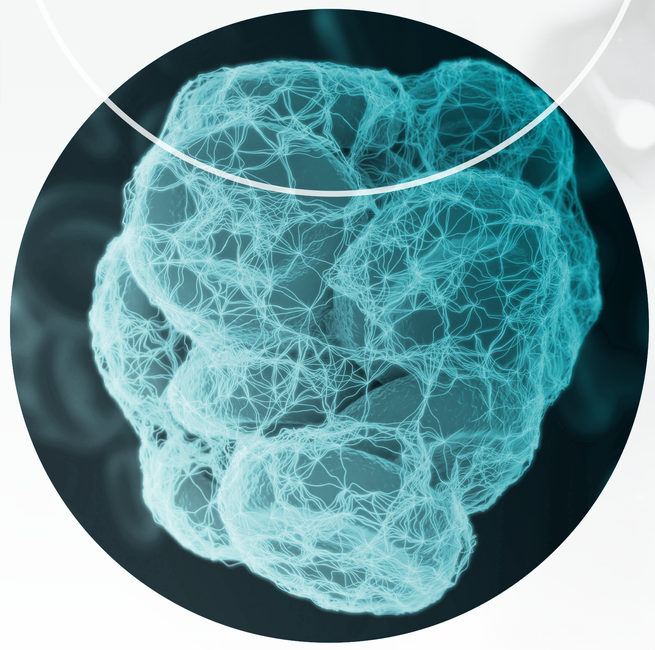
Performance of factor VIII extended half-life product measurement – a global external quality assurance program study



Elysse Dean[1], Anna Williams[2] and Piet Meijer[3]

1 RCPAQAP, Sydney, Australia.
2 UK NEQAS BC, Sheffield, UK.
3 ECAT, Voorschoten, The Netherlands.

Introduction

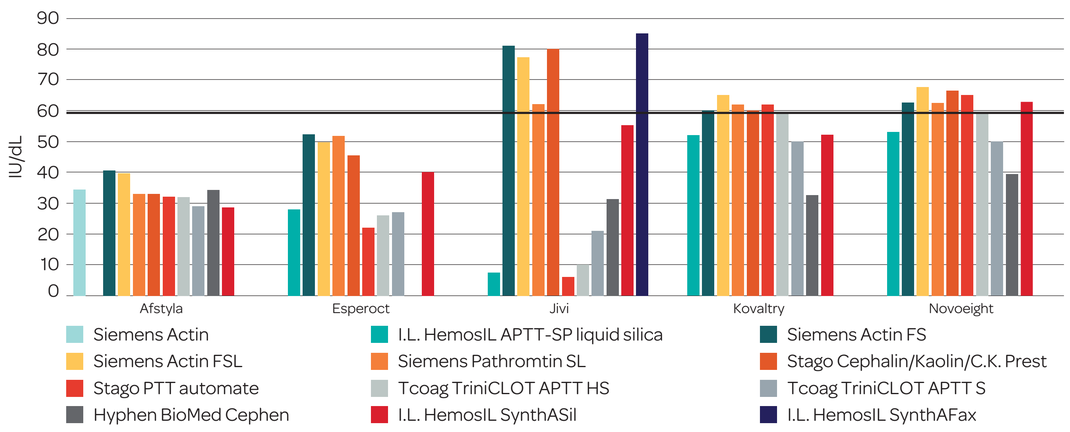
Haemophilia A is characterised by recurrent spontaneous or traumatic bleeding episodes. Historic treatment commonly included intravenous Factor VIII (FVIII) concentrates with short half-lives and therefore frequent and burdensome infusions. New extended half-life (EHL) FVIII products have been introduced with the expected outcome of longer time between treatment intervals but no loss of efficacy[1,2]. Here we explore whether laboratory testing can accurately measure FVIII levels pre and post FVIII EHL product treatment.

Aim

To assess the effect of spiking plasma samples with five different FVIII EHL products on FVIII measurements across multiple methods in three external quality assurance (EQA) programs.

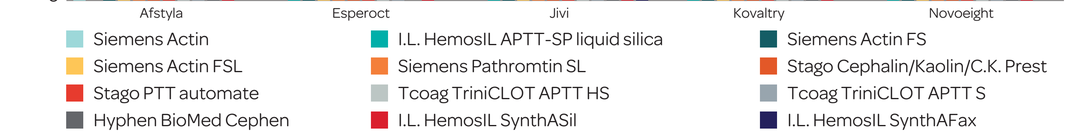
Methods

In 2023, three EQA providers (RCPAQAP, UKNEQAS and ECAT) conducted a global study to investigate the performance of laboratories measuring FVIII in samples spiked with FVIII extended half-life products. The lyophilised plasma samples were spiked with Afstyla, Esperoct, Jivi, Kovaltry and Novoeight at ~6 IU/dL and ~60 IU/dL to represent pre and post FVIII treatment levels. 275 laboratories from Australasia (RCPAQAP n= 25), Europe (ECAT, n=150) and the UK (NEQAS, n=100) performed FVIII assays utilising their routine methods and provided detailed information via an online questionnaire including assay methodology, instrumentation, reagent/kit and calibration material.



Black line represents potency level of FVIII product & expected recovery.

