Validation plan of the Intercept process for pathogen inactivation in plasma units in Switzerland

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1. Introduction

The INTERCEPT Blood System for Plasma is a medical device that is intended for the preparation of pathogen-inactivated plasma. The INTERCEPT Blood System for Plasma received CE Mark registration in 2006. This allows market distribution of the devices broadly in Europe. The system has been implemented in 20 sites and 8 countries. To date, more than 5'000 INTERCEPT units have been transfused to patients in the course of Phase III clinical studies and more than 55'000 plasma transfusions have been monitored by an active hemovigilance program.

The goal of this document is to provide a general template of the validation plan for the Intercept-plasma process, to be used by each blood center to elaborate its own validation plan.

For successful implementation of the INTERCEPT Blood System in a blood center, there are two aspects in the process validation. First, the plasma components before INTERCEPT treatment need to be verified to meet the guardband requirements. Second, the plasma components after INTERCEPT treatment must meet the local QC requirements.

The scope of this validation is limited to the Intercept process itself; the production of plasma compliant with the Intercept guardbands (see below), the traceability and IT aspects of the Intercept implementation, or regular blood bank operations not specific to Intercept (e.g. tubing seal, sterile connections…) shall be validated separately according to local quality insurance systems.

2. Intercept guardbands

Plasma components (either collected by plasma aphaeresis – *source plasma*-, collected during multi-component apheresis -*concurrent plasma*- or processed from whole-blood -*recovery plasma*-) must meet the Intercept specifications before the Intercept treatment.

	Plasma set
Volume	385-650 mL
Contaminating RBC	$\leq 4.10^6$ /mL
Contaminating leukocytes	$\leq 1.10^6$ per bag

Table 1. Intercept Guardbands.

3. Prerequisites

Prior to starting the validation plan, Cerus Customer Services or a trained contractor will be on site to install and calibrate the INTERCEPT Illuminator. A certificate of service documenting proper calibration and functionality of the INTERCEPT Illuminator will be issued to the blood center.

The blood bank personnel will receive a hands-on training on the INTERCEPT process by a skilled Cerus technician or a trained contractor. If requested, a training binder can be provided to the blood center.

4. Pre-validation phase

The first part in the validation plan is to verify that plasma components prepared for pathogen inactivation meet the guardband requirements as specified in Table 1 with respect to volume, RBC and leukocyte contamination. Additionally, it is required that plasma units meet the Swiss specifications in terms of contaminating platelets. Lastly, baseline levels of Factor VIII and Fibrinogen activities need to be established.

Characteristic	Value	Comment
Number of units (units as they would enter the Intercept process)	12	The statistics of the ABO groups must be representative of the plasma blood bank distribution statistics (a maximum of 4 group O units should be included)
Volume	385-650 mL	100% of units
Contaminating RBC	$\leq 4.10^6$ /mL	100% of units
Contaminating Leukocytes	$\leq 1.10^6$/bag	100% of units
Contaminating platelets	$< 50.10^6$/mL	100% of units
Factor VIII	≥ 0.5 UI/mL	100% of units, half units should be sampled within 8 hours post collection, half units should be sampled 15-18 hours post-collection.[1,2]
Fibrinogen	None specified	Half units should be sampled within 8 hours post collection, half units should be sampled 15-18 hours post-collection.[1,2]

Table 2. Requirements for the pre-validation phase.

Both the pre-validation and the validation phases can be carried out with different plasma sources. All plasma units used should be of the same type for the pre-validation and validation phase:

[1] In case the pre-validation is carried out with thawed plasma, the sampling of Factor VIII and Fibrinogen should be carried out immediatly after thawing. In this case, both time from collection to thawing, and from thawing to sampling, should be reported.

[2]

- Source plasma: plasma units collected by plasmapheresis according to the T-CH collection specifications (Chapter 17C. Collection modalities). Given the plasma components meet the T-CH specifications (Chapter 18C. Specifications: plasma) after sampling, they can enter the routine FFP supply chain.

- Concurrent plasma: single-donor plasma units collected during multi-component apheresis according to the T-CH collection specifications (Chapter 17C. Collection modalities). Given the plasma components meet the T-CH specifications (Chapter 18C. Specifications: plasma) after sampling, they can enter the routine FFP supply chain.

- Recovery plasma: ABO-matched pools of 2-6 whole blood-derived plasma. In this case, the whole blood processing should be thoroughly described (duration and temperature control of whole blood hold before processing, time from collection to sampling of Factor VIII and Fibrinogen). In case the specifications of this product have not been published yet by the T-CH at the time of validation, the pooling and conditioning of plasma units should be described in details. The plasma components should be disposed off and cannot enter the current FFP supply chain.

- Thawed plasma: any plasma units of the above-mentioned type that have previously been frozen according to the prescription of the T-CH, and thawed for the purpose of the validation. The thawing process and time to testing should be described in details. The plasma components should be disposed off and cannot enter the current FFP supply chain.

As the demonstration of proper implementation of Intercept-plasma does not depend on the source of plasma used, the pre-validation and validation phases must be carried out with one source of plasma (the same for the pre-validation and the validation phases). It is the responsibility of the blood bank to validate the use of other sources of plasma (i.e. that other plasma sources comply to Intercept guardbands) according to standard internal procedures.

