HOTLINE: Effective January 11, 2021

New Test **3003651** **Alpha Thalassemia (*HBA1* and *HBA2*) Deletion/Duplication with reflex to Hb Constant Spring** **HBA DDCS**

Available Now

Additional Technical Information

Methodology: Multiplex Ligation-dependent Probe Amplification with Sanger sequencing confirmation of HbCS
Performed: Varies
Reported: 10-14 days; 21 days if reflexed

Specimen Required: Collect: Lavender (EDTA), pink (K_2EDTA), or Yellow (ACD Solution A or B).
Specimen Preparation: Transport 2 mL whole blood. (Min: 1 mL)
Storage/Transport Temperature: Refrigerated.
Stability (collection to initiation of testing): Room Temperature: 7 days; Refrigerated: 1 month

Reference Interval: By report

Interpretive Data:
Background Information: Alpha Globin (*HBA1* and *HBA2*) Deletion/Duplication
Characteristics: Decreased or absent synthesis of the hemoglobin (Hb) alpha-chain resulting in clinical presentations ranging from asymptomatic silent carriers to severe anemia and fetal lethality. Alpha thalassemia silent carrier commonly results from deletion of a single alpha globin gene (-a/aa) and is clinically asymptomatic. Alpha thalassemia trait may be caused by deletion of a single alpha globin gene from both chromosomes (-a/-a), or deletion of the *HBA1* and *HBA2* globin genes from the same chromosome (--/aa). Heterozygosity for Hb Constant Spring (HbCS) is usually asymptomatic but may be associated with mild microcytic anemia. Homozygous HbCS is characterized by overt hemolytic anemia, jaundice and splenomegaly. Hemoglobin H disease occurs due to inactivation of three alpha globin genes and results in hemolysis with Heinz bodies, moderate anemia, and splenomegaly. Hb Bart hydrops fetalis syndrome results from deletion of all four alpha globin genes (--/--) and is lethal in the fetal or early neonatal period. Alpha globin gene duplication results in three or more active alpha globin genes on a single chromosome.
Epidemiology: Carrier frequency of alpha thalassemia in African, African-American (1:3), Mediterranean (1:30-50), Middle Eastern, Southeast Asian (1:20).
Inheritance: Autosomal recessive.
Cause: Pathogenic variants in the alpha globin gene cluster (*HBZ, HBM, HBA2, HBA1, HBQ1*) or regulatory region.
Clinical Sensitivity: Varies by ethnicity, at least 90 percent.
Methodology: Multiplex ligation-dependent probe amplification (MLPA) for the *HBZ, HBM, HBA2, HBA1*, and *HBQ1* genes, the HS-40 regulatory region, and Hb Constant Spring (HbCS) *HBA2* c.427T>C; p.Ter143Gln. To determine copy number of HbCS in absence of a concurrent deletion of *HBA2*, PCR and bidirectional sequencing for HbCS is performed.
Analytical Sensitivity and Specificity: 99 percent.
Limitations: Diagnostic errors can occur due to rare sequence variations. Specific breakpoints of large deletions/duplications will not be determined; therefore, it may not be possible to distinguish variants of similar size. Non-deletional variants within the coding or regulatory regions of the alpha globin cluster genes, other than HbCS, will not be targeted. Individuals carrying both a deletion and duplication within the alpha globin gene cluster may appear to have a normal number of alpha globin gene copies. Rare syndromic or acquired forms of alpha thalassemia associated with *ATRX* gene variants will not be detected.

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.

Note: If a concurrent deletion of *HBA2* is not identified, PCR and bidirectional sequencing for the HbCS copy number will be performed. Additional charges apply.

CPT Code(s): 81269; if reflexed, add 81257

New York DOH Approved.

HOTLINE NOTE: Refer to the Test Mix Addendum for interface build information.