Introduction of Pathogen Inactivation in a Regional Blood Center in Switzerland

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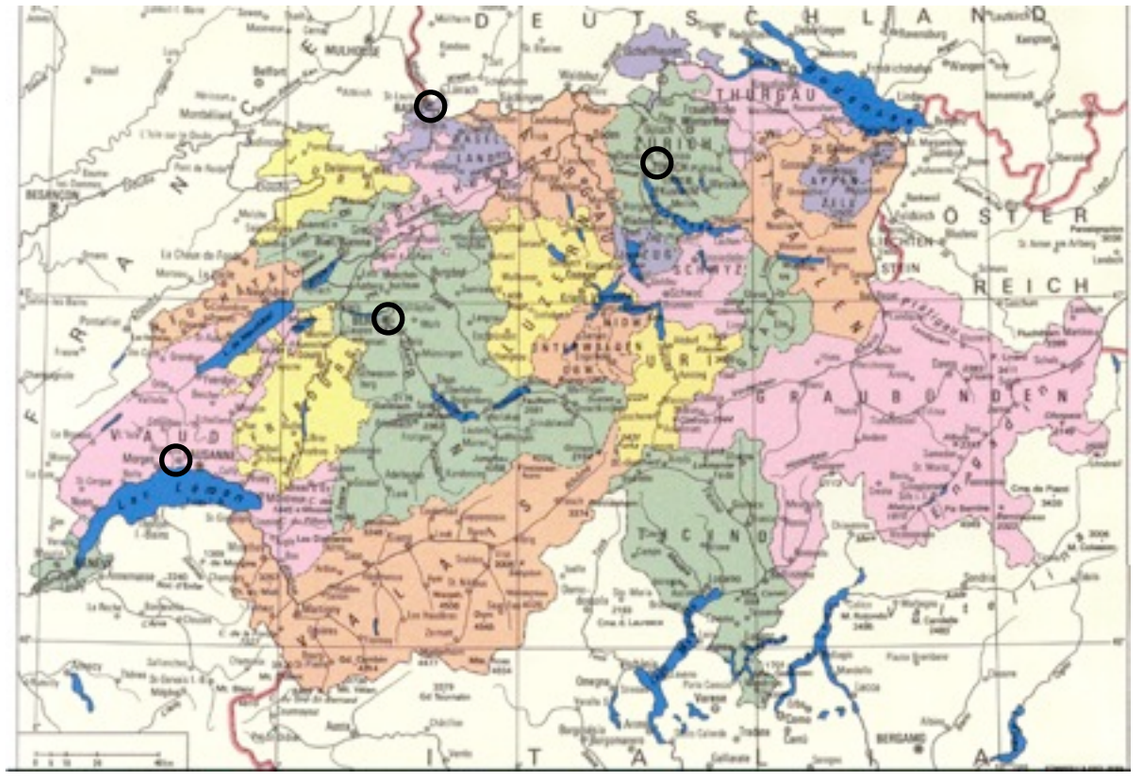
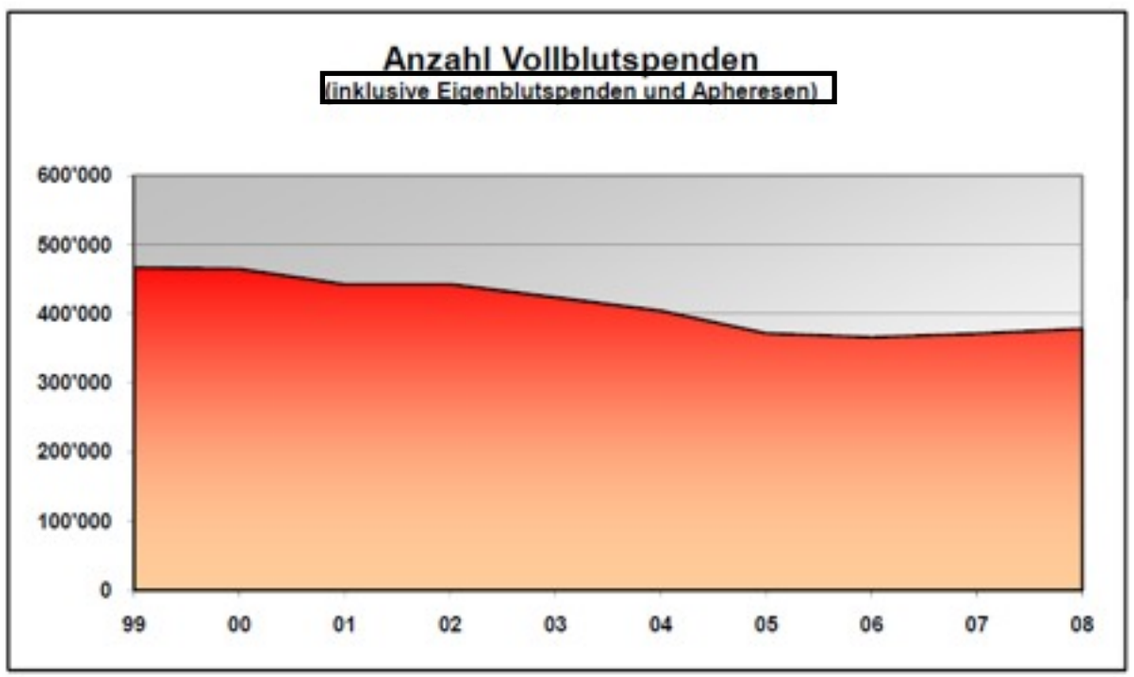
Annual production – Lausanne





