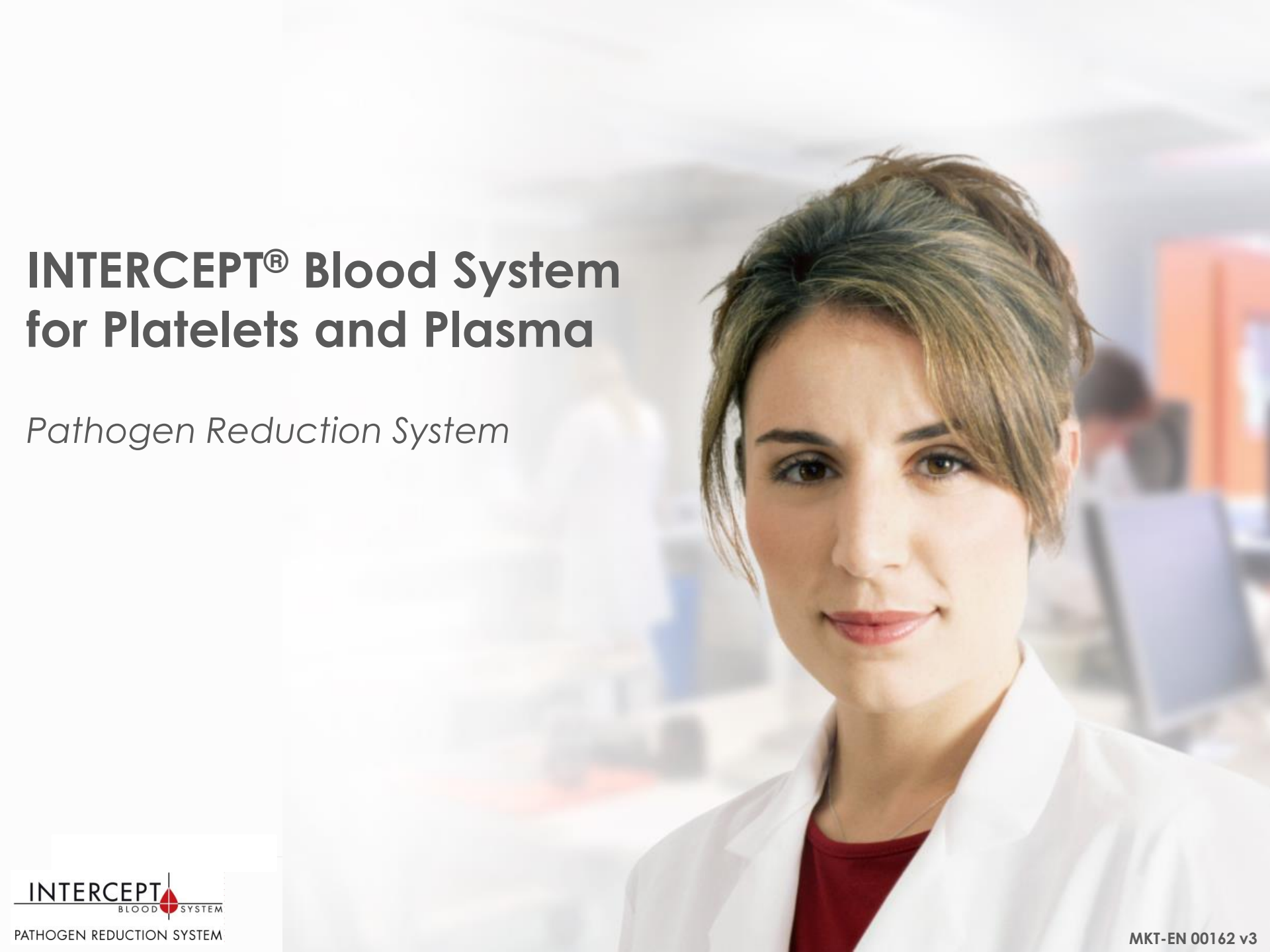
INTERCEPT® Blood System for Platelets and Plasma

Pathogen Reduction System



INTERCEPT BLOOD SYSTEM
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-ethlhexyl)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

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Current Transfusion-Associated Risks