The measurement of Factor VIII is not part of Intercept guardbands, but will be used to estimate the retention of Factor VIII throughout the Intercept process. Because Factor VIII activity is dependent on blood groups, it is requested that the statistics of the blood groups used for the pre-validation be the same as the distribution statistics of FFP units of the local blood bank. A maximum of 4 group O units should be included in the pre-validation phase.

Because Fibrinogen has been shown to be altered by the Intercept process, it is requested to measure baseline levels of Fibrinogen by a standard, approved activity-based technique (such as a Clauss assay, for example). In order to establish the reference ranges for Fibrinogen concentration in the framework of plasma preparation for Intercept treatment, it is requested that half units be sampled within 8 hours post-collection, and half units be sampled within 15-18 hours post-collection. This data will be used to establish reference values for Fibrinogen (see below, paragraph 6).

Once it has been demonstrated that pre-validation plasma units meet the specifications outlined in Table 2, the validation phase of the Intercept treatment can be carried out.

5. Intercept treatment

The INTERCEPT process is a 4-step process. In step 1, the plasma unit is connected via a sterile connection device to an integral processing set and the entire plasma content is passed through a container of amotosalen HCl into an illumination container. In step 2, the plasma amotosalen mixture is illuminated with a 3 J/cm^2 UVA treatment on an INTERCEPT Illuminator. In step 3, the illuminated plasma mixture is passed through a flow compound adsorption device (CAD) by gravity to lower the levels of residual amotosalen and free photoproducts. In step 4, the treated plasma is transferred to and evenly distributed between 2 to 3 plastic containers for storage. The plasma units are then quick-frozen and stored frozen until use. A SOP template for the INTERCEPT Plasma process is attached as companion document.

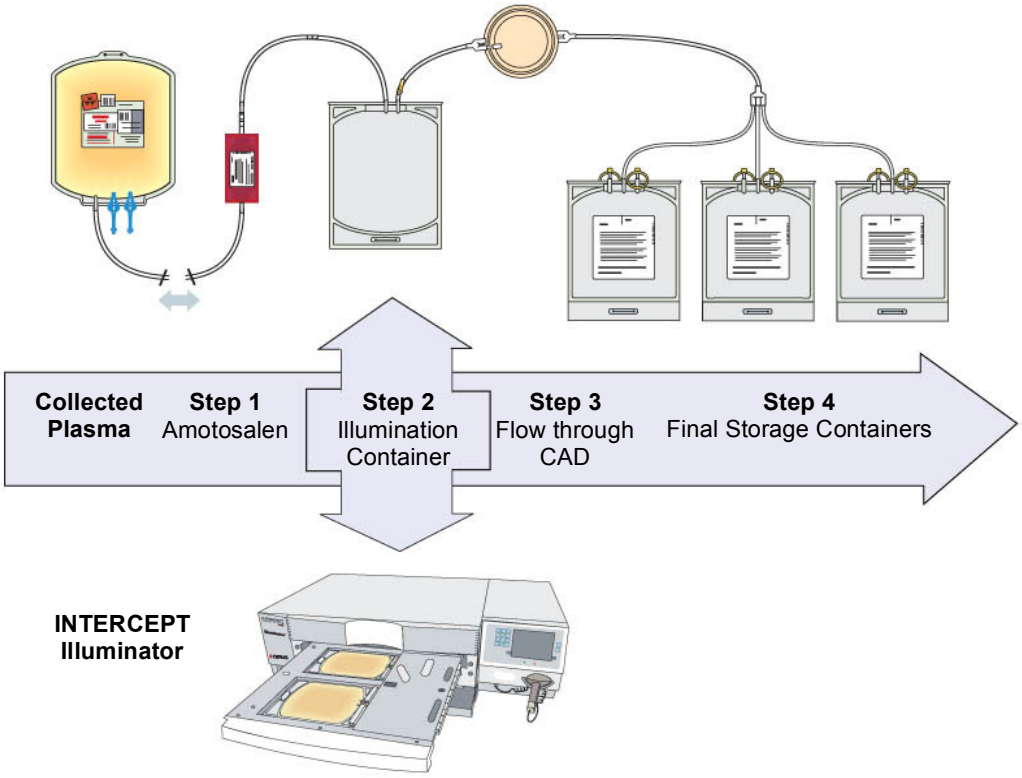


Figure 1. Scheme of the Intercept process for plasma.

6. Validation phase

Once it has been confirmed that the 12 pre-validation units meet the specifications requirements detailed in Table 2, the validation of the Intercept process for plasma can be performed, according to standard operating procedures (a template of SOPs is provided for information in the companion document).

The goal of the validation phase is to demonstrate that the Intercept process is correctly implemented. To do so, 12 plasma units will be processed with the Intercept

treatment, as described in paragraph 5 and according to SOP provided in the companion document.

Characteristic	Value	Commentary
Number of units (units as they would enter the Intercept process)	12	The statistics of the ABO groups must be representative of the plasma blood bank distribution statistics (a maximum of 4 group O units should be included)
Before Intercept treatment		
Volume	385-650 mL	100% of units
Contaminating RBC	$\leq 4.10^6$ /mL	100% of units
Contaminating leukocytes	$\leq 1.10^6$/unit	100% of units
Contaminating platelets	$< 50.10^6$/mL	100% of units
Factor VIII	≥ 0.5 UI/mL	Used for the calculation of the retention
Fibrinogen	none	Used for establishment of a reference range and calculation of the retention
After Intercept treatment		
Volume of final units	200±20 mL	100% of units
Factor VIII	≥ 0.5 UI/mL	100% of units
Residual Amotosalen[3]	< 2 µM	100% of units
Fibrinogen	None	Used for calculation of the retention.

