INTERCEPT® Blood System for Platelets and Plasma

Pathogen Reduction System
Warnings and Contraindications

INTERCEPT Blood System for Platelets and Plasma

There is no pathogen inactivation process that has been shown to eliminate all pathogens.

CONTRAINDICATIONS
Contraindicated for preparation of plasma or platelet components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. Contraindicated for preparation of plasma or platelet components intended for neonatal patients treated with phototherapy devices that emit peak wavelengths 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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The Need for Blood Safety
Current Transfusion-Associated Risks
Testing measures have improved blood safety, but residual risks exist

**Bacteria**
The most frequent transfusion-transmitted infection (TTI)

**New and emerging pathogens**
A risk that current safety measures cannot eliminate

**Screening limitations**
Gaps in current defenses exist, due to the window period and limited screening sensitivity

**Leukocytes**
Residual cells and cytokines can cause harmful post-transfusion reactions such as transfusion-associated graft-versus-host disease (TA-GVHD)

**Known pathogens**
Routine testing covers only a limited number

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INTERCEPT BLOOD SYSTEM PATHOGEN REDUCTION SYSTEM
Bacterial Contamination of Platelets
The most frequent TTI

- Despite implementation of interventions to mitigate bacterial contamination and reduce associated adverse events (AEs), residual risks remain...

- Several recent studies demonstrate that platelets contaminated with bacteria continue to be transfused.1–4

<table>
<thead>
<tr>
<th>Bacterial Contamination Risk</th>
<th>Clinical Sepsis Risk due to Bacteria</th>
<th>Viral Infectious Risk (HIV/HCV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~1:1,500 Units1</td>
<td>~1:5,000 Units5</td>
<td>~1:1,000,000 Units6</td>
</tr>
<tr>
<td>~1:250 Patients5</td>
<td>~1:1,000 Patients5</td>
<td>~1:200,000 Patients</td>
</tr>
</tbody>
</table>

## TA-Sepsis is Often Under Reported

Due to passive vs. active surveillance methods

<table>
<thead>
<tr>
<th></th>
<th>Active Surveillance (n=102,988)</th>
<th>Passive Surveillance (n=135,985)</th>
<th>X – Fold Higher Rate by Active vs. Passive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterially Contaminated Units</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected</td>
<td>50</td>
<td>2</td>
<td>32.0</td>
</tr>
<tr>
<td>Transfused</td>
<td>42</td>
<td>2</td>
<td>27.7</td>
</tr>
<tr>
<td><strong>Septic Transfusion Reactions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic Transfusion Reaction</td>
<td>16</td>
<td>2</td>
<td>10.6</td>
</tr>
<tr>
<td>Septic Transfusion Reaction with Bactermia</td>
<td>5</td>
<td>1</td>
<td>6.6</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

TA-Sepsis is Under Reported
Due to passive vs. active surveillance methods

- Consistent with previous studies, 1–4 the Hong et al. recently demonstrated that platelets contaminated with bacteria continue to be transfused.5
- Transfusion-related sepsis is greatly under-reported due to passive vs. active surveillance methods. Patient risk is 10- to 40-fold higher when comparing active vs. passive surveillance.5

~1:2,500 units is contaminated with bacteria
~1:10,700 units implicated in clinical sepsis
~1:1,700 patients develop clinical sepsis (6 AP* Exposure)


*Apheresis platelet unit
Emerging Pathogens
Risk of spreading pathogens such as chikungunya, dengue, Zika
Emerging Pathogens
Global portals of transfusion-transmitted infection – daily air routes

http://openflights.org
Emerging Pathogens
Current mitigations

- No FDA commercially licensed test for donor screening exists.
- AABB Bulletin released February 2016: Zika, chikungunya, dengue travel deferrals
- Post donation information/illness reporting
  - Risk still exists with components transfused from asymptomatic donors
- Stop routine collections, attain components elsewhere
  - Puerto Rico, Florida due to Dengue (One Blood in 2013)
  - Not ideal for platelets, disruptive due to limited shelf-life and shipping time
- Pathogen reduction (PR)
  - FDA approved for arboviruses including chikungunya, dengue, WNV
  - FDA Guidance released February 2016 recommends PR for areas with active transmission of ZIKV
  - WHO Guidance released February 2016 recommends PR for areas with active transmission of ZIKV