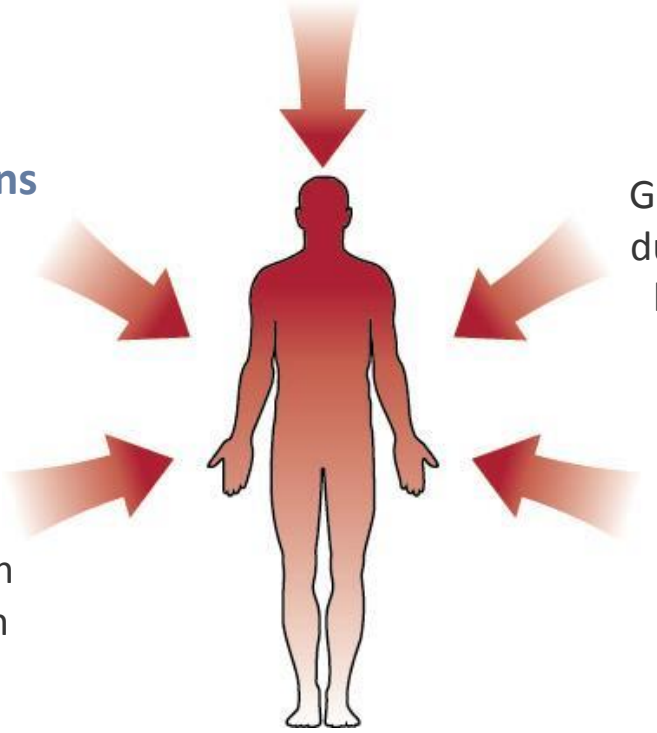
Testing measures have improved blood safety, but residual risks exist

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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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]

Bacterial Contamination Risk	Clinical Sepsis Risk due to Bacteria	Viral Infectious Risk (HIV/HCV)
 ~1:1,500 Units[1]	 ~1:5,000 Units[5]	 ~1:1,000,000 Units[6]
 ~1:250 Patients[5]	 ~1:1,000 Patients[5]	 ~1:200,000 Patients

[1]Dumont, LJ et al. *Transfusion*. 2010 Mar;50(3):589–99.|[2]Pearce, S et al. *Transfus Med.* 2011 Feb;21(1):25–32.
[3]Murphy, WG et al. *Vox Sang.* 2008 Jul;95(1)13–9. | [4]Walther-Wenke, G et al. *Vox Sang*. 2011 May;100(4):359–66.
[5]Kleinman, S et al. *Transfusion*. 2013 Jul;53(7):1603–18. | [6]Zou, S et al. *Transfusion.* 2010 Jul;50(7):1495–504.

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TA-Sepsis is Often Under Reported

Due to passive vs. active surveillance methods

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

Jacobs, MR et al. *Clin Infect Dis.* 2008 Apr 15;46(8):1214–20.

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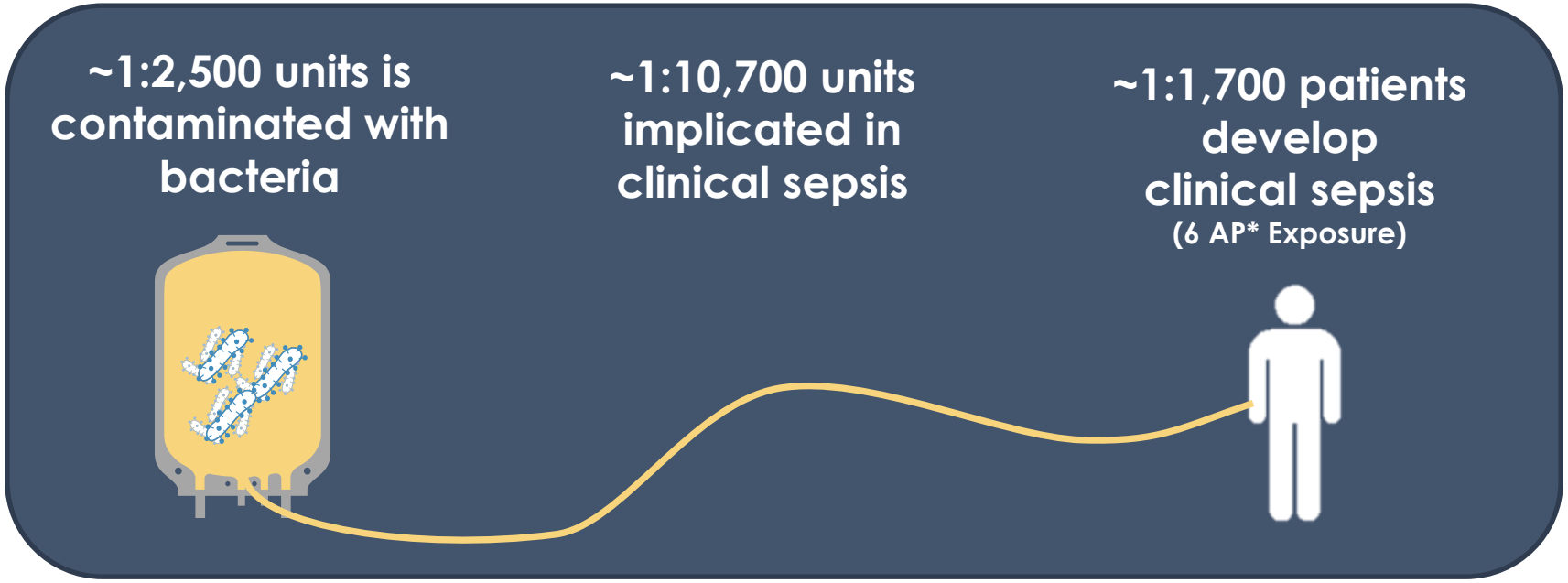
TA-Sepsis is Under Reported

