The Evolution of Blood Safety Mitigation Measures

IPFA 2016, Lisbon

Adonis Stassinopoulos, Ph.D
VP Global Scientific Affairs and Research
Outline

• Unsustainability of Testing as the main method of protection against new pathogens

• PI vs. NAT

• Introduction to INTERCEPT 10+ year experience

• Applications of PI in residual safety and new safety issues
  • Bacteria
  • Emerging Pathogens

Conclusions
Emerging Pathogens: Is testing a sustainable solution?

Development time, cost, continual addition of new pathogens

25 years of testing = protection against 9 agents
HIV, Hepatitis B, Hepatitis C, HTLV, bacteria, West Nile virus, T. Cruzi, Syphilis, Leukocytes

- HIV-1
- HBc
- ALT
- HCV 1.0
- HIV-1/2
- HCV 2.0
- HIV-1 p24
- Widespread Leukoreduction
- HIV-HCV NAT
- WNV NAT
- T. Cruzi

Bacterial Detection
AABB Rule 5.1.5.1

New pathogens continue to emerge

Cost

$250
$200
$150
$100


RBC price data adapted from B Custer & J S Hoch, Transfusion Medicine Reviews, 23, No 1 (January), 2009: pp 1-12

2003 Pathogen Inactivation
Pathogen Inactivation vs. Testing

Pathogen Inactivation

- One intervention per blood product
- Proactive
- Does not require prior knowledge of the pathogen, or additional development time
- If properly designed, ensures robust, broad inactivation
- Simpler business model

Nucleic Acid, or Ab Testing

- Developed per pathogen, and can be bundled, i.e. triplex vs. singlex
- Reactive
- Requires development and validation for sensitivity and specificity with characterized samples
- Sometimes needs to be used in addition to orthogonal assays, i.e. Ab and NAT
- Business model required for each pathogen
When pathogens are unable to replicate, they are considered “inactivated” and cannot infect patients. Donated plasma or platelet component(s) may contain harmful agents such as bacteria, viruses, protozoans, and/or white blood cells. Donated Plasma or Platelet Component contaminated with pathogens. INTERCEPT locks the DNA or RNA to prevent replication. Pathogen-reduced component can then be transfused into the patient.
10+ Years of Routine Global Use

>100 Blood Centers in 25 Countries with kits sold to produce over 3,500,000 INTERCEPT platelet and plasma units

Centers in Routine Use

Commerciably Available

Regulatory Activity Initiated / Application Pending Review

Last update: May 2016
# Select Regulatory Approvals

**Status as of May 2016**

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Approval Authority</th>
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<td>2006</td>
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<td>2010</td>
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<td>Mexico* (COFEPRIS)</td>
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<tr>
<td>2011</td>
<td>US</td>
<td>US (FDA)</td>
</tr>
<tr>
<td>2014</td>
<td>Brazil</td>
<td>Brazil (ANVISA)</td>
</tr>
</tbody>
</table>

* Approvals shown do not represent a comprehensive list

* For first center approval
Approved Claims by Reg. Authorities

- Use of INTERCEPT platelets and plasma without patient population exclusions
- Replacement of gamma irradiation for the prevention of TA-GvHD
  - Exemptions By AABB for Accredited Labs Internationally
  - Accepted by AABB as an alternative in the US
- Replacement of CMV testing
- Extension of platelet shelf life to 7 days, when that is allowed
- Satisfies AABB requirement 5.1.5.1, as an alternative to BD
- Approved PI claims
INTERCEPT Blood Systems for All components

for Platelets

for Plasma

for RBC

\(^1\)The INTERCEPT System for RBC is not approved for use
Common Mechanism of Action and Target Different compounds for PC/PL and RBC

- **S-59 Amotosalen**
  - Targeting
  - Helical region of DNA and RNA
  - Intercalation
  - Crosslinking
  - UVA Illumination