Table 3. Characteristics of validation plasmas.

Plasma components used for the validation phase should be of the same type as those used for the pre-validation phase (source, concurrent, recovery or thawed plasma). In order to properly validate the authorized limits of the Intercept process, at least half the plasma units should be processed by the Intercept process 15-18 hours post-collection, and frozen within 20 hours.

Additionally, the CAD time (time to pass the whole treated plasma unit through the resin to deplete residual Amotosalen) should be documented for each process.

In order to properly assess the effect of the Intercept treatment on Factor VIII and Fibrinogen activities, retention of factor activity (i.e. difference between activities measured before and after the treatment divided by the value before the treatment) should be calculated. It is expected that retention values will be above 70%.

As there is no normative value for Fibrinogen, values measured during the pre-validation phase and before Intercept treatment during the validation phase will be grouped into two sets of values to establish reference ranges:

- Group A: plasma sampled within 8 hours post-collection before the Intercept treatment.

[3] Amotosalen residual levels should be measured in a Cerus-approved laboratory and documented as analysis certificates.

- Group B: plasma sampled at 15-18 hours post-collection before the Intercept treatment.

For each group, reference range for Fibrinogen activity (as expressed in mg/dL) will be calculated in the following way: if μ is the mean Fibrinogen activity of the group and σ is the standard deviation of Fibrinogen activity within the group, the reference range is defined as μ±3σ (so that given Fibrinogen activities follow a normal distribution, 99.7% of all plasmas fall in this reference range).

Beyond retention of Fibrinogen activity (percentage of Fibrinogen activity maintained during the Intercept treatment), an important feature of the validation will be to demonstrate that Fibrinogen activities after the Intercept treatment fall within the normal reference ranges of groups A and B.

Lastly, in order to assess the quality of the final product (plasma bag treated with the Intercept process, frozen according to the T-CH specifications), the 12 plasma units used in the validation phase must be thawed, and Factor VIII and Fibrinogen activities must be assessed.

After Intercept treatment, freezing and thawing of plasma bags		
Factor VIII	≥ 0.5 UI/mL	100% of units
Fibrinogen	None	Used for assessment of Fibrinogen in final units.

Table 4. Factor VIII and Fibrinogen requirements after thawing of final products.

Plasma units treated during the Intercept validation must not be distributed.

7. Sample collection for coagulation factor analysis

This validation plan requires to measure Fibrinogen and Factor VIII activity prior and after the Intercept treatment. Factor VIII is a particularly labile coagulation factor. Pre-analytical handling of samples is thus of paramount importance in evaluating the effect of the Intercept treatment on coagulation factors. There are two aspects that need to be taken into account:

- The measurement of Factor VIII and fibrinogen must reflect the effect of the Intercept treatment alone independently of other biases.
- In order to be able to compare activity values from site to site, the sampling of plasmas for coagulation factor analysis must be standardized as much as possible.

7.1. Sample collection

Samples should be collected just prior the Intercept treatment (baseline samples) and just after the completion of the treatment (post-CAD samples).

If pooled or previously frozen plasma is used, the plasma should be mixed thoroughly before sampling. Unmixed plasma from a tubing line is not appropriate for coagulation factor measurement.

Both baseline and post-CAD samples should be of equal volume, so that they undergo the same freezing process, which is known to affect coagulation factor activity.

During Intercept treatment, baseline samples should be kept at the same temperature as the plasma bag undergoing the treatment, so that differences in coagulation factor activities stem primarily from the Intercept treatment itself and not from different sample processing.

7.2. Tubes for sample collection

The number of tubes taken must be adapted to the logistics of the lab that will perform the coagulation factor analysis; it is generally recommended to take at least two different tubes for each sample (at least one back-up tube should be kept).

It is recommended to use 2 mL polypropylene screw-top tubes (with O ring), which are adapted to cold storage and thawing in a water bath. Tubes should be filled with 1.0-1.5 mL of plasma, so that the volume of air remains minimal above the solution, while allowing for volume expansion during freezing.

7.3. Sample freezing and storage

Both baseline and post-CAD sample should be frozen together, as soon as possible after completion of the Intercept treatment. Tubes should be frozen in a sample rack (the use of sample boxes can slow down the freezing process). Samples should be frozen down to the lowest temperature available (ideally ≤ -65°C) in a freezer that is not frost-free (defrosting procedures can result in temporary thawing of plasma samples).

7.4. Sample analysis

Samples should be thawed in a water bath at 37°C just to the liquid state, gently mixed manually, and immediately processed for analysis.

Paired samples (baseline and post-CAD) should be processed together, one after the other to limit assay variability between samples of the same process.