*Data for pathogen reduction of Zika by INTERCEPT Blood System, pathogen reduction system, has not been submitted for FDA review.*
Emerging Pathogens
Current mitigations – Pathogen Reduction

- Per FDA Guidance released 16 February 2016:

In areas with active Zika virus transmission (http://www.cdc.gov/zika/geo/index.html), the FDA recommends that Whole Blood and blood components for transfusion be obtained from areas of the U.S. without active transmission. **Blood establishments may continue collecting and preparing platelets and plasma if an FDA-approved, pathogen-reduction device is used.** The guidance also recommends blood establishments update donor education materials with information about Zika virus signs and symptoms and ask potentially affected donors to refrain from giving blood.
Testing Challenges

Present TTI risk, increased logistics burden to hospitals

- Escaped bacterial detection by early culture\(^1\)
- Point of issue (POI) testing presents significant challenges
  - High false-positive rates can lead to significant product discard rates\(^2,3\)
  - Presents logistic and cost burdens: need for re-testing if not transfused in \(\leq 24\) hours; repeat testing algorithm for positive POI units\(^3\)
- Reactive approach presents a TTI risk due to emerging pathogens\(^4\)

\(^4\)Kleinman S et al. Transfusion 2010, 50 2592-2606
The INTERCEPT® Blood System
pathogen reduction system

Overview
INTERCEPT Blood System
A proactive approach to reducing TTI risk

- FDA-approved pathogen reduction system
  - Safety, efficacy demonstrated in prospective clinical trials
  - 10+ Years routine, global use
  - Effective January 1, 2016 – Permanent, hospital outpatient billing codes (P-codes) established for PR-treated platelets and plasma

- Reduces transfusion-transmitted infectious (TTI) risk through the comprehensive inactivation of viruses, bacteria, and parasites that can be found in plasma and platelet components

- Potentially lowers the risk of transfusion-associated graft-versus-host disease (TA-GVHD) in platelet units through T-cell inactivation

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.

1. [https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Hospital-Outpatient-Regulations-and-Notices-Items/CMS-1633-FC.html?DLPage=1&DLEntries=10&DLSort=2&DLSortDir=descending](https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Hospital-Outpatient-Regulations-and-Notices-Items/CMS-1633-FC.html?DLPage=1&DLEntries=10&DLSort=2&DLSortDir=descending)
INTERCEPT Blood System

Indications for Use

INTERCEPT Platelets

For the ex vivo preparation of pathogen-reduced apheresis platelet components in order to:

- Reduce the risk of TTI, including sepsis
- Potentially reduce the risk of TA-GVHD

INTERCEPT Plasma

For the ex vivo preparation of pathogen-reduced, whole blood derived or apheresis plasma in order to reduce the risk of TTI

When pathogens are unable to replicate, they are considered “inactivated” and cannot infect patients. Pathogen-reduced component can then be transfused into the patient.
Mechanism of Action
Targeting DNA and RNA to prevent pathogen proliferation\(^1,2\)

1. Intercalates Into Regions of DNA and RNA
2. Crosslinks Upon UVA Illumination
3. Blocks Replication, Transcription and Translation

**Broad Spectrum Inactivation**

**A proactive approach to reducing TTIs**

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. For a full list of pathogens, please refer to package inserts.

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### GRAM-NEGATIVE BACTERIA

- Klebsiella pneumoniae*◊#
- Yersinia enterocolitica*◊#
- Escherichia coli*
- Pseudomonas aeruginosa*
- Salmonella choleraesuis*
- Enterobacter cloacae*
- Serratia marcescens*
- Anaplasma phagocytophilum#

### GRAM-POSITIVE BACTERIA

- Staphylococcus epidermidis*◊#
- Staphylococcus aureus*
- Streptococcus pyogenes*
- Listeria monocytogenes*
- Corynebacterium minutissimum*
- Bacillus cereus (vegetative) *
- Lactobacillus species*
- Bifidobacterium adolescentis*
- Propionibacterium acnes*
- Clostridium perfringens (vegetative) *