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]Dumont, LJ et al. *Transfusion*. 2010 Mar;50(3):589–99.|[2]Pearce, S et al. *Transfus Med*. 2011 Feb;21(1):25–32.
[3]Murphy, WG et al. *Vox Sang*. 2008 Jul;95(1)13–9.
[4]Walther-Wenke, G et al. *Vox Sang*. 2011 May;100(4):359–66.|[5]Hong H, et al. *Blood*. 2016;127(4):496-502.
*Apheresis platelet unit

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Emerging Pathogens

Risk of spreading pathogens such as chikungunya, dengue, Zika

Chikungunya Cases Spike In New York And New Jersey

Reuters

examiner.com

LIFE/ HEALTH & FITNESS/ DISEASE & ILLNESS

Dengue and chikungunya in the Americas, the U.S. and Florida: 2014

January 3, 2015

SCIENTIFIC AMERICAN™

HEALTH

Zika Virus Threatens U.S. from Abroad

Exclusive: An interactive map, based on data from 50 state health departments, the mosquito-borne disease made its way to America in travelers' bloodst

By Dina Fine Maron on January 26, 2016

Fifth case of chikungunya confirmed in Texas

Hawaii mayor declares state of emergency to address dengue fever outbreak

transmitted to people through bites from mosquitoes of the Aedes species – the same dengue and chikungunya viruses. CBS NEWS

Tweet / Stumble / Email

ND -- Hawaii County Mayor Billy Kenoi has declared a state of ith the growing dengue fever outbreak in the state.

