Macopharma is an innovator in global healthcare with expertise in the fields of Transfusion, Infusion and Biotherapy. One of Macopharma’s aims is to provide a comprehensive range of products for the pathogen reduction of infectious agents in plasma, platelets and red cells. This is aligned with Macopharma’s product development strategy of the continuous quest, through partnerships, for improved safety, efficacy, and quality of transfusion, infusion and cellular therapy.

The **THERAFLEX MB-Plasma** system has been designed to inactivate both recognized and emerging pathogens in plasma. The Pathogen Reduction technology for plasma has been developed in partnership with the Blood Centre of the German Red Cross Chapters of NSTOB, Springe. It is a user-friendly in-house treatment for single units of plasma adapted for the inactivation of pathogens in Fresh Frozen Plasma from aphaeresis or whole blood. MB-treated plasma produced with the Macopharma THERAFLEX MB-Plasma procedure is in clinical use in 18 countries worldwide and more than 6 Million MB-plasma units have been treated and subsequently transfused to date.

The development of the **THERAFLEX UV-Platelets** system is a joint project between the Research Foundation of the German Red Cross Blood Services and Macopharma to inactivate recognized and emerging pathogens in platelets. The technology is based on the exposure of plasma-reduced platelet concentrates to UV-C light only, requiring no additional photoactive substance. It is a simple and fast, one-step inactivation process using **SSP+** as an additive solution and substitute for plasma. Clinical trials are in progress and commercialisation is expected in 2016.

The **P-Capt** filter has been designed to prevent v-CJD blood transmission. It is a dockable sterile, single-use prion reduction filter compatible with red cell concentrates originating from any collection and processing system. Red blood cells are passed through the filter under gravity and a highly specific affinity adsorbent material captures and removes any v-CJD prion protein. The P-Capt filter incorporates a prion-specific affinity resin developed by PRDT and supplied by ProMetic to Macopharma and it is manufactured under licence and distributed by Macopharma. The product is CE-marked since 2006 and is available for sale in Europe.

The Platelet Additive Solution **SSP+** ("PAS-E") is the most suitable PAS on the market. It is designed to partially replace plasma in the preparation and storage of buffy-coat derived platelet concentrates or apheresis platelet units. The recommended ratio is up to 80% SSP+ / 20% plasma. The solution enables platelets to be stored at 22°C ± 2°C, under gentle agitation, for up to 7 days following collection and according to local regulations.

Macopharma is proud to share with you the most relevant articles showing the benefits of these blood safety technologies.

We wish you an enjoyable and fruitful reading.
## Blood Safety - Bibliography - 2014

**THERAFLEX MB-Plasma, THERAFLEX UV-Platelets, SSP+ & P-CAPT**

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors, title and references</th>
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<tbody>
<tr>
<td>2011</td>
<td>Seghatchian J, Struff WS, Reichenberg S. <strong>Main properties of the THERAFLEX MB-Plasma system for pathogen reduction.</strong> Transfusion Medicine and Hemotherapy 2011;38:55-64.</td>
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Blood Safety
Abstracts Scientific Publications 2012-2014

THERAFLEX MB-PLASMA
Factor VIII and fibrinogen recovery in plasma after Theraflex methylene blue-treatment: effect of plasma source and treatment time

André Rapaille\textsuperscript{1}, Stefan Reichenberg\textsuperscript{2}, Tome Najdovski\textsuperscript{1}, Nicolas Cellier\textsuperscript{1}, Nicolas de Valensart\textsuperscript{1}, Véronique Deneys\textsuperscript{1}

\textsuperscript{1}Belgian Red Cross, Blood Service, Sruilée, Belgium; \textsuperscript{2}Maccopharma International GmbH, Langen, Germany

\textbf{Background.} The quality of fresh-frozen plasma is affected by different factors. Factor VIII is sensitive to blood component storage processes and storage as well as pathogen-reduction technologies. The level of fibrinogen in plasma is not affected by the collection processes but it is affected by preparation and pathogen-reduction technologies.

\textbf{Materials and methods.} The quality of plasma from whole blood and apheresis donations harvested at different times and treated with a pathogen-reduction technique, methylene blue/light, was investigated, considering, in particular, fibrinogen and factor VIII levels and recovery.

\textbf{Results.} The mean factor VIII level after methylene blue treatment exceeded 0.5 IU/mL in all series. Factor VIII recovery varied between 78% and 89% in different series. The recovery of factor VIII was dependent on plasma source as opposed to treatment time. The interaction between the two factors was statistically significant. Mean levels of fibrinogen after methylene blue/light treatment exceeded 200 mg/dL in all arms. The level of fibrinogen after treatment correlated strongly with the level before treatment. There was a negative correlation between fibrinogen level before treatment and recovery. Pearson's correlation coefficient between factor VIII recovery and fibrinogen recovery was 0.58.

\textbf{Discussion.} These results show a difference in recovery of factor VIII and fibrinogen correlated with plasma source. The recovery of both factor VIII and fibrinogen was higher in whole blood plasma than in apheresis plasma. Factor VIII and fibrinogen recovery did not appear to be correlated.

\textbf{Keywords:} factor VIII, fibrinogen, methylene blue, MB-FFP.
Anhydrous MB chloride (85 μg) in the form of a dry pill was sufficient to obtain a concentration of 1 μM based on a plasma unit having a volume of 266 mL (range, 230-318 mL). The pill, in the transfer line, dissolved in the plasma during transfer. The packs were illuminated using the MacroTonic (Macopharma) plasma illumination system. The peak emission wavelength for the lamps was 590 nm. This procedure delivers the required dose of 180 J/cm². Illuminated plasma was filtered through a Blueflex filter to eliminate at least 90% of MB and its photoresidues. The whole procedure was performed in accordance with the manufacturer’s instructions.

Plasma collected by apheresis was split into two or three units and leucodepleted with the Plasmaflex PLAS4 filter before MB-treatment.

All plasma units (MB-treated or not) were frozen to −30 °C with the same procedure within 60 minutes using a shock freezer (MBP42, Dometic, Hosingen, Luxembourg) in respect of the Council of Europe recommendations. WB plasma collections were frozen within 18 hours of collection; apheresis plasmas within 6 hours of collection. They were stored for 2 to 20 days (mean 7 days for WB plasmas and 12 days for apheresis plasmas) at −30 °C. They were thawed in a water bath at 30 °C for 60 minutes and immediately treated by the MB procedure.

