and is cleared or approved by the FDA or Competent Authority.</td>
</tr>
</tbody>
</table>

Safety Study of >20,000 Platelet doses
Routine Use of Psoralen Treated Platelets$^{31,39}$

- Longitudinal studies conducted over 13 years at 26 centers across 15 countries
- **No** reported instances of transfusion-transmitted infection (TTI)
- There was no irradiation in over 97% of the psoralen treated treated platelets. No reported instances of transfusion-associated graft-versus-host disease (TA-GVHD)

<table>
<thead>
<tr>
<th>Study (years)</th>
<th>Psoralen/UVA Platelet Doses</th>
<th>Patients</th>
<th>Patient Primary Diagnosis</th>
<th>AEs (SAEs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV1$^{31}$ (2003-2005)</td>
<td>5,106</td>
<td>651</td>
<td>30%</td>
<td>0.8% (0.0%)</td>
</tr>
<tr>
<td>HV2$^{31}$ (2005-2007)</td>
<td>7,437</td>
<td>1,400</td>
<td>18%</td>
<td>0.7% (0.0%)</td>
</tr>
<tr>
<td>HV3$^{31}$ (2006-2010)</td>
<td>6,632</td>
<td>2,016</td>
<td>52%</td>
<td>0.4% (0.1%)</td>
</tr>
<tr>
<td>HV5$^{39}$ (2013-2016)</td>
<td>2,373</td>
<td>698</td>
<td>0.4% (0.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Total:</strong> (2003-2016)</td>
<td><strong>21,548</strong></td>
<td><strong>4,765</strong></td>
<td></td>
<td><strong>0.6%† (0.0%)</strong></td>
</tr>
</tbody>
</table>


*AE: Adverse Event; SAE: Serious Adverse Event
†Conventional platelet AE rate has been shown to be 0.63%$^3$
No Transfusion Transmitted Sepsis (TTS) or Fatalities with Psoralen Treated Platelets

Outcome Data for >700,000 psoralen treated platelet transfusions

<table>
<thead>
<tr>
<th>Country</th>
<th>(Year)</th>
<th>Conventional Platelets</th>
<th>psoralen treated Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Units Transfused (n)</td>
<td>TTS (Fatalities)</td>
<td>Units Transfused (n)</td>
</tr>
<tr>
<td>France</td>
<td>2006-2016</td>
<td>2,860,529</td>
<td>50 (10)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>2005-2016</td>
<td>156,719</td>
<td>16 (9)</td>
</tr>
<tr>
<td>Belgium</td>
<td>2009-2015</td>
<td>294,477</td>
<td>9 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>3,311,725</td>
<td>75 (13)</td>
<td>705,577</td>
</tr>
</tbody>
</table>

45. Benjamin et al. Transfusion 2017;57:2946-57
Comparison of Platelet Use During the 21 months Before and After Psoralen/UVA Light Treatment Introduction in Innsbruck, Austria

<table>
<thead>
<tr>
<th>All Patients</th>
<th>Pre-psoralen/UVA treatment (N=1797)</th>
<th>Post-psoralen/UVA treatment (N=1694)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Platelets transfused</td>
<td>4.8 ± 9.7</td>
<td>4.5 ± 8.9</td>
<td>0.44</td>
</tr>
<tr>
<td>Courses</td>
<td>1.5 ± 1.6</td>
<td>1.4 ± 1.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Average Interval</td>
<td>0.9 ± 0.9</td>
<td>0.8 ± 0.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Days of Support</td>
<td>5.9 ± 14.7</td>
<td>5.0 ± 11.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RBCs Transfused</td>
<td>13.7 ± 18.8</td>
<td>13.0 ± 17.0</td>
<td>0.53</td>
</tr>
<tr>
<td>Plasma Transfused</td>
<td>7.0 ± 30.4</td>
<td>4.3 ± 22.8</td>
<td>0.11</td>
</tr>
<tr>
<td>AE per patient</td>
<td>24/1797 (1.3%)</td>
<td>23/1694 (1.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>AE per transfusion</td>
<td>32/8611 (0.4%)</td>
<td>24/7705 (0.3%)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