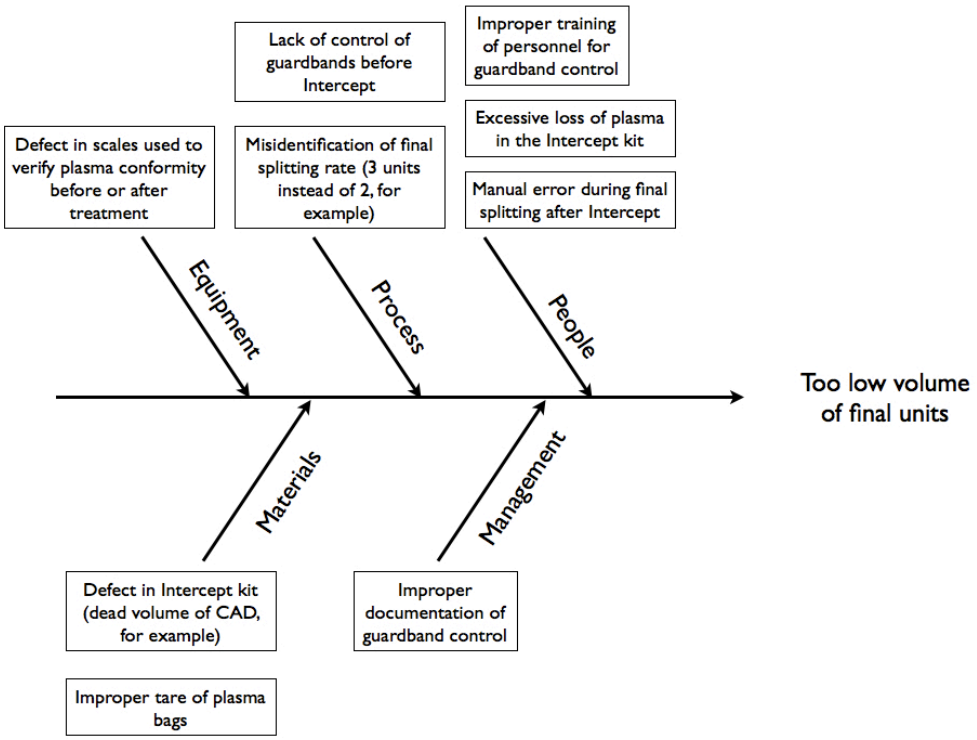
Coagulation factor analysis should be completed within two hours after thawing of samples.