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- 30’000 RBC concentrates (400’000 in Switzerland; ZH > BE > VD)
- 3’000 platelet concentrates (apheresis, 37% double doses)
- 6’000 fresh frozen plasmas
- 8’000 liters of plasma for fractionation

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Agenda

Decision Process for Implementing Pathogen Inactivation

Operational Changes in Component Laboratories
Meeting INTERCEPT processing input requirements
Optimization of buffy coat pooling process

Impetus for BC pooling

- Increase overall production of platelet concentrates: external supply between 4 and 100 PCs per year (+2’000% in 3 years) despite an increase in production (20% in 3 years)

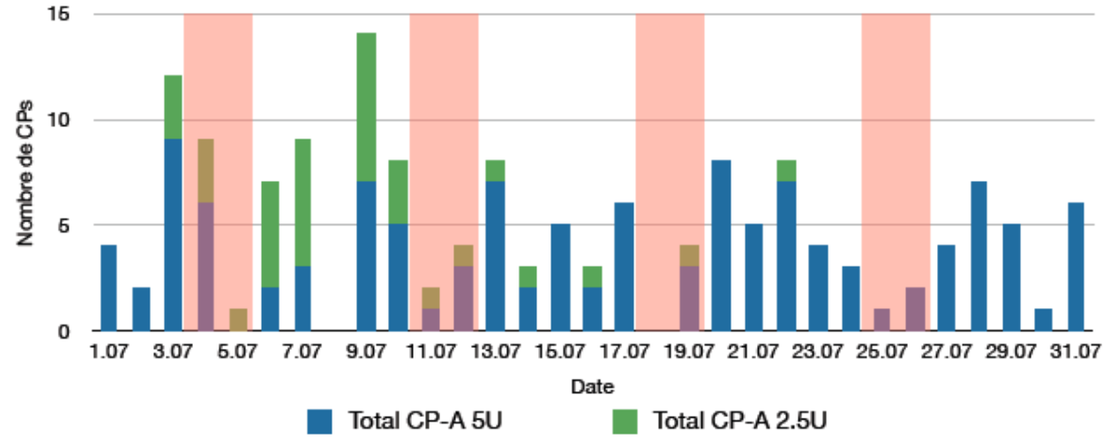
- Increase PCs availability during long weekends

- Possibility to produce PCs “on demand”

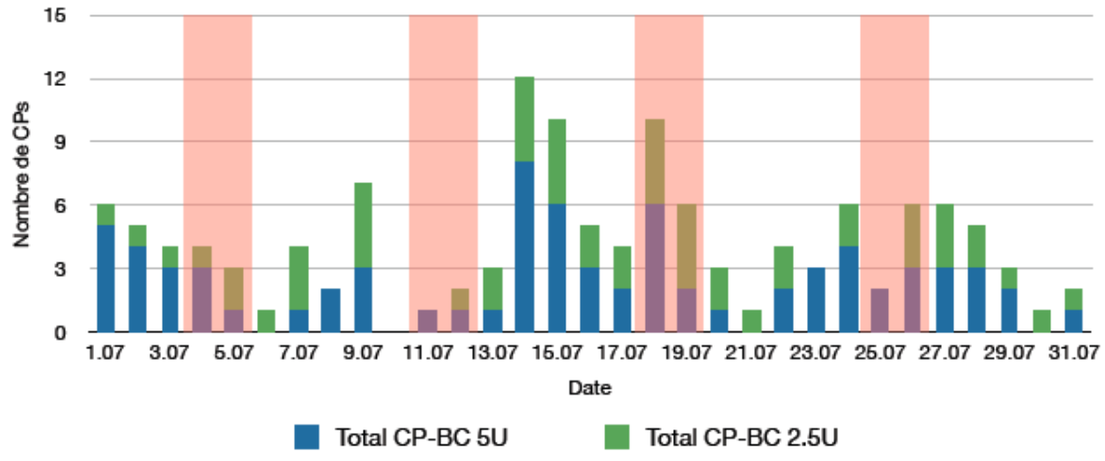
- Transition to platelet additive solution (PAS) - beneficial for transfusion reactions

Before Intercept approval

- Apheresis platelets only for:
  - Pregnant women
  - Pediatry
  - Oncology
  - Patients immunized against HLA or HPA



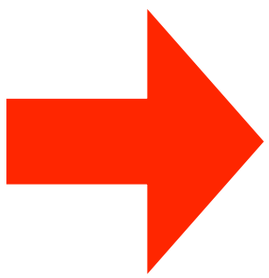
- Apheresis or Buffy Coat derived platelets for all others



Demand for each type of product is highly fluctuating, adding one level of complexity to blood bank

After Intercept approval

- PI-treated, BC-derived and apheresis platelets are equivalent products in terms of safety and efficiency.
- They can be used for any kind of patients (including pediatry, oncology...).
- We would like to introduce a policy: “fresher platelets for more critical patients”.



