

**Routine Production of Apheresis Plasma Pathogen Inactivated
Using the INTERCEPT Blood System™:
Preservation of Plasma Quality**

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**Presented at the XXXIst International Congress of the
International Society of Blood Transfusion (I.S.B.T.)
Berlin, Germany • June 26th - July 1st, 2010**

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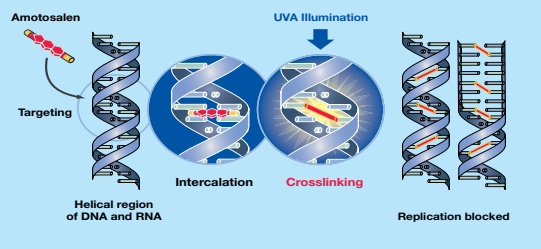


Background

Centre de Transfusion Sanguine des Armées (CTSA) collects 838 apheresis plasma components (600-650 mL) and transfuses approximately 1443 plasma products (200 mL) annually. In 2006 the Agence Française de Sécurité Sanitaire des Produits de Santé (Afssaps) approved plasma treated with the INTERCEPT™ system for transfusion. The INTERCEPT Blood System™ uses a combination of amotosalen and UVA light to inactivate viruses, bacteria, parasites and leukocytes in blood components prior to transfusion (Figure 1). To implement the INTERCEPT system in CTSA, the process was validated with 30 apheresis plasma collections. Preliminary results were reported at SFTS annual meeting 2009 (*Transfusion Clinique et Biologique* 2009; 16:3:317).

Figure 1: INTERCEPT Mechanism of Action

The INTERCEPT Blood System uses a combination of amotosalen HCl and long wavelength ultraviolet A (UVA) light. The amotosalen compound penetrates cellular and nuclear membranes and intercalates into the helical regions of DNA and RNA. Covalent crosslinks to the nucleic acid base pairs form upon exposure to UVA light, blocking DNA and RNA replication. This process inactivates leukocytes and pathogens, rendering them unable to cause disease, while retaining the function of plasma/platelets, which do not require nucleic acid replication for therapeutic efficacy.



Aims

The objective of this study was to evaluate the impact of INTERCEPT Blood System on routine production and whether the quality of INTERCEPT plasma meets the local quality requirement for transfusion: per unit volume of ≥ 200 mL, mean Factor VIII activity ≥ 0.70 IU/mL, mean total proteins > 50 g/L and residual amotosalen < 2 μ M. In this study, results on 784 INTERCEPT treated plasma units (200-300 mL) from 6 months of routine production are reported.

Methods

284 apheresis plasma components (600-650 mL) were collected using the Haemonetics MCS@+ device and stored at ambient temperature prior to treatment (Table 1). INTERCEPT treatment was performed as soon as possible to allow freezing of treated plasma products within 8 hours of collection. INTERCEPT treatment involves the addition of amotosalen (150 μ M) to the apheresis component, the illumination (3 J/cm² UVA) of the plasma mixture, and reduction of the amotosalen concentration by a flow-through compound adsorption device (CAD, <30 minutes). The treated plasma was evenly divided into 3 or 2 storage containers (≥ 200 mL) (Figure 2 and 3). Post-treatment samples were taken for analysis of residual amotosalen by HPLC, coagulation Factor VIII by standard coagulation assays and total proteins by Biuret reaction.

Table 1: Plasma collection for INTERCEPT treatment

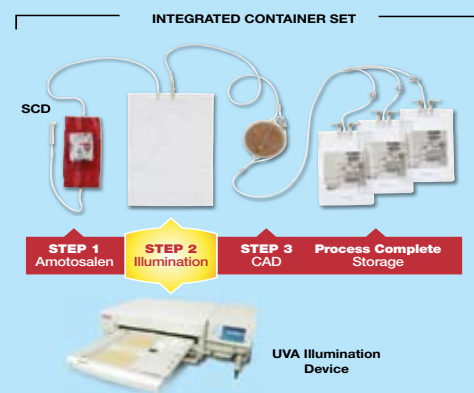
	Plasma collection for INTERCEPT treatment
Routine production period	6 months (March-August, 2009)
Total plasma components	284 apheresis plasma
Collection platform	Haemonetics MCS@+ Set 792 P
Average plasma volume	600-650mL

Figure 3: Apheresis plasma before and after INTERCEPT treatment



Figure 2: The INTERCEPT Blood System for Plasma

Using a sterile connecting device (SCD), the plasma container is sterilely connected to the INTERCEPT kit. Amotosalen (1) is added by gravity flow and the plasma mixture is illuminated with UVA light (2). Residual amotosalen and its photoproducts in the plasma mixture are reduced to low levels using a compound adsorption device (CAD) (3) before the plasma is transferred to the storage containers.



Results

Prior to INTERCEPT implementation, 30 apheresis plasma collections were validated for the treatment of INTERCEPT and evaluated for plasma functions (Table 2). Following INTERCEPT implementation, routine use of 284 apheresis plasma components treated with INTERCEPT was reported. The mean volume of the apheresis plasma components was 637 ± 29 mL (450-650mL) with acceptable RBC contamination for treatment by visual inspection. All collections met the input requirements of INTERCEPT processing parameters.

After INTERCEPT treatment, the mean volume of the three plasma products was 211 ± 4 mL, and 288 ± 19 mL when two plasma products were produced. There was an average $27 \text{ mL} \pm 3 \text{ mL}$ (18 - 37mL) volume loss for each INTERCEPT process (n=234), representing approximate 4% plasma loss. The mean activity of Factor VIII was 0.9 ± 0.1 IU/mL and total proteins were 64.1 ± 3.3 g/L (n=24), meeting the local requirement of 0.7 IU/mL and 50 g/L respectively. The residual amotosalen concentration in treated plasma products (n=21) was consistently low with a mean of 0.8 ± 0.1 μ M, within the 2 μ M limit approved by the French authorities (Table 3).

Table 2: Factors in apheresis plasma before and after INTERCEPT treatment*

	Pre-treatment (n=30)	Post-treatment (n=30)	% recovery
Factor VII (IU/mL)	1.01 ± 0.2	0.8 ± 0.1	79%
Factor VIII (IU/mL)	1.23 ± 0.4	0.77 ± 0.3	64%
Factor IX (IU/mL)	1.04 ± 0.2	0.82 ± 0.2	78%
Fibrinogen (mg/mL)	3.18 ± 0.7	2.51 ± 0.7	79%
Proteins (g/L)	66 ± 3	65 ± 4	99%

*Data presented at SFTS 2009

Table 3: Quality control of INTERCEPT plasma

	Quality control of INTERCEPT-plasma (total=784 units)	Local requirement
Volume/unit n=784	288 ± 19 mL (two final products)* 211 ± 4 mL (three final products)	≥ 200 mL
Residual amotosalen (μ M) n=21	0.8 ± 0.1 (0.62 - 1.0)	< 2 μ M
Factor VIII (IU/mL) n=24	0.9 ± 0.1 (0.8 - 0.9)	≥ 0.7 IU/mL
Proteins (g/L) n=24	64.1 ± 3.3 (60.2 - 70.7)	> 50 g/L

*Two plasma units were produced due to low weight of plasma resulted from extra sampling and some production error during the process

Conclusions

- INTERCEPT Blood System for plasma has been integrated into routine production at CTSA without adding additional personnel or laboratory space.
- Apheresis plasma treated with INTERCEPT maintained proper function of plasma factors.
- Quality of INTERCEPT treated plasma was consistent and met the local requirements for plasma transfusion.