Process Validation of the INTERCEPT Blood System™ for Pathogen Inactivation of Apheresis Plasma at a Regional Center (EFS-Auvergne Loire)

Olivier Garraud, Patricia Chavarin, Céline de Putter, Françoise Boussoulade, Madeleine Vidal, Sophie Acquart

EFS Auvergne Loire, Saint- Etienne, France

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

CONTACT

Prof. Olivier Garraud MD PhD
olivier.garraud@efs.sante.fr

EFS Auvergne Loire,
25 Boulevard Pasteur,
42023 Saint- Etienne,
France
+33 4 77 81 42 55

Process Validation of the INTERCEPT Blood System for Pathogen Inactivation of Apheresis Plasma at a Regional Center (EFS-Auvergne Loire)

Olivier Garraud, Patricia Chavarin, Céline de Putter, Françoise Boussoulade, Madeleine Vidal, Sophie Acquart

EFS Auvergne Loire, Saint- Etienne, France

Background

The INTERCEPT Blood System™ for plasma is CE marked as Class III medical device for the inactivation of a wide range of pathogens in plasma (**Figure 1 and 2**). In 2006 the Agence Française de Sécurité Sanitaire des Produits de Santé (Afssaps) approved plasma treated with the INTERCEPT™ system for transfusion. To implement the INTERCEPT system in France, each center must validate the INTERCEPT process according to national regulatory requirements. EFS-Auvergne Loire collects ~5,000 apheresis plasma components for therapeutic use (split into 3 products) and transfuses approximately 15,000 plasma products annually.

Figure 2: 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.

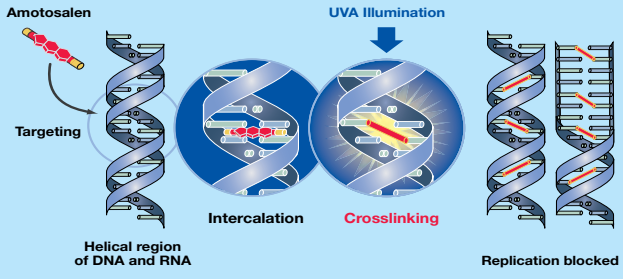
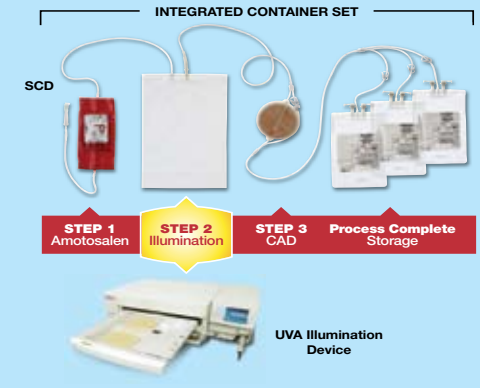


Figure 1: The INTERCEPT Blood System for Plasma

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.



Aims

The objective of this study was to validate the INTERCEPT plasma process at EFS-Auvergne Loire. The validation procedure requires that: 1) plasma collections meet the input requirements of the INTERCEPT processing parameters: 385-650 mL with <4x10^6 RBC/mL, and 2) INTERCEPT treated plasma products meet the national quality requirement for transfusion: per unit volume of ≥200 mL, mean Factor VIII activity ≥0.70 IU/mL, and residual amotosalen <2 µM.

Results

The mean volume of the apheresis plasma components before INTERCEPT treatment was 643 ±5 mL (n=36, 621-647 mL) containing 0.004 ±0.004 x10^6 RBC/mL, 0.167 ±0.0x10^3 WBC/mL and 1.0 ±0.0x10^9 platelets/mL. All collections met the input requirements of INTERCEPT processing parameters (**Table1**).

After INTERCEPT treatment, the mean volume of the three plasma products was 209 ± 5 mL (n=105, 199-221mL). There was an average loss of 5% of the plasma volume during the process (**Table 2**). The mean activity of Factor VIII was 0.87 ± 0.05 IU/mL (n=36, range 0.8-0.9 IU/mL). The residual amotosalen concentration in treated plasma products was consistently low with a mean of 0.79 ± 0.07 µM, well within the 2 µM limit approved by the Afssaps and (**Table 3**).

Table 1: Plasma Parameters of Pre-INTERCEPT Treatment

	Plasma volume (mL)	Plt count (x10^9/L)	RBC (x10^6/mL)	WBC (x10^6/L)
Average	643	1.0	0.004	0.167
SD	5	0.0	0.004	0.000
Max	647	1.0	0.020	0.167
Min	621	1.0	0.001	0.167
N	36	36	36	36

Table 2: INTERCEPT Plasma Processing

	Timing between collection and freezing (hh:mm)	Plasma volume loss during process (mL)
Average	5:28	32
SD	1:14	3
Max	7:40	39
Min	3:15	27
N	36	36

Table 3: Quality Control of INTERCEPT Plasma

	Plasma Volume/ unit (mL)	Factor VIII (IU/mL)	Residual Amotosalen (µM)
Average	209	0.87	0.79
SD	5	0.05	0.07
Max	221	0.90	0.91
Min	199*	0.80	0.03
N	105	36	36

*plasma <200ml was due to the sampling on the first day.

Methods

The production laboratory personnel at EFS Auvergne-Loire were trained on the INTERCEPT process in 3 days (4 persons). The validation of the INTERCEPT Blood System has been done during this period.

Collection:

- 36 apheresis plasma components, 12 per day, were collected In St Etienne and Clermont Ferrand using the Auto C®.
- Plasma components have been stored at ambient temperature prior to treatment.

Production:

- 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 µM) to the apheresis component, the illumination (3 J/cm^2 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 storage containers (approximately 200 mL).

Quality control:

- Plasma volume determination by weight.
- Post treatment samples randomly selected from the three containers were taken for analysis of residual amotosalen by HPLC and coagulation Factor VIII by standard assays (chronometric measure).

Conclusions

- **The implementation of INTERCEPT for plasma has been successful in EFS-Auvergne Loire and was made available within a short period of time; no difficulty has been encountered. The INTERCEPT process was reproducible.**
- **Quality of INTERCEPT treated plasma met the local requirement for plasma transfusion.**
- **INTERCEPT treated plasma products produced in EFS-Auvergne Loire are currently in routine clinical use: 1,771 units – split between the relevant blood groups – have been produced over a 3 month period to constitute the inventory; during that period of time, appropriate information about the product has been delivered to physicians; from mid-Oct. to the end of Dec. 2009, 2,256 units have been transfused.**

Presented at the XXXIst International Congress of the International Society of Blood Transfusion (I.S.B.T.)

Berlin, Germany • June 26th - July 1st, 2010