The production ratio apheresis / BC-derived depends only on operational and financial considerations

Previous situation (2009)- no BC-derived platelets

Platelets produced by apheresis only:
2200-2300 apheresis procedures
Platelets collected and stored in 100% plasma

30’000 whole blood donations
Filtration of whole blood
Separation of RBCs, dry BC, and plasma

Process optimized for RBC and plasma production

Close future

60% of platelets produced by apheresis
(1’500-1’600 procedures) in PAS
40 % of platelets derived from BC (in PAS,
32-47% plasma)

30’000 whole blood donations
Separation of RBCs, “plasma-rich” BC, and plasma for fractionation
filtration of CE

Process optimized for BC production

Decisions for BC pooling

- Isogroup pooling of A or O BCs
- Pooling of Rhesus negative BC, if possible
- No a priori selection of BCs (gender, PLT content...); only AINS are taken into account.
- No further testing of CMV or isohemolysins
- As much as possible, we want to be able to match the production objectives (20 BC-derived PCs per week) with on-site collections only

    ➡ pooling of 4 BCs

Transition to using INTERCEPT

- Conversion of the process for the production of BCs for pooling
- Target: plasma content between 32 and 47% in the pooled platelet concentrate
- Modification of the Optipress backplate to increase plasma content
- Pooling of 4 BC + 280 mL of Intersol
- Optimization of soft centrifugation conditions
- Optimization of platelet extraction

Process optimization and validation

- input requirements of INTERCEPT (apheresis and BC platelets)

	Small Volume	Large Volume		Dual Storage
Suspension Medium*	**PAS**	**PAS**	**Plasma**	**PAS**
Plt Count	$2.5\text{-}6.0\text{x}10^{11}$	$2.5\text{-}7.0\text{x}10^{11}$	$2.5\text{-}7.0\text{x}10^{11}$	$2.5\text{-}7.0\text{x}10^{11}$
Volume	255-325 mL	300-420 mL	255-390 mL	300-420 mL
Plasma	32 – 47%	32 – 47%	100%	32 – 47%
RBC	$<4\text{x}10^{6}$/mL	$<4\text{x}10^{6}$/mL	$<4\text{x}10^{6}$/mL	$<4\text{x}10^{6}$/mL
CAD time	4–16 hrs	6-16 hrs	16-24 hrs	6-16 hrs
Integrated Storage Containers	1	1	1	2
Approved Storage	7 days	7 days	5 days	7 days

- Treated components must meet local quality guidelines
  - > 2.4 x 1011 platelets per unit
  - pH above 6.4
  - shelf-life of 5 days, 7-day shelf life permitted

BC adjustments

- Adjust plasma content per BC to PI requirement for 4 and 5 BCs
- Verification of RBC concentrates
- Verification of plasma units

Two main transitions in the whole blood process

Filtration of whole blood
Separation of RBCs, dry BC, and plasma

Separation of RBCs, dry BC, and plasma
Filtration of CE

Filtration of whole blood
Separation of RBCs, “plasma-rich” BC, and plasma

RBC	Plasma
Vol = 268.8±15.7 mL Hb = 52.1 ± 5.4 g/bag	Vol = 269.0 ± 19.9 mL
Vol = 259.7±12.3 mL Hb = 52.0 ± 4.2 g/bag	Vol = 279.0 ± 12.2 mL
Vol = 257.9±16.5 mL Hb = 49.9 ± 4.9 g/bag	Vol = 249.8 ± 16.9 mL

