Les plasmas thérapeutiques d'aujourd'hui et de demain

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Déclaration de liens d'intérêt

- Sur ces 5 dernières années,
  - Honorariums et invitations reçus de Cerus-Europe, Macopharma-France
  - Invitations reçues de Terumo-BCT
  - Visite de la plateforme de production du FVIII d'Octapharma (voyage et visite)
- Recherche subventionnée
  - CNR-MAT, APHP : co-investigateur principal → Étude rétrospective de l'efficacité et de la tolérance du plasma inactivé par l'Amotosalen dans les échanges plasmatiques pour PTT (Cerus-Europe)

Le détail de la conférence est disponible dans :

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TRANSFUSION
CLINIQUE ET BIOLOGIQUE

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Update article

Plasma for direct therapeutic use, for today and tomorrow: A short critical overview

Un état des lieux et les nouvelles questions à propos du plasma à usage thérapeutique direct

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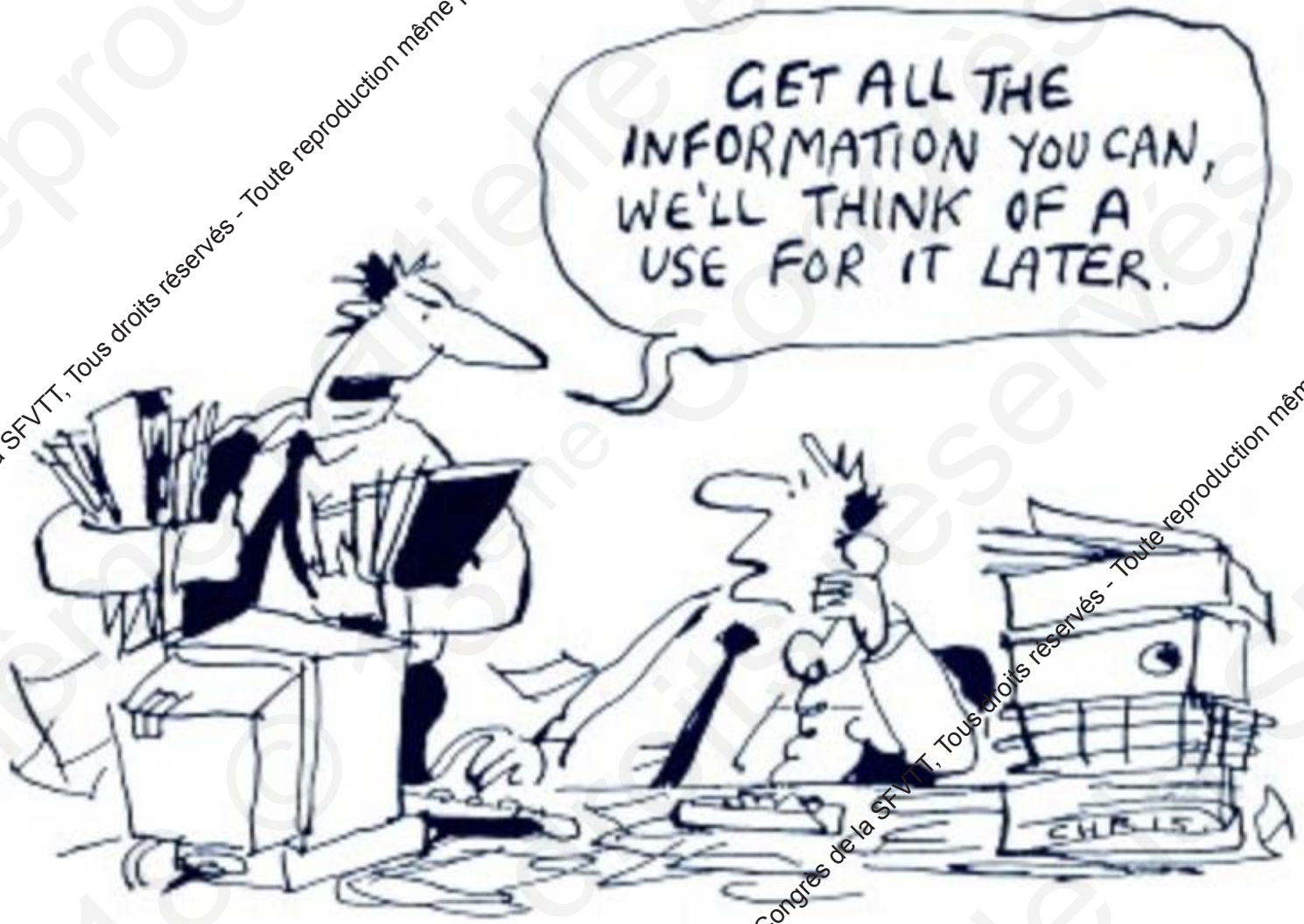

