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EMICIZUMAB CARRY OVER IN ANALYSIS OF ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT)

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None of the authors has any conflicts of interest to disclose.

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Background

Emicizumab (Hemlibra ®) is a procoagulant antibody used for treatment of Hemophilia A. In September of 2020, clinical laboratories received a field safety notice regarding the potential risk of sample contamination from patient samples containing Emicizumab in automated assays based on the Activated Partial Thromboplastin Time (APTT) on the Sysmex CS- and CA- coagulation analyzers. Emicizumab carry-over has previously been described in the Diagnostica Stago coagulation analyzers.
The aim was to evaluate the magnitude of the shortened APTT caused by carry over of Emicizumab between patient samples.

Methods

Eleven anonymized samples with APTT 40–110s were analyzed using the Dade Actin FS APTT-reagent (Siemens) using the Sysmex® CS-5100 (Sysmex). The assay has a reference range of 20s–30s, and a CV% ≤1,5 at levels 25s and 60s. Samples were analyzed before and after analysis of six anonymized samples with known concentrations of Emicizumab (13-80 µg/mL).
All samples were frozen at -70° C and were thawed for 5 minutes in a 37° water bath. After the complete series an additional rinse probe was performed and a last APTT was measured to control for sample drift, due to coagulation factor consumption. Three samples were excluded because they had changed > 11%.

Results

Results of analysis are presented in table 1. Shortened APTT was compared to pre-APTT for the first four rows and compared to post-APTT for the last two rows, to correct for sample drift.

Conclusions

The sample contamination from Emicizumab only affected samples with very prolonged APTT. Although unfortunate, we concluded that the clinical effects are acceptable. In the routine workflow, samples from patients with Emicizumab cannot be identified and isolated. The option of introducing an additional probe rinse after every sample analyzed on the automated coagulation analyzers was declined. The potential for sample contamination was communicated to the coagulation specialists.

				APTT (s)				
APTT pre Emicizumab	**40 s**	**48 s**	**57 s**	**68 s**	**70 s**	**72 s**	**89 s**	**110 s**
Δ post 13 µg/mL Emi	-1	-1	0	0	1	-1	2	-3
Δ post 24 µg/mL Emi	0	-2	1	1	0	-1	4	-6
Δ post 40 µg/mL Emi	-1	-2	0	1	1	-1	3	-6
Δ post 49 µg/mL Emi	-1	-4	0	0	1	-2	3	-8
Δ post 66 µg/mL Emi	0	-1	0	0	-1	1	-6	-16
Δ post 80 µg/mL Emi	0	-1	0	2	0	1	-5	-18
APTT post rinse	**38 s**	**45 s**	**57 s**	**67 s**	**72 s**	**69 s**	**99 s**	**119 s**

Table 1. Decrease (-Δ) in APTT after sample contamination from samples with Emizicumab.