

Validation of Pooled Buffy Coat Platelet Components Suspended in a Mixture of Plasma and SSP+ Treated with INTERCEPT™ Pathogen Inactivation at Center for Transfusion Services (CTS) in Luxembourg

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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

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). The original INTERCEPT™ CE Mark was for the treatment of platelet components (PCs) suspended in a mixture of plasma and InterSol™. This label claim has been expanded to include the use of a

new commercially available platelet additive solution SSP+ (MacoPharma) (Figure 2). The input parameters for the INTERCEPT Large Volume (LV) set are: 2.5-7.0x10¹¹ platelets, 300-420 mL, 32-47% plasma, and <4x10⁶/mL RBC (Table 1). The CTS of Luxembourg produces 3,700 PCs each year, of which 2,300 PCs are prepared from whole blood donations.

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.

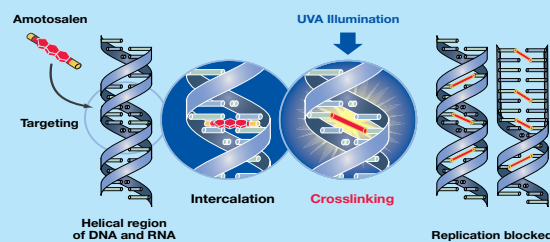
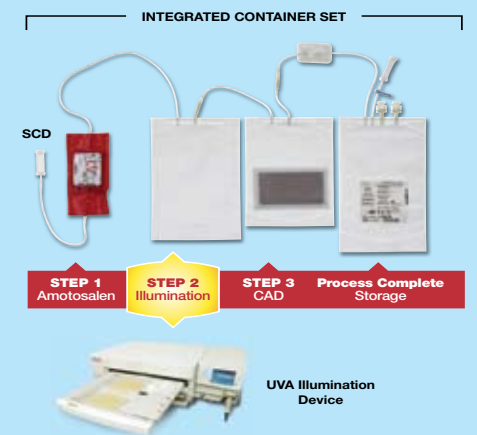


Table 1: INTERCEPT Large Volume (LV) Set PC Input Parameters

Parameters	Input requirement (LV)
Plt dose (x10 ¹¹)	2.5 -7.0
Volume (mL)	300 -420
Plasma content (%)	32 -47
InterSol or SSP+ (%)	53 -68
RBC (x10 ⁶ /mL)	< 4
WBC	Per local requirement

Figure 2: The INTERCEPT Blood System for Platelets

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



Aims

The objective of this study was to validate the INTERCEPT process using pooled buffy coat (BC) platelet components suspended in plasma/SSP+, including:

- 1) Production of BC PCs meeting the input requirements of the INTERCEPT process
- 2) Verification of in vitro parameters after INTERCEPT treatment
- 3) Demonstration of process compatibility with routine operations

Methods

BCs from whole blood donations (500 mL) were prepared using Optipure® bag UGR6495 and Optipress® II. For each PC, four ABO-matched BCs were pooled with 250 mL SSP+. After low speed centrifugation, PCs were collected by expressing the supernatant through a leuko-reduction filter and stored with shaking at 22±2°C before treatment.

A total of 30 PCs were evaluated for quality control before and after INTERCEPT treatment with the INTERCEPT LV set. Platelet counts pre- and post-INTERCEPT treatment were measured. Platelet swirling scores were compared on pre- and post-treatment units. Prior to product release, platelet count, pH, and swirling scores were also measured.

Results

Between August and October of 2009, 31 BC PCs prepared in SSP+ were evaluated for the INTERCEPT input parameters (Table 2). All met the requirements for platelet dose (3.4x10¹¹ SD 0.49), plasma (36-41%), and volume (324-360 mL). All but one (97%) BC PC passed visual inspection of RBC contamination (<4 x10⁶ RBC/mL). The PCs (n=30) were treated with INTERCEPT within 26 hours of whole blood donation. The mean contact time with the compound adsorption device (CAD) was an average of 17.4 hours.

After treatment the mean platelet content was 3.1x10¹¹ (SD 0.4), corresponds to a mean platelet processing loss of 8.8%, a level which was within the established ranges for the INTERCEPT procedure and consistent

with results from other blood centers. The mean platelet swirling score was 3 (Table 3).

After INTERCEPT treatment and 3-5 days of storage, mean platelet content (n=30) was 2.9x10¹¹ (2.1-4.0 x10¹¹) in a mean volume of 313 mL (289-330 mL). The mean pH value was 7.1 (range 6.9-7.2). The mean swirling score was 2.9 (range 2-3). These measurements indicated that INTERCEPT treated platelets were within the local requirements for transfusion (Table 3). The INTERCEPT pathogen inactivation process was validated within 3 months, and was compatible with routine CTS Luxembourg operations with some modifications required especially for the management of CAD phase to stay within the maximum of 16 hours.

Table 2: INTERCEPT platelet Input Parameters and Processing Parameters

Parameters	Input (n=31)
Platelet (x 10 ¹¹)	3.4 ± 0.49
Volume (mL)	325 - 360
% Plasma	36 - 41
RBC content	<4 x 10 ⁶ /mL*
Parameters	Processing
CAD (hrs)	17.4 ± 8.5
Total Processing time	within 26 hrs after WB donation
Platelet loss (%)	8.8%
Volume loss (mL/unit)	23 ± 4

* measured against color chart, one BC PC had >4x10⁶RBC/mL.

Table 3: INTERCEPT Platelet Functions

Parameters (n=30)	Post-INTERCEPT	Release/expiry (3-5 days storage)
Platelet (x 10 ¹¹)	3.1 ± 0.4	2.9 ± 0.5
Volume (mL)	316 ± 10	313 ± 10
pH	n.d.	7.1 ± 0.1
Swirling score	3.0 ± 0	2.9 ± 0.3

Conclusions

- All platelet components with the exception of one prepared from a pool of 4 buffy-coats in a mixture of plasma and SSP+ were within the ranges of INTERCEPT processing requirement.
- INTERCEPT process can be made compatible with the routine operation of CTS of Luxembourg with management of the CAD phase to within 6 - 16 hours.
- Platelet loss (<10%) resulting from INTERCEPT treatment was acceptable.
- In vitro platelet quality parameters met local guidelines.