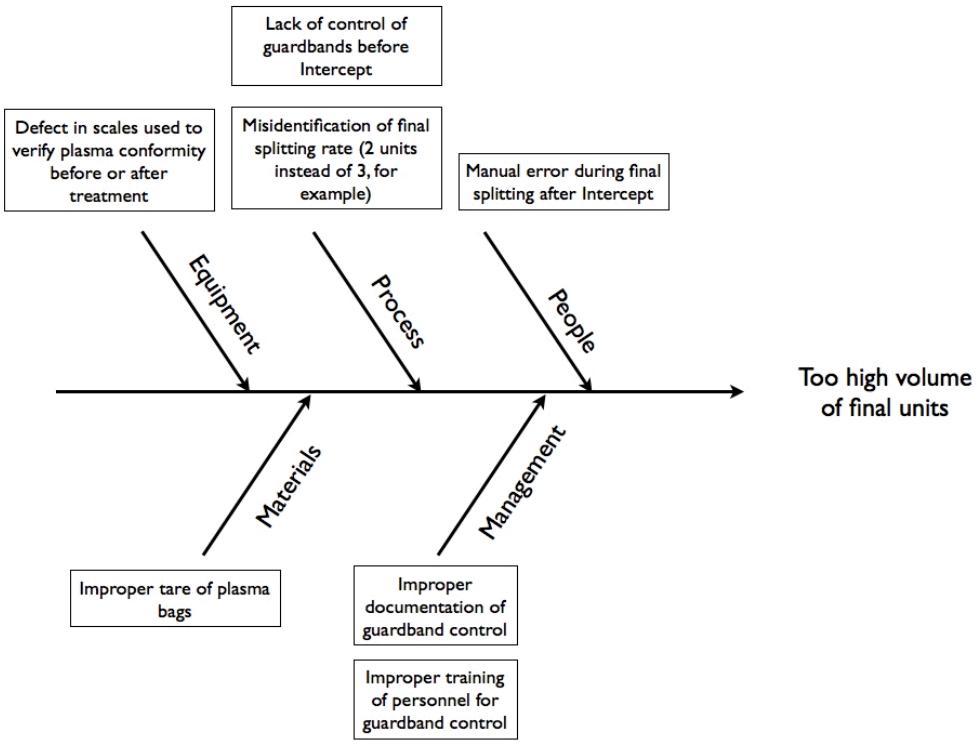
7.5. Results reporting

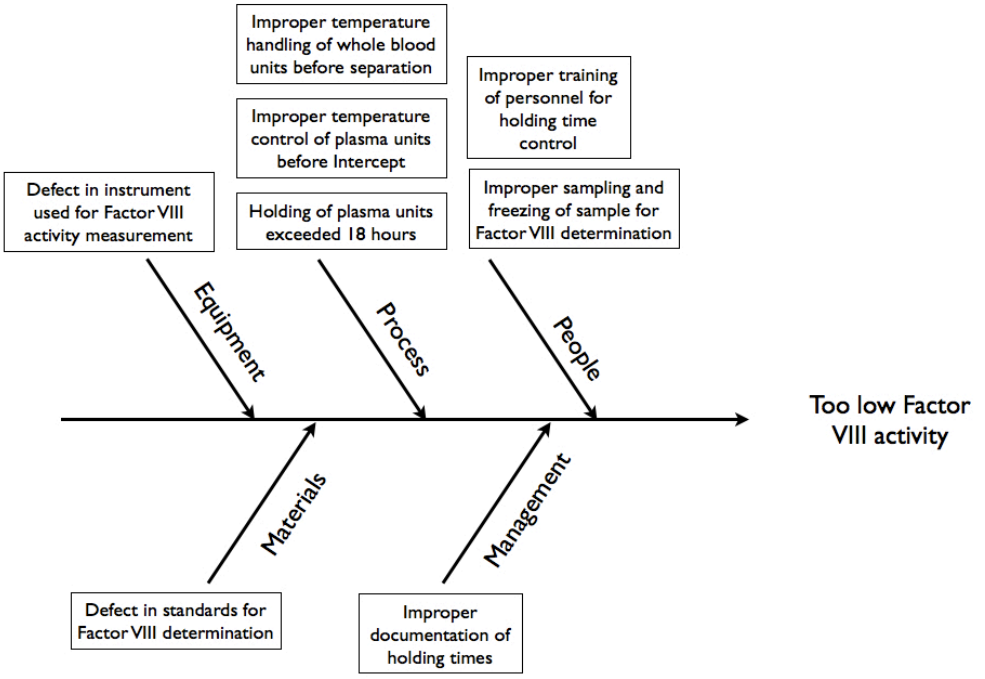
For both fibrinogen and factor VIII, absolute values (baseline and post-CAD) should be reported, as well as retention of Fibrinogen and Factor VIII activity (percent activity of coagulation factor compared to the baseline value).

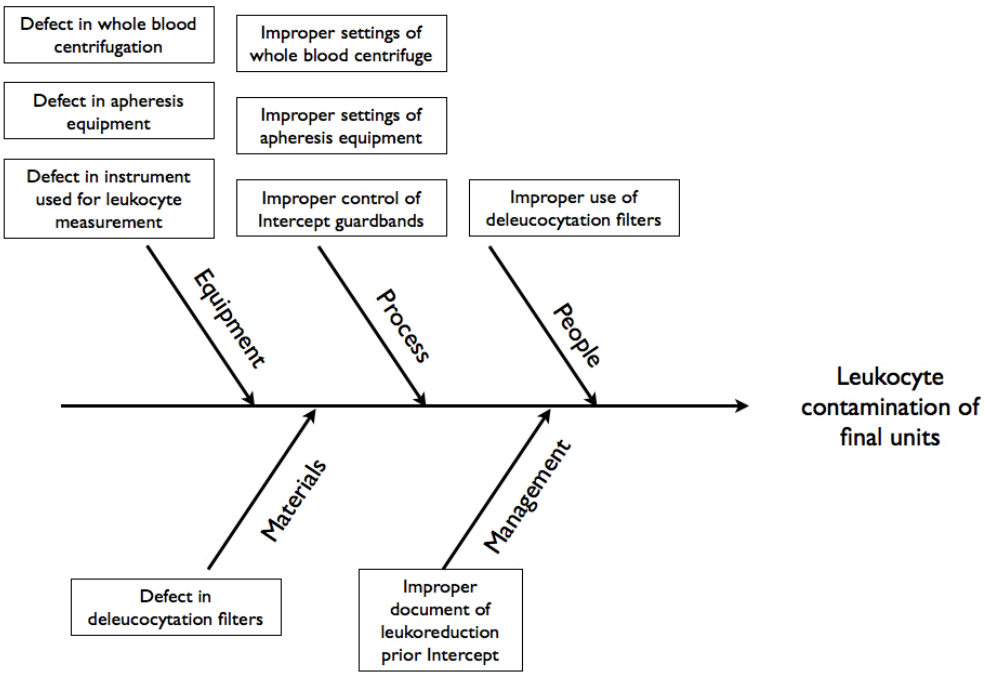
8. Risk analysis

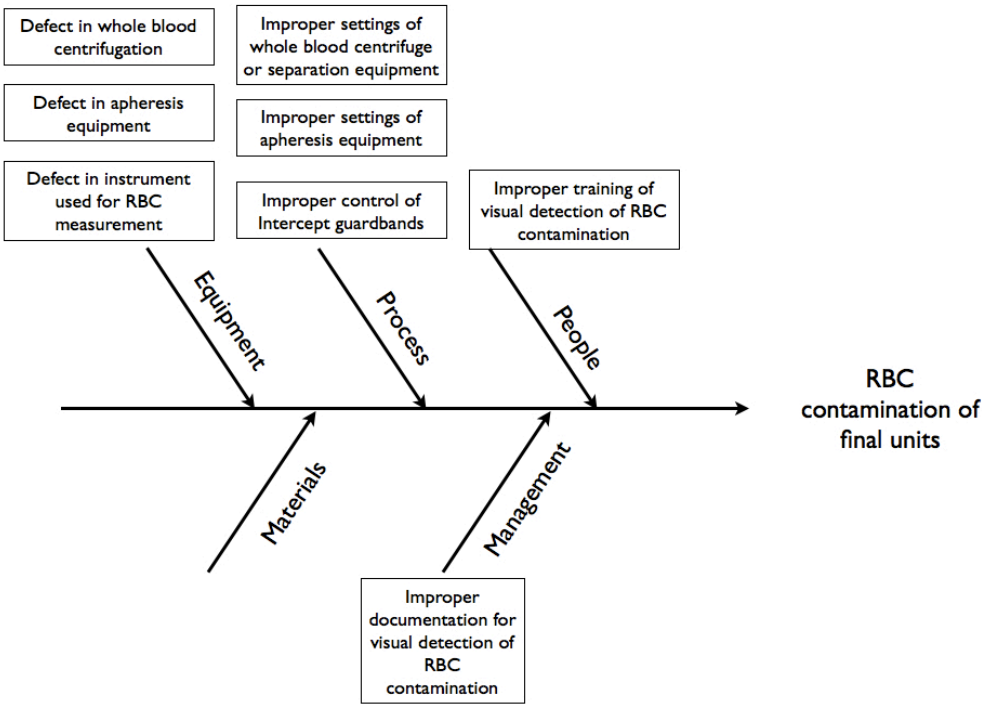
The goal of this very general risk analysis is to identify the potential problems and difficulties that can arise during the validation of Intercept-plasma, and some of their potential causes. It should by no mean exempt end-users to perform their own risk analysis. In order to simplify error tracking, Fishbone diagrams are provided for main potential problems.