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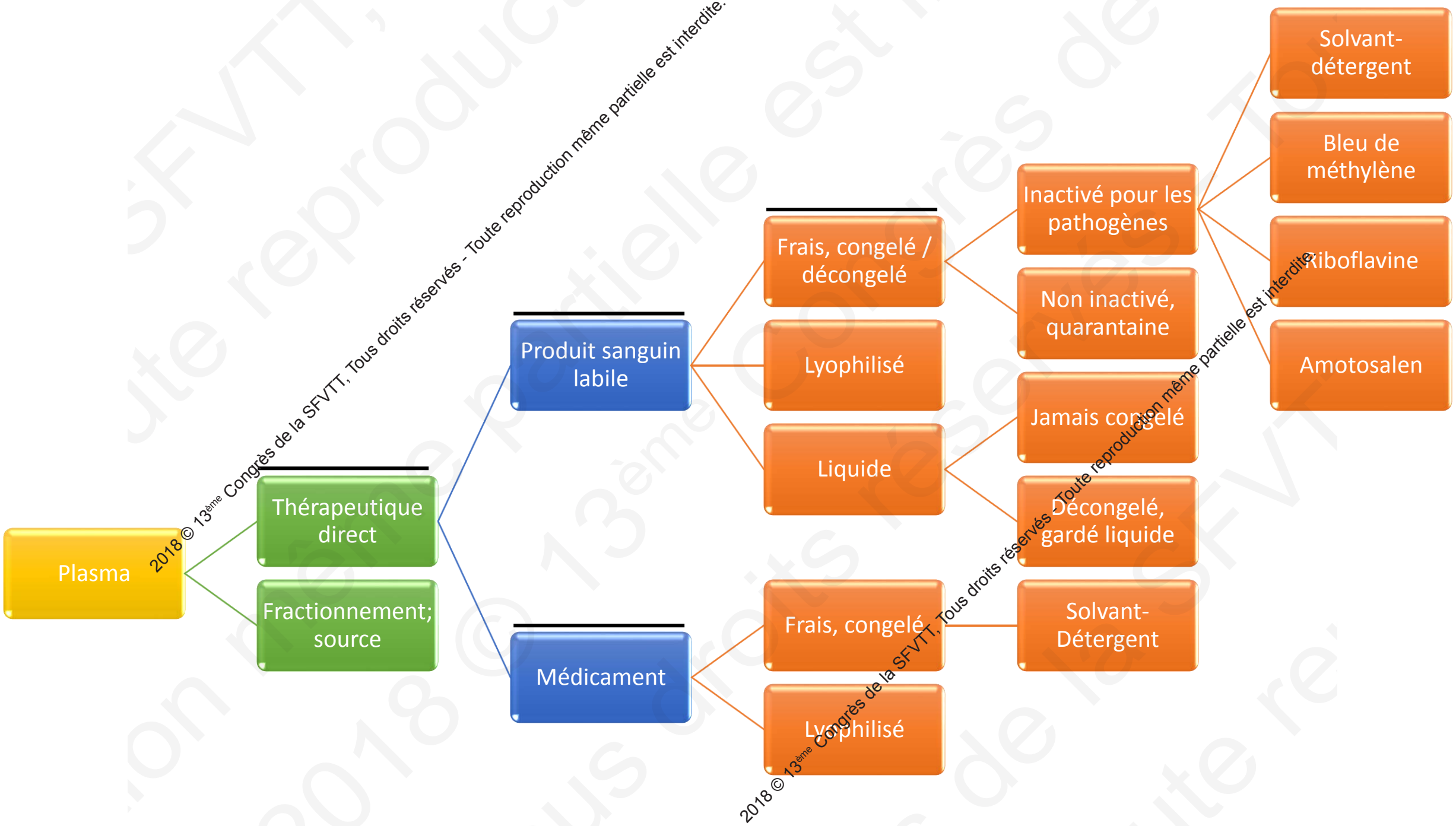

Table 1
The distinct presentations of "plasma for direct therapeutic use" yet available or in evaluation worldwide.

	LBC										Drug[a]	
	FFP					LYO			Liquid		FFP	LYO
	Quarantine secured	Solvent-Detergent	Amotosalen inactivated	Methylene Blue inactivated	Riboflavin inactivated	PLYO®	–	Never frozen	Thawed	24 h RT hold***, thawed		
Safety method	For several months: frequently 2–3 (in France, for 60 days) NAT tested or not	Tween and Triton X-100	Amotosalen (psoralen) and UVA illumination	Methylene Blue and visible light illumination	Ribloflavin and UVA + B + C illumination	Amotosalen inactivated	Solvent-Detergent	None NAT tested or not	None or Amotosalen-inactivated NAT tested or not	None NAT tested or not	Solvent-Detergent Tween and Triton X-100	Quarantine NAT tested
Number of donations	Single (Apheresis or whole blood supernatant)	In general in pools (used to be × 100 in mean in France) Exists in minipools for the Middle-East supply	Single or several in minipools (no more than 6) Per French law, no more than 5 donations to make 6 products	Single	Single	Minipools (no more than 12; per French law, no more than 10)	Pooled	Single or minipools	Single or minipools	Single or minipools	Large pools, in mean > 1000	Single (apheresis)
ABO compatibility	Single donation: ABO compatibility strictly required	In pools: universal	Required (single or in Minipools of no more than 6)	Required	Required	ABO mixed and referred to as "universal"	Universal	Required (single); Minipools may be ABO mixed becoming "universal"	Required (single); Minipools may be ABO mixed becoming "universal"	Required (single); Minipools may be ABO mixed becoming "universal"	Required Could be ABO mixed in theory but not-yet done	Required

Table 1 (*Continued*)

	LBC										Drug[a]	
	FFP					LYO			Liquid		FFP	LYO
	Quarantine secured	Solvent-Detergent	Amotosalen inactivated	Methylene Blue inactivated	Riboflavin inactivated	PLYO®	–	Never frozen	Thawed	24 h RT hold***, thawed		
Haemostatic activity	Unmanipulated plasma Often considered as a standard FFP	Has been considered to be standard for therapeutic plasma exchange Often considered as a standard FFP also	Proved to be safely used in therapeutic plasma exchange and liver transplantation	Generally considered haemostatic but the French have banned this plasma as judged at risk of carrying adverse reactions Weakness would be inconsistent fibrinogen level	Lack of randomized clinical trials so far	Principally evaluated in disaster situations Proved to provide good haemostasis in massive haemorrhage situations	Little specific information available Should be equivalent to mate products	To be further evaluated (depends on how long it is stored)	To be further evaluated (depends on how long it is stored)	Discussed	Has been considered a standard for therapeutic plasma exchange Often considered to be a standard FFP also Often used as a comparator in clinical trials	
Main users	Largely used worldwide; the main one issued in France at the time being	Pools discontinued in France Minipools largely used in the Middle-East	Large worldwide experience Has been largely used in France	Very large worldwide experience	Some users in former Easter European countries and other unique users	More or less restricted to military use (and civilian disasters) in France Used by special operation forces in the USA thanks to a specific contract (evaluation)	Produced by the South-African Blood Establishment and restricted to national use	Used in some hospitals in the UK and the USA (and others)	Used in some hospitals in Sweden the UK and the USA (and others)	Used in some hospitals in the UK and the USA (and others)	Largely used worldwide Sometimes manufactured from a given country's collected plasma and shipped back as SD-FFP (with use restricted to this country)	Produced by the German Red Cross and available on the Plasma Derivative market

LBC: Labile Blood Component; FFP: Fresh Frozen Plasma; LYO: Lyophilized therapeutic plasma; NAT: Nucleic Acid Testing.

[a] Going by the status of a Plasma Derived Drug or Plasma Derivative.

frontiers in Medicine

MINI REVIEW
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Blood and Blood Components: From Similarities to Differences

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Blood transfusion is made possible because, in most countries and organizations, altruistic individuals voluntarily, anonymously, and generously donate (without compensation) either whole blood or separated components that are then processed and distributed by professionals, prior to being allocated to recipients in need. Being part of modern medicine, blood transfusion uses so-called standard blood components when relative to cellular fractions and fresh plasma. However, as will be discussed in this paper, strictly speaking, such so-called labile blood components are not completely standard. Furthermore, the prevalent system based on voluntary, non-remunerated blood donation is not yet universal and, despite claims by the World Health Organization that 100% of blood collection will be derived from altruistic donations by 2020 (postponed to 2025), many obstacles may hinder this ambition, especially when relative to the collection of the enormous amount of plasma destined for fractionation into plasma derivative or drugs. Finally, country organizations also vary due to the economy, sociology, politics, and epidemiology. This paper then, discusses the particulars (of which ethical considerations) of blood transfusion diversity and the consequences for donors, patients, and society.

