HOTLINE: Effective May 20, 2019

**New Test** **3001399** ***SHOX*-Related Disorders, Sequencing** **SHOX FGS**

Additional Technical Information

Patient History for *SHOX*-Related Disorders

**Methodology:** Polymerase Chain Reaction/Sequencing
**Performed:** Sun-Sat
**Reported:** 12-14 days

**Specimen Required:** Collect: Lavender (EDTA) or Pink ($K_2$ EDTA).
Specimen Preparation: Transport 3 mL whole blood. (Min: 1 mL)
Storage/Transport Temperature: Refrigerated.
Stability (collection to initiation of testing): Ambient: 1 week; Refrigerated: 1 month; Frozen: 6 months

**Interpretive Data:**
**Background Information for *SHOX*-Related Disorders, Sequencing:**
**Characteristics of *SHOX*-related disorders (*SHOX* deficiency):** Short stature, mesomelia, and abnormal alignment of the radius, ulna and carpal bones at wrist (Madelung deformity). Variable expressivity results in some affected individuals with syndromic short stature and additional findings (eg, Leri-Weill dyschondrosteosis (LWD) or Langer mesomelic dysplasia (LMD)), while others have isolated short stature (ISS).
**Prevalence of *SHOX* deficiency:** 1 in 1,000
**Inheritance:** *SHOX* is located in pseudoautosomal region 1 (PAR1) on the X and Y chromosomes and escapes X-inactivation. Thus, inheritance is pseudoautosomal dominant for ISS and LWD, and pseudoautosomal recessive for LMD.
**Penetrance:** High, with variability in expression.
**Cause:** One pathogenic variant (haploinsufficiency) of the *SHOX* gene causes ISS and LWD. Two pathogenic variants in *SHOX* (complete loss of *SHOX*) cause LMD.
**Clinical Sensitivity:** Approximately 10-20 percent of disease-causing variants in *SHOX* are sequence variants.
**Methodology:** Bidirectional Sanger sequencing of the *SHOX* coding regions, including exon 6a and 6b, and intron-exon boundaries.
**Analytical Sensitivity and Specificity:** Greater than 99 percent.
**Limitations**: Diagnostic errors can occur due to rare sequence variations. Large deletions/duplications, repeat element insertions, deep intronic variants, and some regulatory region variants are not detected.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

See Compliance Statement C: www.aruplab.com/CS

**CPT Code(s):** 81405

New York DOH approval pending. Call for status update.

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