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

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/13/2021
Sex:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Hemophilia A (F8) Sequencing

ARUP test code 3004241

Hemophilia A (F8) Specimen	Whole Blood
Hemophilia A (F8) Interp	Negative

RESULT
No pathogenic variants were detected in the F8 gene.

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the F8 gene. This result decreases the likelihood of, but does not exclude, a diagnosis of hemophilia A. Please refer to the background information included in this report for the clinical sensitivity and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended. If this individual is suspected to be affected with hemophilia A, targeted testing for the F8 intron 22-A and intron 1 inversions (ARUP test code 2001759) and F8 deletion/duplication analysis (Deletion/Duplication Analysis by MLPA, ARUP test code 3003144) are recommended.

COMMENTS
Likely benign and benign variants are not included in this report.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Hemophilia A (F8) Sequencing

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

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

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: Sequencing detects 76-98 percent of variants causing mild or moderate hemophilia A and 43-51 percent of variants causing severe hemophilia A.
GENE TESTED: F8 (NM_000132.4)
METHODOLOGY: Capture of all coding exons and exon-intron junctions of the F8 gene, followed by massively parallel sequencing. Sanger sequencing is performed as necessary to fill in regions of low coverage and confirm reported variants.
ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.
LIMITATIONS: A negative result does not exclude a diagnosis of or carrier status for hemophilia A. This test only detects variants within the coding regions and intron-exon boundaries of the F8 gene. Variants in regions that are not included in the preferred transcript are not detected. This assay will not detect the common intron 22-A and intron 1 inversions. Regulatory region variants and deep intronic variants will not be identified. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. In males, lack of massively parallel sequencing coverage of one or more F8 exons may suggest the presence of a large deletion; however, this should be confirmed by a validated method. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Hemophilia A (F8) Specimen	21-319-102963	11/15/2021 10:27:00 AM	11/15/2021 10:27:34 AM	11/15/2021 10:32:00 AM
Hemophilia A (F8) Interp	21-319-102963	11/15/2021 10:27:00 AM	11/15/2021 10:27:34 AM	11/15/2021 10:32:00 AM

END OF CHART

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