DESIGN AND VALIDATION OF A NOVEL SET TO POOL, FILTER AND SPLIT 6 UNITS OR 1500ML OF RECOVERED PLASMA PRIOR TO PATHOGEN INACTIVATION WITH INTERCEPT

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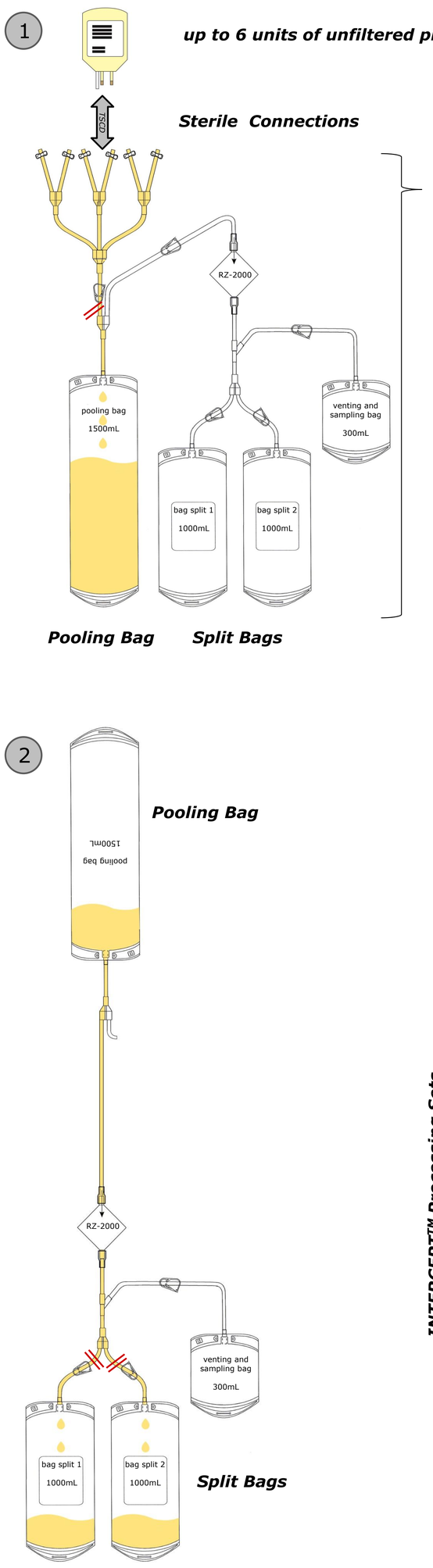
Introduction and Purpose

INTERCEPT™ pathogen inactivation (PI) technology is used for source and recovered plasma. To treat recovered plasma, approx. 2.5 plasma units should be pooled to use full capacity of the *INTERCEPT™* processing set (650mL). Hence, 5 units are pooled and separated into 2 splits of 650mL each with a commercially available set. Since this set has no filter, filtered plasma must be used to meet Swiss specifications, which leads to tradeoffs. For example, if whole blood filtration is used, buffy-coats lack platelets (plts). If component filtration is applied, often expensive blood collection sets have to be used. The latter approach is particularly uneconomic when most plasma is not used for transfusion but for fractionation not requiring filtered plasma. To solve this issue, we have developed a set with integrated filter.

Methods

We previously showed that whole blood filter RZ-2000 can remove white blood cells (WBC) from large volumes of plasma without getting clogged (Goslings et al., Vox Sang 2012;103; suppl.1). Therefore, we designed a set based on this filter (Fig.1). Blood was collected with set NGR6428 (Fenwal) and separated into erythrocytes, buffy-coat and unfiltered plasma. Although our set has been designed to pool 5 or 6 of these plasma units, we pooled up to 7 units for validation purposes to challenge the system. Furthermore, 8 of the 26 unfiltered plasma pools made were spiked with WBCs to increase WBC concentrations far above standard conditions.

Figure 1: Use of PurePlas 6 (Plasma Pooling Set with Leucocyte Filter)



Steps 1-3 of Figure 1 explained:

(1) Sterile connect up to 6 units of unfiltered plasma to the pooling set PurePlas 6. (For validation purposes up to 7 units were used to challenge the system.)

