

# ECAT Survey Results for Low Levels of Factor VIII and IX

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# What is the Significance of External Surveys in Coagulation Factor Assessment?

It may give your answers to the following questions:

- **Are the results of my laboratory comparable to other laboratories?**  
Although the assigned values are not the nominal values, your results may give an indication of the accuracy of your results.
- **Are the results of my laboratory consistent from one survey to the other and are there trends in the results?**  
It may not always be easy to detect trends in internal quality controls.
- **Is the method that is used in the laboratory the best method for the purpose of the laboratory?**  
Dividing results in different groups facilitates method comparison.



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External quality Control of diagnostic Assays and Tests  
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9th Participants meeting 2014

# Treatment strategy of Haemophilia patients: Prophylactic treatment

Treatment strategy of patients is very much dependent on the native factor VIII of a person with haemophilia:

- Persons with severe haemophilia (<1% factor VIII) need to be treated prophylactically in order to prevent spontaneous joint bleedings.
- Persons with moderate or mild haemophilia generally do not need prophylactic treatment as at least 1% factor VIII is needed to prevent spontaneous bleeding under normal circumstances.



# Treatment strategy of Haemophilia patients: Prophylactic treatment

Treatment strategy of patients is very much dependent on the native factor VIII of a person with haemophilia:

- Persons with severe haemophilia ( $<1\%$  factor VIII) need to be treated prophylactically in order to prevent joint bleedings.
- Persons with moderate or mild haemophilia generally do not need prophylactic treatment as at least  $1\%$  factor VIII is needed to prevent spontaneous bleeding under normal circumstances.



**The  $1\%$  limit of native factor VIII activity is crucial in the decision concerning prophylactic treatment of haemophilia A patients.**



# Treatment strategy of Haemophilia patients during bleedings: Target values of Factor VIII levels during treatment of bleedings in Haemophilia Patients\*

Severity of bleeding	Initial FVIII target plasma level	Lowest FVIII target during intermittent treatment	Target FVIII activity during continuous application		
Light#	30%	n.a.	n.a.		
Severe	50%	>25%	>40%		
Life threatening	100%	>50%	>80%		

# light bleedings in mild haemophilia are treated with DDAVP

\*Dutch Guidelines for Diagnosis and Treatment of Haemophilia and Additional Hemostasis Abnormalities (2009)



## The accuracy of Factor VIII assay may be important at different levels in different clinical situations!

- Around 1% with respect to decision concerning prophylactic treatment.
- Around 10% concerning the choice of treatment: DDAVP versus FVIII concentrate in mild hemophiliacs.
- Around 30% with respect to the lowest acceptable level during treatment of severe bleedings and as desirable lowest level in DDAVP treatment.
- Around 50% with respect to the lowest acceptable level during treatment of life threatening bleedings.
- Around 100% with respect to the desirable initial level during treatment of life threatening bleedings



