

Overview

Useful For

Determining the etiology of hereditary persistence of fetal hemoglobin (HPFH), or delta-beta-thalassemia

Diagnosing less common causes of beta-thalassemia; these large deletional beta-thalassemia mutations result in elevated hemoglobin (Hb) A2 and usually have slightly elevated Hb F levels

Distinguishing homozygous Hb S disease from a compound heterozygous Hb S/large beta-globin cluster deletion disorder (ie, Hb S/beta zero thalassemia, Hb S/delta beta zero thalassemia, Hb S/HPFH, Hb S/gamma-delta-beta-thalassemia)

Diagnosing complex thalassemias where the beta-globin gene and 1 or more of the other genes in the beta-globin cluster have been deleted

Evaluating and classifying unexplained increased Hb F percentages

Evaluating microcytic neonatal anemia

Evaluating unexplained long standing microcytosis in the setting of normal iron studies and negative alpha thalassemia testing/normal Hb A2 percentages

Confirming gene fusion hemoglobin variants such as Hb Lepore and Hb P-Nilotic

Confirming homozygosity vs hemizyosity of mutations in the beta-like genes (*HBB*, *HBD*, *HBG1*, *HBG2*)

Testing Algorithm

This test is recommended to identify a variety of conditions involving large deletions or duplications within the beta-globin gene cluster locus region including:

-Identifying large deletions causing increased hemoglobin (Hb) F levels such as hereditary persistence of fetal hemoglobin (HPFH), delta-beta thalassemias, and gamma-delta-beta-thalassemia

-Identifying beta thalassemia conditions in cases where beta gene sequencing did not find a beta-thalassemia mutation

-Confirming gene fusion hemoglobin variants such as Hb Lepore and Hb P-Nilotic

-Investigating newborns with unexplained microcytic anemia that is suspected to be caused by epsilon-gamma-delta-beta-thalassemia

-Confirming homozygosity vs hemizyosity of mutations in the beta-like genes (*HBB*, *HBD*, *HBG1*, *HBG2*)

-Investigating individuals older than 12 months of age with unexplained microcytosis and normal hemoglobin electrophoresis for whom more common causes of microcytosis such as iron deficiency and alpha-thalassemia have been excluded

This test may result as a reflex secondary to testing from several evaluations (HAEVP / Hemolytic Anemia Evaluation; HBELC / Hemoglobin Electrophoresis Cascade, Blood; MEVP / Methemoglobinemia Evaluation; REVE / Erythrocytosis Evaluation; THEVP / Thalassemia and Hemoglobinopathy Evaluation).

Method Name

Only orderable as a reflex. For more information see:

- HAEVP / Hemolytic Anemia Evaluation
- HBELC / Hemoglobin Electrophoresis Cascade, Blood
- MEVP / Methemoglobinemia Evaluation
- REVE / Erythrocytosis Evaluation
- THEVP / Thalassemia and Hemoglobinopathy Evaluation

Polymerase Chain Reaction (PCR) Analysis/Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen**Specimen Type**

Whole Blood EDTA

Specimen Required

Only orderable as a reflex. For more information see:

- HAEVP / Hemolytic Anemia Evaluation
- HBELC / Hemoglobin Electrophoresis Cascade, Blood
- MEVP / Methemoglobinemia Evaluation
- REVE / Erythrocytosis Evaluation
- THEVP / Thalassemia and Hemoglobinopathy Evaluation

Specimen Type: Peripheral blood

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)

Specimen Volume: 4 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in the original tube.

Specimen Minimum Volume

2 mL

Reject Due To

No specimen should be rejected.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated		

Clinical and Interpretive

Clinical Information

Large deletions involving the beta-globin cluster locus on chromosome 11 manifest with widely variable clinical phenotypes. Up to 10% of beta-thalassemia cases (dependent on ethnicity) are caused by large deletions in the beta-globin cluster. Other thalassemias including delta-beta-thalassemia, gamma-delta-beta-thalassemia, and epsilon-gamma-delta-beta-thalassemia also result from functional loss of genes or the locus control region (LCR) that controls globin gene expression. In addition, hereditary persistence of fetal hemoglobin (HPFH) is caused by deletions of variable size along the beta globin cluster locus. Most, but not all, of the large deletion beta globin cluster disorders are associated with variably elevated hemoglobin (Hb) F percentages that persist after 2 years of age. In addition, most manifest in microcytosis. A notable exception is HPFH, which can have normal to minimal decreased mean corpuscular volume (MCV) values. The correct classification of these deletions is important as they confer variable predicted phenotypes and some are more protective than others when found in combination with a second beta globin mutation, such as Hb S or beta thalassemia. In addition, identification of these deletions can explain lifelong microcytosis in the setting of normal iron studies and negative alpha-thalassemia molecular results.

Reference Values

Only orderable as a reflex. For more information see:

- HAEVP / Hemolytic Anemia Evaluation
- HBELC / Hemoglobin Electrophoresis Cascade, Blood
- MEVP / Methemoglobinemia Evaluation
- REVE / Erythrocytosis Evaluation
- THEVP / Thalassemia and Hemoglobinopathy Evaluation

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

Nondeletional subtypes of beta-thalassemia or hereditary persistence of fetal hemoglobin (HPFH) are not detected

by this assay.

Hemoglobin electrophoresis and sequencing analysis of the beta-globin gene will be performed prior to this test to exclude other diagnoses or to indicate the diagnostic utility of this testing platform.

This test is not useful for diagnosis or confirmation of alpha-thalassemia, the most common beta-thalassemias or hemoglobin variants. It also does not detect nondeletional hereditary persistence of fetal hemoglobin.

In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.

Clinical Reference

1. Hein MS, Oliveira JL, Swanson KC, et al: Large Deletions Involving the Beta Globin Gene Complex: Genotype-Phenotype Correlation of 119 cases. *Blood* 2015;126:3374
2. Kipp BR, Roellinger SE, Lundquist PA, et al: Development and clinical implementation of a combination deletion PCR and multiplex ligation-dependent probe amplification assay for detecting deletions involving the human alpha-globin gene cluster. *J Mol Diagn* 2011 Sep;13(5):549-557. doi: 10.1016/j.jmoldx.2011.04.001. Epub 2011 Jun 25
3. Rund D, Rachmilewitz E: Beta-thalassemia. *N Engl J Med* 2005;353:1135-1146
4. Nussbaum R, McInnes R, Willard H: Principles of Molecular Disease: Lessons from the Hemoglobinopathies. In Thompson and Thompson Genetics in Medicine. Seventh edition. Philadelphia, PA, Saunders Elsevier, 2007, pp 323-342
5. Wood WG: Hereditary persistence of fetal hemoglobin and delta beta thalassemia. In Disorders of Hemoglobin, First edition, Cambridge University Press, New York, NY, 2001, pp 356-388

Performance

Method Description

Multiplex ligation-dependent probe amplification (MLPA) is utilized to test for the presence of large deletions in the beta-globin gene.

PDF Report

No

Day(s) and Time(s) Test Performed

Wednesday; 10 a.m., Friday; 2 p.m.

Analytic Time

5 days

Specimen Retention Time

Whole Blood: 2 weeks; DNA: 3 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81363-HBB (hemoglobin, beta, beta-globin) (eg, beta thalassemia), duplication/deletion analysis

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
WBDDR	Beta Globin Cluster Locus Del/Dup,B	In Process

Result ID	Test Result Name	Result LOINC Value
48356	Beta Globin Cluster Locus Del/Dup	50397-9
48355	Reviewed by	18771-6
48357	Interpretation	59466-3