Figure 1 Overall median results for 6 IU/dL samples by one-stage assay APTT reagent



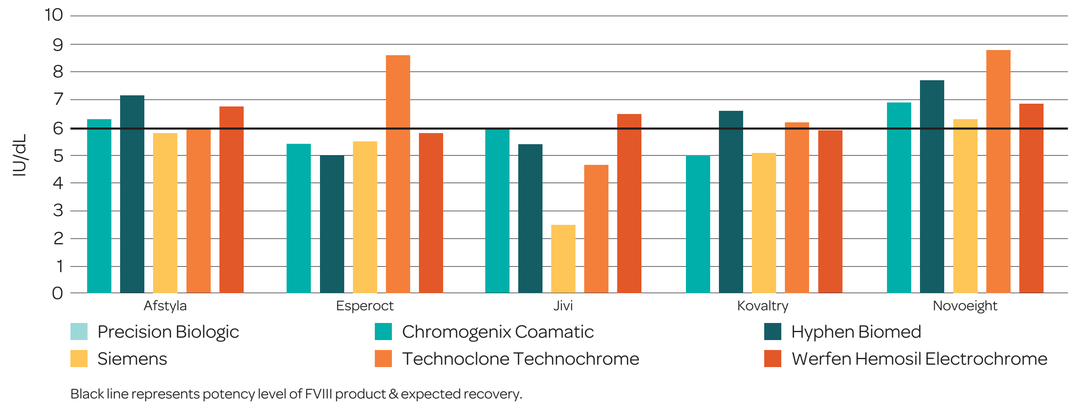
Black line represents potency level of FVIII product & expected recovery.

Figure 2 Overall median results for 60 IU/dL samples by one-stage assay APTT reagent

Results

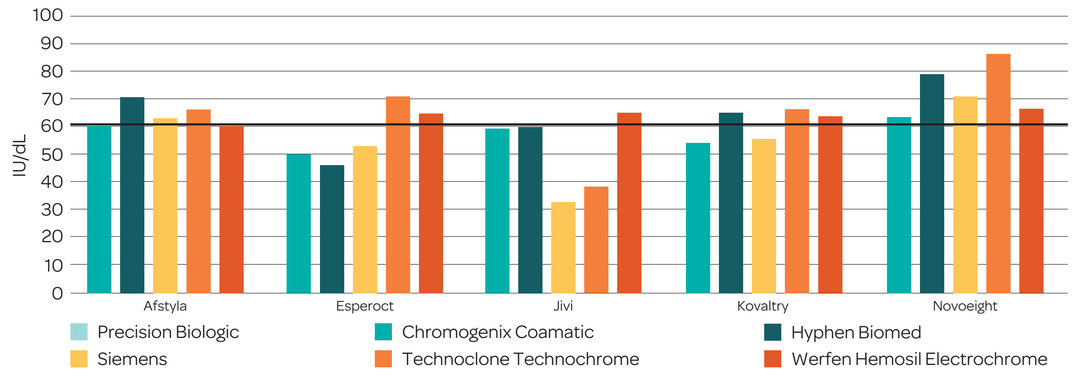
For laboratories utilising one stage clotting assays (OSA) (n=203) the medians (IU/dL) are as follows for the ~6IU/dL and ~60IU/dL samples respectively: Afstyla 4.9IU/dL; 33.8IU/dL, Esperoct 5.0IU/dL; 43.0IU/dL, Jivi 7.8IU/dL; 64.0IU/dL, Kovaltry 7.0IU/dL; 57.1IU/dL, and Novoeight 7.3IU/dL; 63.5IU/dL. Refer to figures 1 and 2 for breakdown by APTT reagent.

For laboratories utilising chromogenic assays (CA) (n=156) the medians are as follows for the ~6IU/dL and ~60IU/dL samples: Afstyla 6.4IU/dL; 62.1IU/dL, Esperoct 5.5IU/dL; 48.8IU/dL, Jivi 5.0IU/dL; 55.3IU/dL, Kovaltry 6.0IU/dL; 59.0IU/dL, and Novoeight 7.0IU/dL; 72.1IU/dL. Refer to figures 3 and 4 for breakdown by chromogenic assay kit.



Black line represents potency level of FVIII product & expected recovery.

Figure 3 Overall median results for 6IU/dL samples by chromogenic assay kit



Black line represents potency level of FVIII product & expected recovery.

Figure 4 Overall median results for 60IU/dL samples by chromogenic assay kit

Results submitted by participants demonstrate that FVIII assays do not provide consistent results of EHL products with both an under- and over-estimation of the expected recovery based on sample concentration.

In the OSAs, Afstyla and Esperoct underestimate FVIII at both concentrations, and Jivi has wide variation between reagents. While the chromogenic assays displayed more consistent results across products, the variation between kits for Jivi remains.

Conclusion

This collaborative EQA study demonstrates the potential assay variability that is encountered when measuring FVIII EHL products in vitro. Utilisation of both OSA and CA methods is recommended to monitor patients on FVIII EHL treatment effectively. Product-specific calibration curves could also be considered to reduce variability when testing with OSA or CA alone[3]. Ultimately, the provision of accurate FVIII results in patients on treatment with EHL products lowers their risk of bleeding and thrombotic complications.

References:

1. Graf L. Extended half-life factor VIII and factor IX preparations. *Transfus Med Hemother.* 2018;45:86–91.
2. Young G, Mahlangu JN. Extended half-life clotting factor concentrates: results from published clinical trials. *Haemophilia.* 2016;22(Suppl 5):25–30.
3. Gu JM, Ramsey P, Evans V, Tang L, Apeler H, Leong L. Evaluation of the activated partial thromboplastin time assay for clinical monitoring of PEGylated recombinant factor VIII (BAY 94-9027) for haemophilia A. *Haemophilia.* 2014;20:593–600.

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

NATA Accredited Proficiency Testing Scheme Provider.
Number 14863 Accredited to ISO/IEC 17043:2010

T: 1300 78 29 20
E: heamatology@rcpaqap.com.au

rcpaqap.com.au