Keywords: transfusion, blood donation, blood processing, blood components, ethics

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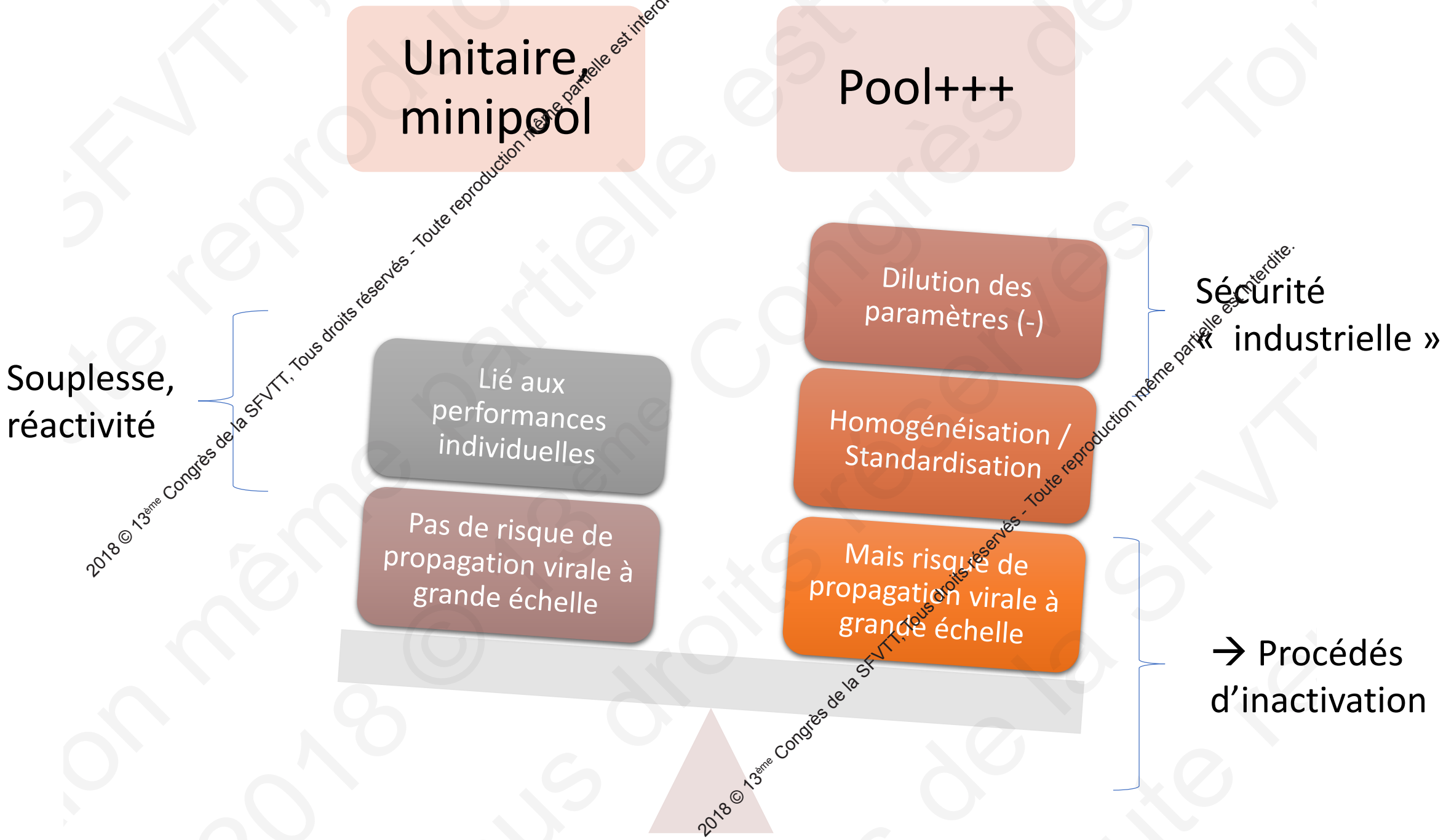
INTRODUCTION

TABLE 1 | Parameters having proven or theoretical influence on the quality of the processed blood component (BC).

Main categories	Main items adding diversity	Level of diversity
Donor dependent parameters (genetically controlled)	• Sex/gender • Immunogenetic characteristics (blood groups) • Natural iso-antibodies • …	• Two • By the thousands (millions if applied also to HLA antigens) • Variable
Donor dependent parameters (only partly genetically controlled)	• Immunization status • Nutrition, metabolism • Hygiene and intoxications (therapeutic and recreational drugs, supplements, alcohol, tobacco) • Meal; or fast • Nycthemeral cycle • Genital cycle and periods • Outside temperature condition • …	Hundreds of influential parameters
Donor independent parameters (BC processing)	• Shipping time and temperature • Needles, plastics and bags, rotators, automats for collection and intermediate storage • Devices for cell separation • Working temperature • Additives (anticoagulant, solutions, pathogen inactivation, etc.) • Filtration steps (meshes, temperature, timing, etc.) • Pooling steps • Preservation conditions • Physical interactions in shelf-life conditions (stacking, shocks, thermic differences, shipping, etc.)	• Variable • Dozens influential parameters
Patient (recipient, beneficiary) dependent parameters	• Blood group • Immunization status • Matching conditions	• By the thousands

Each parameter being independent from the preceding one, diversity is created by the multiplication as opposed to the addition of all. The final diversity goes by the million or more. Not all parameters are equally influential but it clearly appears from the table that one given BC collected by one individual, despite being "standardized" to a norm, is unlikely to be "standard."



https://www.toutsurlatransfusion.com/transfusion-sanguine/medecine-transfusionnelle/indications-et-qualifications-des-produits-sanguins.php

Transfusion de plasmas frais congelés

Les plasmas frais congelés (PFC) apportent l'ensemble des protéines plasmatiques (en particulier les facteurs de la coagulation et les fractions du complément), même si certaines proteines plasmatiques ont une perte d'activité lors de l'atténuation des agents pathogènes.