### Psoralen/UVA Light Treatment - Summary

**Replacement of critical tests and/or procedures**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria</strong></td>
<td>• The FDA Guidance(^{52}) and AABB Standard 5.1.5.2(^{53}) state that PRT can be used in place of bacterial testing.</td>
</tr>
<tr>
<td><strong>T-cells</strong></td>
<td>• FDA and AABB Standard 5.19.3.1 have approved psoralen treated as an alternative to gamma irradiation for the prevention of TA-GVHD(^*).(^{53,23})</td>
</tr>
<tr>
<td><strong>CMV</strong></td>
<td>• Psoralen treated provides Cytomegalovirus (CMV) inactivation levels(^{23}) meeting the AABB Standard 5.19.2(^{53}) policy requiring methods to reduce CMV transmission risk.</td>
</tr>
<tr>
<td><strong>Protozoan Parasites</strong></td>
<td>• In early 2018 the FDA approved the first test for a parasite, Babesia.(^{54}) The psoralen treated Blood system was FDA approved to reduce the risk of Babesia, T. Cruzi and Plasmodium transmission in 2014.(^{23})</td>
</tr>
<tr>
<td><strong>Emerging Pathogens</strong></td>
<td>• WHO(^{55}), European Centre for Disease Prevention and Control (ECDC)(^{56}) and FDA Guidance(^{24}) for Zika state that PRT(^{**}) can be used in place of Zika testing or importing from non-endemic areas.</td>
</tr>
</tbody>
</table>

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\(^{53}\) AABB, 30th edition, 2015. \([53]\)  
\(^{23}\) The psoralen treated Blood System for Platelets Package Insert, Cerus Corporation; July 17, 2018.  
\(^{54}\) FDA. Babesiosis. Silver Spring, MD 2018 \([54]\)  
\(^{55}\) WHO. Interim Zika guidance. February 2016. \([55]\)  
\(^{56}\) ECDC. Zika Virus and Safety of Substances of Human Origin, July 2016. \([56]\)  
\(^{24}\) FDA Zika Guidance for Industry, August 2016.  

\(^*\) Transfusion-Associated Graft vs. Host Disease  
\(^{**}\) Data for pathogen reduction of ZIKA by the psoralen treated Blood System, pathogen reduction system, has been submitted for FDA review.
Warnings and Contraindications

CONTRAINDICATIONS
Contraindicated for preparation of platelets or plasma intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. Contraindicated for preparation of platelet components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

WARNINGS AND PRECAUTIONS
Only INTERCEPT Processing Sets for plasma or platelet components are approved for use in the INTERCEPT Blood System. Use only the INT100 Illuminator for UVA illumination of amotosalen-treated plasma or platelet components. No other source of UVA light may be used. Please refer to the Operator's Manual for the INT100 Illuminator. Discard any plasma or platelet components not exposed to the complete INT100 illumination process.

Tubing components and container ports of the INTERCEPT Blood System for Plasma and Platelets contain polyvinyl chloride (PVC). Di(2-ethylhexyl)phthalate (DEHP) is known to be released from PVC medical devices, and increased leaching can occur with extended storage or increased surface area contact. Blood components will be in contact with PVC for a brief period of time (approx. 15 minutes) during processing. The risks associated with DEHP released into the blood components must be weighed against the benefits of therapeutic transfusion.

PLATELETS
INTERCEPT processed platelets may cause the following adverse reaction: Acute Respiratory Distress Syndrome (ARDS). An increased incidence of ARDS was reported in a randomized trial for recipients of INTERCEPT processed platelets, 5/318 (1.6%), compared to recipients of conventional platelet components (0/327). Monitor patients for signs and symptoms of ARDS.

PLASMA
Amotosalen-treated plasma may cause the following adverse reaction: Cardiac Events. In a randomized controlled trial of therapeutic plasma exchange (TPE) for TTP, five patients treated with INTERCEPT Blood System processed plasma and none with conventional plasma had adverse events in the cardiac system organ class (SOC) reported. These events included angina pectoris (n=3), cardiac arrest (n=1), bradycardia (n=1), tachycardia (n=1) and sinus arrhythmia (n=1). None of these events resulted in documented myocardial infarction or death. Monitor patients for signs and symptoms of cardiac events during TPE for TTP.

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Hypersensitivity to Psoralsens

USA Package Insert

- Contraindicated for preparation of plasma or platelets intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralsens.

