Laboratory Monitoring of New Hemostatic Agents for Hemophilia

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Prophylactic infusions of coagulation factor concentrates result in a reduction in bleeding related morbidity and mortality in patients with severe hemophilia. Such infusions are commonly provided through central venous access devices (CVADS) and less commonly through peripheral venous access. Such frequent CVAD access may result in CVAD related complications such as infections. Infusion of the current generation of standard half-life concentrates requires either twice or three times weekly infusions for factor IX and VIII respectively. However, individualized pharmacokinetics (PK) direct optimal prophylactic dosing. Available clinical data on extended half-life (EHL) factor replacement products indicates a potential for a significant reduction in the need for frequent infusions, e.g., potentially once a week for factor IX and twice a week for factor VIII. The available data on the EHL factor replacement products also confirms similar individualized variability. Optimal dosing of these therapies relies on accurate assays, of which there is a variety, although performance characteristics vary with the specific product being tested.

The FVIII and FIX assays are performed using activators of the intrinsic or contact activation pathway. The most commonly used assays are the one stage assay, chromogenic assays are less commonly used. A variety of regents with different types of activators and phospholipid content are available for one stage assays, there are fewer available chromogenic assays.

Accurate results of the respective post infusion clotting factor activity is essential for cost effective dosing. Variability in factor recovery of plasma samples spiked with the long acting factors has been demonstrated, the extent of variability depends on the molecular modification.

During this session, the available data on outcomes of field studies of the various long acting concentrates will be described along with the manufacturers recommended assay methodology.