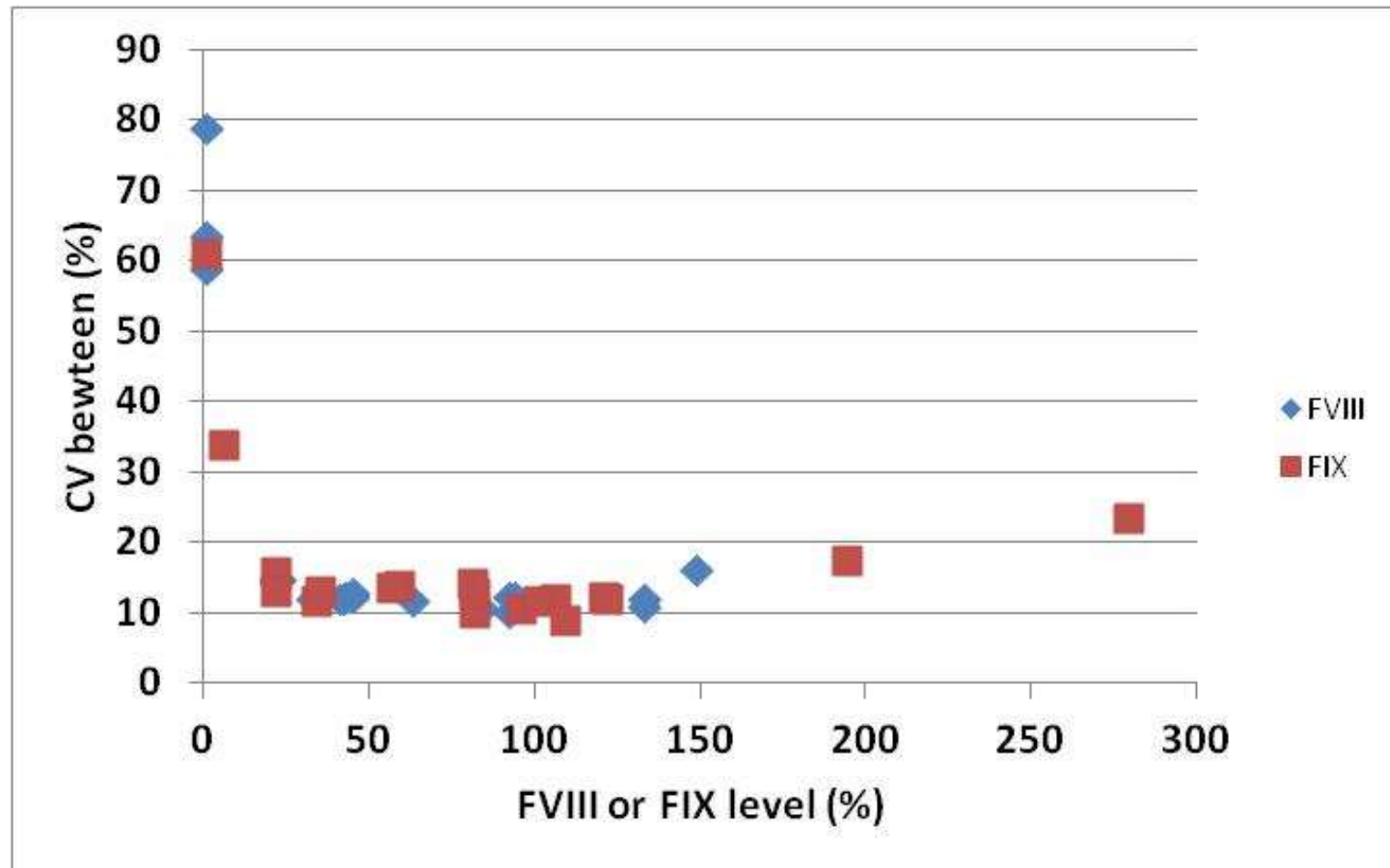
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- Around 50% with respect to the lowest acceptable level during treatment of life threatening bleedings.
- Around 100% with respect to the desirable initial level during treatment of life threatening bleedings

 **Do ECAT results indicate sufficient precision at these factor VIII levels?**



# Coefficient of variation of factor VIII/IX results in ECAT surveys





# Severe Haemophilia A

N = 201

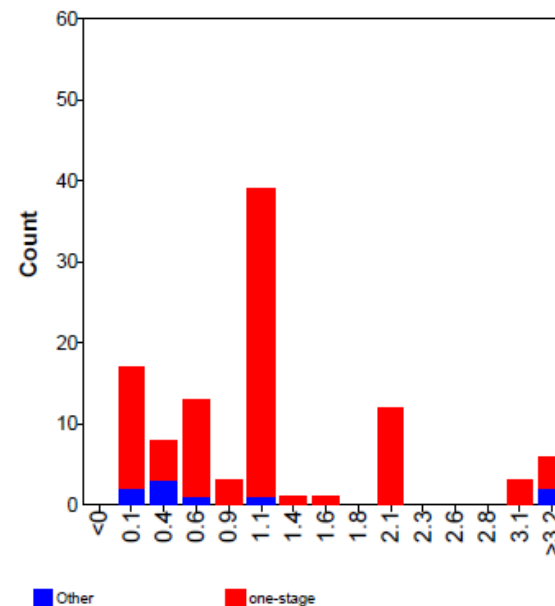
98x < [value] : 16 x < [0.1 – 0.9]  
69 x < 1  
13 x < [2 – 12] (13%)

103 numerical results

Robust mean : 0.95%  
Median : 1.00%  
SD : 0.75%  
Range : 0 – 41%

Result > 1% : 22 (21%)

Overall: 17% reported a result > 1% FVIII



# Variation in samples with FVIII around 1%

## Possible causes of high variation

- **Quality of deficient plasma, reagent, pre-dilution**
- **Residual factor VIII activity in factor VIII deficient plasma\***
- **Presence of lupus inhibitors**
- **Presence of pre-activated factor to be assayed**
- **Influence of high factor XI activity**
- **Role of type of APTT reagent**