Psoralen treated products have been in routine use in Europe (16+ years) and USA (3+ years) with over 6 million psoralen treated components administered with no hypersensitivity reaction to psoralsen reported to date.

Psoralens in Food

Psoralens are present in a wide variety of foods

<table>
<thead>
<tr>
<th>FOODS RICH IN PSORALEN¹</th>
<th>Anise Seeds</th>
<th>Cilantro</th>
<th>Fennel</th>
<th>Lovage (Leaf Parsley)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caraway Seeds</td>
<td>Coriander Seeds</td>
<td>Figs</td>
<td>Mustard Seed</td>
<td></td>
</tr>
<tr>
<td>Carrots</td>
<td>Cumin Seeds</td>
<td>Grapefruit</td>
<td>Parsnips</td>
<td></td>
</tr>
<tr>
<td>Celeriac</td>
<td>Dill</td>
<td>Lemon/Lime</td>
<td>Root Parsley</td>
<td></td>
</tr>
<tr>
<td>Celery</td>
<td>Chevril (French Parsley)</td>
<td>Orange</td>
<td>Turnips</td>
<td></td>
</tr>
</tbody>
</table>

Use with Neonatal Phototherapy

An old issue … addressed by new technology

- **USA Package Insert**¹,²:
  - *Contraindicated for preparation of platelet components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm*, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

- **American Academy of Pediatrics-Clinical Practice Guidelines**³
  - Recommended spectrum for intensive phototherapy: 430 – 490 nm
  - Use special blue tubes or LED light source with output in the visible blue-green spectrum for intensive phototherapy
  - Cautionary language around use of halogen lamps (to avoid burns)

- **None of the neonatal phototherapy devices marketed in the US today emit a peak wavelength below 425 nm with a lower bound of the emission bandwidth less than 375 nm**⁴

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Amotosalen Absorbance

Amotosalen absorbs in the UV spectrum, diminishing significantly past 375nm. Therefore, the small amount of amotosalen left in platelet products could react if exposed to wavelengths within the absorption spectrum.

A lower bound of 375nm and minimum peak of 425nm is meant to reduce that potential risk further.
Warnings and precautions: PLATELETS

INTERCEPT processed platelets **may cause the following adverse reaction: Acute Respiratory Distress Syndrome (ARDS)** An increased incidence of ARDS was reported in a randomized trial for recipients of INTERCEPT processed platelets, 5/318 (1.6%), compared to recipients of conventional platelet components (0/327). Monitor patients for signs and symptoms of ARDS.

This effect has not been seen since these results were documented in clinical trial results used for the FDA approval process. **This is not a contraindication for use.**

PIPER study is being done to confirm that this is no longer an issue.
PIPER: Evaluating respiratory risk in routine use in the US

- Based on data from European HV systems, FDA approved INTERCEPT PCs, but requested confirmatory data from a Phase IV post-marketing study as the product entered routine use in the US.

- **PIPER Study**
  - Population: Hematology-Oncology patients requiring 1 or more PCs
    - 3000 patients in sequential cohorts
  - Non-inferiority design
  - Intervention: PRT platelet components
  - Comparison: Conventional platelet components
  - Outcome: Incidence of assisted ventilation
    - Intubation
    - Tight fitting mask with PEEP or BPAP > 5 cm H₂O
  - Timing: Platelet support for up to 21 days
    - Assisted ventilation up to 7 days after last PC transfusion
    - AE (including transfusion reactions) 24 hours after each study PC transfusion
    - SAE for 7 days after last PC transfusion up to day 21
Psoralen Treated Product Labeling

- Labeled as **APHERESIS PLATELETS LEUKOCYTES REDUCED, PSORALEN-TREATED**
- Platelet dose is the same as conventional platelets.
- Pre-meds and hang time are the same as conventional platelets.
- 1.3 LITER BAG with INTERCEPT BLOOD SYSTEM embossed across the top of the bag
New Psoralen Treated Platelets

Conventional Platelet Bag Size

Psoralen-Treated Platelet Bag Size
Storage on Rotator Shelf
Permanent Outpatient Billing Code for INTERCEPT® Blood System Pathogen Reduced Apheresis Platelets