Published On: Thu, Sep 12th, 2013

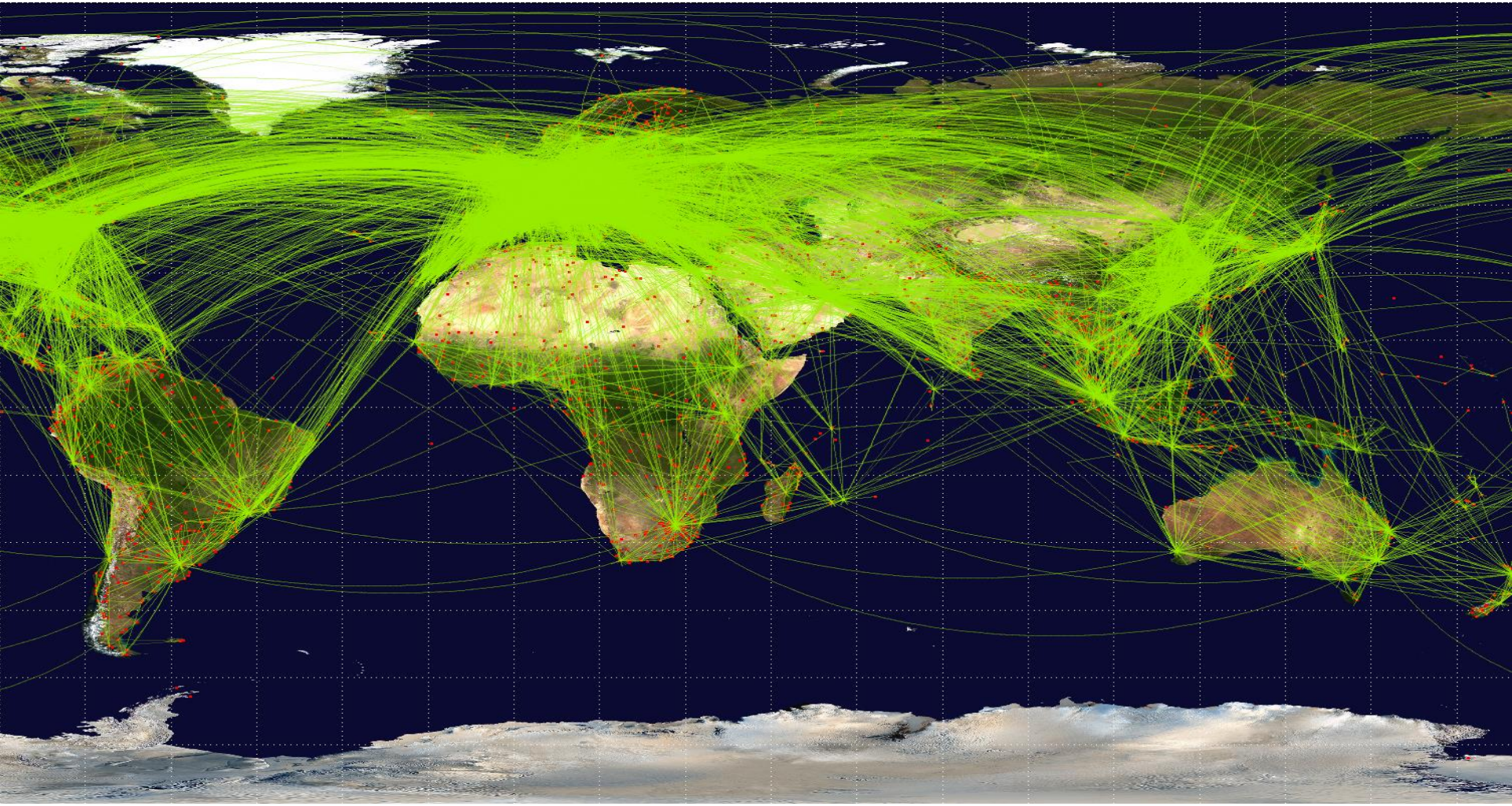
Hometown News / Outbreak News | By Robert Herriman

Florida Blood Bank, OneBlood, Temporarily Suspends Blood Donations From Martin And St. Lucie Counties Due To Dengue Fever

ION SYSTEM

Emerging Pathogens

Global portals of transfusion-transmitted infection – daily air routes



http://openflights.org

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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.

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Emerging Pathogens

Current mitigations – Pathogen Reduction

- Per FDA Guidance released 16February2016:

FDA News Release

FDA issues recommendations to reduce the risk for Zika virus blood transmission in the United States

For Immediate Release

February 16, 2016

Release

As a safety measure against the emerging Zika virus outbreak, today the U.S. Food

*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.*

area with active Zika virus transmission during the prior three months, and those who have traveled to areas with active transmission of Zika virus during the past four weeks.

*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 ≤ 24 hours; repeat testing algorithm for positive POI units[3]
- Reactive approach presents a TTI risk due to emerging pathogens[4]

[1]Benjamin, R et al. *Vox Sanguinis* 2013. | [2]Jacobs MR *et al. Transfusion* 2011;51:2573. | [3]Harm et al. *Transfusion* 2013;843-850.
[4]Kleinman S et al. *Transfusion* 2010, 50 2592-2606

The INTERCEPT® Blood System

pathogen reduction system

Overview

INTERCEPT BLOOD SYSTEM

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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[1]

- **Reduces transfusion-transmitted infectious (TTI) risk through the comprehensive inactivation of viruses, bacteria, and parasites that can be found in plasma and platelet components**[2,3]

- **Potentially lowers the risk of transfusion-associated graft-versus-host disease (TA-GVHD) in platelet units through T-cell inactivation**[3]

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.