The study comprised six study arms each involving 30 plasmas (Table I). In one branch, whole blood-derived (WB) plasmas were separated and treated within 6 hours of collection (D0), separated after whole blood storage on eutectic plates at 20 °C and processed within 18 hours of collection (D1) or treated after freezing and thawing (F-T). In the other branch, apheresis plasmas (Aph) were treated within 6 hours (D0), stored on eutectic plates at 20 °C and treated within 18 hours (D1) or treated after freezing and thawing (F-T).

**Fibrinogen and factor VIII measurement**

The concentration of fibrinogen (factor I) was measured following Clauss’s method with thrombin reagent (Dade Behring) on a CA-7000 automated coagulation analyser (Sysmex Ltd., Milton Keynes, UK). FVIII was quantified using one-stage clotting times with Actin-FS (Dade-Behring) on a CA-1500 automated instrument (Sysmex Ltd.). Clotting factor-deficient plasmas consisted of human immune-adsorbed plasmas and were obtained from Dade-Behring.

**Statistical analysis**

The values were analysed using the Anderson-Darlin test for normal distribution. All results are expressed as the mean±standard deviation (SD) and range for each study arm. Comparisons of FVIII and fibrinogen recovery between the various groups were performed using analysis of variance (ANOVA) for independent groups and two factors: source (WB or apheresis) and treatment time (D0, D1, F-T). Subsequent statistical analyses were performed with Student’s t-test to uncover which groups were different. Correlations were examined using Pearson’s correlation coefficient (r). The rates of FVIII exceeding 0.5 UI/mL and fibrinogen exceeding 200 mg/dL between different groups were evaluated with Pearson’s chi-square association test. Differences and correlations were considered to be statistically significant when the P value was lower than 0.05. All analyses were performed using Minitab® Statistical Software (State College, Pennsylvania, USA).

**Results**

**Plasma factor VIII**

Detailed results including mean SD, minimum and maximum, are presented in Table II for both FVIII and fibrinogen. The means of FVIII after MB treatment from all arms of the study exceeded 0.50 IU/mL. The percentage of plasmas in which the FVIII level exceeded 0.5 IU/mL varied between 83% for the WB and frozen-thawed plasma and 100% for the WB plasma on day 0. The Pearson’s chi-square result (0.258, p=0.879) showed no difference in the proportion of plasma with FVIII exceeding 0.50 IU/mL between the different groups.

**Table I - Sampling design.**

<table>
<thead>
<tr>
<th>Study arm</th>
<th>WB plasma</th>
<th>Apheresis plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Treatment time</td>
<td>Day 0</td>
<td>Day 1</td>
</tr>
<tr>
<td>Number units</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Group O</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Group A, B, AB</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Volume before treatment (mL)</td>
<td>272±16</td>
<td>279±13</td>
</tr>
</tbody>
</table>

Sampling taken before and after treatment.
Fibrinogen

ANOVA results showed a significant effect of treatment time (p<0.05) but no significant effect of the plasma source on fibrinogen data before treatment. The interaction between plasma source and treatment time was not statistically significant. Means of fibrinogen levels in the different groups before treatment were not statistically different with Student's t-tests except for the comparison between apheresis plasma treated D1 and F-T. The mean levels of fibrinogen after MB treatment in all the study arms exceeded 200 mg/dL (Table II). The lowest percentage of plasmas in which the fibrinogen level exceeds 200 mg/dL was observed in the apheresis plasma treated on day 1 (63%).

The Pearson's chi-square result (0.863, p=0.649) showed no difference in the numbers of plasmas with fibrinogen exceeding 200 mg/dL in different groups. ANOVA results of fibrinogen after treatment were not statistically different between different groups.

Factor VIII recovery

We compared the recovery of FVIII before and after MB treatment (Figure 1). Higher results were obtained with WB plasma treated on day 0 and day 1 (Table II). The comparison of FVIII recovery in the different arms by Student's t-test revealed a statistically significant difference (p<0.001) in the recovery of FVIII between the WB plasma processed at day 0 (89±6%) or day 1 (82±10%) and apheresis plasma on day 0 (80±10%), day 1 (78±8%) or frozen/thawed (83±5%). The lowest result was obtained in apheresis plasma treated on day 1 (78±8%). All treated plasmas of the six arms had a FVIII recovery above 50%. ANOVA results showed a significant effect of plasma source (p<0.001) but not of treatment time (p=0.218). The interaction between the two factors was statistically significant (p<0.001).

The FVIII concentration after MB treatment showed a strong correlation with the FVIII level before treatment (r=0.941, p<0.001). There was no correlation between the level of FVIII before treatment and FVIII recovery (r=0.013, p=0.859).

Figure 1 - Means of factor VIII recovery with confidence interval at 95%.
was higher than that in the plasmas from the others arms of this study (85-87%) (Figure 2). This difference was statistically significant (p<0.05) except for WB plasma on day 1 vs apheresis plasma on day 1 (Table II).

Fibrinogen levels after treatment correlated strongly with those before treatment (r=0.939, p<0.001). In contrast to the findings for FVIII, the correlation between fibrinogen levels before treatment and recovery was negative (r=−0.195, p<0.01), implying that the loss was greater when the units contained higher pre-treatment levels.

**Correlation between factor VIII and fibrinogen recovery**

Pearson's correlation coefficient was 0.58 (p<0.001) when all data were considered (Figure 3). It was above 0.50 for the three series with WB plasma and for the series with apheresis plasma on day 0 (Table III). In contrast, the correlation coefficient of the D1 and F-T apheresis plasma was very low (r=−0.23 and 0.21).

**Discussion**

It is well-known that FVIII is sensitive to blood component storage conditions, pathogen-reduction technology processes and blood groups\textsuperscript{11,12}. For this reason we compared the recovery of FVIII before and after MB treatment. The percentage of plasmas in which the FVIII level after MB treatment exceeded 0.5 IU/mL was the highest in the WB plasma on day 0 (100%).

The mean recovery of FVIII after treatment with MB in the different series was above 80%, except in the apheresis day 1 arm (78%). These results are better than those obtained in the initial validation in our centre which was performed in 2003 (data not shown) (89% vs 83% for the WB plasma treated on day 1 and 83% vs 81% for the series with WB frozen/thawed plasma). This can be explained by the improved skills of technicians over years. The results of this study are notably better than those published by Rock\textsuperscript{3} (67%), Hornsey et al.\textsuperscript{13} (75%) and Garwood et al.\textsuperscript{14} (median between 76% and 71%). However, they are comparable to those published by Moog et al.\textsuperscript{14} (85%) and Politis et al.\textsuperscript{15} (82%). Mean FVIII recovery in WB plasma treated on day 0 and day 1 (89%) was higher than that in the plasma in the other arms of this study.