Le plasma est indiqué lors de déficits complexes rares en facteurs de coagulation ou lorsque les fractions coagulantes spécifiques ne sont pas disponibles. Les facteurs de coagulation non disponibles comme médicaments dérivés du sang sont le facteur V, la protéine S et le plasminogène. Le plasma thérapeutique est également nécessaire en cas de déficit en protéines autres que celles de la coagulation telle que la métalloprotéase ADAMTS 13.

Les plasmas doivent également être prescrits lors d'une hémorragie ou d'un geste à risque hémorragique associé à une anomalie sévère de l'hémostase. Il existe deux types de situation hémorragique :

- Hémorragies aiguës qui vont conduire à une transfusion massive, on la retrouve essentiellement en milieu chirurgical, obstétrical et traumatologique.
- Hémorragie lente, rencontrée tant en milieu médical que chirurgical

Les indications du plasma sont très différentes entre ces deux situations. Dans la première situation, les transfusions de plasma sont réalisées précocemment et exclusivement basées sur la gravité clinique du patient. Pour le second type d'hémorragie, les transfusions de plasma doivent être limitées. L'indication de transfusion de plasma doit être en relation entre des signes cliniques et des résultats biologiques traduisant le déficit en facteurs de coagulation. Les résultats biologiques ne doivent pas être le seul facteur de la décision de transfuser.

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TRANSFUSION DE PLASMA THÉRAPEUTIQUE :
PRODUITS, INDICATIONS
ACTUALISATION 2012

RECOMMANDATIONS

En résumé, les indications du plasma thérapeutique sont :

- hémorragie d'intensité modérée, peu évolutive ou contrôlée (guidée en priorité par les tests de laboratoire avec un ratio temps de Quick patient/témoin > 1,5)
- choc hémorragique et situations à risque d'hémorragie massive, en association à des concentrés de globules rouges avec un ratio PFC/CGR compris entre 1/2 et 1/1
- en neurochirurgie en l'absence de transfusion massive (TP < 50 % lors de la surveillance du traumatisé crânien grave et < 60 % pour la pose d'un capteur de pression intracrânienne)
- au cours de la chirurgie cardiaque, en cas de persistance d'un saignement microvasculaire et de déficit en facteurs de coagulation (TP < 40 % ou TCA >1,8/ témoin en présence d'un temps de thrombine normal ou de facteurs de coagulation < 40 %)
- CIVD obstétricale, lorsque le traitement étiologique ne permet pas de contrôler rapidement l'hémorragie
- CIVD avec effondrement des facteurs de la coagulation (TP inférieur à 35-40 %), associée à une hémorragie active ou potentielle (acte invasif)
- micro-angiopathie thrombotique (purpura thrombotique thrombocytopénique et syndrôme hémolytique et urémique avec critères de gravité) :
    - en cas de déficit en un facteur de la coagulation et impossibilité d'obtenir rapidement une préparation de facteur purifié, dans le cadre d'une situation d'urgence hémorragique,
    - en tant que produit de substitution et non de remplissage vasculaire, chez les patients sans facteur de risque hémorragique traités par des échanges plasmatiques rapprochés
    - chez le nouveau-né et l'enfant, les indications sont similaires à celles de l'adulte. Chez l'enfant de moins de 29 semaines de gestation en détresse vitale, la transfusion de PFC est recommandée lorsque les facteurs de coagulation sont inférieurs à 20 %, même en l'absence de syndrôme hémorragique clinique
    - en cas de surdosage grave en AVK, dans deux rares situations : absence de concentrés de complexe prothrombinique (CCP) et absence de CCP ne contenant pas d'héparine en cas d'antécédents de TIH.

L'utilisation de plasma thérapeutique n'est pas recommandée dans les situations suivantes :

- comme prophylaxie du saignement en cas d'altération mineure ou modérée de l'hémostase
- comme soluté de remplissage en cas de brûlures
- en cas de chirurgie cardiaque, en l'absence d'un saignement
- en cas d'insuffisance hépatocellulaire chronique, en l'absence de saignement
- en cas d'insuffisance hépatique aiguë sévère, chez un sujet ne saignant pas et non exposé à un geste vulnérant, dans le seul but de corriger les anomalies de l'hémostase
- en cas de poussées aiguës d'oedème angioneurotique héréditaire (OAH)
- en cas d'hémorragie associée aux nouveaux anticoagulants oraux, il n'y a pas de données cliniques justifiant l'intérêt d'une transfusion de PFC dans le seul but d'antagoniser leurs effets
- chez l'enfant et chez le nouveau-né en cas de :
    - syndrôme hémolytique et urémique typique post-diarrhéique (STEC+),
    - infection néonatale sans CIVD, à titre de traitement adjuvant au traitement antibiotique
    - hypovolémie sans syndrôme hémorragique et sans trouble de l'hémostase
    - prévention des hémorragies intraventriculaires du prématuré en l'absence de coagulopathie
    - avant acte chirurgical (nouveau-né).

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bjh BRITISH JOURNAL OF HAEMATOLOGY

bjh guideline

British Society of Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding

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Table IV. Plasma selection for patients who have undergone ABO-mismatched haematopoietic stem cell (HSC) transplantation

Recipient ABO blood group	Donor ABO blood group	Category of ABO mismatch	Phase II (when HSC are infused)		Phase III*
			First choice	Second choice	
O	A	Major	A	AB	Donor
	B	Major	B	AB	Donor
	AB	Major	AB		Donor
A	O	Minor	A	AB	Donor
	B	Major and minor	AB		Donor
	AB	Major	AB		Donor
B	O	Minor	B	AB	Donor
	A	Major and minor	AB		Donor
	AB	Major	AB		Donor
AB	O	Minor	AB		Donor
	A	Minor	AB		Donor
	B	Minor	AB		Donor

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*Phase III starts when both forward and reverse grouping in the recipient are consistent with the donor ABO type.