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
2. INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.
3. INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.

INTERCEPT BLOOD SYSTEM
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INTERCEPT Blood System
Indications for Use

INTERCEPT Platelets[1]

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[2]

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

[1]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[2]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.

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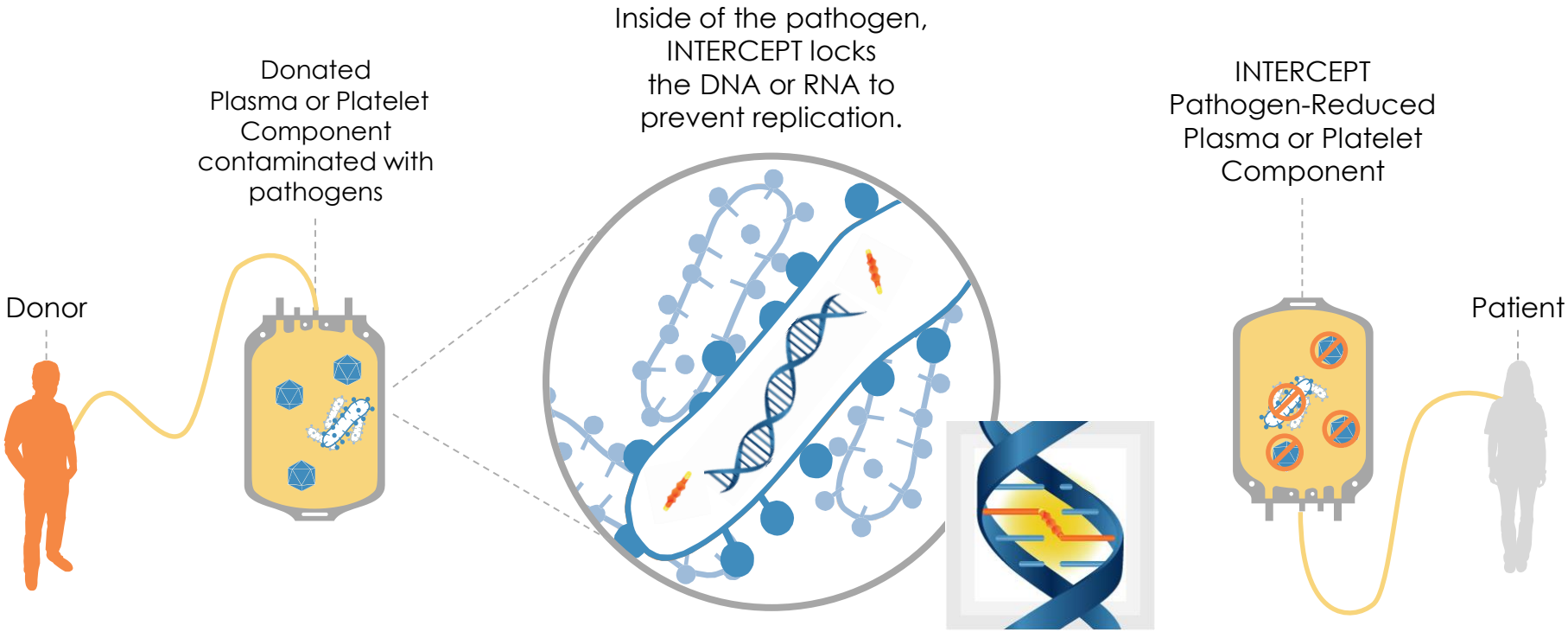
INTERCEPT Blood System

Pathogen reduction system[1,2]



Donated plasma or platelet component(s) may contain harmful agents such as bacteria, viruses, protozoans, and/or white blood cells.

When pathogens are unable to replicate, they are considered "inactivated" and cannot infect patients.

Pathogen-reduced component can then be transfused into the patient

[1]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[2]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015,

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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

[1]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[2]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.

