INTRODUCTION
Factor XIII (FXIII) protransglutaminase circulates in plasma as Aβ₂ tetramer, the A subunit being the functional form. When activated by thrombin and calcium to FXIIa, it acts in the last step of the coagulation cascade and contributes to Fibrin crosslinking and clot stiffness. Measurement of FXIII is of high usefulness in many contexts (congenital or acquired FXIII deficiencies, low FXIII with bleeding complications in trauma or surgery, FXIII autoantibodies, monitoring FXIII substitutive therapy…). BIOPHEN™ Factor XIII is a new automated chromogenic assay for the rapid testing of FXIII concentration in citrated human plasma, measured through FXIIla transglutaminase activity, and usable on any analyzer with 340nm wavelength.

AIM
The aim of this study is to evaluate performances of the new chromogenic FXIII assay adapted on CS coagulation analyzers and to compare tests results with those obtained with the reference method.

RESULTS
The test showed good performance characteristics with low intra-assay coefficients of variation (2.7% to 4.9%) and inter-assay coefficients of variation (1.5% to 1.9%) on CS-series (Table 1).

<table>
<thead>
<tr>
<th>Mean (FXIII %)</th>
<th>CV% intra-series</th>
<th>CV% inter-series</th>
</tr>
</thead>
<tbody>
<tr>
<td>QC1</td>
<td>102</td>
<td>2.7%</td>
</tr>
<tr>
<td>QC2</td>
<td>29</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

Table 1: Performance of BIOPHEN™ Factor XIII on CS-5100 using lyophilized control plasmas, intra-series (n=40) and inter-series (n=30, 10 runs, 5 days).

Using a calibration curve from 0 to 150%, the dynamic range is from 5 to 300% with automated redilution (Figure 1) with a very good recovery at very low FXIII levels (0 to 10%).

Figure 1: Linear regression analysis for Factor XIII following preparation of dilution series with spiked plasmas. Linearity for the BIOPHEN™ Factor XIII reagent (A). Linearity of low range (B).

Specificity is verified with FXIII deficient plasma (<0.1%) and reference interval in normal plasmas is from 60 to 146% (n=120). Interference study is performed using 2 levels of controls (Table 2).

<table>
<thead>
<tr>
<th>Hemoglobin</th>
<th>Bilirubin</th>
<th>Intralipids</th>
<th>Heparin*</th>
<th>DOACs**</th>
<th>Fibrinogen</th>
<th>Ammonium</th>
</tr>
</thead>
<tbody>
<tr>
<td>No interference up to 250 mg/dL</td>
<td>60 mg/dL</td>
<td>250 mg/dL</td>
<td>2 µL/mL</td>
<td>400 ng/mL</td>
<td>6 g/L</td>
<td>0.5mM</td>
</tr>
</tbody>
</table>

Table 2: Interferences in BIOPHEN™ Factor XIII on CS-series using spiked lyophilized plasmas. “Heparins tested are UFH and LMWH, ** DOACs tested are Dabigatran, Rivaroxaban, Apixaban and Edoxaban.

Extended stability is measured: 5 days on board, 1 week at 2–8°C, 48 hours at room temperature and 2 months frozen.

Good correlation with predicate devices on CS-2500 (r=0.989, p < 0.001), and between analyzers (r = 0.997, p < 0.0001). Very low concentrations are correctly measured (Figure 2).

Figure 2: Correlation results of relevant samples assessed in this study and shown by regression analysis, Bland and Altman difference plot and Compare Pairs (deficient plasmas), using reference method or analyzer. (A) Correlation and (B) Bland and Altman difference plot of BIOPHEN™ Factor XIII and Berichrom FXIII (n = 102), (C) Compare Pairs using 10 individuals deficient plasmas (FXIII < 5%), (D) Correlation of BIOPHEN™ Factor XIII on CS-2500 and CS-5100 (n = 98). Statistical significance was defined by a hypothesis test yielding a P-value of less than 0.05.

Analysis done by Bland and Altman difference plot showed good agreement between both reagents. A slight measurement difference, especially in low and very low range measurement, is observed (Figure 2B and 2C). This difference may be due to the higher blank value and higher LOQ value of the reference reagent.

CONCLUSIONS
BIOPHEN Factor XIII is a simple, automated (usable on all analyzers with 340nm wavelength), highly stable, and reliable method for measurement of FXIII activity in citrated human plasma. It is accurate and precise, with low CVs, well correlated to existing methods, and offers an extended dynamic range, with high on-board stability.

REFERENCES

ACKNOWLEDGEMENTS
J. PATHMANATHAN, HYPHEN BioMed, Neuville-sur-Oise, France.