Recommendations

- **Plasma of donors with identical ABO blood group to the recipient should be used as the first choice. If this is not possible, ABO non-identical plasma is acceptable if it has 'low-titre' anti-A or anti-B activity (1B).**
- **Group O plasma should only be given to group O patients (1B).**
- **Fresh frozen plasma and cryoprecipitate of any RhD group may be transfused. If RhD positive plasma is given to an RhD negative individual, no anti-D prophylaxis is required (1B).**

Recommendations

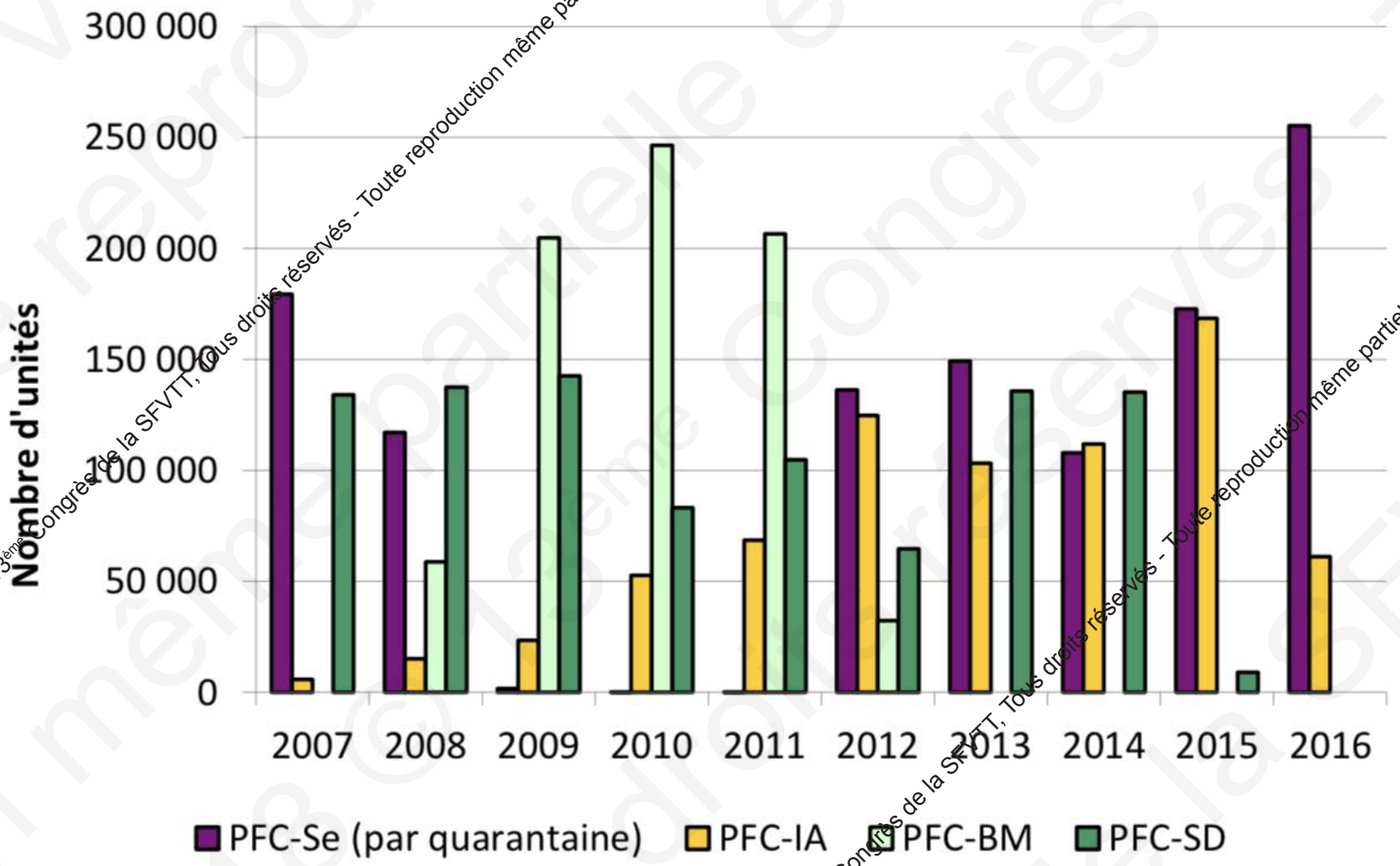
- **Following ABO minor mismatched solid organ transplant, plasma components should be of recipient's ABO group (1C).**
- **Following ABO major mismatched solid organ transplant, plasma should be of donor's ABO group until organ accommodation (usually 4 weeks after transplant) (1C).**
- **Following ABO bidirectional mismatched solid organ transplant, group AB plasma should be given until organ accommodation (usually 4 weeks after transplant) (1C).**

Supplemental Table 1: Types of plasma for direct therapeutic use issued in France 2008-2016

	Types of fresh frozen plasma in use in France (2008-2016)			
	Solvent-Detergent inactivated plasma	Quarantine plasma	Methylene Blue inactivated plasma	Amotosalen-HCl-UVA inactivated plasma
2008	+	+	+	-
2009	+	discontinued	+	-
2010	+	-	+	+
2011	+	-	+	+
2012	+	+	discontinued	+
2013	+	+	-	+
2014	-	+	-	+
2015	-	+	-	+
2016	-	+	-	+