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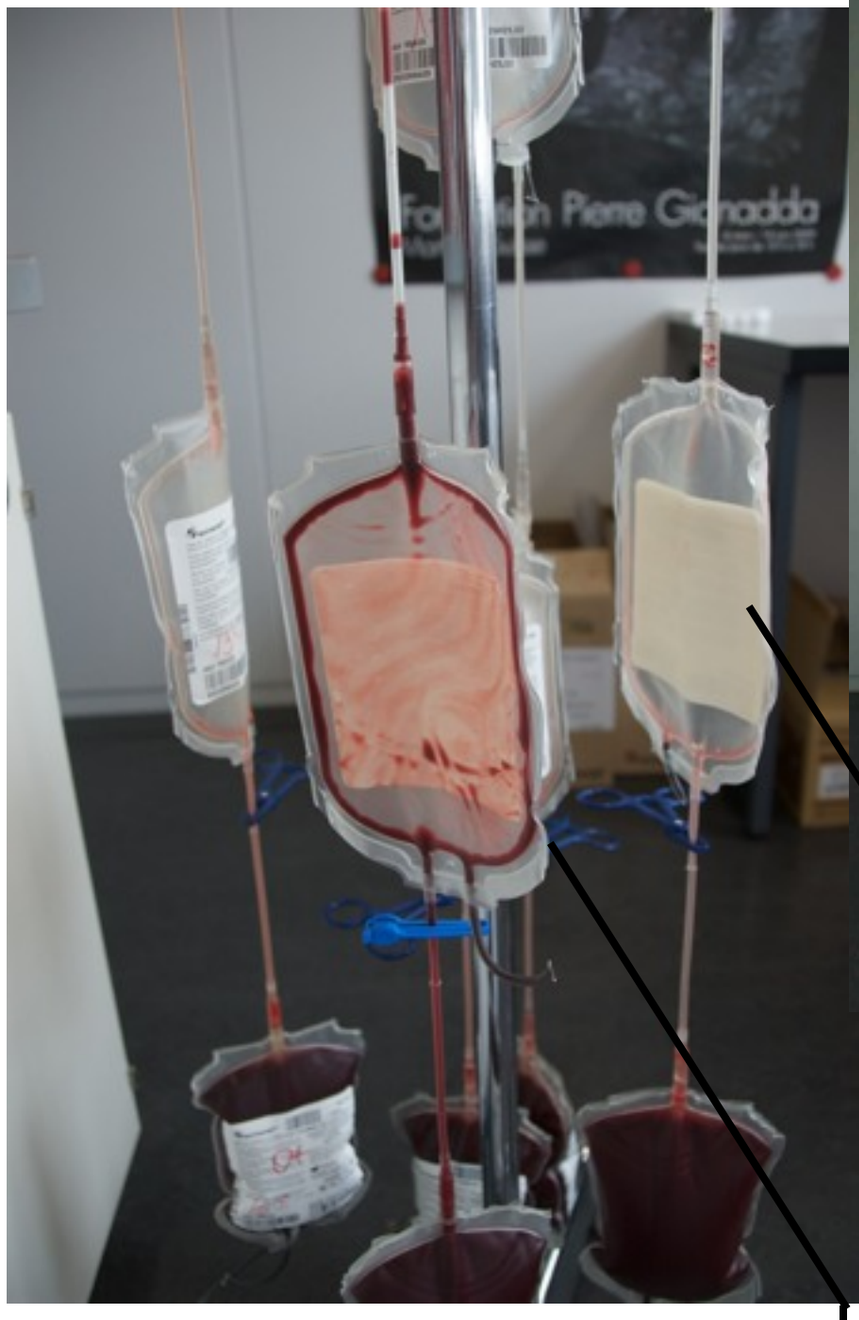
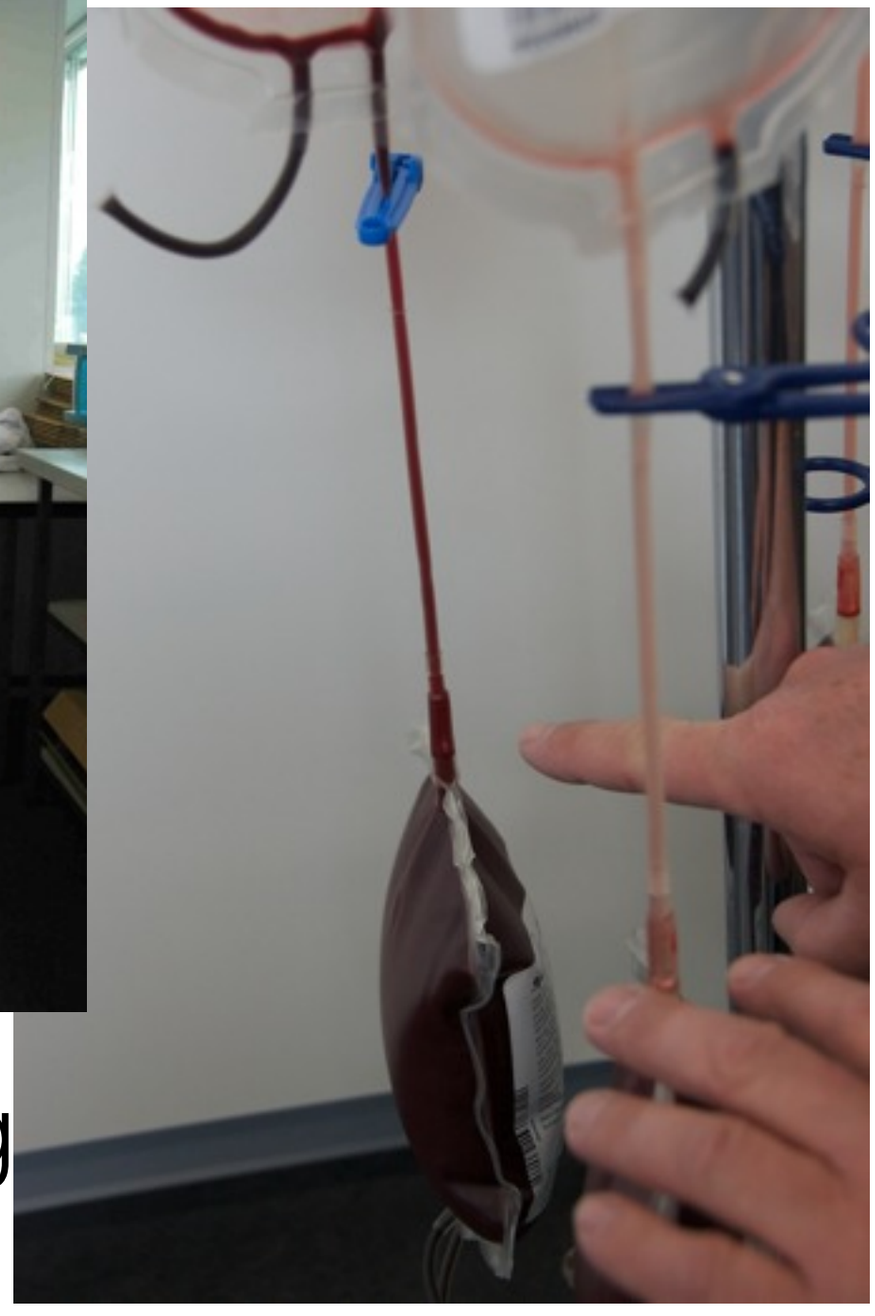
Process optimization: train rinsing with PAS