- **S-303**
  - Effector
  - Anchor
  - Linker
  - Intercalation
  - Crosslinking
  - Chemical Reaction
  - Degradation
  - S-300 (Non-reactive)

**Platelets and Plasma**

**RBC**
Agents Inactivated by INTERCEPT (Amotosalen)

ROUNTELY TESTED AGENTS

CERUS’S COMPREHENSIVE SPECTRUM PROTECTION

ENVELOPED VIRUSES
- HIV-1
- HIV-2
- HBV
- HCV
- HTLV-I
- HTLV-II
- DH BV

ENVIRONMENTALLY VIRUS
- BVDV
- CMV
- WNV
- SARS
- Vaccinia
- Chikungunya
- Dengue
- Influenza A

GRAM-NEGATIVE BACTERIA
- Klebsiella pneumoniae
- Yersinia enterocolitica
- Escherichia coli
- Pseudomonas aeruginosa
- Salmonella choleraesuis
- Enterobacter cloacae
- Serratia marcescens
- Anaplasma
- phagocytophilum
- Orientia tsutsugamushi

SPIROCHETES
- Treponema pallidum
- Borrelia burgdorferi

PROTOZOA
- Trypanosoma cruzi
- Plasmodium falciparum
- Leishmania sp.
- Babesia microti

GRAM-POSITIVE BACTERIA
- Staphylococcus epidermidis
- Staphylococcus aureus
- Streptococcus pyogenes
- Listeria monocytogenes
- Corynebacterium minutissimum
- Bacillus cereus (vegetative)
- Lactobacillus sp.
- Bifidobacterium adolescentis
- Propionibacterium acnes
- Clostridium perfringens

LEUKOCYTES
- T-cells

Agents Inactivated by INTERCEPT (Amustaline)

**ROUTINELY TESTED AGENTS**

**ENVELOPED VIRUSES**
- HIV-1
- HIV-2
- HBV
- HCV
- HTLV-I
- HTLV-II
- DH BV
- BVDV
- CMV
- WNV
- SARS
- Vaccinia
- Chikungunya
- Dengue
- Influenza A

**ENVELOPED VIRUSES**
- DH BV
- Treponema pallidum
- Borrelia burgdorferi
- Bluetongue virus, type 11
- Simian adenovirus 15
- Feline calicivirus
- Parvovirus B19
- Human Adenovirus 5

**GRAM-NEGATIVE BACTERIA**
- Klebsiella pneumoniae
- Yersinia enterocolitica
- Escherichia coli
- Pseudomonas aeruginosa
- Salmonella choleraesuis
- Enterobacter cloacae
- Serratia marcescens
- Anaplasma phagocytophilum
- Orientia tsutsugamushi

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- Propionibacterium acnes
- Clostridium perfringens

**PROTOZOA**
- Trypanosoma cruzi
- Plasmodium falciparum
- Leishmania sp.
- Babesia microti
- T-cells

**SPIROCHETES**
- Treponema pallidum
- Borreli burgdorferi

**BACTERIA**
- Staphylococcus epidermidis
- Staphylococcus aureus
- Streptococcus pyogenes
- Listeria monocytogenes
- Corynebacterium minutissimum
- Bacillus cereus (vegetative)
- Lactobacillus sp.
- Bifidobacterium adolescentis
- Propionibacterium acnes
- Clostridium perfringens

Hemovigilance Programs
Demonstrated safety in routine use

>300,000 INTERCEPT Platelets Evaluated in Routine Use

<table>
<thead>
<tr>
<th></th>
<th>French National Hemovigilance(^1)</th>
<th>Swiss National Hemovigilance(^2)</th>
<th>Multicenter Cerus HV(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td># INTERCEPT Platelet Transfusions</td>
<td>180,762</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>

(2) SwissMedic Haemovigilance Annual Reports, 2010 - 2014.
BACTERIA
FDA Revised Draft Guidance for Bacterial Safety\(^1\)

Recognizes bacterial risk in platelets, includes pathogen reduction as option to help mitigate risk

- Addresses industry concerns on the high risk of bacterial contamination in platelets.
- Includes pathogen reduction as an alternative to testing, strengthens language for day 4 and 5 secondary testing requirements.