### ENVELOPED VIRUSES

- HIV-1 *◊#
- DHBV (model for HBV)*◊#
- BVDV (Model for HCV)*◊#
- HTLV-I*#
- HTLV-II*#

**Enveloped Viruses**

- CMV*
- WNV*◊#
- Chikungunya*◊#
- Dengue*◊
- Influenza A*#

### NON-ENVELOPED VIRUSES

- Bluetongue virus**
- Adenovirus*◊#
- Parovirus B19#

### PROTOZOA

- Trypanosoma cruzi*◊#
- Plasmodium falciparum**

### SPIROCHETES

- Treponema pallidum**
- Borrelia burgdorferi**

### LEUKOCYTES

- Human T-Cells*◊#

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* pathogen reduced Amicus apheresis platelets in PAS-3
◊ pathogen reduced Trima apheresis platelets in 100% plasma
# pathogen reduced plasma

Permanent Outpatient Billing Codes
Established for pathogen reduced platelets and plasma

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

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>P-9070</td>
<td>Plasma, pooled multiple donor, pathogen reduced, frozen, each unit</td>
<td>$73.08</td>
</tr>
<tr>
<td>P-9071</td>
<td>Plasma (single-donor), pathogen reduced, frozen, each unit</td>
<td>$72.56</td>
</tr>
<tr>
<td>P-9072</td>
<td>Platelets, pheresis, pathogen reduced, each unit</td>
<td>$641.85</td>
</tr>
</tbody>
</table>

HCPCS = Hospital Common Procedure Coding System; P-Code = Permanent Code

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Hospital-Outpatient-Regulations-and-Notices-Items/CMS-1633-FC.html?DLPage=1&DLEntries=10&DLSort=2&DLSortDir=descending
The INTERCEPT Blood System
For Platelets
INTERCEPT Blood System for Platelets

Proactively defends patients against TTI*

- First FDA-approved pathogen reduction system for platelets
  - Safety, efficacy demonstrated in prospective clinical trials
  - 10+ Years routine, global use

- Reduces transfusion-transmitted infectious (TTI) risk, including sepsis
  - Broad spectrum of bacteria frequently implicated in TTI
  - Emerging pathogens, such as chikungunya, dengue, Plasmodium species.
  - Established threats such as HIV-1, HBV**, HCV**, WNV

- Potentially reduce risk of transfusion-associated graft-versus-host disease (TA-GVHD) through reduced contaminating T-cell activity\(^1\)

- Approved for use with Amicus apheresis platelets in PAS-3 and Trima apheresis platelets in 100% plasma\(^^\)

* 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. ** Pathogen reduction demonstrated for DHBV and BVDV, model viruses for HBV and HCV respectively. \(^^\) Please refer to the package insert for full prescribing information.

INTERCEPT Blood System for Platelets

Populations studied in clinical trials1-6

- Patients with various hematological malignancies (acute myeloid / lymphoid leukemia, lymphoma, multiple myeloma, myelodysplasia, hairy cell leukemia, solid tumors).

- Patients undergoing peripheral blood progenitor cell transplantation or bone marrow transplantation.

3Janetzko, L et al. Transfusion 2005 Sep;45:1443–52.
Nearly 1000 Subjects Evaluated in Clinical Trials
Primary endpoints met in controlled, randomized studies for the INTERCEPT Blood System for Platelets

