Pathogen reduction (PR) as alternative to testing

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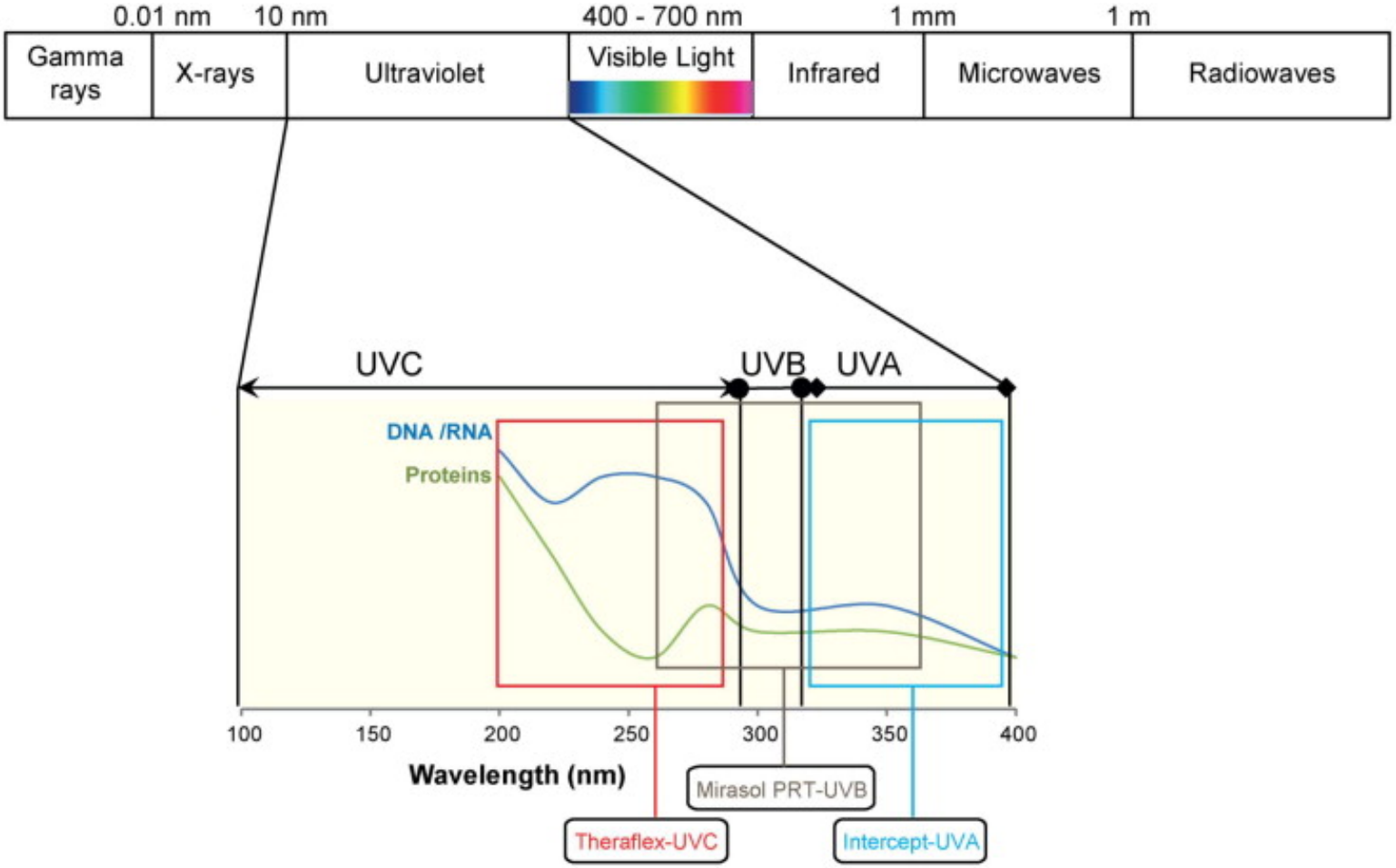
Current methods of Pathogen Reduction in blood products

Method	**Amotosalen/UVA**	**Riboflavin/UV**	**UVC**
Manufacturer	Cerus	Terumo	Macopharma
Product	FFP	FFP	
	PC	PC	
In clinical trial	RCC	RCC	PC
		WB	

Scheme representing electromagnetic wavelength spectra, zooming into the ultraviolet range and positioning UV-light based pathogen reduction treatments