- Draft Guidance includes:
  - Blood centers - must either:
    - Perform **pathogen reduction**, or
    - Perform primary bacterial testing (use of culture detection method on a sample taken \(\geq\) 24 hours post-collection)
  - Hospital transfusion service – can use either:
    - **Pathogen reduced** platelets – no further measures necessary
    - Conventional platelets, already negative in primary bacterial testing -- must perform secondary testing at day 4 and 5 per methods in guidance document

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High Log Inactivation for Broad Spectrum of Bacteria in Platelet Concentrates

<table>
<thead>
<tr>
<th>Gram-positive (Aerobes and Anaerobes)</th>
<th>PC/PAS</th>
<th>PC/PL</th>
<th>Gram-negative</th>
<th>PC/PAS</th>
<th>PC/PL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>&gt; 6.6</td>
<td>&gt;7.4¹</td>
<td>Escherichia coli</td>
<td>&gt; 6.4</td>
<td>≥7.3</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>6.6</td>
<td>&gt;7.6</td>
<td>Serratia marcescens</td>
<td>&gt; 6.7</td>
<td>&gt;7.1</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>&gt; 6.8</td>
<td>&gt;6.1</td>
<td>Klebsiella pneumoniae</td>
<td>&gt; 5.6</td>
<td>≥6.7</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>&gt; 6.3</td>
<td>&gt;6.6</td>
<td>Pseudomonas aeruginosa</td>
<td>4.5</td>
<td>≥6.8</td>
</tr>
<tr>
<td>Corynebacterium minutissimum</td>
<td>&gt; 6.3</td>
<td>&gt;6.4</td>
<td>Salmonella choleraeuis</td>
<td>&gt; 6.2</td>
<td>&gt;5.9</td>
</tr>
<tr>
<td>Bacillus cereus (vegetative)</td>
<td>&gt; 6.0</td>
<td>≥5.6</td>
<td>Yersinia enterocolitica</td>
<td>&gt; 5.9</td>
<td>&gt;7.3</td>
</tr>
<tr>
<td>Lactobacillus sp</td>
<td>&gt; 6.9</td>
<td>&gt;6.1</td>
<td>Enterobacter cloacae</td>
<td>5.9</td>
<td>≥6.0</td>
</tr>
<tr>
<td>Bifidobacterium adolescentis</td>
<td>&gt; 6.5</td>
<td>-</td>
<td>Spirochetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>&gt; 6.7</td>
<td>&gt;6.7</td>
<td>Treponema pallidum</td>
<td>6.8 - 7.0</td>
<td>-</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>&gt; 7.0</td>
<td>&gt;6.0</td>
<td>Borrelia burgdorferi</td>
<td>&gt; 6.8</td>
<td>-</td>
</tr>
</tbody>
</table>

- Robust Inactivation of Bacteria is critical to protect against them, as bacteria can grow in blood products