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Primary End Point</th>
<th>Primary End Point Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II Randomized, controlled, single-blind, cross-over trial to evaluate the viability of INTERCEPT Platelets, clearance of amotosalen, healthy patients¹ (n=65)</td>
<td>Recovery/survival, clearance of amotosalen</td>
<td>✓</td>
</tr>
<tr>
<td>Phase II Randomized, controlled, double-blind, cross-over study to evaluate the safety/efficacy of INTERCEPT Platelets, thrombocytopenic patients² (n=32)</td>
<td>Bleeding time</td>
<td>✓</td>
</tr>
<tr>
<td>Phase III Randomized, controlled, double-blind, parallel trial to evaluate the safety/efficacy of INTERCEPT Platelets, thrombocytopenic patients³ (n=645)</td>
<td>WHO Grade 2 bleeding</td>
<td>✓</td>
</tr>
<tr>
<td>Phase III Randomized, controlled, double-blind, parallel trial to evaluate the safety/efficacy of INTERCEPT Platelets, thrombocytopenic patients⁴ (n=43)</td>
<td>1-Hour CCI</td>
<td>✓</td>
</tr>
<tr>
<td>Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT in routine setting⁵ (n=51)</td>
<td>Frequency of acute transfusion reactions was 1.6%</td>
<td></td>
</tr>
<tr>
<td>Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT routine setting⁶ (n=46)</td>
<td>Frequency of acute transfusion reactions was 2%</td>
<td></td>
</tr>
<tr>
<td>Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT, routine setting⁷ (n=169)</td>
<td>Frequency of acute transfusion reactions was 2.4%</td>
<td></td>
</tr>
</tbody>
</table>

Hemovigilance Programs
Demonstrated safety in routine use

>300,000 INTERCEPT Platelets Evaluated in Routine Use

<table>
<thead>
<tr>
<th></th>
<th>French National Hemovigilance</th>
<th>Swiss National Hemovigilance</th>
<th>Multicenter Cerus HV</th>
</tr>
</thead>
<tbody>
<tr>
<td># INTERCEPT Platelets Transfusions</td>
<td>180,782</td>
<td>130,843</td>
<td>19,175</td>
</tr>
<tr>
<td># Patients Receiving INTERCEPT Platelets</td>
<td>~30,000</td>
<td>~20,000</td>
<td>4,067</td>
</tr>
<tr>
<td>INTERCEPT ATR Rate</td>
<td>~0.3%₄</td>
<td>~0.3%₅</td>
<td>~0.6%</td>
</tr>
<tr>
<td>Conventional ATR Rate</td>
<td>~0.3%₄</td>
<td>~0.4%₅</td>
<td>NA</td>
</tr>
</tbody>
</table>

Demonstrated Sepsis Prevention
With routine use of INTERCEPT platelet units

- Hemovigilance (HV) programs provide a comprehensive view of transfusions and potential adverse events.
  - 300,000+ INTERCEPT platelet units have been transfused in French and Swiss national HV programs
  - No reported TTIs and sepsis-related fatalities to-date

<table>
<thead>
<tr>
<th>HV Program</th>
<th>Conventional Platelets</th>
<th>INTERCEPT Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Platelet Units Transfused</td>
<td>TTIs (Fatalities)</td>
</tr>
<tr>
<td>France 2006–2014¹²</td>
<td>2,299,334</td>
<td>49 (8)</td>
</tr>
<tr>
<td>Switzerland 2010–2014¹³</td>
<td>36,500</td>
<td>1 (0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,335,834</strong></td>
<td><strong>50 (8)</strong></td>
</tr>
</tbody>
</table>

Reduction of T-Cells
To a level that potentially reduces the risk of TA-GVHD

- INTERCEPT processed platelets exhibited a $4 \log_{10}$ reduction of viable T-cells.
- DNA modification assay in components processed with the INTERCEPT Blood System demonstrated high DNA modification densities to help ensure inactivation of most genes:

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

**INTERCEPT Platelets 1:83 adduct formed: base pair**

Animation courtesy of AuBuchon, JK.

No Reports of TA-GVHD in Routine Use
With INTERCEPT treated platelets

- Longitudinal studies conducted in 21 centers, across 11 countries over 7-years in broad patient populations
  - Large proportion of hematology/oncology patients
- 97% of Platelet components (PCs) were not treated with gamma irradiation

<table>
<thead>
<tr>
<th>Study</th>
<th>PCs</th>
<th>Patients</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV1</td>
<td>5,106</td>
<td>651</td>
<td>INTERCEPT PCs</td>
<td>Safety</td>
<td>2003–2005</td>
</tr>
<tr>
<td>HV2</td>
<td>7,437</td>
<td>1,400</td>
<td>INTERCEPT PCs</td>
<td>Safety</td>
<td>2005–2007</td>
</tr>
<tr>
<td>HV3</td>
<td>6,632</td>
<td>2,016</td>
<td>INTERCEPT PCs</td>
<td>Safety</td>
<td>2006–2010</td>
</tr>
<tr>
<td>Total</td>
<td>19,175</td>
<td>4,067</td>
<td>INTERCEPT PCs</td>
<td>Safety</td>
<td>2003–2010</td>
</tr>
</tbody>
</table>

