Pathogen reduction (PR) as alternative to testing

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## Current methods of Pathogen Reduction in blood products

<table>
<thead>
<tr>
<th>Method</th>
<th>Amotosalen/UVA</th>
<th>Riboflavin/UV</th>
<th>UVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Cerus</td>
<td>Terumo</td>
<td>Macopharma</td>
</tr>
<tr>
<td>Product</td>
<td>FFP</td>
<td>FFP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>PC</td>
<td></td>
</tr>
<tr>
<td>In clinical trial</td>
<td>RCC</td>
<td>RCC</td>
<td>PC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WB</td>
</tr>
</tbody>
</table>
Scheme representing electromagnetic wavelength spectra, zooming into the ultraviolet range and positioning UV-light based pathogen reduction treatments.

Salunkhe V et al. Transfusion and Apheresis Science, Volume 52, Issue 1, 2015, 19 - 34
Pathogen reduction treatments: products, demands, solutions and geography

Salunkhe V et al. Transfusion and Apheresis Science, Volume 52, Issue 1, 2015, 19 - 34
## Potential redundant safety measures

<table>
<thead>
<tr>
<th>Product</th>
<th><strong>Amotosalen/UVA</strong></th>
<th><strong>Riboflavin/UV</strong></th>
<th><strong>UVC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>FFP</td>
<td>Bacteria?</td>
<td>Bacteria?</td>
<td></td>
</tr>
<tr>
<td>PC</td>
<td>Bacteria</td>
<td>Bacteria</td>
<td>Bacteria</td>
</tr>
<tr>
<td></td>
<td>Irradiation</td>
<td>Irradiation</td>
<td>NK</td>
</tr>
<tr>
<td></td>
<td>APC filtration</td>
<td>APC filtration</td>
<td>NK</td>
</tr>
<tr>
<td></td>
<td>CMV</td>
<td>CMV</td>
<td>CMV</td>
</tr>
<tr>
<td>RCC</td>
<td>Bacteria</td>
<td>Bacteria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Irradiation</td>
<td>Irradiation</td>
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<tr>
<td></td>
<td>APC filtration</td>
<td>APC filtration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HTLV-I/II</td>
<td>HTLV-I/II</td>
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</tr>
<tr>
<td></td>
<td>CMV, EBV, HHV-8</td>
<td>CMV, EBV, HHV-8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T Cruzi Ab</td>
<td>T Cruzi Ab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plasmodium Ab</td>
<td>Plasmodium Ab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Babesia NAT</td>
<td>Babesia NAT</td>
<td></td>
</tr>
</tbody>
</table>
In vitro evidence of efficacy of Mirasol in WB

1. **Nucleated white cells**
   (Marschner et al. Transfusion 2010; Fast et al. Transfusion 2013)

2. **Enveloped viruses (HIV-1, HCV, HBV)**

3. **Non-enveloped viruses (HAV, HEV, B19V)**
   (Marschner et al. Transfus Med Hemother 2011)

4. **Intra-cellular viruses (HHV-8, CMV?)**
   (Allain et al. unpublished)

5. **Bacteria**
   (Goodrich et al. Biologicals 2010)

6. **Parasites (Babesia, Plasmodium, Trypanosoma Cruzi, Leishmania)**
PR applied to whole blood (WB)

- Single operation, single cost
- WB is the main blood product in Sub-Saharan Africa
- Need evidence that PR WB produce safe components
- Allows redundancy of multiple costly safety measures
  - Filtration
  - NAT (HIV-1, HCV, HBV, WNV, HEV, DENV, CHIKV, B19?)
  - HTLV-I/II, CMV, EBV, HHV-8 & irradiation
  - Anti-HBc
  - Bacterial testing
  - Parasite testing (malaria, trypanosoma)
Objective:
• To evaluate the efficacy of Mirasol-treated fresh whole blood (FWB) to prevent malaria transmission via transfusion

Primary and Secondary Endpoints:
• Incidence of transfusion-transmitted malaria (TTM)
  – Plasmodium detection & quantification
  – Microscopy, quantitative PCR, allelic discrimination
• Bacterial contamination of FWB products
• Clinical laboratory parameters in FWB products and study subjects

Safety Endpoints:
• Transfusion reactions and/or transfusion-related adverse events (AEs)
• Treatment emergent adverse events (TEAEs)
Patient Eligibility

• Patients eligible for the study were adults (≥ 18 years of age) in Depts A&E, Medicine or O&G.
  – Blood group O
  – Expected to receive 1-2 WBU and 3d stay in hospital
  – Follow-up at 1, 3, 7 and 28d post-transfusion

• Exclusion from the study were:
  – Pregnant women
  – Patient with massive bleeding expected to require more than 2 unit of FWB
  – Patients having been transfused less than a month prior to being considered for the study
  – Patients receiving anti-malarial treatment
Definition of TTM based on Freimanis et al, Transfusion 2013

1. No parasitaemia pre-transfusion
2. Parasitaemia in at least 2 consecutive samples post-TX
3. Same parasite species in donation & patient
4. Sequence homology donation-patient *Plasmodium*
5. >95% homology in at least 2 of 3 alleles: MSP1, MSP2, 3D7 or FC27, GLURP