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Broad Spectrum Inactivation

A proactive approach to reducing TTIs

GRAM-NEGATIVE BACTERIA

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

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

NON-ENVELOPED VIRUSES

Bluetongue virus*#
Adenovirus*◊#
Parovirus B19#

PROTOZOA

*Trypanosoma cruzi**◊#
*Plasmodium falciparum**#
*Babesia microti**#

SPIROCHETES

*Treponema pallidum**#
*Borrelia burgdorferi**#

LEUKOCYTES

Human T-Cells*◊#

* pathogen reduced Amicus apheresis platelets in PAS-3
◊ pathogen reduced Trima apheresis platelets in 100% plasma
pathogen reduced 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. For a full list of pathogens, please refer to package inserts.

INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.
INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.

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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**

New CY2016 HCPCS P-Code	New HCPCS P-Code Long Descriptor	Final CY 2016 OPPS Payment Amount
P-9070	Plasma , pooled multiple donor, pathogen reduced, frozen, each unit	**$73.08**
P-9071	Plasma (single-donor), pathogen reduced, frozen, each unit	**$72.56**
P-9072	Platelets, pheresis, pathogen reduced, each unit	**$641.85**

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

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The INTERCEPT Blood System

For Platelets

INTERCEPT BLOOD SYSTEM

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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 [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[1]FDA Press Release: FDA approves pathogen reduction system to treat platelets. December 19, 2014.

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INTERCEPT Blood System for Platelets

Populations studied in clinical trials[1-6]

- 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.

[1]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[2]McCullough, J et al. *Blood* 2004 Sep;104(5):1534–41.|[3]Janetzko, L et al. *Transfusion* 2005 Sep;45:1443–52.
[4]Slichter, SJ et al. *Transfusion* 2006 Oct;46:731–40.|[5]Schlenke, P et al. *Ann Hematol* 2011 Dec;90(12):1457–65.
[6]Infanti, L et al. *Transfus Apher Sci* 2011 May;45(2):175–181.

INTERCEPT BLOOD SYSTEM
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Nearly 1000 Subjects Evaluated in Clinical Trials

Primary endpoints met in controlled, randomized studies for the INTERCEPT Blood System for Platelets

Study Description	Primary End Point	Primary End Point Met?
Phase II Randomized, controlled, single-blind, cross-over trial to evaluate the viability of INTERCEPT Platelets, clearance of amotosalen, healthy patients[1] **(n=65)**	Recovery/survival, clearance of amotosalen	✓
Phase II Randomized, controlled, double-blind, cross-over study to evaluate the safety/efficacy of INTERCEPT Platelets, thrombocytopenic patients[2] **(n=32)**	Bleeding time	✓
Phase III Randomized, controlled, double-blind, parallel trial to evaluate the safety/ efficacy of INTERCEPT Platelets, thrombocytopenic patients[3] **(n=645)**	WHO Grade 2 bleeding	✓
Phase III Randomized, controlled, double-blind, parallel trial to evaluate the safety/ efficacy of INTERCEPT Platelets, thrombocytopenic patients[4] **(n=43)**	1-Hour CCI	✓
Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT in routine setting[5] **(n=51)**	Frequency of acute transfusion reactions was 1.6%	
Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT routine setting[6] **(n=46)**	Frequency of acute transfusion reactions was 2%	
Observational Single-arm, uncontrolled, open label study evaluating the safety of INTERCEPT, routine setting[7] **(n=169)**	Frequency of acute transfusion reactions was 2.4%	

[1]Snyder, E et al. *Transfusion.* 2004 Dec;44(12):1732–40.|[2]Slichter SJ et al. *Transfusion.* 2006 May;46(5):731–40.
[3]McCullough et al. *Blood.* Sep 2004;104(5):1534–41.|[4]Janetzko et al. *Transfusion.* 2005 Sep;45(9):1443–52.
[5]Schlenke P et al. *Ann Hematol.* 2011 Dec;90(12):1457–65.|[6] Infanti L et al. *Transfus Apher Sci.* 2011 Oct;45(2):175–81.
[7] INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA; Cerus Corporation. 2016.