¹ In blue latest claims that have not been reviewed by TUV yet

No Sepsis Fatalities with INTERCEPT Platelets when Used in Routine

French and Swiss National hemovigilance data

<table>
<thead>
<tr>
<th>Year</th>
<th>Conventional Platelets</th>
<th>INTERCEPT Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Units Transfused (n)</td>
<td>Transfusion Transmitted Infections (Fatalities)</td>
</tr>
<tr>
<td>2006</td>
<td>231,853</td>
<td>4 (0)</td>
</tr>
<tr>
<td>2007</td>
<td>232,708</td>
<td>9 (2)</td>
</tr>
<tr>
<td>2008</td>
<td>239,349</td>
<td>6 (1)</td>
</tr>
<tr>
<td>2009</td>
<td>241,634</td>
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<tr>
<td>2010</td>
<td>253,149</td>
<td>2 (1)</td>
</tr>
<tr>
<td>2011</td>
<td>267,785</td>
<td>3 (1)</td>
</tr>
<tr>
<td>2012</td>
<td>275,834</td>
<td>7 (2)</td>
</tr>
<tr>
<td>2013</td>
<td>278,234</td>
<td>4 (1)</td>
</tr>
<tr>
<td>2014</td>
<td>278,788</td>
<td>5 (0)</td>
</tr>
<tr>
<td>2010</td>
<td>29,900</td>
<td>1 (0)</td>
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<tr>
<td>2011</td>
<td>6,600</td>
<td>0</td>
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<tr>
<td>2012</td>
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<td>0</td>
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<tr>
<td>2013</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2014</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>2,335,834</td>
<td>50 (8)</td>
</tr>
</tbody>
</table>

Swiss HV data: SwissMedic Haemovigilance Annual Reports, 2010-2014.
EMERGING PATHOGENS
Emerging Pathogens
The risk of spreading pathogens – Chikungunya, Dengue, Zika
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.
Emerging Pathogens
Current mitigations: Pathogen Reduction

WHO Guidance, February 2016

Maintaining a safe and adequate blood supply during Zika virus outbreaks
Interim guidance
February 2016
WHO GUIDELINES FOR MANAGEMENT OF EMERGING PATHOGENS

1. Introduction
   1.1 Background
   These guidelines have been developed in recognition that
   infection with Zika virus may present a risk to blood safety,
   and in consideration of the declaration on 1 February 2016
   by the WHO Director-General of a Public Health
   Emergency of International Concern with regard to clusters
   of microcephaly and other neurological disorders,
   potentially associated with Zika virus. Currently there is
   other severe neurological complications was
   supported during a 2013–2014 outbreak in French
   Polynesia and remains under investigation [6, 14].
   During the Zika virus outbreak in French Polynesia
   between November 2013 and February 2014, a total of
   1,055 healthy blood donors were tested by nucleic acid
   amplification technology (NAT)-based assays, with 42
   (23%) confirmed positive for Zika virus RNA. Blood
   donors positive for Zika virus RNA were contacted
   retrospectively to investigate the occurrence of "Zika fever-
   conjugate" and/or "Zika".
   For the 42 donors that tested
   yes had a Zika fever-like
   try they gave blood. No
   though transfusion was
   1%. However, transmission
   and West Nile virus by
   documented [2, 14, 25],
   of Zika virus transmission
   reported from Cameroon,

   c. Pathogen reduction of blood components
   Pathogen reduction technology (PRT) may be implemented.
   PRT is currently available for plasma and platelets, but not
   for whole blood or red blood cells. Different PRTs have
   been shown to be effective against other flaviviruses (e.g.
   West Nile, dengue) [10,11,20] and, in the absence of Zika-
   specific information, are presumed as equally effective
   against Zika virus.

   Clinical symptoms of Zika virus infection, and probable
   cases of sexual transmission have been described [1, 3, 14, 15].
   A link between Zika virus infection during pregnancy and
   microcephaly in infants is suspected and currently being
   investigated for causal association [12, 21]. An association
   of Zika virus with Guillain-Barre syndrome (GBS) and

   mk-EN 00156 v4
The INTERCEPT Blood System
Maintaining a safe and adequate blood supply during arboviral outbreaks

INTERCEPT has been called upon to help sustain platelet availability during arboviral outbreaks:

- **2005 CHIKV epidemic on Ile de La Réunion, France**¹
  - All PC were treated with INTERCEPT allowing collections of PC in the island

- **CHIKV outbreaks in Guadeloupe and Martinique, French Polynesia**²
  - PC were treated with INTERCEPT
  - Other components were either quarantined with enhanced PDI collection, or tested with NAT
  - CHIKV positive donations was transfused to 10 recipients without clinical symptoms³