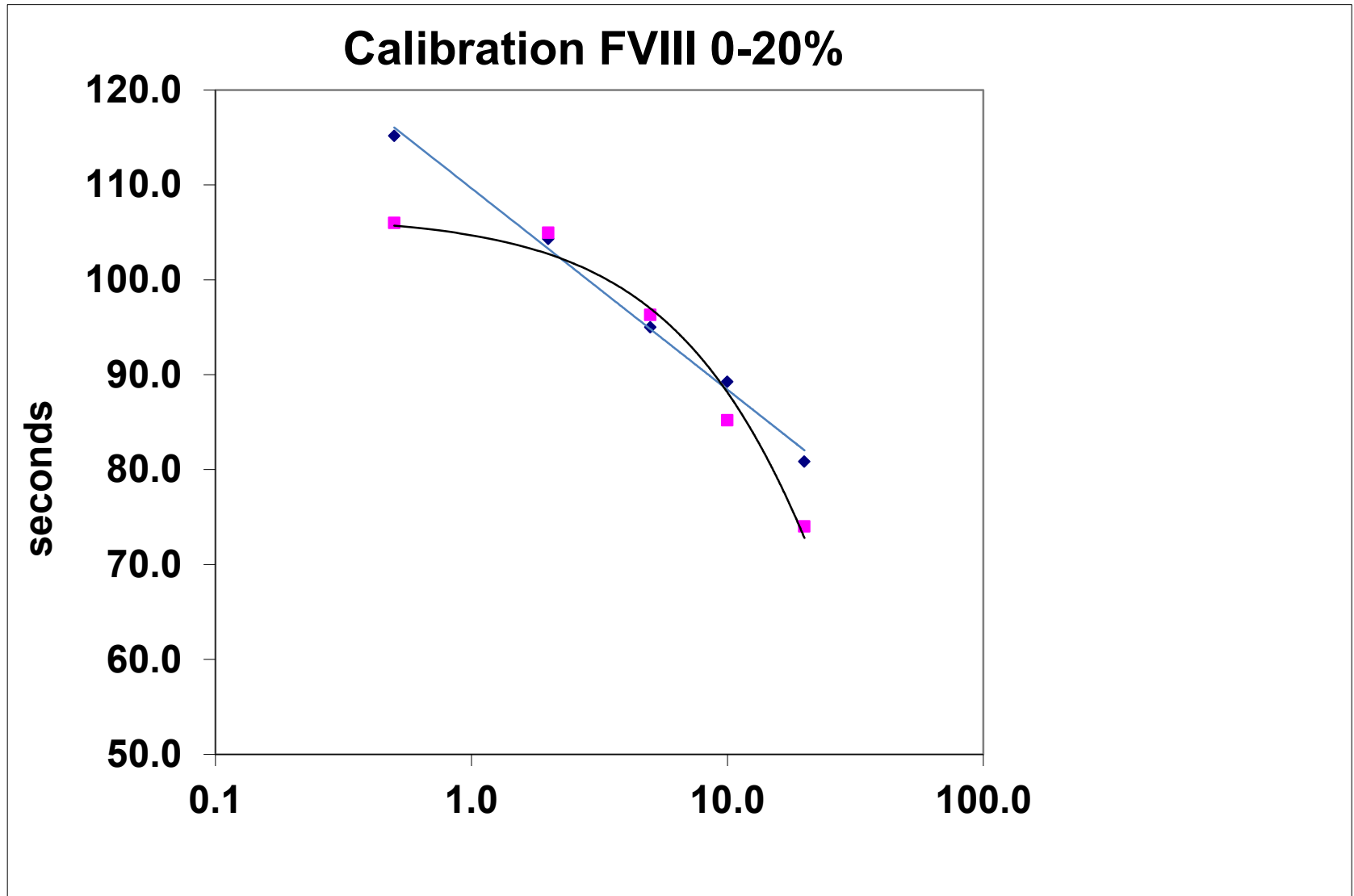


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# Quality of Factor VIII Deficient Plasma