The difference between the WB plasma on day 0 and frozen-thawed plasma was also noted by Garwood et al.\textsuperscript{14}, who found an 8% reduction due to freeze/thawing. Unfortunately, the authors were not able to identify a root cause. Zeiler et al.\textsuperscript{16} observed only minimal loss of FVIII and fibrinogen due to freezing and thawing. The difference observed between WB plasma on day 0 and day 1 on the one hand and apheresis plasma on day 0 on the other hand could be explained by the use of different anticoagulants. Preston\textsuperscript{1} and Myllylä\textsuperscript{2} noted that the type of anticoagulant and the amount of citrate were factors that influenced plasma quality. Preston\textsuperscript{1} pointed out the importance of pH on the stability of factor VIII. Carlebjörk et al.\textsuperscript{17} observed the difference in activity and stability of FVIII in blood collected into different anticoagulants (CPD-A and ACD vs citrate). The higher pH in blood collected with citrate might give rise to lower activity and instability. Back in 1965, Weiss\textsuperscript{18} had demonstrated that FVIII was less stable at pH values higher than 7.3. Prowse et al.\textsuperscript{19} demonstrated that collecting WB into half the

**Table III** - Pearson's product-moment correlation between FVIII and fibrinogen recovery in the six arms.

<table>
<thead>
<tr>
<th>Study arm</th>
<th>WB D0</th>
<th>WB D1</th>
<th>WB F-T</th>
<th>Aph D0</th>
<th>Aph D1</th>
<th>Aph F-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson's correlation coefficient</td>
<td>0.59</td>
<td>0.80</td>
<td>0.89</td>
<td>0.57</td>
<td>−0.23</td>
<td>0.12</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.212</td>
<td>0.543</td>
</tr>
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</table>

Temperature. At the same time, Rock et al. postulated that the use of anticoagulants with lower levels of citrate was an advantage to the generation of FVIII. Beck et al. confirmed that reduced citrate concentrations in apheresis collections resulted in better preservation of FVIII activity. In our apheresis collections, we currently use the citrate concentration recommended by Beck et al. In our study, plasmas were collected into two different anticoagulants, CPD (citrate concentration 105 mM) for WB collection and citrate 4% (citrate concentration 136 mM) for apheresis collection. The higher pH and citrate concentration of anticoagulant for the apheresis collections could explain the lower recovery of FVIII for apheresis plasma. The routine quality control data from previous years tends to support this hypothesis.

The level of fibrinogen in the plasma before treatment is not affected by the preparation processes, unlike FVIII which is sensitive to different processes and blood groups. Even after treatment, fibrinogen is imperceptibly affected by the plasma preparation processes. The percentage of plasmas in which the fibrinogen level exceeded 200 mg/dL varied from 63% for the apheresis plasma treated on day 1 to 90% for the WB plasma treated on day 0. On the other hand, we observe a significant difference in the recovery of fibrinogen between the WB plasma processed on day 0 or 1 compared with frozen/thawed WB plasma and apheresis plasma on day 0 or frozen/thawed.

The average recovery of fibrinogen after MB treatment was above 80%. These results were higher than those of the initial validation conducted in our centre in 2003 (data not shown) (89% vs 78% for the WB plasma on day 1 and 85% vs 76% for WB frozen/thawed plasmas). The results of our study are significantly better than those published by Rock et al. and Garwood et al. (median 79% and 72%). They are comparable to those published by Moog et al. (78%) and Politis et al. (82%). We confirm the results of Politis et al. who described a negative correlation between data before treatment and recovery of fibrinogen implying that the loss was greater when the units had higher pre-treatment levels. The reason for this is unknown. The MB/light-induced reduction of functional fibrinogen, measured by the Clauss method, has been explained previously by a modification of histidine residues. It can be assumed that there might be an optimal relation of total amount or concentration of MB and fibrinogen which results in a maximum effect. Interestingly, the lowest fibrinogen concentrations after treatment occurred in the plasmas with the lowest starting volume (i.e. highest MB concentration because of the addition of a constant amount of MB [85 μg] per unit).

Three groups of WB plasma and one apheresis plasma on day 0. Conversely, the correlation coefficient for frozen/thawed apheresis plasma was very low (0.12).

In summary, these results show a difference in recovery of FVIII and fibrinogen in relation to the source of plasma. Recovery levels of both factors were higher in WB plasma than in apheresis plasma. This observation could be related to the anticoagulant composition or pH.

Both studied factors affect the quality of fresh-frozen plasma. FVIII recovery is influenced by both treatment time and the pathogen-reduction process. FVIII recovery is indeed representative of the preparation process as Lawrie et al. suggested. The level of fibrinogen in fresh-frozen plasma is a clinically significant factor.

Nevertheless it has been shown previously that the thrombin generation of MB-treated plasma is only slightly or not changed.

FVIII and fibrinogen recovery did not appear to be correlated. Politis et al. made the same observation. The combined effects of the preparation and MB-treatment seem to be coagulation factor-dependent.

The results of the FVIII recovery comply with Belgian legislation (recovery >50%). All treated plasmas in the six arms had a recovery greater than 50%. Loss of coagulation factor activity was within the internationally accepted range. All means of FVIII after treatment in the six arms complied with Council of Europe recommendations (average exceeding 0.5 IU/mL).

In our routine production, 90-95% of MB-treated plasma comes from WB processed within 18 hours of collection and only 5 to 10% of MB-treated plasmas come from apheresis, frozen-thawed collection with Autopheresis-C mainly of AB, A or B MB-treated stock. This production strategy gives us confidence both in the FVIII and fibrinogen content of our MB-treated fresh-frozen plasma.

Acknowledgements
We thank Prof. Stéphane Eeckhoudt, at the Coagulation Laboratory, St. Luc University Hospital, Brussels for FVIII and fibrinogen assays.

Conflicts of interest disclosure
This work was partly supported by Macopharma, Tourcoing, France.

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Paired analysis of plasma proteins and coagulant capacity after treatment with three methods of pathogen reduction.

Coene J, Devreese K, Sabot B, Feys HB, Vandekerckhove P, Compernolle V


BACKGROUND: The effect of photochemical pathogen reduction (PR) methods on plasma quality has been the subject of several reports but solid comparative data for the different technologies are lacking.