INTERCEPT BLOOD SYSTEM
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Hemovigilance Programs

Demonstrated safety in routine use

>300,000 INTERCEPT Platelets Evaluated in Routine Use

	French National Hemovigilance[1]	Swiss National Hemovigilance[2]	Multicenter Cerus HV[3]
# INTERCEPT Platelets Transfusions	**180,782**	**130,843**	**19,175**
# Patients Receiving INTERCEPT Platelets	~30,000	~20,000	4,067
INTERCEPT ATR Rate	~0.3%[4]	~0.3%[5]	~0.6%
Conventional ATR Rate	~0.3%[4]	~0.4%[5]	NA

[1]French National Agency for Medicine and Health Product Safety/ANSM, Hemovigilance Activity Reports, 2006 - 2014.
[2]SwissMedic Haemovigilance Annual Reports, 2010 - 2014. | [3]Knutson F et al. Vox Sanguinis 2015.
[4]French National Agency for Medicine and Health Product Safety/ANSM, Hemovigilance Activity Reports, 2009-2011.
[5]SwissMedic Haemovigilance Annual Report 2014; conventional : 2008-2010, INTERCEPT: 2011-2014.

INTERCEPT BLOOD SYSTEM
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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

HV Program	Conventional Platelets		INTERCEPT Platelets	
	Platelet Units Transfused	TTIs (Fatalities)	Platelet Units Transfused	TTIs
France 2006–2014[1,2]	2,299,334	49 (8)	180,762	0
Switzerland 2010–2014[1,3]	36,500	1 (0)	130,843	0
Total	**2,335,834**	**50 (8)**	**311,605**	**0**

[1] Sweeney J, Lozano M. *Platelet Transfusion Therapy*. Bethesda: AABB Press, 2013.
[2] French National Agency for Medicine and Health Product Safety/ANSM, *Hemovigilance Activity Reports*, 2012–2014.
[3] SwissMedic *Haemovigilance Annual Reports*, 2010–2014.

INTERCEPT BLOOD SYSTEM
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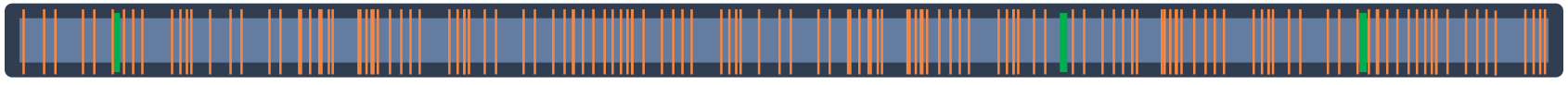
Reduction of T-Cells

To a level that potentially reduces the risk of TA-GVHD[1]

- INTERCEPT processed platelets exhibited a 4 $\log_{10}$ reduction of viable T-cells.[2]
- 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[3,4] amotosalen adduct formed: base pair



Animation courtesy of AuBuchon, JK.

[1]FDA Press Release: *FDA approves pathogen reduction system to treat platelets*. December 19, 2014. | [2]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016. | [3]Grass, JA et al. *Blood*. 1998 Mar 15;91(6):2180-8. | [4]Setlow, RB, Setlow, JK. *Effect of radiation on polynucleotides*. Baldwin, ML, Jeffries, LC (eds). *Irradiation of blood components*. Bethesda, MD. AABB, 1992 p1.

INTERCEPT BLOOD SYSTEM

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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

Study	PCs	Patients	Intervention	Outcome	Timing
HV1	5,106	651	INTERCEPT PCs	Safety	2003–2005
HV2	7,437	1,400	INTERCEPT PCs	Safety	2005–2007
HV3	6,632	2,016	INTERCEPT PCs	Safety	2006–2010
Total	**19,175**	**4,067**	**INTERCEPT PCs**	**Safety**	**2003–2010**

Knutson, F et al. *Vox Sang*. 2015 May 15. doi:10.1111/vox.12287. [Epub ahead of print]

The INTERCEPT Blood System

For Plasma

INTERCEPT BLOOD SYSTEM

PATHOGEN REDUCTION SYSTEM

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]**

* 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.

[1]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.

INTERCEPT BLOOD SYSTEM
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INTERCEPT Blood System for Plasma

Populations studied in clinical trials[1]

- 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]

[1]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.|[2]Mintz, PD et al. *Blood*. 2006 May1;107(9):3753-60.
[3]de Alarcon, P et al. *Transfusion* 2005 Aug;45(8):1382-72.|[4]Mintz, PD et al. *Transfusion* 2006 Oct;46(10):1693-704.
[5] Cinqualbre, J et al. *Vox Sang* 2012 103(Supplement 1):247-48.