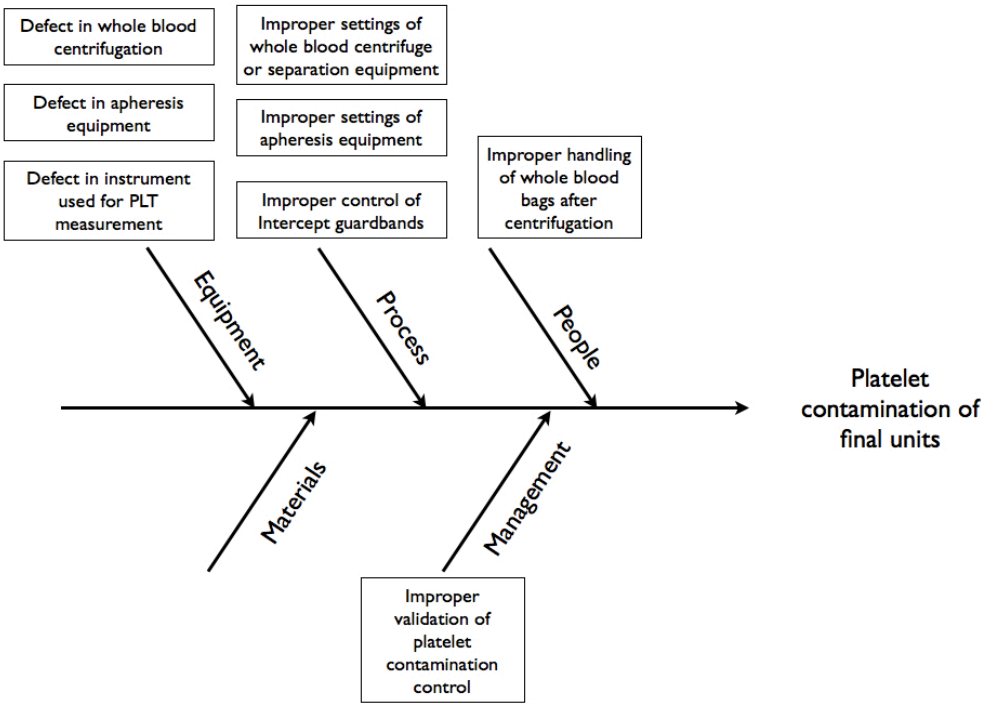

Lack of control of guardbands before Intercept
Improper training of personnel for guardband control
Excessive loss of plasma in the Intercept kit
Defect in scales used to verify plasma conformity before or after treatment
Misidentification of final splitting rate (3 units instead of 2, for example)
Manual error during final splitting after Intercept
Equipment
Process
People
Too low volume of final units
Materials
Management
Defect in Intercept kit (dead volume of CAD, for example)
Improper documentation of guardband control
Improper tare of plasma bags


Lack of control of guardbands before Intercept
Defect in scales used to verify plasma conformity before or after treatment
Misidentification of final splitting rate (2 units instead of 3, for example)
Manual error during final splitting after Intercept
Equipment
Process
People
Too high volume of final units
Materials
Management
Improper tare of plasma bags
Improper documentation of guardband control
Improper training of personnel for guardband control


Improper temperature handling of whole blood units before separation
Improper training of personnel for holding time control
Improper temperature control of plasma units before Intercept
Defect in instrument used for Factor VIII activity measurement
Holding of plasma units exceeded 18 hours
Improper sampling and freezing of sample for Factor VIII determination
Equipment
Process
People
Too low Factor VIII activity
Materials
Management
Defect in standards for Factor VIII determination
Improper documentation of holding times


Defect in whole blood centrifugation
Improper settings of whole blood centrifuge
Defect in apheresis equipment
Improper settings of apheresis equipment
Defect in instrument used for leukocyte measurement
Improper control of Intercept guardbands
Improper use of deleucocytation filters
Equipment
Process
People
Leukocyte contamination of final units
Materials
Management
Defect in deleucocytation filters
Improper document of leukoreduction prior Intercept