The INTERCEPT Blood System
For Plasma
INTERCEPT Blood System for Plasma
A proactive approach for blood centers to reduce TTI risk*

- **Reduces transfusion-transmitted infection (TTI) risk**¹
  - Broad spectrum inactivation with ≥4 log reduction for most pathogens
  - Emerging pathogens, such as chikungunya, *Plasmodium* species
  - Established threats such as HIV-1, HBV**, HCV**, WNV

- **Approved for use with whole blood derived or apheresis plasma**¹

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* 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. ** Pathogen reduction demonstrated for DHBV and BVDV, model viruses for HBV and HCV respectively.

Acquired coagulation factor deficiencies\(^1,2\)

Congenital coagulation factor deficiencies\(^1,3\)

Those undergoing therapeutic plasma exchange (TPE) due to thrombotic thrombocytopenic purpura (TTP)\(^1,4\)

Those undergoing liver transplantation\(^1,5\)

\(^2\)Mintz, PD et al. Blood. 2006 May 1;107(9):3753-60.
Hemovigilance (HV) programs - a comprehensive view of transfusions and potential adverse events.

HV programs tracking the **routine use of >200,000 INTERCEPT Plasma** units in Europe have demonstrated therapeutic efficacy with an adverse event profile consistent with untreated plasma. 

<table>
<thead>
<tr>
<th>Year</th>
<th>Product</th>
<th>Plasma Units</th>
<th>Acute Transfusion Reactions per 1,000 Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Untreated Plasma</td>
<td>348,725</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>INTERCEPT Plasma</td>
<td>22,933</td>
<td>0.52</td>
</tr>
<tr>
<td>2010</td>
<td>Untreated Plasma</td>
<td>329,757</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>INTERCEPT Plasma</td>
<td>52,692</td>
<td>0.47</td>
</tr>
<tr>
<td>2011</td>
<td>Untreated Plasma</td>
<td>311,482</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>INTERCEPT Plasma</td>
<td>68,440</td>
<td>0.31</td>
</tr>
</tbody>
</table>

1 Subset HV data shown above, French HV data.
### Safety, Efficacy Evaluated in Prospective Trials

Studies met primary endpoints for the INTERCEPT Blood System for Plasma

<table>
<thead>
<tr>
<th>Study Design*</th>
<th>Primary Result(s)</th>
<th>Primary Endpoint Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase I</strong></td>
<td>Randomized, single-blind, crossover with healthy subjects (N=15)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Comparable coagulation factor levels attained between test and control FFP.</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phase II</strong></td>
<td>Randomized, single-blind, crossover with healthy subjects, warfarin anticoagulated (N=27)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td><strong>Comparable prothrombin time and FVII kinetics between test and control FFP.</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phase II</strong></td>
<td>Randomized, double-blind, parallel group, multiple coagulation deficiencies (N=13)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>INTERCEPT plasma was <strong>safe and well tolerated by patients impaired with hepatic function. Comparable hemostatic activity attained between test and control FFP.</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phase IIIa</strong></td>
<td>Open label, single arm, congenital coagulation deficiencies (N=34)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Comparable recovery, pharmacokinetic performance, and PT/PTT attained between test and control FFP.</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phase IIIb</strong></td>
<td>Randomized, double-blind, parallel group, acquired coagulation deficiencies (N=121)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td><strong>Comparable coagulation responses and clinical hemostasis were attained between test and control FFP.</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phase IIIc</strong></td>
<td>Randomized, double-blind, parallel group, thrombotic thrombocytopenic purpura (TTP) (N=35)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td><strong>Remission rates, time to remission, relapse rates, and time to relapse, as well as number of TPE and volume of FFP required were comparable between INTERCEPT Plasma and conventional FFP.</strong></td>
<td>✓</td>
</tr>
</tbody>
</table>

*Sample size (N) is the total of test and control patient samples.