STUDY DESIGN AND METHODS: Plasma (n = 24) photoinactivated with methylene blue (MB), riboflavin (RF), or amotosalen (AS) was compared using a pool-and-split design. Samples were taken before and after treatment with each method and tested for coagulation factors (fibrinogen, Factor [F] II, FV, FVIII, F IX, FXI), natural coagulation inhibitors (Protein C [PC], protein S [PS], antithrombin III [AT]), prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin generation (TG). The three methods were mutually compared by repeated-measures analysis of variance.

RESULTS: All three PR methods cause significant reduction (p < 0.01) of activity of the procoagulant proteins fibrinogen, FII, FV, FVIII, F IX, and FXI. Coagulation is also affected, with significant changes in PT, APTT, and TG. RF treatment causes a significantly higher decrease in concentration of coagulation factors, PS, and AT than the other methods (p < 0.01). PT, APTT, and TG are also affected most by RF treatment. FII, FVIII, F IX, PC, AT, and PT are best preserved with the MB method and FV, FXI, and TG after AS treatment (p < 0.01). Coagulation factor loss due to the volume loss during PR treatment is more important for MB and AS than for RF.

CONCLUSION: PR treatment of plasma affects coagulation proteins and coagulant capacity. For the RF method this effect is most pronounced, although to some extent compensated by a smaller volume loss.
Update on the use of pathogen-reduced human plasma and platelet concentrates.

Seltsam A, Müller TH


The use of pathogen reduction technologies (PRTs) for labile blood components is slowly but steadily increasing. While pathogen-reduced plasma is already used routinely, efficacy and safety concerns impede the widespread use of pathogen-reduced platelets. The supportive and often prophylactic nature of blood component therapy in a variety of clinical situations complicates the clinical evaluation of these novel blood products. However, an increasing body of evidence on the clinical efficacy, safety, cost-benefit ratio and development of novel technologies suggests that pathogen reduction has entered a stage of maturity that could further increase the safety margin in haemotherapy. This review summarizes the clinical evidence on PRTs for plasma and platelet products that are currently licensed or under development.
A regional haemovigilance retrospective study of four types of therapeutic plasma in a ten-year survey period in France

Bost V, Odent-Malaure H, Chavarin P, Benamara H, Fabrigli F & Garraud O

Vox Sang. 2013; 104(4):337-341

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 (Al)] 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 Al led, respectively, to 7·14, 4·86, 1·05 and 4·16 AEs per 10 000 deliveries.
Two pathogen reduction technologies-methylene blue plus light and shortwave ultraviolet light-effectively inactivate hepatitis

Steinmann E, Gravemann U, Friesland M, Doerrbecker J, Müller TH, Pietschmann T, Seltsam A.

*Transfusion.* 2013; 53(5):1010-1018

**BACKGROUND:** Contamination of blood products with hepatitis C virus (HCV) can cause infections resulting in acute and chronic liver diseases. Pathogen reduction methods such as photodynamic treatment with methylene blue (MB) plus visible light as well as irradiation with shortwave ultraviolet (UVC) light were developed to inactivate viruses and other pathogens in plasma and platelet concentrates (PCs), respectively. So far, their inactivation capacities for HCV have only been tested in inactivation studies using model viruses for HCV. Recently, a HCV infection system for the propagation of infectious HCV in cell culture was developed. Contamination of blood products with hepatitis

**STUDY DESIGN AND METHODS:** Inactivation studies were performed with cell culture-derived HCV and bovine viral diarrhea virus (BVDV), a model for HCV. Plasma units or PCs were spiked with high titers of cell culture-grown viruses. After treatment of the blood units with MB plus light (Theraflex MB-Plasma system, MacoPharma) or UVC (Theraflex UV-Platelets system, MacoPharma), residual viral infectivity was assessed using sensitive cell culture systems.

**RESULTS:** HCV was sensitive to inactivation by both pathogen reduction procedures. HCV in plasma was efficiently inactivated by MB plus light below the detection limit already by 1/12 of the full light dose. HCV in PCs was inactivated by UVC irradiation with a reduction factor of more than 5 log. BVDV was less sensitive to the two pathogen reduction methods.

**CONCLUSIONS:** Functional assays with human HCV offer an efficient tool to directly assess the inactivation capacity of pathogen reduction procedures. Pathogen reduction technologies such as MB plus light treatment and UVC irradiation have the potential to significantly reduce transfusion-transmitted HCV infections.
Storage of thawed plasma for a liquid plasma bank: impact of temperature and methylene blue pathogen inactivation


*Transfusion* 2012; 52(3):529-536.

**BACKGROUND:** Rapid transfusion of fresh-frozen plasma (FFP) is desired for treating coagulopathies, but thawing and issuing of FFP takes more than 40 minutes. Liquid storage of plasma is a potential solution but uncertainties exist regarding clotting factor stability. We assessed different storage conditions of thawed FFP and plasma treated by methylene blue plus light (MB/light) for pathogen inactivation.

**STUDY DESIGN AND METHODS:** Fifty thawed apheresis plasma samples (approx. 750 mL) were divided into three subunits and either stored for 7 days at 4°C, at room temperature (RT), and at 4°C after MB/light treatment. Clotting factor activities (Factor [F] II, FV, FVII through FXIII, fibrinogen, antithrombin, von Willebrand factor antigen, Protein C and S) were assessed after thawing and on Days 3, 5, and 7. Changes were classified as “minor” (activities within the reference range) and “major” (activities outside the reference range).

**RESULTS:** FFP storage at 4°C revealed major changes for FVIII (median [range], 56% [33%-114%]) and Protein S (51% [20%-88%]). Changes were more pronounced when plasma was stored at RT (FVIII, 59% [37%-123%]; FVII, 69% [42%-125%]; Protein S, 20% [10%-35%]). MB/light treatment of thawed FFP resulted in minor changes. However, further storage for 7 days at 4°C revealed major decreases for FVIII (47% [12%-91%]) and Protein S (49% [18%-95%]) and increases for FVII (150% [48%-285%]) and FX (126% [62%-206%]).

**CONCLUSION:** Storage of liquid plasma at 4°C for 7 days is feasible for FFP as is MB/light treatment of thawed plasma. In contrast, storage of thawed plasma for 7 days at RT or after MB/light treatment at 4°C affects clotting factor stability substantially and is not recommended.
<table>
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<th>Year</th>
<th>Authors, title and references</th>
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Abstracts Scientific Publications 2012-2014

THERAFLEX UV-Platelets

2014
The efficacy of the ultraviolet C pathogen inactivation system in the reduction of *Babesia divergens* in pooled buffy coat platelets

Castro E, González LM, Rubio JM, Ramiro R, Gironés N, Montero E.