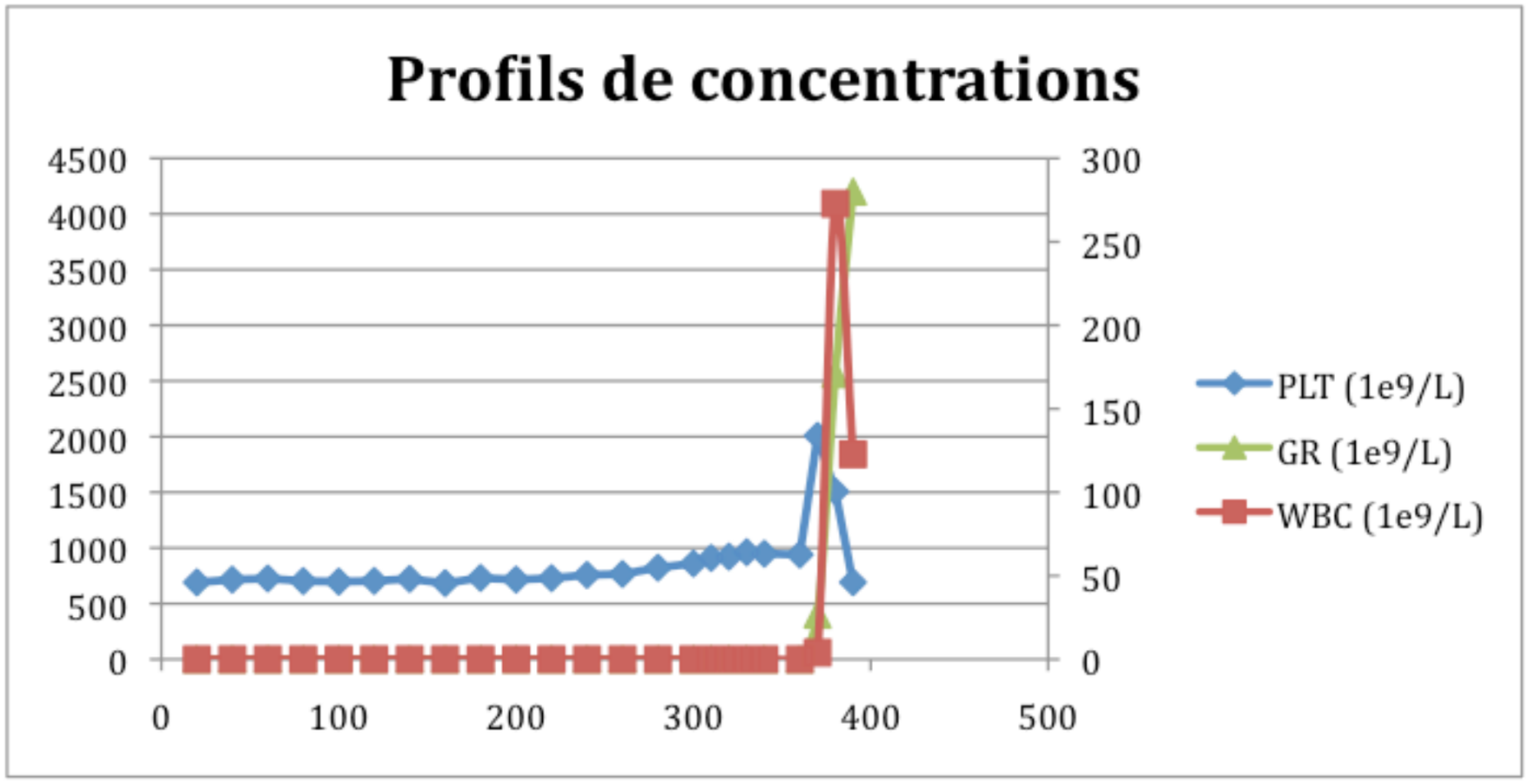




Correct rinsing

Incorrect rinsing

Characteristic of the interface Platelets/Red Cell



The interface is very rich in platelets

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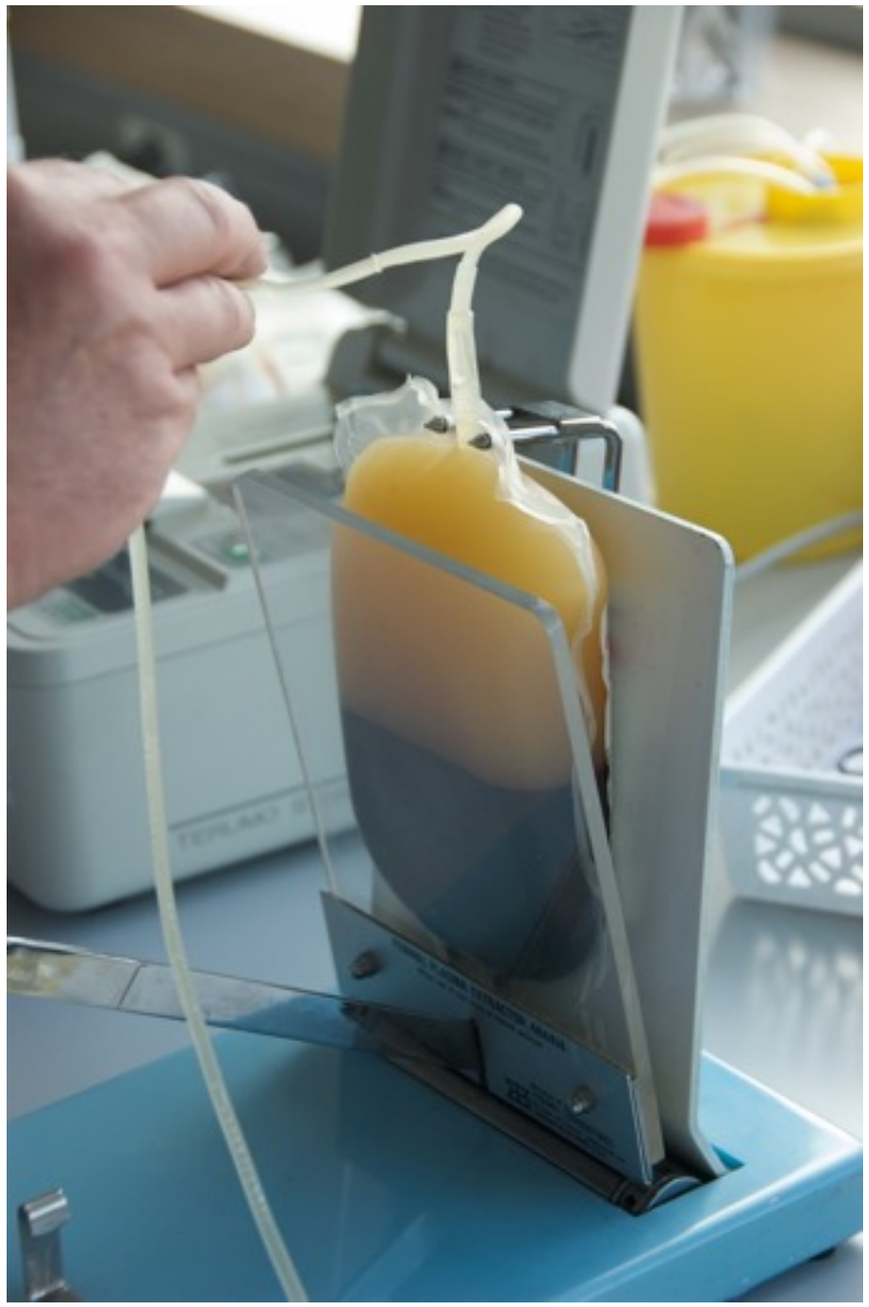
Importance of soft centrifugation optimization



Clear cut between PRP and Red Cell layers
Most diffuse possible Platelet layer above Red Cell

Platelet expression into a transfer bag

Push the platelets as far as possible into the transfer bag

BC and PLT characteristics prior to PI (4 BC)