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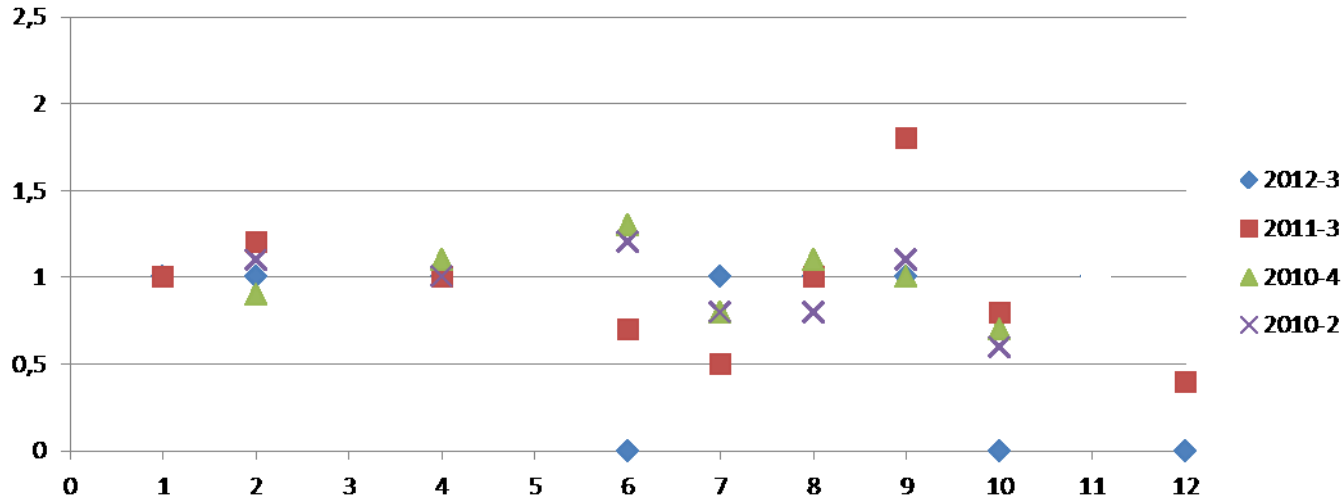
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# Variation in samples with FVIII around 1%

(Mean of at least 5 participants)

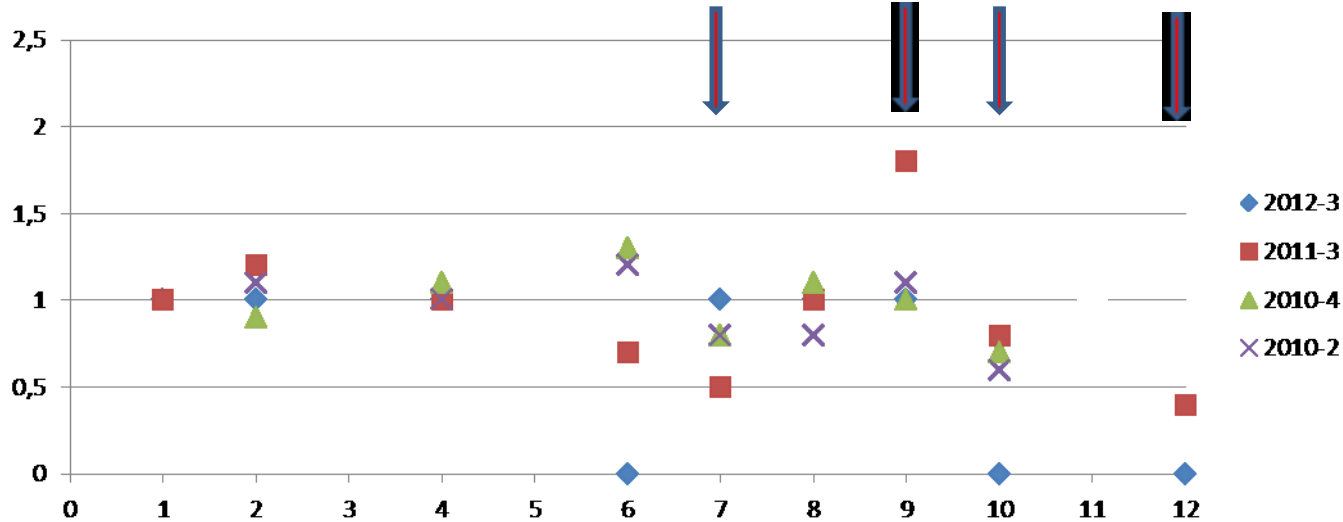


1	STA Cephascreen (Stago)
2	STA APTT Kaolin(Stago)
3	PTT-LA (Stago)
4	PTT a (Stago)
5	PTT Reagent (Stago)
6	Synthasil (HemosIL) (IL)
7	APTT-SP (HemosIL) (IL)
8	Actin® FSL (Siemens)
9	Actin® FS (Siemens)
10	Pathromtin SL (Siemens)
11	Platelin® LS (Biomerieux)
12	Coamatic