*Transfusion* 2014; doi: 10.1111/trf.12598

**BACKGROUND:** *Babesia* spp. is an intraerythrocytic parasite that causes human babesiosis and its transmission by transfusion has been extensively demonstrated. The aim of this study was to ascertain the efficacy of an ultraviolet C (UVC)-based pathogen inactivation system in the reduction of *Babesia divergens*-infected platelet (PLT) concentrates and to determine the parasite’s ability to survive in PLT concentrates stored under blood bank conditions.

**STUDY DESIGN AND METHODS:** This study was conducted using *in vitro* cultures of *B. divergens*. The detection limit of the culture assay was established and, subsequently, 15 buffy coat–derived PLT concentrates (BC-PCs) were inoculated with $10^7$ *B. divergens*-infected red blood cells. Infected BC-PCs were irradiated with 0.2 J/cm² UVC light using the THERAFLEX UV-Platelets method (Macopharma). Viability and parasite growth were evaluated before and after inactivation. Culture growth kinetics were monitored by DNA incorporation of $[^3H]$thymidine. The ability of *B. divergens* to survive in PLT concentrates was also analyzed.

**RESULTS:** The limit of detection in cultures was established at $0.1 \times 10^{-6}\%$ parasites. The THERAFLEX UV-Platelets system inactivated *B. divergens* to below the limit of detection in 12 of 15 BC-PCs (log reduction, >6.0) and to the limit of detection (log reduction, 5.0) in three of 15. It was also demonstrated that *B. divergens* remains viable in BC-PCs stored up to 7 days.

**CONCLUSION:** Since *B. divergens* can survive in PLT concentrates and given the performance of UVC, this system could be considered as an alternative to prevent *B. divergens* and other *Babesia* species from being transmitted through PLT transfusions.
Two pathogen reduction technologies-methylene blue plus light and shortwave ultraviolet light-effectively inactivate hepatitis

Steinmann E, Gravemann U, Friesland M, Doerrbecker J, Müller TH, Pietschmann T, Seltsam A.


BACKGROUND: Contamination of blood products with hepatitis C virus (HCV) can cause infections resulting in acute and chronic liver diseases. Pathogen reduction methods such as photodynamic treatment with methylene blue (MB) plus visible light as well as irradiation with shortwave ultraviolet (UVC) light were developed to inactivate viruses and other pathogens in plasma and platelet concentrates (PCs), respectively. So far, their inactivation capacities for HCV have only been tested in inactivation studies using model viruses for HCV. Recently, a HCV infection system for the propagation of infectious HCV in cell culture was developed. Contamination of blood products with hepatitis

STUDY DESIGN AND METHODS: Inactivation studies were performed with cell culture-derived HCV and bovine viral diarrhea virus (BVDV), a model for HCV. Plasma units or PCs were spiked with high titers of cell culture-grown viruses. After treatment of the blood units with MB plus light (Theraflex MB-Plasma system, MacoPharma) or UVC (Theraflex UV-Platelets system, MacoPharma), residual viral infectivity was assessed using sensitive cell culture systems.

RESULTS: HCV was sensitive to inactivation by both pathogen reduction procedures. HCV in plasma was efficiently inactivated by MB plus light below the detection limit already by 1/12 of the full light dose. HCV in PCs was inactivated by UVC irradiation with a reduction factor of more than 5 log. BVDV was less sensitive to the two pathogen reduction methods.

CONCLUSIONS: Functional assays with human HCV offer an efficient tool to directly assess the inactivation capacity of pathogen reduction procedures. Pathogen reduction technologies such as MB plus light treatment and UVC irradiation have the potential to significantly reduce transfusion-transmitted HCV infections.
Pathogen inactivation of platelets using ultraviolet C light: effect on in vitro function and recovery and survival of platelets


BACKGROUND: We evaluated the effect of treating platelets (PLTs) using ultraviolet (UV)C light without the addition of any photosensitizing chemicals on PLT function in vitro and PLT recovery and survival in an autologous radiolabeled volunteer study.

STUDY DESIGN AND METHODS: For in vitro studies, pooled or single buffy coat-derived PLT concentrates (PCs) were pooled and split to obtain identical PCs that were either treated with UVC or untreated (n = 6 each) and stored for 7 days. PLT recovery and survival were determined in a two-arm parallel autologous study in healthy volunteers performed according to BEST guidelines. UVC-treated or untreated PCs (n = 6 each) were stored for 5 days and were compared to fresh PLTs from the same donor.

RESULTS: There were no significant differences on Day 7 of storage between paired UVC-treated and control PC units for pH, adenosine triphosphate, lactate dehydrogenase, CD62P, CD63, PLT microparticles, and JC-1 binding, but annexin V binding, lactate accumulation, and expression of CD41/61 were significantly higher in treated units (p < 0.05). Compared with control units, the recovery and survival of UVC-treated PC were reduced after 5 days of storage (p < 0.05) and when expressed as a percentage of fresh values, survival was reduced by 20% (p = 0.005) and recovery by 17% (p = 0.088).

CONCLUSION: UVC-treated PLTs stored for 5 days showed marginal changes in PLT metabolism and activation in vitro and were associated with a degree of reduction in recovery and survival similar to other pathogen inactivation systems that are licensed and in use.
Characteristics of the THERAFLEX UV-Platelets pathogen inactivation system - An update

Seghatchian J, Tolksdorf F.


