ECAT survey results for low levels of Factor VIII

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A correct diagnosis of factor VIII deficiency and the assessment of the severity of haemophilia are essential for a patient-tailored treatment strategy. The bleeding risk in haemophilia patients is increasing with decreasing factor VIII levels and becomes threatening at factor VIII activity levels ≤1.0%. Therefore it is very important to use a factor VIII assay with a high accuracy at very low levels of factor VIII activity.
During the last six years (since 2008) the ECAT foundation distributed 4 samples with an assigned factor VIII between 0% and 2.0%. The mean factor VIII activity with different APTT reagents and one chromogenic assay are summarized in table 1. Only reagents which are used by at least 5 participants have been included.

Table 1.

	Survey #:	**2012-3**	**2011-3**	**2010-4**	**2010-2**
	Type of sample:	Severe Hemophilia A patient	Patient with FVIII <2%	Patient with FVIII <1%	Sample with FVIII <2%
1	Haemosil APTT-SP liq sil (IL)	1	0.5	0.8	0.8
2	Haemosil Synthasil (IL)	0	0.7	1.3	1.2
3	ACTIN FS (Siemens)	1	1.8	1	1.1
4	Actin FSL (Siemens)	1	1	1. 1	0.8
5	Pathromtin SL (Siemens)	0	0.8	0.7	0.6
6	PTT Automate (Stago-Roche)	1	1	1.1	1
7	Cephalin/Kaolin (Stago-Roche)	1	1.2	0.9	1.1
8	Cephascreen (Stago-Roche)	1	1	-	-
9	Tcoag TriniClot APTT-HS	1	1	-	-
10	Chromogenic Substrate Coamatic	0	0.4	-	-

The mean results of the different samples vary in the different one-stage assays from less than 1% (lowest value 0%) to more than 1% (highest value 1.8%). The results of two reagents (Haemosil APTT-SP liq sil® and Pathromtin SL®) were ≤ 1% in all four samples and the results of one reagent (Actin FS) was ≥ 1% in all samples. The results correlate with those described in a manuscript published by our group in 2008 (*Verbruggen et al,* Haemophilia (2008), 14 (Suppl. 3), 76–82).

However, unfortunately, the genotypes of the subjects and/or FVIII antigen concentrations of the survey samples are not known. This renders it difficult to establish the nominal values of the samples and therefore conclusions on the accuracy of the different reagents cannot be drawn.

Conclusion: The assay of very low factor VIII activities measured with one-stage assays in samples of severe and/or moderate hemophilia A patients show variations which do not meet clinical requirements. The nominal value of the samples which are used for external surveys need improved characterization.