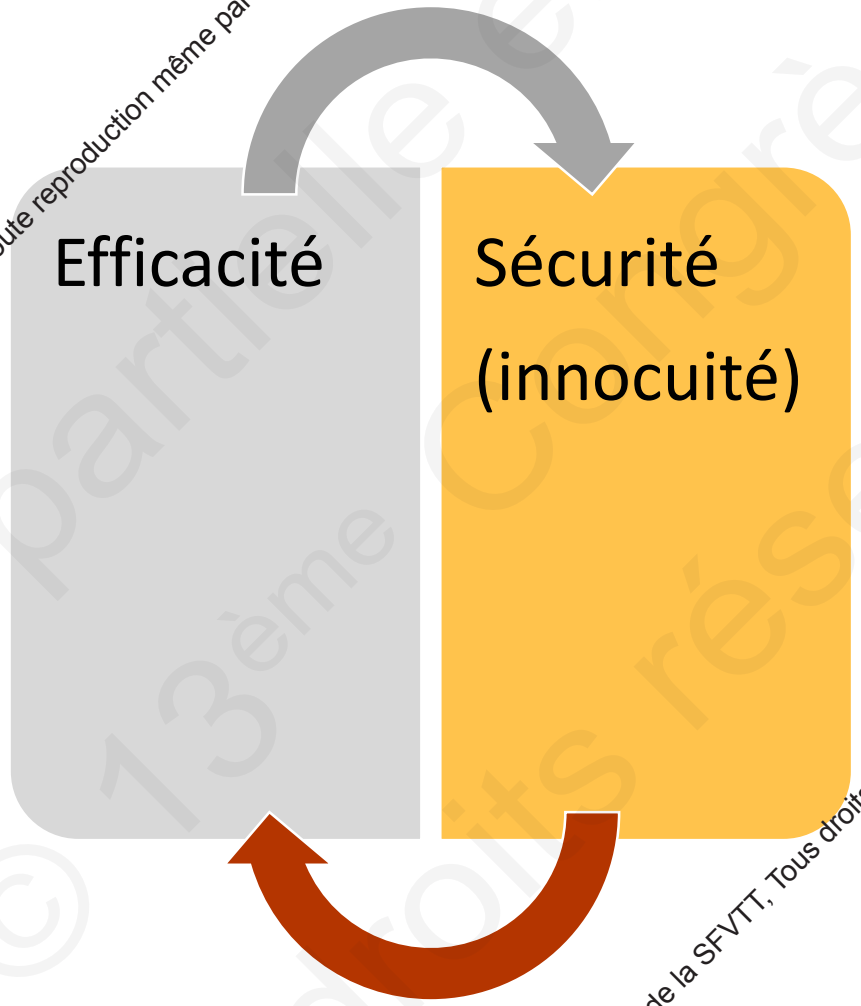
Considered Period

Figure 7 : Evolution du nombre de plasmas thérapeutiques cédés, 2007-2016



Source : CRH-ST et EFS

Source : ANSM, 2017



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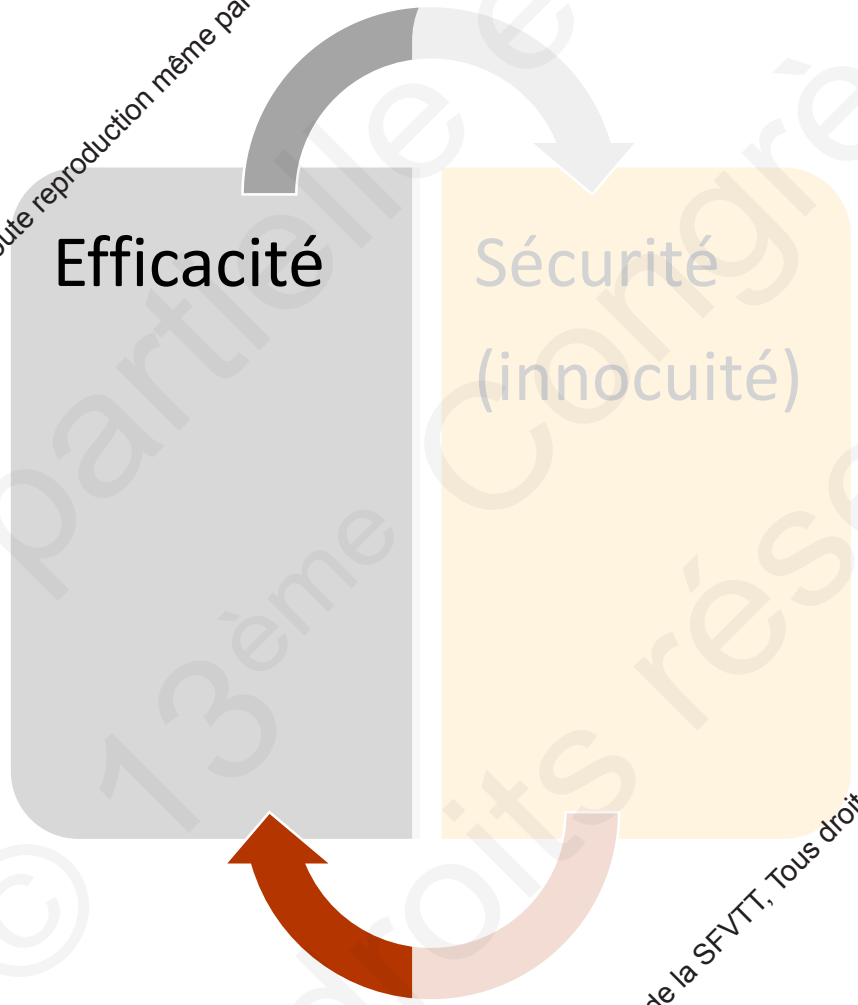

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Source: FDA, 2014

J. Irsch et al Vox Sang 2009,
DOI: 10.1111/j.1423-0410.2009.01224.x

Study method: This study was conducted at two blood centers. Test samples were derived from whole blood plasma, which was processed and frozen within 24 hours. Sixty two pools, (186 total units) of plasma were collected. A portion of each pool was separated, frozen and tested as the untreated control. The remaining portion of each pool was processed using the INTERCEPT system, frozen, and then tested in parallel with untreated control samples. A summary of study results is presented in the table below.

In Vitro Study Results

Test	IBS processed plasma		Control plasma	
	Mean±SD	Range	Mean±SD	Range
pH	7.38±0.03	7.35 – 7.45	7.41±0.05	7.34 – 7.58
Osmolality (mOsm/kg)	308±5	294 –321	309±5	295 – 322
PT (s)	14.4±0.7	12.7 – 16.9	13.1±0.3	11.6 – 15.3
aPTT (s)	27.0±1.7	23.1 – 31.3	24.2±1.4	20.4 – 27.6
Fibrinogen (g/L)	2.43±0.37	1.70 – 3.74	2.81±0.36	2.28 – 4.10
Prothrombin (IU/mL)	0.93±0.09	0.72 – 1.14	1.03±0.10	0.85 – 1.28
Factor V (IU/mL)	0.82±0.11	0.51 – 1.19	0.91±0.13	0.56 – 1.27
Factor VII (IU/mL)	0.81±0.13	0.60 – 1.22	0.99±0.14	0.71 – 1.41
Factor VIII (IU/mL)	0.73±0.20	0.35 – 1.21	0.91±0.25	0.44 – 1.52
Factor IX (IU/mL)	0.93±0.17	0.58 – 1.56	1.12±0.19	0.71 – 1.66
Factor X (IU/mL)	0.83±0.13	0.53 – 1.18	0.95±0.14	0.62 – 1.33
Factor XI (IU/mL)	0.90±0.13	0.66 – 1.28	1.02±0.14	0.77 – 1.43
vWF R:Co (IU/mL)	0.97±0.24	0.46 – 1.55	1.01±0.25	0.51 – 1.56
ADAMTS-13 antigen (%)	128.8±20.6	94.0 – 181.4	124.7±17.9	90.4 – 173.4
ADAMTS-13 activity (%)	87.5±11.0	64.0 – 114.8	93.4±10.3	68.0 – 114.8
Antithrombin III (IU/mL)	0.93±0.06	0.73 – 1.07	0.98±0.06	0.76 – 1.11
Protein C (IU/mL)	0.86±0.09	0.67 – 1.01	0.95±0.10	0.79 – 1.20
Protein S (IU/mL)	1.04±0.10	0.84 – 1.26	1.08±0.11	0.84 – 1.30
Alpha-2-plasmin Inhibitor (IU/mL)	0.85±0.07	0.63 – 1.02	1.00±0.08	0.72 – 1.18
TAT (IU/mL)	2.3±0.8	2.0 – 6.3	2.4±0.8	2.0 – 6.7
Factor VIIa (ng/mL)	<3.6	<3.6	<3.6	<3.6
NAPTT (s)	91.8±11.4	70.3 – 121.9	91.8±10.6	69.9 – 118.4
C3a (ng/mL)	50.4±38.4	13.0 – 216.2	134.7±57.0	66.8 – 359.0

IX. SUMMARY OF PRIMARY CLINICAL STUDIES

The safety and effectiveness of IBS processed plasma were investigated in eight clinical studies summarized in the table below (N=704).

