HOTLINE: Effective November 15, 2021

2001755 Hemophilia A (*F8*) 2 Inversions, Fetal F8 INV FE

Interpretive Data:

Background Information for Hemophilia A (*F8*) 2 Inversions:

Characteristics: Hemophilia A is characterized by deficiency of factor VIII clotting activity. Less than 1 percent factor VIII activity results in severe deficiency associated with spontaneous joint or deep muscle bleeding. Moderate deficiency (1-5 percent activity) and mild deficiency (6-40 percent activity) are associated with prolonged bleeding after tooth extractions, surgery, or injuries, and recurrent or delayed wound healing. Female carriers of hemophilia A may have increased bleeding tendencies.

Epidemiology: 1 in 5,000 live male births worldwide

Cause: Pathogenic *F8* germline variants

Inheritance: X-linked recessive. In the estimated 30 percent of cases that appear to be de novo, the mother is found to be a carrier at least 80 percent of the time.

Penetrance: 100 percent in males. Approximately 30 percent of female carriers have factor VIII activity levels of less than 40 percent and are at risk for bleeding symptoms typically consistent with mild hemophilia A.

Clinical Sensitivity: 51 percent of variants causing severe hemophilia A are detected by *F8* inversion testing. This assay does not detect *F8* variants associated with mild or moderate hemophilia A in males.

Methodology: Intron 22-A and intron 1 inversions detected by inverse PCR and electrophoresis.

Analytical Sensitivity/Specificity: 99 percent

Limitations: A negative result does not exclude a diagnosis of or carrier status for hemophilia A. Diagnostic errors can occur due to rare sequence variations. *F8* variants, other than the *F8* type 1 or type 2 intron 22-A and intron 1 inversions, will not be detected. Rare *F8* intron 22-A and intron 1 inversions with different breakpoints may not be detected by this assay.

For quality assurance purposes, ARUP Laboratories will provide a confirmation of the above result at no charge. Following delivery, please collect a cord blood sample from the infant in a lavender (EDTA) or yellow (ACD Solution A or B) top tube and transport 1mL cord blood at 2-8 °C. Please specify on the test request form that this is a confirmatory study to be performed at no charge. Please provide the mother's name for specimen identification purposes.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.