Background
The blood transfusion service Zurich introduced the pathogen inactivation (PI) method INTERCEPT™ for platelets in 2011 and considers now to introduce INTERCEPT™ for plasma as well (Fig. 1). Pathogen inactivated fresh-frozen plasma (PI-FFP) has several advantages compared to quarantine plasma. Apart from further reducing the risk of transfusion related infections, plasma management is facilitated and availability of FFP increases since PI-FFP can be delivered for transfusion immediately after freezing. To use INTERCEPT™ plasma processing sets with recovered plasma several units need to be pooled prior PI. Ideally a pool of 5 units (approx. 1300mL) is evenly distributed on 2 PI-sets. To reduce cost and optimize workflows only the fraction of recovered plasma intended for transfusion is leukodepleted with a filter integrated into the pooling-set. However, no such set is commercially available yet (Fig. 2). Since whole blood filters are designed to cope with much higher amounts of residual cells than plasma filters for component filtration, we decided to build a pooling-set prototype based on a whole blood filter.

Methods
A pooling-set was built by connecting a 2000mL-bag (R42041, Fenwal) with the Asahi RZ-2000 filter taken from Fenwal set NGR6449. The RZ-2000 outlet was connected via y-piece to a dual-bag-set (2x500mL, VDE40003XA, Macopharma). 6 Plasma-pools (each containing 5 non-filtered recovered plasma units) were processed with this prototype (Fig. 3). Each of the 2 bags of the dual-set is supposed to be connected to an INTERCEPT™-set. However, for economic reasons, the filter was operated in 1 PI-set only resulting in 3 PI-FFP per INTERCEPT™-set used. Time from donation to freezing was 5-8h. 1 PI-FFP unit per pool was thawed for analysis at first month of storage. Residual cells and Factor VIII were assessed by FACS and photometry, respectively.

Aims
The objective of this study was to identify a filter suitable to quickly process 1300mL non-filtered recovered plasma to meet process entry criteria for INTERCEPT™ (guard bands: vol. 385-650mL, <4x10^9 RBC/mL and Swiss specifications for FFP with respect to residual cells and Factor VIII (<1x10^6 WBC/unit, <5x10^9 RBC/unit, <50x10^9 platelets/L, Factor VIII ≥1.14IU/mL)).

Results
Before filtration average pool-volume (n=6) was 1335mL (1310-1358) and mean WBC concentration in pools was 0.0233x10^6/L (range 0.0087-0.0697x10^6/L) which is equivalent to 4.7x10^9WBC/200mL-FFP. RBC ranged 0.19-0.65x10^11/L, platelets 11.91-23.67x10^10/L and Factor VIII was 1.14IU/mL (0.97-1.40, n=5). After filtration (max. 9min), volume loss was 56-69mL and WBC ranged 0.0000-0.0001x10^6/L (equivalent to 0.0-0.02x10^6WBC/200mL-FFP). RBC were reduced to 0.07-0.36x10^11/L and platelets to 0.13-0.62x10^9/L while Factor VIII was still in average 1.14IU/mL (1.00-1.29, p=0.686). PI was performed with 611-634mL filtered plasma and in 3 PI-sets Factor VIII of the PI-FFP was in average 0.78IU/mL (0.70-0.94) (Tab. 1-4). While loss of Factor VIII through freezing was not significant (p=0.102), PI significantly decreased Factor VIII by 25% (p=0.042) (Fig. 4).

Parameters Measured During Production of PI-FFP with Prototype

- **Volume before filtration**: 1335mL (1310-1358)
- **WBC concentration**: 0.0233x10^6/L (range 0.0087-0.0697x10^6/L)
- **RBC concentration**: 0.19-0.65x10^11/L
- **Platelets**: 11.91-23.67x10^10/L
- **Factor VIII**: 1.14IU/mL (0.97-1.40, n=5)

**Table 1**: Specifications for volume and RBCs according to INTERCEPT

**Table 2**: Specifications for WBCs and Factor VII according to Swiss regulations

**Table 3**: Parameters after freezing and thawing

**Table 4**: Parameters after pathogen inactivation

**Table 5**: Factor VIII Recovery in plasma at different processing steps

**Figure 1**: The INTERCEPT™ Process for Plasma

**Figure 2**: Principle of Plasma Pooling prior to INTERCEPT™

**Figure 3**: Prototype in Use

**Figure 4**: Factor VIII Recovery

Summary/Conclusions
All plasma-pools met guard bands after filtration and all PI-FFP met Swiss specifications. The RZ-2000 seems to be well suited to filter 1300mL plasma for INTERCEPT™ without having any negative impact on Factor VIII. Due to these promising results further development of plasma pooling-set using RZ-2000 is desirable.

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