Clinical Trials of IBS Processed Plasma

Trial	Phase	Design	Clinical Setting	N	Objectives
C-001-97	1	Randomized Crossover Blinded	Healthy Subjects	15	Amotosalen kinetics Safety
C-002-97	2	Randomized Crossover Blinded	Anticoagulated Healthy Subjects	27	Warfarin reversal Factor kinetics Safety
C-002-98	2	Randomized Parallel Group Blinded	Acquired Coagulopathy Liver Disease	13	Pilot study Logistics Clinical response
F3A99UC*	3	Single Group Open Label	Congenital Coagulopathy	34	Factor kinetics Clinical response Safety
F3B99	3	Randomized Parallel Group Blinded	Acquired Coagulopathy Liver Disease	121	Clinical response to invasive surgery Safety
F3C99	3	Randomized Parallel Group Blinded	TTP with therapeutic plasma exchange	35	Clinical response Safety
CLI 00080	Post marketing in Europe	Retrospective Cohort Controlled Comparative Efficacy	TTP	31	Clinical response
EFS Alsace/ Strasbourg University	Post marketing in Europe	Retrospective Cohort Controlled Comparative Efficacy	Liver Transplant	427	Clinical response Safety

**Not discussed in detail as the data are not adequate to support the indication*

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ORIGINAL PAPER

Characterization of efficacy and safety of pathogen inactivated and quarantine plasma in routine use for treatment of acquired immune thrombotic thrombocytopenic purpura

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Comparative effectiveness of plasma prepared with amotosalen-UVA pathogen inactivation and conventional plasma for support of liver transplantation

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TRANSFUSION 2015;55;1710–1720

AI-FFP

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Centre de référence des microangiopathies thrombotiques

Amotosalen-Inactivated Fresh Frozen Plasma Is Comparable to Solvent-Detergent Inactivated Plasma to Treat Thrombotic Thrombocytopenic Purpura

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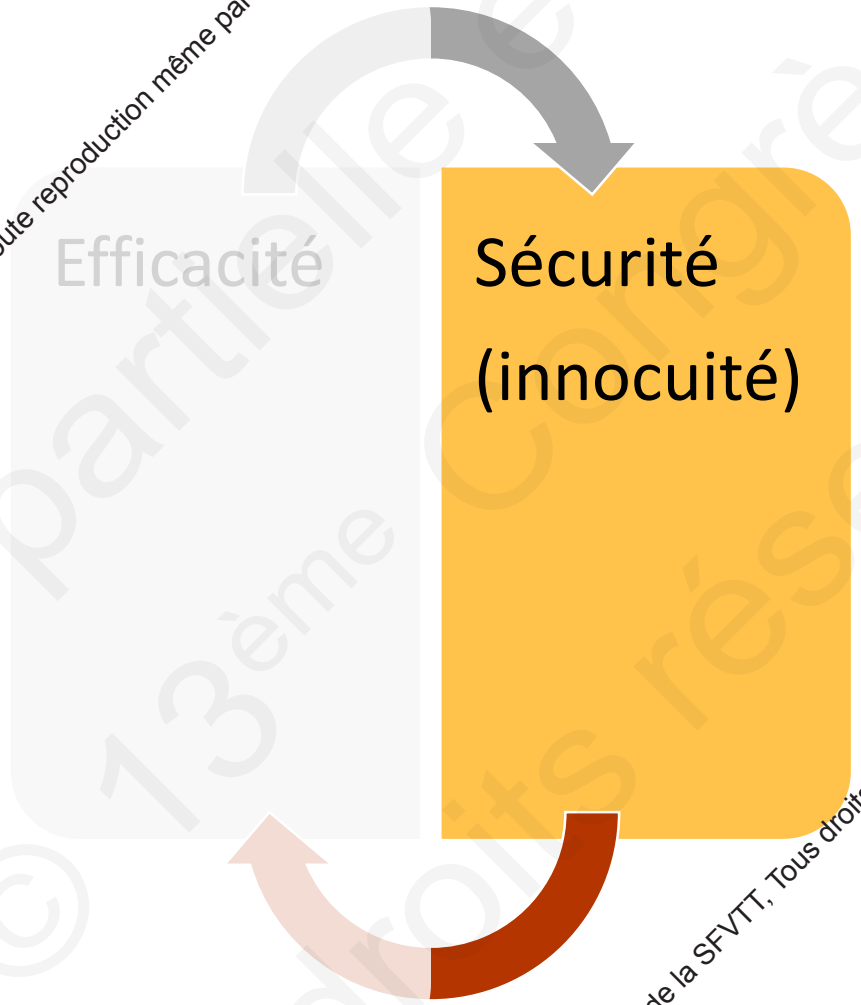

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ORIGINAL PAPER

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A regional haemovigilance retrospective study of four types of therapeutic plasma in a ten-year survey period in France

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Vox Sanguinis

Background and objectives Our objective was to compare the frequency of adverse events (AEs) due to any of the 4 types of fresh-frozen plasma (FFP) prepared and delivered by the French Blood Establishment (EFS) over a 10-year period. Surveillance of AEs and vigilance was performed according to a homogeneous policy. The four types of FFP comprised of one type (methylene blue [MB] that was stopped since then and of another type [amotosalen (AI)] that was recently introduced, along with two conventional products [quarantine (Q) and solvent–detergent (SD)].

Materials and Methods This is a retrospective study based on the national AE reporting database and on the regional database system for deliveries. AEs recorded after the delivery of 1 of the 4 types of FFP were pairwise compared, with appropriate statistical corrections.

Results 105 964 FFP units were delivered (38·4% Q, 17·9% SD, 9·7% MB and 34% AI).

Statistical comparisons of AEs identified only a difference in AE rates between quarantine and solvent–detergent plasma.

Conclusions FFP was confirmed to be extremely safe in general, especially if one considers 'severe' AEs. All types of FFP were associated with extremely low occurrences of AEs. Q, SD, MB and AI led, respectively, to 7·14, 4·86, 1·05 and 4·16 AEs per 10 000 deliveries.