Defect in whole blood centrifugation
Improper settings of whole blood centrifuge or separation equipment
Defect in apheresis equipment
Improper settings of apheresis equipment
Defect in instrument used for RBC measurement
Improper control of Intercept guardbands
Improper training of visual detection of RBC contamination
Equipment
Process
People
RBC contamination of final units
Materials
Management
Improper documentation for visual detection of RBC contamination


Defect in whole blood centrifugation
Improper settings of whole blood centrifuge or separation equipment
Defect in apheresis equipment
Improper settings of apheresis equipment
Defect in instrument used for PLT measurement
Improper control of Intercept guardbands
Improper handling of whole blood bags after centrifugation
Equipment
Process
People
Platelet contamination of final units
Materials
Management
Improper validation of platelet contamination control

9. Appendix A – proposed specifications of Intercept-treated plasma in the scope of the validation runs

These proposed specifications for final plasma units treated by the Intercept process are provided for information. They complete the validation plan and should be used to prepare the operational implementation of the Intercept process.

The tests and controls described in the validation plan remain compulsory in the scope of the validation, and the quality controls proposed below are purely indicative to prepare the implementation of Intercept in routine.

It is the responsibility of the T-CH to provide definitive, approved plasma product specifications, and this document is thus just a proposal that should be used with all due caution.

9.1. *Pooled, ABO*-matched, whole blood-derived, fresh frozen plasma, leukocyte-depleted, treated with the Intercept pathogen inactivation technique

Definition

ABO-matched, whole blood plasma, coming from 2-6 blood donations, leukocyte-depleted, pathogen-inactivated with the Intercept process.

Donor selection criteria

Conform to the selection criteria of the STS CRS.

Blood bags, filters and anticoagulants

Conform to the list of material approved by the STS CRS.

Biological qualification

Conform to the rules prescribed by the STS CRS.

Characteristics and packaging

Volume	200±20 mL
Leukocytes	≤ 1.10^6/unit
Platelets	< 50.10^6/mL
Red blood cells	< 4.10^6 /mL
Factor VIII	≥ 0.5 UI/mL

Freezing	20 hours following donation at the latest
Freezing process	≤ 1 hour at ≤-30°C
Shelf life	2 years
Storage	≤ -25°C

Transportation	≤ -20°C during max. 24 hours

In order to protect the plasma bag against damages due to freeze/thawing, the plasma bag must be packaged under vacuum in a plastic bag.

Labeling

Fixed data	Variable data	Warnings
• Name and address of the producer • Product name • Volume: 200±20 mL • Leukocyte content: < 1.10^6 per unit • Prepared and tested according to the law on therapeutic products and STS CRS prescriptions. • Prepared from 2-6 whole blood donations • Prepared with the Intercept process ZL-N°58.835 (Swissmedic) • Declaration of the stabilizing solution	• Donation number • ABO blood group • Donation date • Expiry date • Lot number of the plasma bag • Warning about blood groups[4]	• Store without interruption at ≤ -25°C • Use a transfusion tubing with a filter of 170-200 µm • Do not re-use partially transfused units • Thaw at 37°C just before transfusion • Refer to the notice of the Compendium Suisse des Médicaments

Quality controls

Parameter	Criterium	Modality	Frequency[5]
Visual control	[6]	Upon delivery	All bags
Volume	200±20 mL	After processing	1%/month
Leukocytes	≤ 1.10^6/unit[7]	Before the Intercept process	4/month
Red blood cells	≤ 4.10^6 /mL	Before the Intercept process	4/month
Platelets	< 50.10^6/mL	After processing	4/month
Factor VIII	≥ 0.5 UI/mL (pool)	During first month, after freezing and	10 units (unitary titration of pool)

[4] AB group : for any recipient ; A group : for recipients of group A or O ; O group : only for recipients of group O ; B group : for recipients of group B or O.

[5] Quality control by final units

[6] Unitary control of each unit to detect any defect of the bag or its content (turbidity, color change, hemolysis, clots).

[7] 90% of controled units must reach this threshold.

		thawing[8]	every three months independently of lot numbers.

[8] Plasma must be thawed in a liquid bath at 25°C or 37°C or by an equivalent technique. The use of a derivation or satellite bag is authorized given the procedure has been validated. Factor VIII activity must be measured by an internationally recognized technique.

9.2. Apheresis fresh frozen plasma, leukocyte-depleted, treated with the Intercept pathogen inactivation technique

Definition

Plasma coming from a single donor, leukocyte-depleted, pathogen-inactivated with the Intercept process.

Donor selection criteria

Conform to the selection criteria of the STS CRS.

Blood bags, filters and anticoagulants

Conform to the list of material approved by the STS CRS.

Biological qualification

Conform to the rules prescribed by the STS CRS.

Characteristics and packaging

Volume	200±20 mL
Leukocytes	≤ 1.10^6/unit
Platelets	< 50.10^6/mL
Red blood cells	≤ 4.10^6 /mL
Factor VIII	≥ 0.5 UI/mL

Freezing	20 hours following donation at the latest
Freezing process	≤ 1 hour at ≤ -30°C
Shelf life	2 years
Storage	≤ -25°C
Transportation	≤ -20°C during max. 24 hours

In order to protect the plasma bag against damages due to freeze/thawing, the plasma bag must be packaged under vacuum in a plastic bag.