Let the plasma flow into the pooling bag.

Sterile disconnect (//) the emptied plasma bags and the attached octopus tubing system.

(2) Let the pooled plasma flow through the RZ-2000 filter.

Sterile disconnect (//) the two split bags.

(3) Sterile connect each split bag to a INTERCEPT™ processing set.

Results

Pools contained 1500-1899mL plasma with WBC concentrations up to $0.597x10^3/\mu L$, plts up to $33.56x10^9/L$, and RBCs up to $0.47x10^6/mL$ (n=26). After filtration, WBCs were below estimated detection limit of FACS ($0.0005 \times 10^3/\mu L$), plts were $\leq 4.09x10^9/L$, and RBCs $\leq 0.05x10^6/mL$. Factor VIII and fibrinogen concentrations did not change significantly ($p>0.05$, n=18). On standard conditions, average total volume loss was 40mL and filtration times were <9min (n=22) (Tab. 1 and 2, Fig. 2).

Table 1: Residual Cells and Volume before Filtration with PurePlas 6

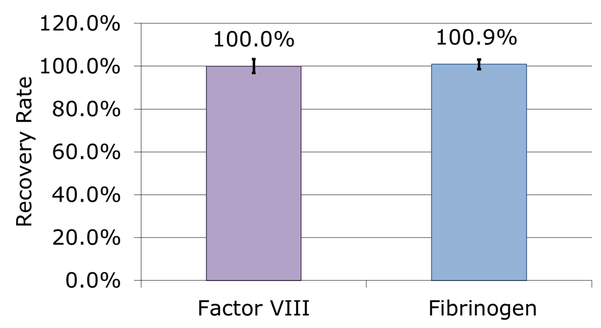
	Average	Median (	Range	)	Specification*	pass/fail
Volume [mL]	1770	1825	(1500 -	1899)	n.a.	n.a.
WBC						
[1x10⁶/200 mL]	26.20	3.76	(0.80 -	119.40)	< 1	96% fail
[1x10³/µL]	0.131	0.019	(0.004 -	0.597)	n.a.	n.a.
RBC [1x10⁶/mL]	0.28	0.25	(0.12 -	0.47)	< 4	100% pass
Plts [1x10⁹/L]	19.96	18.98	(8.50 -	33.56)	< 50	100% pass

Table 2: Residual Cells and Volume Loss after Filtration with PurePlas 6

	Average	Median (	Range	)	Specification*	pass/fail
Volume Loss [mL]	40	40	(34 -	49)	n.a.	n.a.
WBC						
[1x10⁶/200 mL]	BDL	BDL	(BDL -	BDL)	< 1	100% pass
[1x10³/µL]	BDL	BDL	(BDL -	BDL)	n.a.	n.a.
RBC [1x10⁶/mL]	0.03	0.03	(0.01 -	0.05)	< 4	100% pass
Plts [1x10⁹/L]	0.68	0.49	(0.15 -	4.09)	< 50	100% pass

*Tables 1 and 2: * Specifications according to Swiss requirements for fresh frozen plasma (Limits for WBCs are per unit; 1 unit ≈200mL); WBC=White Blood Cell; RBC=Red Blood Cell; plts=platelets; BDL=Below Detection Limit; n=26; WBCs were reduced from out of specification values to levels below estimated detection limit (0.0005 x $10^3/\mu L$). Levels of RBCs and plts already fulfilled requirements before filtration and were further reduced by using PurePlas 6.*

Figure 2: Recovery of Factor VIII and Fibrinogen



Full recovery of factor VIII and fibrinogen in plasma being processed with PurePlas 6; p >0.05 and n=18 for factor VIII and for fibrinogen.

Summary/Conclusions

Our set PurePlas 6 efficiently filters up to 6 units or 1500 mL of plasma for PI without affecting factor VIII and fibrinogen concentrations. Concentrations of WBCs were reduced from out of specification values to levels below estimated detection limit of FACS. Concentrations of RBCs and plts already fulfilled Swiss specifications for fresh frozen plasma and were even further reduced by using PurePlas 6.