Key words: adverse events, fresh-frozen plasma, haemovigilance, therapeutic plasma, transfusion safety.

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Table 1 Distribution of Fresh-Frozen Plasma types in the Auvergne-Loire Region (France) from 2000 to 2011, Adverse Event record and pairwise comparison of adverse event by plasma type

Type of plasma component (FFP)	Total FFP transfused (January 2000–October 2011)	Number of FFP units eliciting an AE (Minor + Mild + Severe + Lethal = Total)	Pairwise comparison of FFP units and their *P* values using the FDR control methods
(a) Possible, probable and certain adverse events (AE)			
Quarantine (Q)	40 631	17 + 11 + 1 + 0 = **29** (*7/10·000*)	**Q vs. SD: P = 0·0009, S** Q vs. BM: *P* = 0·6308, NS Q vs. AI: *P* = 0.1463, NS
Solvent–Detergent (SD)	19 015	1 + 1 + 0 + 0 = **2** (*1/10·000*)	SD vs. MB: *P* = 0·1411, NS SD vs. AI: *P* = 0·1411, NS
Methylene Blue (MB)	10 283	4 + 0 + 1 + 0 = **5** (*4·8/10·000*)	MB vs. AI, *P* = 0·7879, NS
Amotosalen (AI)	36 035	11 + 2 + 2 + 0 = **15** (*4·1/10·000*)	-
Total	105 964	Total = **48** (*4·5/10·000*)	
(b) Probable and certain adverse events (AE)			
Quarantine (Q)	40 631	12 + 10 + 1 + 0 = **23** (*5·7/10·000*)	**Q vs. SD: P = 0·0102, S** Q vs. BM: *P* = 0·4043, NS Q vs. AI: *P* = 0573, NS
Solvent–Detergent (SD)	19 015	1 + 0 + 0 + 0 = **1** (*0·5/10·000*)	SD vs. MB: *P* = 0·2548, NS SD vs. AI: *P* = 0·2657, NS
Methylene Blue (MB)	10 283	2 + 0 + 1 + 0 = **3** (*2·9/10·000*)	MB vs. AI, *P* = 0·7169, NS
Amotosalen (AI)	36 035	6 + 1 + 1 + 0 = **8** (*2·2/10·000*)	-
Total	105 964	Total = **35** (*3·3/10·000*)	

FCR, false discovery rate; FFP, fresh-frozen plasma.
Bold stands for significant (S) and italics stand for non significant (NS).

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SHORT REPORT

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Independent evaluation of tolerance of therapeutic plasma inactivated by amotosalen-HCl–UVA (Intercept™) over a 5-year period of extensive delivery

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Vox Sanguinis

Amotosalen-HCl–UVA (AI) is a process to inactivate pathogens in therapeutic plasma (FFP). Tolerance is the main residual issue in FFP transfusion, and only large series observations are powered enough to identify significantly elevated levels of hazards. We report here on 15 133 new transfusions of AI-FFP, over the previously published 36 035, which in all represents one of the largest series observed by means of a highly standardized surveillance (51 168 observations). There is no noticeable difference in terms of tolerance of AI-FFP compared to 5875 transfusions of Quarantine (Q)-FFP. There was no significant difference in terms of advance events, between the two types of FFP ($P = 0{\cdot}98$); further, no difference was recorded either when the total number of AI-FFP (51 168) was compared to the corresponding number of Q-FFP (5875; $P = 0{\cdot}62$).

Key words: amotosalen, haemovigilance, pathogen reduction, safety, therapeutic plasma.

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Table 2 Comparison of FFP tolerance with two types of plasma in our regional setting of the national blood service in France (period 2001–2013; 51 168 amotosalen-HCl–UVA inactivated (AI) FFP units); the accountability used for recording the hazardous events was 1 and above

	Severity 2	Severity 3	Severity 4	Total	No. observations	Incidence	Statistical significance
(A) New FFP transfusions							
AI-FFP	3	2	0	5	15 133	0·00033	NS
Q-FFP	2	0	0	2	5875	0·00034	$P = 0·98$
(B) Comparison between observations with 2 FFP types (same period of time)							
AI-FFP	5	7	0	12	51 168	0·00024	NS
Q-FFP	2	0	0	2	5875	0·00034	$P = 0·62$

FFP, fresh frozen plasma.

Table 3 Clinical details on adverse events recorded after the transfusion of AI-FFP and Q-FFP

Type of plasma	Date	Severity	Diagnostics	Associated pathology
AI-FFP	December 2011	3	Allergy (shock)	
AI-FFP	April 2012	2	Allergy (localized urticaria)	Associated urticaria on puncture sites; latex allergy suspected
Q-FFP	November 2012	2	Allergy (cutaneous rash and dyspnea)	
Q-FFP	December 2012	2	Allergy (localized urticaria)	
AI-FFP	January 2013	3	Oedema (face and thorax); considered allergic type	Associated urticarial on puncture sites; latex allergy suspected
AI-FFP	March 2013	2	Hypotension; considered allergic type	Associated allergy to antibiotics and disinfectant
AI-FFP	September 2013	2	Hypotension; considered allergic type	Suspected sepsis (*Staphylococcus hominis*)

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Réduction de pathogènes,
Exemple : Amotosalen-HCl-UVA (IINTERCEPT®)

Summary of Pathogen Reduction Study Results

Pathogen	Log Reduction
Virus (Enveloped)	
HIV-1 IIIB, cell-associated	≥6.2
HIV-I IIIB cell-free	≥6.1
DHBV	4.4 to 4.5
BVDV (model for HCV)	≥4.5
HTLV-I	≥4.1
HTLV-II	≥4.7
West Nile virus	≥6.7
SARS-Associated Coronavirus	≥4.0
Chikungunya virus (CHIKV)	6.5
Influenza A virus (H_5N_1 Avian Influenza)	≥5.7
Virus (Non-Enveloped)	
Parvovirus B19	1.8
Bluetongue virus	≥4.0
Adenovirus 5	≥5.6
Bacteria	
Klebsiella pneumoniae	≥6.7
Yersinia enterocolitica	≥6.6
Staphylococcus epidermidis	≥6.6
Treponema pallidum	≥5.4
Borrelia burgdorferi	≥9.9
Anaplasma phagocytophilum (HGE agent)	≥3.6
Protozoan Parasite	
Plasmodium falciparum	≥5.9
Babesia microti	≥4.9
Trypanosoma cruzi	>5.0

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Hepatitis E transmission by transfusion of Intercept blood system–treated plasma

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