CHARGE Syndrome (CHD7)

**Indications for Ordering**
Confirms a clinical diagnosis or suspected diagnosis of CHARGE syndrome

**Test Description**
Bidirectional sequencing of entire coding region and intron/exon borders of the CHD7 gene

**Tests to Consider**
- CHARGE Syndrome, CHD7 Sequencing 2012609
  - Genetic testing to confirm a diagnosis of CHARGE syndrome
- CHARGE Syndrome (CHD7) Sequencing, Fetal 2012717
  - Prenatal test for a fetus with ultrasound findings suggestive of CHARGE syndrome

**Disease Overview**

**Incidence** ~1/10,000

**Symptoms**
- CHARGE is an acronym for the major features of the condition
  - Ocular coloboma
  - Choanal atresia
  - Heart defects
  - Restriction growth and delayed development
  - Genital abnormalities
  - Ear anomalies
- Condition is highly variable

**Diagnostic criteria**
- Diagnosis is based primarily on clinical findings and temporal bone imaging
- Clinical criteria for CHARGE syndrome
  - Four major characteristics, or three major and three minor characteristics
- Clinical criteria for possible/probable CHARGE syndrome
  - Two major and several minor characteristics

**Minor characteristics**
- Genital hypoplasia
- Developmental delay
- Cardiovascular malformation
- Growth deficiency
- Orofacial cleft
- Tracheoesophageal fistula
- Characteristic facial features

**Genetics**

**Gene** – CHD7

**Inheritance** – autosomal dominant

**Penetrance** – 100%, though severity of the condition is highly variable

**De novo variants**
- Almost always de novo
- Rare parent-to-child transmission has been reported

**Variants**
- Most variants are sequence variants
- Partial or full deletions of CHD7 are rare

**Test Interpretation**

**Sensitivity/specificity**
- Clinical sensitivity ~90% in individuals or fetuses fulfilling clinical criteria for CHARGE syndrome
- Analytical sensitivity/specificity >99%

**Results**
- Positive
  - One copy of a pathogenic variant detected
    - Confirms a diagnosis of CHARGE syndrome
- Negative
  - No pathogenic variant detected
    - Likelihood of CHARGE syndrome is reduced, but still possible

**Limitations**
- Diagnostic errors can occur due to
  - Rare sequence variations
  - Primer- or probe-site variants
- Not detected
  - Large deletions and duplications
  - Regulatory region variants
  - Deep intronic variants
References