ClinLab
Clinical Testing Laboratory, Inc.

Clinical Testing Lab of Washington
2150 Pennsylvania Avenue NW
Washington, DC 20037
Phone: 202-555-1212

Specimen Number	Specimen Type	Control Number	Account Number	Account Phone Number	Route
	Peripheral Blood				

Patient Last Name	Patient Barcode

Patient First Name	Patient Middle Name
Marco	

Patient SS#	Patient Phone	Total Volume

Age (Y/M/D)	Date of Birth	Sex	Fasting
2 y.o.		Male	

Patient Address	Indication: Hemophilia Family History: Family history of uncontrolled bleeding in males Ethnicity: Mixed race - European Caucasian & African

Date and Time Collected	Date Entered	Date and Time Reported	Physician Name	NPI	Physician ID
			Jane Ferreiro, MD		

Tests Ordered
Hemophilia Mutation Evaluation

General Comments
Please send a copy of the final report to the Molecular Science/M1 Training office via Fax at (202) 555-1212

Clinical test results for DNA Hemophilia Mutation Evaluation

GENE	TEST RESULTS	EXPLANATION
near F8 (Xq28) gene region	NG_011403.1: g.4980_5005del	**This result is reported due to a request for reporting all variants in gene regions known to be associated with those associated with Hemophilia.** Based on current knowledge, we have discovered a **variant of uncertain significance (VUS)**. Please note that knowledge about variants is constantly evolving. Please consider revisiting research about this variant in the future. A PCR/sequencing study has detected one copy of the variant NG_011403.1(F8):g.4980_5005del. When mapping the sequenced region to the nucleotide record indicated (which includes 5000 base pairs upstream from the transcriptional start site), a 25 base pair deletion upstream and including the transcriptional start site was found. While we have no specific information about this particular variant, this missing region maps to a site where critical gene expression regulatory sequences, such as promoter elements, are often found. When diagnosing genetic disorder, any assertion should be interpreted in the context of clinical presentation and results of other laboratory tests (e.g., APTT, Factor VIII Activity, etc.). For X-linked disorders, male patients are particularly susceptible to genetic variant impact as they have only one copy of the X chromosome.
F9 (Xq27.1)	Negative	

INDICATIONS FOR TESTING
Individuals with a diagnosis of hemophilia, appropriate at-risk female relatives of probands with identified mutations, and hemophilia carriers with genetic counseling, are candidates for testing.

METHODOLOGY

Factor VIII & IX sequencing: The gene regions for Factor VIII and IX including up- and down-stream regions are analyzed by direct DNA sequence analysis using an automated fluorescent sequencing machine. When a mutation is detected, confirmation is carried out on an independent amplification of PCR using a second prep (B-prep) by sequencing in the opposite direction. If no mutation is found, sequence analysis is performed in both directions.

PERFORMANCE

Factor IX sequencing: From previous experience, we have been able to detect factor VIII or IX gene mutations in about 99% of individuals with the diagnosis of hemophilia with specificity of mutation detection in probands and carrier detection is also estimated to be greater than 99%.

LIMITATIONS

The sequence analysis will not detect mutations located in regions that are not analyzed. The sequencing method also will not detect gross genetic alterations including most duplications, inversions, or deletions (in females). Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance.

CLINICAL DESCRIPTION

Hemophilia A and B are characterized by a deficiency of either factor VIII and IX clotting activity, respectively, that results in prolonged oozing after injuries, tooth extractions, or surgery, and delayed or recurrent bleeding prior to complete wound healing. These are X-linked recessive bleeding disorders with an incidence of about 1 per 30,000 live male births. Hemophilia affects males; however, all male offspring will be normal, and although all female offspring will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of carriers of hemophilia have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

The age of diagnosis and frequency of bleeding episodes are related to the level of factor VIII and/or IX clotting activity. In severe hemophilia, spontaneous joint or deep-muscle bleeding is the most frequent symptom. Individuals with severe hemophilia are usually diagnosed during the first two years of life; without prophylactic treatment, they may average up to two to five spontaneous bleeding episodes each month. Individuals with moderate hemophilia seldom have spontaneous bleeding; however, they do have prolonged or delayed oozing after relatively minor trauma and are usually diagnosed before age five to six years; the frequency of bleeding episodes varies from once a month to once a year. Individuals with mild hemophilia do not have spontaneous bleeding episodes; however, without pre- and post-operative treatment, abnormal bleeding occurs with surgery or tooth extractions; the frequency of bleeding may vary from once a year to once every ten years. Individuals with mild hemophilia are often not diagnosed until later in life. In any individual with hemophilia, bleeding episodes may be more frequent in childhood and adolescence than in adulthood. Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia) and are thus symptomatic carriers, although symptoms are usually mild. After major trauma or invasive procedures, prolonged or excessive bleeding usually occurs, regardless of severity.