INTERCEPT Blood System Inactivates *Enterococcus faecalis*, Multiple Species of *Streptococcus* and *Serratia liquefaciens* in Platelet Components in Platelet Additive Solution and in Plasma

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Background
A photochemical treatment process utilizing 150 mW ultramollas (590-600 and 312 nm) long wavelength ultraviolet light (UVA), the INTERCEPT Blood System, has been developed to inactivate high titers of a large number of Gram positive and Gram negative bacteria, both cell-free and cell-associated, enveloped and nonenveloped viruses, and protozoan parasites (Table 1). It is currently in use in more than 100 sites in 20 countries and has recently been approved for use in the US.

Previous studies have shown inactivation of Streptococcus pyogenes and Serratia marcescens by the INTERCEPT Blood System for platelets. Additional species of Serratia and Streptococcus have recently emerged as organisms of concern to blood transfusion in the UK. The INTERCEPT mechanism of action is not species specific and evaluation of these additional species offers the opportunity to demonstrate this breadth of efficacy.

Aims
The aim of these studies was to demonstrate that the inactivation of Serratia marcescens and Streptococcus pyogenes is representative of the two genera by showing that inactivation of Serratia marcescens, Streptococcus agalactiae, Streptococcus mitis, Streptococcus pneumoniae and Enterococcus faecalis by INTERCEPT treatment is comparable to that previously demonstrated for Serratia marcescens and Streptococcus pyogenes.

Methods
Apheresis platelet components containing 3-4 x 10^11 platelets in 330-400 mL of 100% plasma or 35% plasma/65% Platelet Additive Solution (PAS) were inoculated to a 100% plasma or 35% plasma/65% PAS solution. Additional species of Serratia and Streptococcus have recently emerged as organisms of concern to blood transfusion in the UK. The INTERCEPT mechanism of action is not species specific and evaluation of these additional species offers the opportunity to demonstrate this breadth of efficacy.

Figure 1: INTERCEPT Mechanism of Action Targeting DNA and RNA to Prevent Pathogen Proliferation

Small molecules (amotosalen) penetrate cellular and nuclear membranes and intercalate into helical regions of DNA or RNA present.

Figure 2: The INTERCEPT Blood System for Platelets
Using a sterile connecting device (SCD), the platelet container is connected directly to the INTERCEPT kit. Amotosalen (1) is added by gravity flow and the platelet mixture is illuminated with UVA light (2). Residual amotosalen and its photoproducts in the platelet mixture are reduced to low levels using a compound adsorption device (CAD) (3) before the platelets are transferred to the storage container.

Results
Historical data for inactivation of S. marcescens and S. pyogenes in PC in PAS are shown in Table 3. Using the data obtained in the current studies. In the current study, inactivation of at least 6.5 log10 of one additional species of Serratia and four additional species of Streptococcus/Enterococcus was demonstrated in PC suspended in 100% plasma or 35% plasma/65% PAS.

Table 1: Pathogen Inactivation by the INTERCEPT Blood System

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Platelets in 100% Plasma</th>
<th>Platelets in 35% Plasma/65% PAS</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. marcescens</em></td>
<td>-6.7±0.1</td>
<td>≥7.3±0.3 (≥6.3)</td>
</tr>
<tr>
<td><em>S. pyogenes</em></td>
<td>-6.8±0.2</td>
<td>≥7.3±0.3</td>
</tr>
<tr>
<td><em>S. agalactiae</em></td>
<td>-6.9±0.2</td>
<td>≥7.3±0.3</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>-6.7±0.1</td>
<td>≥7.3±0.3</td>
</tr>
<tr>
<td><em>E. faecalis</em></td>
<td>-6.8±0.2</td>
<td>≥6.3±0.3</td>
</tr>
</tbody>
</table>

Conclusions

• INTERCEPT treatment inactivates high titers of multiple species of Serratia and Streptococcus in platelet components suspended in PAS and in plasma.

• These results support the applicability of inactivation data obtained using one species as a model for efficacy across a genus.