Considerable progress has been made in the last decade in producing purer, safer, leucocyte and plasma reduced platelet concentrates (PC) with an extended shelf life. The development of different pathogen inactivation technologies (PIT) has made a substantial contribution to this trend. Preceding platelet PIT (INTERCEPT Blood System/Cerus Corporation, Concord, CA, USA; MIRASOL/Caridian BCT, Lakewood, CO, USA) are based on adding a photosensitive compound to PC. The mixture is then activated by UV light in the UVB and/or UVA spectral regions. A novel procedure, THERAFLEX UV-Platelets (MacoPharma, Mouvaux, France), was recently developed that uses short-wave ultraviolet light (UVC), without addition of any photoactive agent. This technology has proven to be highly effective in sterilising bacteria (the major cause of morbidity/mortality after platelet transfusion) as well as inactivating other transfusion transmitted DNA/RNA containing pathogens and residual leucocytes. Any PIT reflects a balance between the efficacy of pathogen inactivation and preservation of platelet quality and function. A broad spectrum of in vitro tests have become available for the assessment of platelet storage lesion (PSL), aiming to better predict clinical outcome and untoward effects of platelet therapy. Recent paired studies on the release of platelet-derived cytokines, as new platelet performance indicators, revealed a parallel increase in both THERAFLEX UV-treated and control PC throughout storage, supporting the notion that the bioavailability of platelet function is not grossly affected by UVC treatment. This is corroborated by some newer technologies for proteomic analysis, showing that the THERAFLEX UV-Platelets system results in limited disruption of integrin-regulating extracellular disulfide bonds and minimal protein alterations when compared to UVB and gamma irradiation. Moreover, standard in vitro parameters reflecting activation, metabolic activity and function of platelets are useful indicators of the overall performance of processing and storage and may be used as surrogate markers of platelet quality in vivo. However, there is some doubt as to what degree each marker alone or in combination reflects the true clinical outcome of transfused platelets. Therefore, an appropriate clinical programme has been initiated. The preclinical
evaluation demonstrated tolerability and immunological safety of THERAFLEX UV-Platelets using an animal model. Additionally, the system has successfully completed two autologous Phase I trials on recovery and survival. Preliminary results suggest that the recovery and survival rates are consistent with other pathogen reduced platelet products that are licensed and in use. The method is currently under evaluation for safety and tolerability of UVC-treated platelets in healthy volunteers. Presently the THERAFLEX UV-Platelets system is the simplest and purest PIT easily adaptable to the existing blood bank setting. In the future, extension of the application range of the THERAFLEX UV-Platelets system is expected, in order to make this new technology compatible with a broad spectrum of collection and processing platforms, and with other blood products.
Evaluation of the tolerability and immunogenicity of ultraviolet C-irradiated autologous platelets in a dog model.


Transfusion 2012 Nov; 52(11):2414-26

BACKGROUND: The THERAFLEX ultraviolet (UV) platelets (PLTs) pathogen reduction system for PLT concentrates (PCs) operates using ultraviolet C (UVC) light at a wavelength of 254 nm. UVC treatment can potentially alter proteins, which may affect drug tolerance in humans and influence the immunogenicity of blood products. This preclinical study in beagle dogs was designed to evaluate the safety pharmacology of UVC-irradiated PCs after intravenous administration and to determine whether they are capable of eliciting humoral responses to PLTs and plasma proteins.

STUDY DESIGN AND METHODS: Six beagle dogs each were transfused once every other week for 10 weeks with UVC-irradiated or nonirradiated PCs. All PCs were autologous canine single-donor products prepared from whole blood. Safety pharmacology variables were regularly assessed. The impact of UVC irradiation on PLT and plasma proteomes was analyzed by one- and two-dimensional gel electrophoresis. Serum samples were tested for UVC-induced antibodies by Western blot and flow cytometry.

RESULTS: Dogs transfused with UVC-irradiated PCs showed no signs of local or systemic intolerance. Few but significant changes in PLT protein integrity were observed after UVC irradiation. Even after repeated administration of UVC-irradiated PCs, no antibodies against UVC-exposed plasma or PLT proteins were detected.

CONCLUSIONS: Repeated transfusions of autologous UVC-treated PCs were well tolerated in all dogs studied. UVC irradiation did not cause significant plasma or PLT protein modifications capable of inducing specific antibody responses in the dogs. High-resolution proteomics combined with antibody analysis introduces a comprehensive and sensitive method for screening of protein modifications and antibodies specific for pathogen reduction treatment.
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Parallel comparison of apheresis-collected platelet concentrates stored in four different additive solutions


BACKGROUND AND OBJECTIVES: Partially replacing plasma with additive solutions in platelet (PLT) concentrates (PCs) may help to reduce transfusion reactions. Constituents of PLT additive solutions (PASs) have been revealed to affect the quality of PCs. Previous studies involved pairwise comparison of identical PLTs with two different PASs or multicomparison using random PLTs with three or more PASs. In this study, we performed parallel comparison using PCs from identical donors with four PASs. In addition to traditional parameters, the release of bioactive substances and plasma proteins was assessed.

MATERIALS AND METHODS: Platelets collected four times by apheresis from three donors were suspended in Intersol, SSP+, Composol or M-sol with 35% autologous plasma. The PC parameters, including PLT activation markers, glucose consumption, chemokines and plasma proteins, were assessed during 5-day storage.

RESULTS: Mean PLT volumes were decreased in SSP+, Composol and M-sol after 5-day storage, with significant differences, whereas the hypertonic shock response (HSR) was decreased only in Intersol. Glucose consumption was faster in Intersol and M-sol than in SSP+ or Composol. PLT activation, determined as CD62P, sCD62P, sCD40L and RANTES, was significantly higher in Intersol than the other three PASs. No marked change was observed in fibrinopeptide A and C3a in any PASs.

CONCLUSIONS: M-sol, SSP+ and Composol effectively preserved the quality of PCs. PLT activation was significantly enhanced in Intersol compared with the other three PASs. These effects seem to depend on magnesium and potassium as a constituent. Parallel comparison further verified that the PC quality largely depended on PASs but not donors.
Current status of additive solutions for platelets

Alhumaidan H, Sweeney J.

The storage of platelets in additive solution (PAS) had lagged behind red cell concentrates, especially in North America. The partial or complete removal of anticoagulated plasma and storage of platelet concentrates in AS presents many advantages. The PAS can be formulated to optimize aerobic metabolism or decrease platelet activation, thus abrogating the platelet storage lesion and potentially improving in vivo viability. Plasma removal has been shown to reduce allergic reactions and the plasma harvested could contribute to the available plasma pool for transfusion or fractionation. PAS coupled to pathogen reduction technology results in a platelet product of equivalent hemostatic efficacy to conventionally stored platelets. Given the above, the likely future direction of platelet storage will be in new generation designer PAS with an extended shelf life and a superior safety profile to plasma stored platelets.
In vitro properties of platelets stored in three different additive solutions

Tynngård N, Trinks M, Berlin G.

Transfusion. 2012 May;52(5):1003-9

BACKGROUND: New platelet (PLT) additive solutions (PASs) contain compounds that might improve the storage conditions for PLTs. This study compares the in vitro function, including hemostatic properties (clot formation and elasticity), of PLTs in T-Sol, Composol, or SSP+ during storage for 5 days.