Centers for Medicare & Medicaid Services (CMS) granted HCPCS Level II codes for pathogen-reduced (PR) platelet components allowing hospitals to bill and secure reimbursement in the outpatient treatment setting.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>HCPCS P-Code Long Descriptor</th>
<th>CMS OPPS CY20 Payment Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>P9073</td>
<td>Platelets, pheresis, pathogen reduced, each unit</td>
<td>$612.01</td>
</tr>
</tbody>
</table>

HCPCS = Hospital Common Procedure Coding System

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Hospital-Outpatient-Regulations-and-Notices-Items/CMS-1679-FC.html?DLPage=1&DLEntries=10&DLSort=2&DLSortDir=descending
Summary: INTERCEPT® Blood System for Platelets

- First, FDA-approved pathogen reduction system for platelets and plasma
- Safety and Efficacy demonstrated in prospective clinical trials
- 16+ years of routine, global use
- Over 6 million kits sold to produce over 6 million doses
- No patient population restrictions, no documented sensitivity to date
- Replaces need for initial bacterial testing at blood center or subsequent point of issue testing at the hospital
- Robust inactivation of a broad spectrum of viruses and bacteria, emerging pathogens, and leukocytes*
- A rational option to meet anticipated FDA guidance for 5-day platelets
- Strong safety profile based on laboratory, clinical trials and >10 years of routine use in all patient groups
- FDA approved alternative to gamma irradiation for the prevention of TA-GVHD;
  - Authorized by AABB Standards as an alternative to irradiation for prevention of TA-GVHD§

*There is no pathogen inactivation process that has been shown to eliminate all pathogens. Certain non-enveloped viruses (eg, HAV, HEV, B19 and poliovirus) and Bacillus cereus spores have demonstrated resistance to the INTERCEPT process.

§Not FDA approved for this purpose
# Hospital Implementation

## IT Systems
- ISBT Codes
- BBIS and HIS Safeguards

## Education & In-services
- Collateral Material
- CLS and RN in-services

## SOP Updates
- Inventory management
- IRR/CMV /PRT

## Product Approval
- Transfusion Committee Approval

## Financial Considerations
- P-Code reimbursement
Verax PGD Rapid Secondary Testing
Verax Biomedical Platelet PGD® Test

- Designed for use with LR or non-LR: RDPs, Pooled RDPs & SDPs
- Results in 30-45 minutes
- ~5 minutes labor per test
- Analytical sensitivity \( \sim 10^3 - 10^4 \) CFU/mL
- 510(k) approved in November, 2009
Rapid Point-of-Release Testing

- Analytic sensitivity of $10^3 - 10^5$ CFU/mL depending on organism and device
- Optimally used at least 72 hours after collection
- Relatively high false positive rate (0.51% with PGD test) → impact to PLT availability

- Cleared by FDA for use as a “safety measure”
- PGD test must be performed within 24 hours prior to transfusion
PGD Test procedure for an Apheresis unit:

Create a fresh 4" Segment & drain it into a sample tube

Transfer 500uL to Microfuge tube

Add 8 drops Reagent 1

Centrifuge 5 min. and decant supernatant

Add 8 drops Reagent 2 and dislodge pellet with Dispo pipette

Add 4 drops Reagent 3 and vortex briefly

Pour in well & Read in 20-25 min

Per Verax:
- Test for one platelet requires tech time of about 5 min with test result after 35 min
- Batch of six tests: 15 min tech time and 45 min to results

Modified Verax PGD slides
### PGD® and 7 Day Dating of SDPs in Plasma

<table>
<thead>
<tr>
<th>Registered with the FDA</th>
<th>Not Registered with the FDA</th>
<th>Licensed with the FDA as a manufacturer</th>
</tr>
</thead>
</table>
| - Write an SOP for implementing 7 Days  
- Determine how you will relabel the bag for 7 Day dating  
- Amend your registration on-line  
- No FDA approval required – start testing and go live | - Write an SOP for implementing 7 Days  
- Determine how you will relabel the bag for 7 Day dating  
- Register on-line  
- No FDA approval required – start testing and go live | - Write an SOP for implementing 7 Days  
- Determine how you will relabel the bag for 7 Day dating  
- File both with the FDA; amend your circular of information  
- Receive approval before going live |
Thank You