INTERCEPT BLOOD SYSTEM
PATHOGEN REDUCTION SYSTEM

INTERCEPT Blood System for Plasma

Demonstrated safety, efficacy in routine use

- Hemovigilance (HV) programs - a comprehensive view of transfusions and potential adverse events.
- HV programs tracking the ***routine use of >200,000 INTERCEPT Plasma***[1] units in Europe have demonstrated therapeutic efficacy with an adverse event profile consistent with untreated plasma.[2-4]

Year	Product	Plasma Units	Acute Transfusion Reactions per 1,000 Units
2009	Untreated Plasma	348,725	0.55
	INTERCEPT Plasma	**22,933**	**0.52**
2010	Untreated Plasma	329,757	0.59
	INTERCEPT Plasma	**52,692**	**0.47**
2011	Untreated Plasma	311,482	0.31
	INTERCEPT Plasma	**68,440**	**0.31**

[1] Subset HV data shown above, French HV data.
[2] INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.
[3] Cazenave JP et al. *Transfusion* 2010;50:1210-1219. | [3]Bost V et al. *Vox Sanguinis* 2013;104:337-341.
[4]Afssaps Rapport Annuel Hemovigilance 2009-2011.

INTERCEPT BLOOD SYSTEM
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Safety, Efficacy Evaluated in Prospective Trials

Studies met primary endpoints for the INTERCEPT Blood System for Plasma[1]

Study Design*	Primary Result(s)	Primary Endpoint Met?
Phase I Randomized, single-blind, crossover with healthy subjects **(N=15)**	**Comparable coagulation factor levels** attained between test and control FFP.[2]	✓
Phase II Randomized, single-blind, crossover with healthy subjects, warfarin anticoagulated **(N=27)**	**Comparable prothrombin time and FVII kinetics** between test and control FFP.[2]	✓
Phase II Randomized, double-blind, parallel group, multiple coagulation deficiencies **(N=13)**	INTERCEPT plasma was **safe and well tolerated by patients impaired with hepatic function. Comparable hemostatic activity attained** between test and control FFP.[3]	✓
Phase IIIa Open label, single arm, congenital coagulation deficiencies **(N=34)**	**Comparable recovery, pharmacokinetic performance, and PT/PTT** attained between test and control FFP.[3]	✓
Phase IIIb Randomized, double-blind, parallel group, acquired coagulation deficiencies **(N=121)**	**Comparable coagulation responses and clinical hemostasis** were attained between test and control FFP.[4]	✓
Phase IIIc Randomized, double-blind, parallel group, thrombotic thrombocytopenic purpura (TTP) **(N=35)**	**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.[5]	✓

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

[1]INTERCEPT Blood System for Plasma [Package Insert]. Concord, CA: Cerus Corporation; 2015.
[2]Hambleton, J et al. *Transfusion.* 2002 Oct;42(10):1302–7. | [3]de Alarcon, P et al. *Transfusion.* 2005 Aug; 45(8):1362–72.
[4]Mintz, PD et al. *Blood.* 2006 May 1;107(9):3753–60. | [5]Mintz PD et al. *Transfusion.* 2006 Oct;46(10):1693-704.

INTERCEPT BLOOD SYSTEM
PATHOGEN REDUCTION SYSTEM

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.

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

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

PATHOGEN REDUCTION SYSTEM

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.

Factor	Untreated Plasma	INTERCEPT Plasma
Anticoagulant Proteins		
Antithrombin III	**0.98**	**0.93**
Protein C (IU/mL)	**0.95**	**0.86**
Protein S (IU/mL)	**1.08**	**1.04**
Proteins of the Fibrinolytic System		
Alpha-2-plasmin inhibitor (IU/mL)	**1.00**	**0.85**
Markers of Coagulation Activation		
Thrombin-Antithrombin Complexes (µg/L)	**2.4**	**2.3**
Factor VIIa (ng/mL)	**<3.6**	**<3.6**

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
PATHOGEN REDUCTION SYSTEM

The INTERCEPT Blood System
Operational Efficiencies

INTERCEPT BLOOD SYSTEM

PATHOGEN REDUCTION SYSTEM

INTERCEPT Blood System

Operational and cost 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.

[1]INTERCEPT Blood System for Platelets [Package Insert]. Concord, CA: Cerus Corporation; 2016.
[2]Berger K, et al. *Onkologie* 2013;36:53–59.

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