Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Hemophilia A (F8) 2 Inversions with Reflex to Sequencing and Reflex to Deletion/Duplication

ARUP test code 2001614

F8 COMP Specimen	Whole Blood
Symptoms for Hemophilia A (F8)	Yes
Family History for Hemophilia A (F8)	Yes
Hemophilia A (F8) Interpretation	See Note

H=High, L=Low, *=Abnormal, C=Critical

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

RESULT
One pathogenic variant detected in the F8 gene.

DNA VARIANT(S)
Pathogenic
Intron 22-A inversion; Heterozygous

INTERPRETATION
One pathogenic inversion was detected in the factor 8 (F8) gene. Thus this individual is a carrier of hemophilia A and has a 10 percent risk of being mildly affected. Her offspring have a 50 percent risk of inheriting the variant regardless of gender.

RECOMMENDATIONS
A baseline factor VIII clotting activity assay should be performed to determine if she is at increased risk for bleeding. Genetic counseling, including a discussion of medical screening and management, is indicated. Testing for the identified variant in other at-risk family members is recommended.

COMMENTS
Reference Sequence: GenBank # NM_000132.3

Inversion Analysis: Positive for inversion, therefore, F8 sequencing and deletion/duplication testing were not performed.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Hemophilia A (F8) 2 Inversions with Reflex to Sequencing and Reflex to Deletion/Duplication

CHARACTERISTICS: Severe deficiency of factor VIII clotting activity is associated with spontaneous joint or deep tissue bleeding. Moderate or mild deficiency is associated with prolonged bleeding after tooth extractions, surgery, or injuries and recurrent or delayed wound healing.
INCIDENCE: 1 in 4,000-5,000 live male births worldwide; rare in females.
INHERITANCE: X-linked recessive. Of simplex cases, 85 percent of mothers are carriers and 10-15 percent of boys have a de novo pathogenic variant.
PENETRANCE: 100 percent in males and 10 percent in females.
CAUSE: Pathogenic F8 gene variants.
CLINICAL SENSITIVITY: 98 percent.
METHODOLOGY FOR INVERSIONS: F8 intron 22-A and intron 1 inversions detected by inverse PCR and electrophoresis.
METHODOLOGY FOR SEQUENCING: Bidirectional sequencing of the F8 coding region and intron-exon boundaries.
METHODOLOGY FOR DELETION/DUPLICATION: Multiplex ligation-dependent probe amplification (MLPA) to detect large deletions/duplications in the F8 coding region.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Regulatory region and deep intronic variants, repeat element insertions, and rare F8 intron 22-A and intron 1 inversions with different breakpoints, will not be detected. Deletions/duplications in exon 23 will not be detected.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
F8 COMP Specimen	19-120-109550	4/30/2019 12:00 00 PM	4/30/2019 1:46:24 PM	4/30/2019 2:49:00 PM
Symptoms for Hemophilia A (F8)	19-120-109550	4/30/2019 12:00 00 PM	4/30/2019 1:46:24 PM	4/30/2019 2:49:00 PM
Family History for Hemophilia A (F8)	19-120-109550	4/30/2019 12:00 00 PM	4/30/2019 1:46:24 PM	4/30/2019 2:49:00 PM
Hemophilia A (F8) Interpretation	19-120-109550	4/30/2019 12:00 00 PM	4/30/2019 1:46:24 PM	4/30/2019 2:49:00 PM

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