- **2014 CHIKV and DENV outbreaks in the Caribbean region**⁴
  - INTERCEPT PC components were deployed in Puerto Rico in response to the epidemic
  - Authorities excluded PI treated components from the quarantine imposed to other components

- **2016 WHO⁵ and US FDA⁶ issued guidances recommending pathogen reduction as an option to mitigate risks related to ZIKV outbreaks; AABB⁷ issued guidance as an option to mitigate CHIKV, DENV, ZIKV**

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# Arbovirus Comparison

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dengue</th>
<th>Chikungunya</th>
<th>Zika</th>
<th>West Nile</th>
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</thead>
<tbody>
<tr>
<td>Virus family</td>
<td>Flaviviridae</td>
<td>Togaviridae</td>
<td>Flaviviridae</td>
<td>Flaviviridae</td>
</tr>
<tr>
<td>Virus genus</td>
<td>Flavivirus</td>
<td>Alphavirus</td>
<td>Flavivirus</td>
<td>Flavivirus</td>
</tr>
<tr>
<td>Serotypes</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>RNA size (kb)</td>
<td>10.7</td>
<td>11.8</td>
<td>10.8</td>
<td>10.3</td>
</tr>
<tr>
<td>Vector</td>
<td><em>Aedes aegypti</em></td>
<td><em>Aedes aegypti</em></td>
<td><em>Aedes aegypti</em></td>
<td><em>Culex Pipiens</em></td>
</tr>
<tr>
<td></td>
<td><em>Aedes albopictus</em></td>
<td><em>Aedes albopictus</em></td>
<td><em>Aedes albopictus</em></td>
<td><em>C. Tarsalis</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>C. quinquefasciaatus</em></td>
</tr>
<tr>
<td>Symptoms / illness</td>
<td>Acute febrile illness</td>
<td>Acute febrile illness</td>
<td>Acute febrile illness</td>
<td>Acute febrile illness,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Sexually Transmitted</em></td>
<td></td>
</tr>
<tr>
<td>Illness outcome</td>
<td>Severe dengue – plasma</td>
<td>Rarely severe,</td>
<td>Rarely severe, Guillian-</td>
<td>Neuroinvasive Disease</td>
</tr>
<tr>
<td></td>
<td>leakage</td>
<td>Arthralgias</td>
<td>Barré Microcephaly</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Encephalitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Polyomyelitis</td>
</tr>
</tbody>
</table>
### Pathogen Inactivation of Arboviruses in Plasma by the INTERCEPT Blood System

<table>
<thead>
<tr>
<th>Arbovirus</th>
<th>Genus</th>
<th>INTERCEPT Log$_{10}$ Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile Virus</td>
<td>Flavivirus</td>
<td>$&gt;6.8$</td>
</tr>
<tr>
<td>Dengue</td>
<td>Flavivirus</td>
<td>$&gt;5.6^1$</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>Alphavirus</td>
<td>$&gt;6.4$</td>
</tr>
<tr>
<td>Zika</td>
<td>Flavivirus</td>
<td>$&gt;6.6^2$</td>
</tr>
</tbody>
</table>

$^1$ Musso D. et al, Transfusion. 2014 54, 2924-30  
$^2$ Aubry M. et al. Transfusion, 2016
**Published Zika PI in INTERCEPT EPT Plasma**

### TABLE 1. Detection of replicative ZIKV and ZIKV titration (log TCID₅₀/mL) in plasma samples before and after inactivation

<table>
<thead>
<tr>
<th>Plasma samples</th>
<th>Initial viral titre</th>
<th>Replicating ZIKV after inactivation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>First passage</td>
</tr>
<tr>
<td>A</td>
<td>6.46</td>
<td>+</td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>5.63</td>
<td>+</td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>5.51</td>
<td>+</td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D (control)</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninactivated sample</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Positive immunofluorescence.  
† Negative immunofluorescence.