STUDY DESIGN AND METHODS: Fifteen buffy coats were pooled and divided into three parts. PLT concentrates (PCs) with 30% plasma and 70% PAS (T-Sol, Composol, or SSP+) were prepared (n = 10). Swirling, PLT count, blood gases, metabolic variables, PLT activation markers, and coagulation by free oscillation rheometry (FOR) were analyzed on Days 1 and 5.

RESULTS: Swirling was well preserved and pH acceptable (6.4-7.4) during storage for all PASs. Storage of PLTs in T-Sol led to a decrease in PLT count whereas the number of PLTs was unchanged in Composol or SSP+ PCs. PLTs in T-Sol showed higher glucose metabolism than PLTs in Composol or in SSP+. At the end of storage PLTs in T-Sol had higher spontaneous activation and lower ability to respond to an agonist than PLTs in Composol or SSP+. PLTs in all the PASs had a similar ability to promote clot formation and clot elasticity.

CONCLUSION: Storage of PLTs in Composol or in SSP+ improved the quality of PCs in terms of better maintained PLT count, lower glucose metabolism, lower spontaneous activation, and improved response to a PLT agonist compared to PLTs in T-Sol. PLTs stored in the various PASs had similar hemostatic properties. These findings make Composol and SSP+ interesting alternatives as PASs.
Evaluation of the automated collection and extended storage of apheresis platelets in additive solution

Johnson L, Winter KM, Hartkopf-Theis T, Reid S, Kwok M, Marks DC.

Transfusion. 2012 Mar;52(3):503-9

BACKGROUND: Collecting apheresis platelets (PLTs) into additive solution has many potential benefits. The new Trima software (Version 6.0, CaridianBCT) allows automated addition of PLT additive solution (PAS) after collection, compared to Trima Version 5.1, which only collects PLTs into plasma. The aim of this study was to compare PLT quality during extended storage, after collection with the different Trima systems.

STUDY DESIGN AND METHODS: Apheresis PLTs were collected using both Trima Accel apheresis systems. The test PLT units (n = 12) were collected using the new Trima Version 6.0 into PLT AS (PAS-IIIM), while the control units (n = 8) were collected into autologous plasma using Trima Version 5.1. All units were stored for 9 days, and in vitro cell quality variables were evaluated during this time.

RESULTS: PLTs collected in PAS-IIIM maintained a stable pH between 7.2 and 7.4, whereas plasma-stored apheresis units exhibited significantly increased acidity during storage, due to lactate accumulation and bicarbonate exhaustion. Plasma-stored PLTs also demonstrated a more rapid consumption of glucose. However, there was little difference in PLT activation or cytokine secretion between PAS-IIIM and control PLTs.

CONCLUSION: These data indicate that apheresis PLT concentrates collected in PAS-IIIM, using Trima Version 6.0 software, maintained acceptable PLT metabolic and cellular characteristics until Day 9 of storage.
Effect of platelet additive solution on bacterial dynamics and their influence on platelet quality in stored platelet concentrates

Greco CA, Zhang JG, Kalab M, Yi QL, Ramirez-Arcos SM, Gyongyossy-Issa MI.

Transfusion. 2010 Nov;50(11):2344-52

BACKGROUND: Platelet additive solutions (PASs) are an alternative to plasma for the storage of platelet concentrates (PCs). However, little is known about the effect of PAS on the growth dynamics of contaminant bacteria. Conversely, there have been no studies on the influence of bacteria on platelet (PLT) quality indicators when suspended in PAS.

STUDY DESIGN AND METHODS: Eight buffy coats were pooled, split, and processed into PCs suspended in either plasma or PAS (SSP+, MacoPharma). PCs were inoculated with 10 and 100 colony-forming units (CFUs)/bag of either Serratia liquefaciens or Staphylococcus epidermidis. Bacterial growth was measured over 5 days by colony counts and bacterial biofilm formation was assayed by scanning electron microscopy and crystal violet staining. Concurrently, PLT markers were measured by an assay panel and flow cytometry.

RESULTS: S. liquefaciens exhibited an apparent slower doubling time in plasma-suspended PCs (plasma-PCs). Biofilm formation by S. liquefaciens and S. epidermidis was significantly greater in PCs stored in plasma than in PAS. Although S. liquefaciens altered several PLT quality markers by Days 3 to 4 postinoculation in both PAS- and plasma-PCs, S. epidermidis contamination did not produce measurable PLT changes.

CONCLUSIONS: S. liquefaciens can be detected more quickly in PAS-suspended PCs (PAS-PCs) than in plasma-PCs by colony counting. Furthermore, reduced biofilm formation by S. liquefaciens and S. epidermidis during storage in PAS-PCs increases bacteria availability for sampling detection. Culture-based detection remains the earliest indicator of bacterial presence in PAS-PCs, while changes of PLT quality can herald S. liquefaciens contamination when in excess of 10(8) CFUs/mL.
The new generation of platelet additive solution for storage at 22 degrees C: development and current experience

Ringwald J, Zimmermann R, Eckstein R.


The storage of platelets (PLTs) in PLT additive solutions (PASs) might have several advantages. It can reduce allergic and febrile transfusion reactions, facilitate AB0-incompatible PLT transfusions, enable pathogen inactivation, and make more plasma available for other purposes (eg, for fractionation). For this reason, there has been considerable focus on the development of new PASs that assure maintenance of good PLT quality throughout storage. Several compounds in PASs such as citrate, acetate, phosphate, potassium, and magnesium have all turned out to be important, and the same applies to the necessary amount of glucose as determined by the plasma carryover. The latest generation of PASs, the modified PAS-III and Composol-PS, contains most or all of those compounds. Recently published data on the in vitro quality of either buffy coat- or apheresis-derived PLT concentrates stored in 70% or even 80% of PAS might encourage transfusion specialists to consider using these PASs in routine blood banking. However, because in vitro tests do not adequately predict clinical effectiveness of PLTs after transfusion, in vivo studies are still needed to assess the quality of PAS-stored PLTs.
Storage of platelets in additive solutions: a multicentre study of the in vitro effects of potassium and magnesium


BACKGROUND AND OBJECTIVES: In a preliminary study, the presence of potassium and magnesium in a modified synthetic medium (PAS-III) was found to have a significant influence on platelet metabolism (using apheresis-derived, as well as buffy-coat-derived platelets) when compared with standard PAS-III. The differences included reduced glycolysis, as evidenced by lower consumption of glucose and lower production of lactate, but also better preservation of pH and hypotonic shock response reactivity. The results suggested that storage in modified PAS-III containing 20% plasma was comparable to storage in standard PAS-III containing 30% plasma. To confirm the preliminary results and to evaluate the effects of different preparation protocols, an international multicentre study, which included 11 different sites, was conducted.