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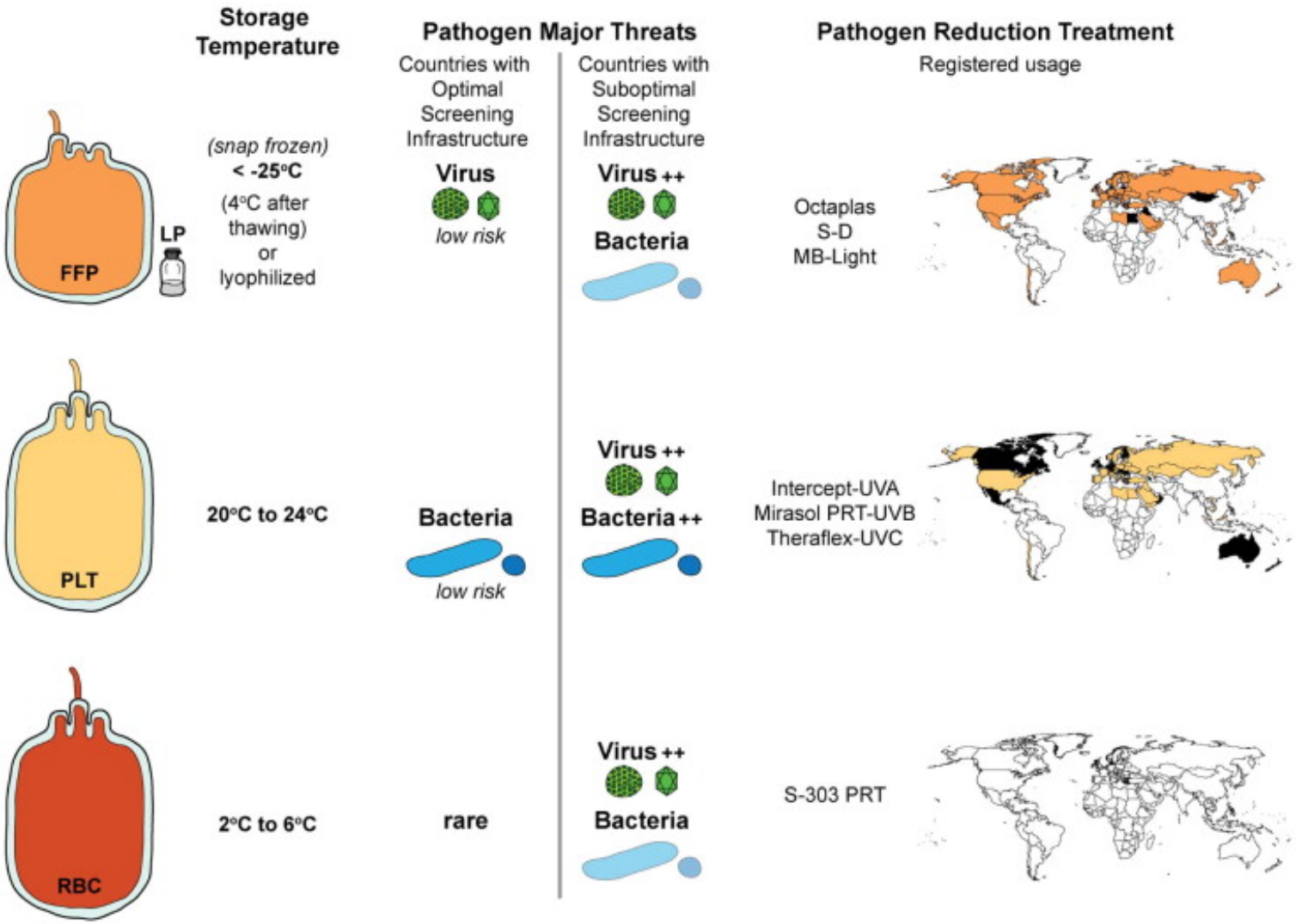
Pathogen reduction treatments: products, demands, solutions and geography



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Potential redundant safety measures

Product	Amotosalen/UVA	Riboflavin/UV	UVC
FFP	Bacteria?	Bacteria?	
PC	Bacteria	Bacteria	Bacteria
	Irradiation	Irradiation	NK
	APC filtration	APC filtration	NK
	CMV	CMV	CMV
RCC	Bacteria	Bacteria	
	Irradiation	Irradiation	
	APC filtration	APC filtration	
	HTLV-I/II	HTLV-I/II	
	CMV, EBV, HHV-8	CMV, EBV, HHV-8	
	T Cruzi Ab	T Cruzi Ab	
	Plasmodium Ab	Plasmodium Ab	
	Babesia NAT	Babesia NAT	

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)

(Goodrich et al. Biologicals 2010; Reddy et al. Transfusion 2013; Allain JP et al 2013, unpublished)

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 unpublished)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)

(Tonetti et al. Transfusion 2013; ElChaar et al, Transfusion 2013; Owusu-Ofori et al. Shock 2014; Tonetti et al. Transfusion 2012, Tonetti et al. Transfusion 2015)

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)

Objectives of the AIMS RCT

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