### TABLE 2. ZIKV RNA quantitation (log copies/mL) in plasma samples before and after inactivation

<table>
<thead>
<tr>
<th>Plasma sample</th>
<th>Initial RNA loads</th>
<th>RNA loads after</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First passage</td>
<td>Second passage</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td>10.22</td>
<td>10.31</td>
</tr>
<tr>
<td>Inactivated sample</td>
<td>9.67</td>
<td>4.07</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td>10.41</td>
<td>10.30</td>
</tr>
<tr>
<td>Inactivated sample</td>
<td>9.44</td>
<td>3.63</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td>10.11</td>
<td>10.43</td>
</tr>
<tr>
<td>Inactivated sample</td>
<td>9.41</td>
<td>3.87</td>
</tr>
<tr>
<td>D (control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preinactivation sample</td>
<td>10.36</td>
<td>10.26</td>
</tr>
<tr>
<td>Noninactivated sample</td>
<td>9.90</td>
<td>9.89</td>
</tr>
</tbody>
</table>

* ZIKV RNA not detected.

>6.57
Infectivity

10.25
PCR

1Aubry et al. Transfusion 2015
Zika Infectivity PI (cfu/mL) $>6.57 \log_{10}$

Zika PCR Reduction (gEq/mL) $10.25 \log_{10}$

$\log_{10} (\text{gEq/mL}) \geq 3.68 + \log_{10} (\text{CFU/mL})$

$1^{st}$ Aubry et al. Transfusion 2015
### Zika Inactivation using the INTERCEPT System for Platelets

<table>
<thead>
<tr>
<th>Conditions</th>
<th>N</th>
<th>Log Titers (pfu/mL)</th>
<th>Log Reduction per mL</th>
<th>Log Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-UVA</td>
<td>Post-UVA</td>
<td></td>
</tr>
<tr>
<td>PC in 100% PLASMA</td>
<td>1</td>
<td>4.3</td>
<td>&lt;0.0</td>
<td>&gt;4.3</td>
</tr>
<tr>
<td>PC in 65% PAS</td>
<td>2</td>
<td>4.0</td>
<td>&lt;-1.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>PC in 65% PAS*</td>
<td>2</td>
<td>6.2</td>
<td>&lt;-0.6</td>
<td>&gt;6.2</td>
</tr>
</tbody>
</table>

*Small volumes
Zika Inactivation using the INTERCEPT System for Red Blood Cells with S-303

<table>
<thead>
<tr>
<th>Replicate</th>
<th>Control</th>
<th>Test</th>
<th>Log Reduction per mL</th>
<th>Log Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 LR</td>
<td>4.3</td>
<td>&lt;-0.7</td>
<td>&gt;4.3</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>2 LR</td>
<td>4.4</td>
<td>&lt;-0.7</td>
<td>&gt;4.4</td>
<td>&gt;5.1</td>
</tr>
<tr>
<td>3 NLR</td>
<td>4.3</td>
<td>&lt;-0.7</td>
<td>&gt;4.3</td>
<td>&gt;5.0</td>
</tr>
<tr>
<td>Mean</td>
<td>4.3</td>
<td>&lt;-0.7</td>
<td>&gt;4.3</td>
<td>&gt;5.0</td>
</tr>
</tbody>
</table>

Conducted at nominal volumes (~280 mL AS-5 RBC)
Conclusions

• Blood Safety is ensured through the use of multiple redundant measures, with testing currently being a key contributor to enhanced blood safety

• There are areas where testing appears inadequate, or cannot be developed and applied fast enough

• PI is increasingly recognized as a technology that can address such areas, as examples from the bacterial contamination and emerging pathogens have demonstrated, in routine use.

• The introduction of PI for RBC will expand the applicability of PI in enhancing blood safety
Thank you!