MATERIALS AND METHODS: Platelets from 30 pools of approximately 20 buffy coat (BC) units each and 24 pooled apheresis platelet units were aliquoted for storage in plasma (reference) or synthetic medium using either a specific additive solution (PAS-III) containing 30% plasma or a modification of PAS-III containing 5.0 mm potassium and 1.5 mm magnesium (PAS-IIIM) and either 30% or 20% plasma. Units were stored at room temperature with agitation for 7 days during which in vitro testing was carried out for biochemical, haematological and functional parameters.

RESULTS: Storage of platelets in PAS-IIIM resulted in a reduction in the rate of glycolysis and better retention of pH and hypotonic shock response reactivity. Storage in PAS-IIIM containing 20% plasma appeared to result in the retention of in vitro properties, similar to those observed during storage in standard PAS-III containing 30% plasma.

CONCLUSIONS: The results of this study confirm the preliminary results. Similar results were seen with platelets prepared by BC and apheresis methods, despite differences in equipment, the preparation technique and in the final platelet contents achieved in the platelet units. Storage of platelets in PAS-IIIM should be considered to improve platelet function and allow plasma reduction to 20%.
Reactions and platelet increments after transfusion of platelet concentrates in plasma or an additive solution: a prospective, randomized study

de Wildt-Eggen J, Nauta S, Schrijver JG, van Marwijk Kooy M, Bins M, van Prooijen HC.


BACKGROUND: Reactions after platelet transfusions are rather common and frequently are caused by plasma constituents. In recent developments, the preparation and storage of platelet concentrates (PCs) in a platelet additive solution (PAS-2) have been shown to result in acceptable storage conditions. A major drawback of the use of these PCs is the progressive increase of P-selectin-positive platelets during storage. The clinical benefit of transfusions of PCs in PAS-2 was studied.

STUDY DESIGN AND METHODS: PCs prepared from buffy coats were suspended in either plasma or PAS-2 and stored for up to 5 days. Clinical responses were evaluated in a prospective study in 21 patients treated with intensive chemotherapy for hematologic malignancies. Eligible patients were randomly assigned to receive prophylactic transfusions of PCs prepared in either plasma or PAS-2. Reactions and CCIs were recorded after each transfusion.

RESULTS: The incidence of reactions in 12 patients given PCs in plasma (n = 192) was 12 percent. Transfusions to 9 patients of PCs in PAS-2 (n = 132) showed a reduction in the incidence of reactions to 5.3 percent (p<0.05). The average 1-hour and 20-hour CCIs after transfusion of PCs in plasma were 20.7 +/- 8.5 and 11.5 +/- 8.0, respectively. CCIs after transfusion of PCs in PAS-2 were significantly lower: the average 1-hour CCI was 17.1 +/- 6.6 (p<0.001) and the average 20-hour CCI was 9.5 +/- 7.0 (p<0.05). Storage conditions of PCs were optimal: in each group, average 1-hour CCIs of both fresh and stored PCs were similar. The 20-hour CCIs after the transfusion of fresh and stored PCs in PAS-2 also were similar.

CONCLUSION: Transfusion of PCs in PAS-2 significantly reduces the incidence of reactions. The 1-hour and 20-hour CCIs after transfusion of PCs in PAS-2 were significantly lower than the CCIs after transfusion of PCs in plasma. Because storage conditions of both PCs were found to be optimal, the decrease in CCIs after transfusion of PCs prepared in PAS-2 may be caused by rapid elimination of a subpopulation of P-selectin-positive platelets from the circulation.
Blood Safety
Scientific Publications

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2014
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<td>2013</td>
<td>Elebute MO, Choo L, Mora A, MacRury C, Llewelyn C, Purohit S, Hicks V, Casey C, Malfroy M, Deary A, Reed T, Meredith S, Manson L, Williamson LM. <em>Transfusion of prion-filtered red cells does not increase the rate of alloimmunization or transfusion reactions in patients: results of the UK trial of prion-filtered versus standard red cells in surgical patients (PRISM A).</em> Br J Haematol 2013;160(5):701-8.</td>
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Blood Safety
Abstracts Scientific Publications 2013
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Removal of exogenous prion infectivity in leukoreduced red blood cells unit by a specific filter designed for human transfusion.

Lescoutra-Etchegaray N, Sumian C, Culeux A, Durand V, Gurgel PV, Deslys JP, Comoy EE. 


BACKGROUND: Five cases of variant Creutzfeldt-Jakob disease (vCJD) infections were attributed to infusion of contaminated blood components, turning to real the interhuman transmissibility of this prion disease from asymptomatic carriers. Preventive policies rely on exclusion from blood donation and benefit of leukoreduction initially implemented against leukotropic viruses. In the absence of available antemortem diagnostic tests, the updated prevalence of silent vCJD infections (1/2000 in the United Kingdom) urges the necessity to enforce blood safety with more efficient active measures able to remove the remaining infectivity.

STUDY DESIGN AND METHODS: Several affinity resins were demonstrated to reduce high levels of brain-spiked infectivity from human leukoreduced red blood cells (L-RBCs). One was integrated in a device adapted to field constraints (volumes, duration) of human transfusion. We assessed here the ability of the resulting removal filter, termed P-Capt, to remove infectivity from human L-RBC units spiked with scrapie-infected hamster brain (≥10,000 infectious units/mL), through inoculation of hamsters with pre- and post-blood filtration samples.

RESULTS: Incubation periods of recipient animals suggest around a 3-log removal of brain-derived prion infectivity by filtration through the P-Capt.

CONCLUSION: On brain-derived spiked infectivity, the P-Capt filter provided a performance similar to the resin packed in columns used for initial proof-of-concept studies, suggesting an appropriate scale-up to efficiently remove infectivity from an individual human blood bag. According to the ability of resin to completely remove apparent endogenous infectivity from hamster leukoreduced blood, the implementation of such a filter, now commercially available, might seriously improve blood safety toward prions.
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<td>THERAFLEX MB-Plasma, THERAFLEX UV-Platelets, SSP+ &amp; P-CAPT</td>
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