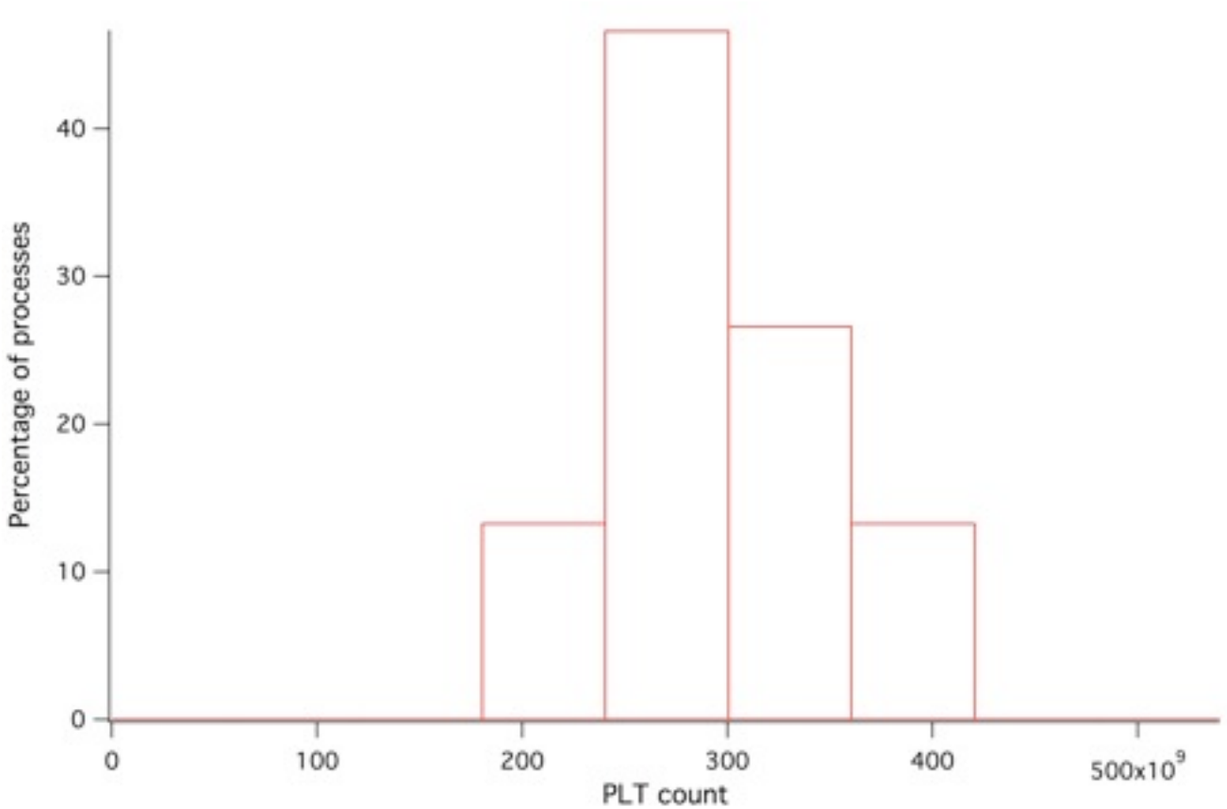
- BC Volume = 68.0 ± 2.5 mL (41.0 ± 2.8 mL of plasma)
- BC Htc = 0.39 ± 0.04
- PLT vol = 340.5 ± 8.3 mL
- PLT num = 3.02 ± 0.53 10^{11} PLT / bag

BC and PLT characteristics prior to PI (5 BC)

- BC Volume = 63.2 ± 1.7 mL (39.0 ± 1.5 mL of plasma, 41.0±1.0% plasma)
- BC Htc = 0.38 ± 0.02
- PLT vol = 338.5 ± 29.0 mL
- PLT num = 4.0 ± 0.4 10^{11} PLT / bag

Actual inactivation data – design qualification

- For pools of 4 Buffy coats
- Average PLT is 2.83±0.55e11 PLT per process (0.71e11 PLT per BC equivalent)
- PLT loss during production is 0.20±0.08e11 PLT per process



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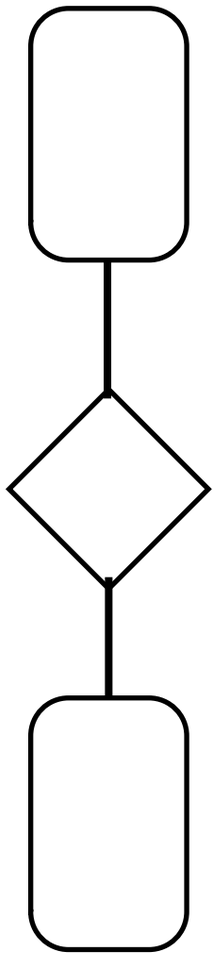
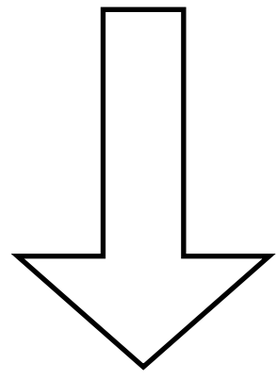
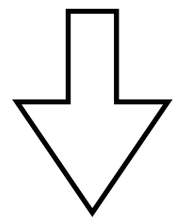
For 4 BCs, need to exclude outliers



BC-derived, non filtered PC > 2.85 10^{11} PLT per bag



100% of PCs > 2.5 10^{11} PLT per bag prior PI



100% of PCs > 2.4 10^{11} PLT per bag after PI

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Take-home messages

- Design qualification is required to produce BC-derived PC in the target yield range
- We need to consider PLT variability for individual BC
- Transition to PAS results in a loss of 20-25 mL plasma per whole blood separation
- Importance of technical partnership with supplier to successfully conduct process adjustments

What about apheresis?