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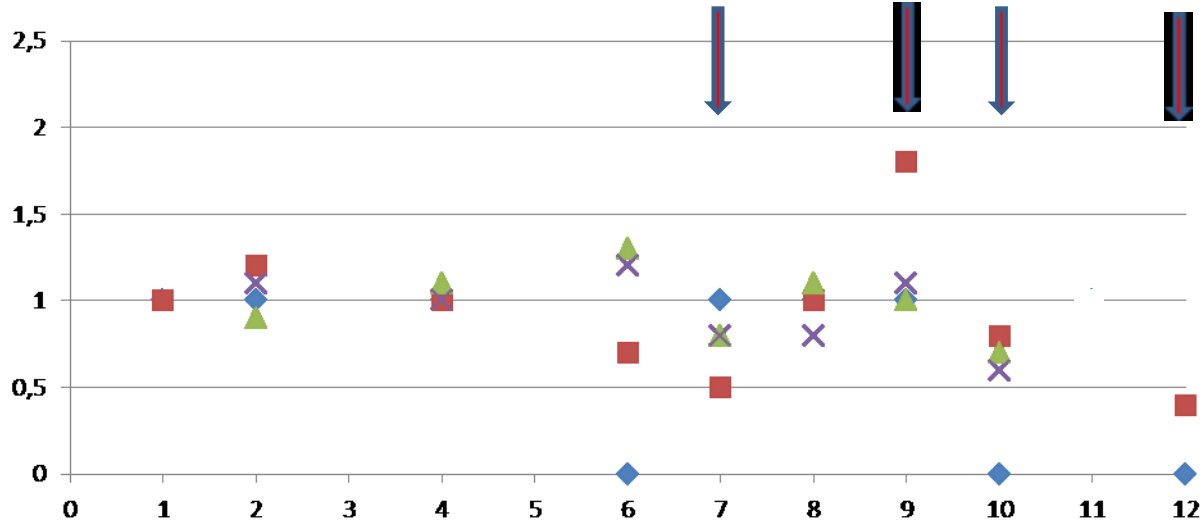
(Mean of at least 5 participants)



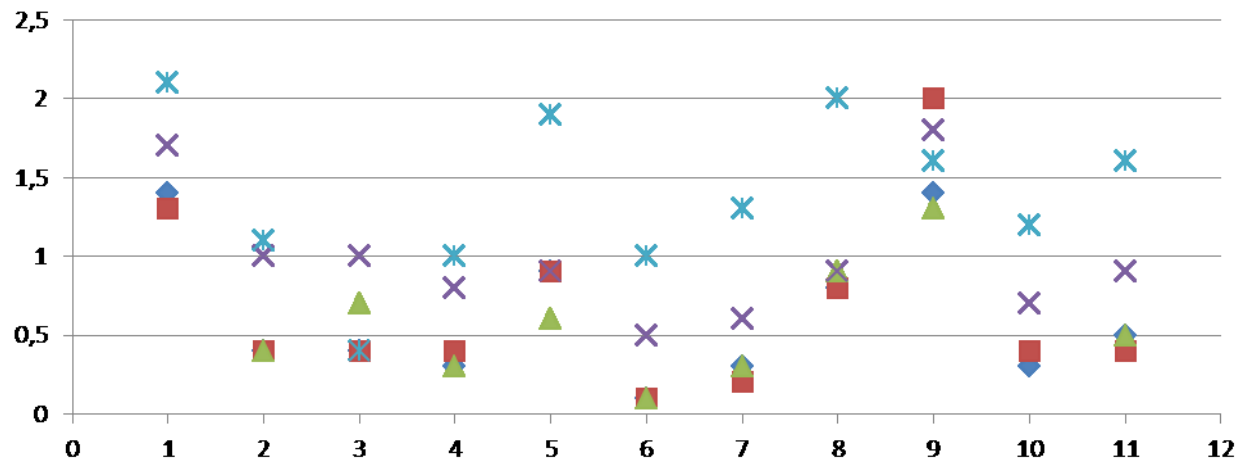
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Haemophilia (2008), 14 (Suppl. 3), 76–82



## Conclusions

- **The ability to detect Factor VIII levels  $<1\%$  is (among other factors) also reagent dependent.**
- **The Coefficient of Variation within a reagent group is general also rather high probably because of other factors which influence the activity.**
- **Consider the use of Chromogenic methods for the diagnosis of severe haemophilia.**