Labeling

Fixed data	Variable data	Warnings
• Name and address of the producer • Product name • Volume: 200±20 mL • Leukocyte content: < 1.10^6 per unit	• Donation number • ABO blood group • Donation date • Expiry date • Lot number of the	• Store without interruption at ≤ -25°C • Use a transfusion tubing with a filter of 170-200 µm • Do not re-use partially

• Prepared and tested according to the law on therapeutic products and STS CRS prescriptions. • Prepared from a single-donor donation • Prepared with the Intercept process ZL-N°58.835 (Swissmedic) • Declaration of the stabilizing solution	plasma bag • Warning about blood groups[9]	transfused units • Thaw at 37°C just before transfusion • Refer to the notice of the Compendium Suisse des Médicaments

Quality controls

Parameter	Criterium	Modality	Frequency[10]
Visual control	[11]	Upon delivery	All bags
Volume	200±20 mL	After processing	1%/month
Leukocytes	$\leq 1.10^6$/unit[12]	Before the Intercept process	4/month
Red blood cells	$\leq 4.10^6$ /mL	Before the Intercept process	4/month
Platelets	$< 50.10^6$/mL	After processing	4/month
Factor VIII	≥ 0.5 UI/mL (pool)	During first month, after freezing and thawing[13]	10 units (unitary titration of pool) every three months independently of lot numbers.

[9] AB group : for any recipient ; A group : for recipients of group A or O ; O group : only for recipients of group O ;B group : for recipients of group B or O.

[10] Quality control by donation set

[11] Unitary control of each unit to detect any defect of the bag or its content (turbidity, color change, hemolysis, clots).

[12] 90% of controled units must reach this threshold.

[13] Plasma must be thawed in a liquid bath at 25°C or 37°C or by an equivalent technique. The use of a derivation or satellite bag is authorized given the procedure has been validated. Factor VIII activity must be measured by an internationally recognized technique.

10. Appendix B: Data to be reported for the pre-validation and validation phases

In order to facilitate data reporting in the scope of this validation plan, data to be reported is described below.

10.1. Pre-validation phase

Plasma source	Description of the source of plasma, including anticoagulant used, pooling procedures (if any)
Time from collection to sampling	For each plasma unit, time from collection to sampling for product characterization should be indicated. A minimum of half units of each blood group should be processed and tested at the maximum time allowed (15-18 hours post-collection for freezing within 20 hours post-collection at the latest).
Handling of plasma units	The conditions of the plasma handling post-collection (temperature, type of temperature control, pooling…) should be described
Volume	Volume prior to any sampling
Residual Red Blood Cells	The measuring technique (counting chamber or flow cytometry, for example) should be indicated
Residual Platelets	The measuring technique (counting chamber or flow cytometry, for example) should be indicated
Residual leucocytes	The measuring technique (counting chamber or flow cytometry, for example) should be indicated
Factor VIII activity	The measuring technique (either immunoassay, chromogenic or clotting assay) should be mentioned. In addition, the processing of the plasma sample for Factor VIII activity determination should be described.
Fibrinogen activity	The measuring technique should be described. In addition, the processing of the plasma sample for Fibrinogen activity determination should be described.

10.2. Validation phase

Pre-inactivation	Plasma source	Description of the source of plasma, including anticoagulant used, pooling procedures (if any)…
	Time from collection	For each plasma unit, time from collection to sampling for production characterization should be indicated. A minimum of half units of each group should be tested at the maximum time allowed (15-18 hours post-collection).
	Handling of plasma units	The conditions of the plasma handling post-collection (temperature, type of temperature control, pooling…) should be described
	Volume	Volume prior to any sampling
	Residual Red Blood Cells	The measuring technique (counting chamber of flow cytometry, for example)
	Residual Platelets	The measuring technique (counting chamber of flow cytometry, for example)
	Residual leucocytes	The measuring technique (counting chamber of flow cytometry, for example)
	Factor VIII activity	The measuring technique (either immunoassay, chromogenic or clotting assay) should be précised. In addition, the processing of the plasma sample for Factor VIII activity determination should be described.
	Fibrinogen activity	The measuring technique should be precised. In addition, the processing of the plasma sample for Fibrinogen activity determination should be described.
Post-inactivation	Pre-inactivation volume	Volume just prior to the Intercept treatment (post-sampling)
	Time to flow through CAD resin	
	Lot number of the Intercept kit	All kits should come from a single lot within one blood bank validation.
	Post-Intercept volume	Prior to any sampling for Factor VIII or Amotosalen determination

	Post-Intercept Factor VIII activity and retention of Factor VIII	The measuring technique (either immunoassay, chromogenic or clotting assay) should be described. In addition, the processing of the plasma sample for Factor VIII activity determination should be described.
	Post-Intercept Fibrinogen activity and retention of Fibrinogen	The measuring technique should be described. In addition, the processing of the plasma sample for Fibrinogen activity determination should be described.
	Residual Amotosalen and photoproducts	Certificates from a certified laboratory should be provided.
	Time from collection to complete freezing	
After Intercept, freezing and thawing	Post-thawing Factor VIII activity	The measuring technique (either immunoassay, chromogenic or clotting assay) should be described. In addition, the processing of the plasma sample for Factor VIII activity determination should be described.
	Post-thawing Fibrinogen activity	The measuring technique should be described. In addition, the processing of the plasma sample for Fibrinogen activity determination should be described.