INTERCEPT Blood System for Plasma

Effective at retaining plasma coagulation function

- INTERCEPT Plasma maintains hemostatic potency, as shown by the retained activity of key coagulation factors.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Untreated Plasma</th>
<th>INTERCEPT Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global Coagulation Parameters</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin Time (seconds)</td>
<td>13.1</td>
<td>14.4</td>
</tr>
<tr>
<td>Activated Partial Thromboplastin Time (aPTT) (seconds)</td>
<td>24.2</td>
<td>27.0</td>
</tr>
<tr>
<td><strong>Coagulation Factors and Proteins of the Hemostatic System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>2.91</td>
<td>2.43</td>
</tr>
<tr>
<td>Factor II (IU/mL)</td>
<td>1.03</td>
<td>0.93</td>
</tr>
<tr>
<td>Factor V (IU/mL)</td>
<td>0.91</td>
<td>0.82</td>
</tr>
<tr>
<td>Factor VII (IU/mL)</td>
<td>0.99</td>
<td>0.81</td>
</tr>
<tr>
<td>Factor VIII (IU/mL)</td>
<td>0.91</td>
<td>0.73</td>
</tr>
<tr>
<td>Factor IX (IU/mL)</td>
<td>1.12</td>
<td>0.93</td>
</tr>
<tr>
<td>Factor X (IU/mL)</td>
<td>0.95</td>
<td>0.83</td>
</tr>
<tr>
<td>Factor XI (IU/mL)</td>
<td>1.02</td>
<td>0.90</td>
</tr>
<tr>
<td>vWF Ristocetin Cofactor Activity</td>
<td>1.01</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Data shown is for whole blood derived plasma frozen within 24 hours. For apheresis plasma, please see package insert. The INTERCEPT Blood System for Plasma Package Insert, 2015.
INTERCEPT Blood System for Plasma
Effective at retaining plasma coagulation function

- INTERCEPT Plasma maintains hemostatic potency, as shown by the retained activity of key coagulation factors.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Untreated Plasma</th>
<th>INTERCEPT Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticoagulant Proteins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>0.98</td>
<td>0.93</td>
</tr>
<tr>
<td>Protein C (IU/mL)</td>
<td>0.95</td>
<td>0.86</td>
</tr>
<tr>
<td>Protein S (IU/mL)</td>
<td>1.08</td>
<td>1.04</td>
</tr>
<tr>
<td><strong>Proteins of the Fibrinolytic System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha-2-plasmin inhibitor (IU/mL)</td>
<td>1.00</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Markers of Coagulation Activation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombin-Antithrombin Complexes (μg/L)</td>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Factor VIIIa (ng/mL)</td>
<td>&lt;3.6</td>
<td>&lt;3.6</td>
</tr>
</tbody>
</table>

Data shown is for whole blood derived plasma frozen within 24 hours. For apheresis plasma, please see package insert. The INTERCEPT Blood System for Plasma Package Insert, 2015.
The INTERCEPT Blood System
Operational Efficiencies
Improved clinical outcomes

The INTERCEPT Blood System for Platelets reduces TTI risk, including sepsis.¹ It also potentially reduces the risk of TA-GVHD.¹ This can result in reduced costs associated with treatment, re-calls and follow-up investigations.²

Avoidance of cost and complexity of bacterial testing

INTERCEPT offers the potential to replace or avoid bacterial detection methods, including point of issue testing, with its ability to reduce the risk of bacterial contamination of platelets and sepsis.¹ This enables hospitals to avoid costs associated with bacterial testing, labor and platelet waste due to potential false positive results.

Improved platelet availability, decreased wastage

INTERCEPT allows for immediate accessibility of platelet units. Early platelet unit receipt provides added flexibility for managing inventory, and enables hospitals to attain fresher platelets.

Permanent outpatient billing codes assigned

Effective January 1, 2016 CMS has granted permanent billing codes for pathogen reduced platelets and plasma components allowing hospitals to bill and secure reimbursement in the outpatient treatment setting.