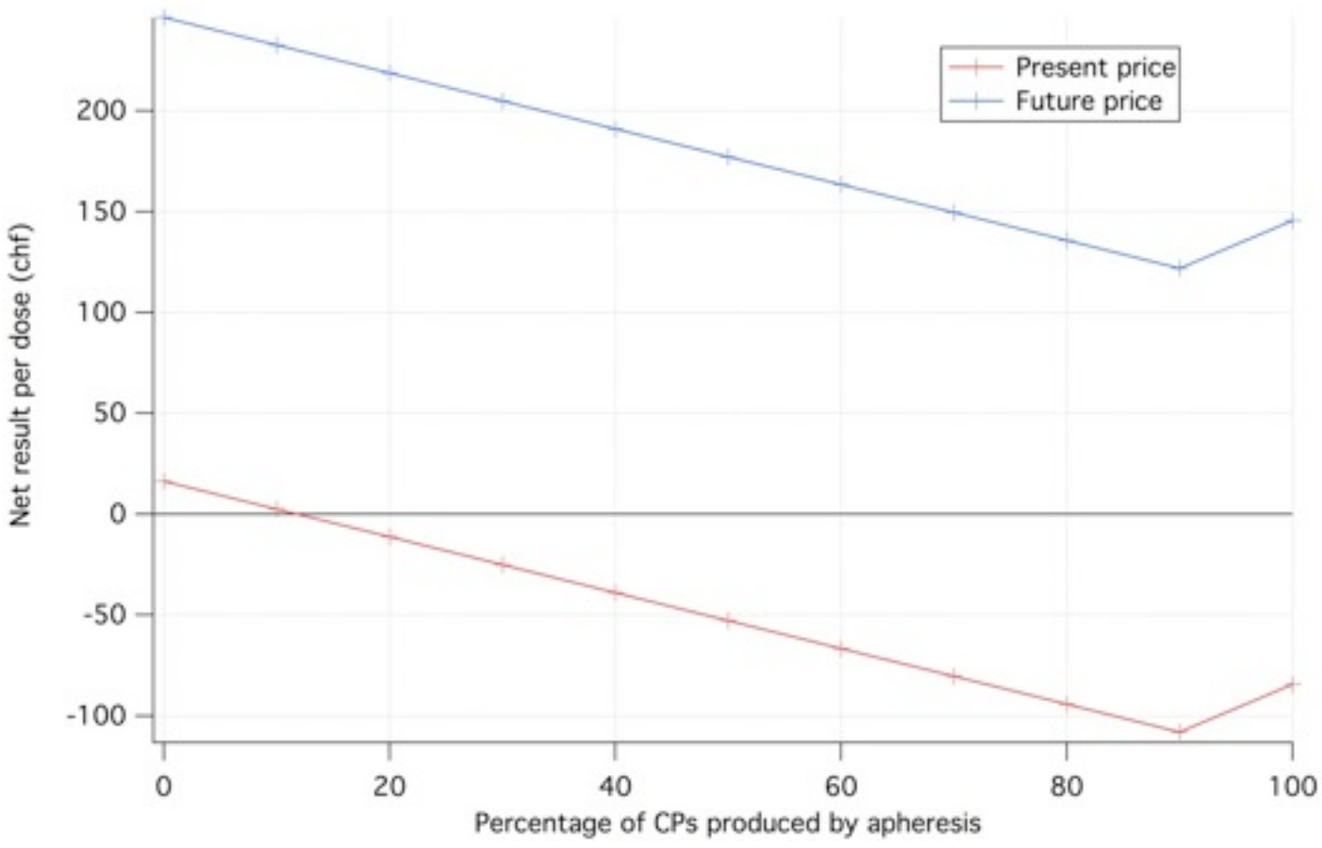
- Need to update our Trima to software version 5.2 for automated PAS addition.

- Expected minor increase in PLT dose (less than 10% to match Intercept specifications).

- Anticipated no change in collection duration.

- Additional plasma collection resulting from conversion to PAS.

Financial analysis



Takes into account:

- plastic and consumable costs
- loss of whole-blood plasma
- gain of plasma from apheresis

Margin to cover investments (illuminators, SCD...) and personnel costs.

Our near-term planning

- May-June 2010: process adjustment.
- June 2010: training staff.
- July-August 2010: consolidation of data and preparation of the validation document (SwissMedic).
- October 2010: production in routine.

We believe that by introducing INTERCEPT in our center, we have a safeguard against not only bacteria but also emerging pathogens.

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Thank You