TEST CHANGE

Spinal Muscular Atrophy (SMA) Copy Number Analysis

2013436, SMA DD

Specimen Requirements:	
Patient Preparation:	
Collect:	Lavender (EDTA), pPink (K2EDTA), or yYellow (ACD sSolution A or B).
Specimen Preparation:	Transport 23 mL whole blood. (Min: 12 mL)
Transport Temperature:	Refrigerated. Also acceptable: Ambient.
Unacceptable Conditions:	
Remarks:	
Stability:	Room TemperatureAmbient: 1 week; Refrigerated: 1 month; Frozen: Unacceptable6 months.
Methodology:	Multiplex Ligation-Ddependent Probe Amplification (MLPA)
Performed:	Varies
Reported:	7-14 days
Note:	
CPT Codes:	81329
New York DOH Approval Status:	This test is New York DOH approved.

Interpretive Data:

Refer to report. Background information for Spinal Muscular Atrophy (SMA) Copy Number Analysis
Characteristics: Spinal muscular atrophy (SMA) is the most common lethal genetic disease in children, and is characterized by progressive muscle weakness due to degeneration of the lower motor neurons. Onset ranges from before birth to adulthood and severity is highly variable. Individuals with SMA have no functioning copies of the *SMN1* gene. Most (95 percent) have homozygous loss of *SMN1* due to deletion or gene conversion, while a minority (5 percent) have a deletion of *SMN1* on one chromosome and a *SMN1* sequence variant on the other. The *SMN2* gene, adjacent and highly homologous to *SMN1*, produces lower levels of survival motor neuron protein compared to *SMN1*. Disease severity has been shown to be modified by *SMN2* gene copy number in some cases, though phenotype cannot be predicted with certainty. An *SMN1* variant, c.*3+80T>G (rs143838139), that is part of a haplotype associated with *SMN1* duplication in silent carriers (2 copies of *SMN1* on one chromosome and no copies on the other), particularly in Ashkenazi Jews, increases the likelihood that 2 copies of *SMN1* are on the same chromosome.
Inheritance: Autosomal recessive.
Cause: Pathogenic variants in the *SMN1* gene.
Variants Tested: For copy number: *SMN1* (NM_000344.3) exon 7 c.840C and exon 8 c.*239G, and

SMN2 (NM_017411.3) exon 7 c.840T. For haplotype associated with *SMN1* duplication (silent carriers): *SMN1* c.*3+80T>G (rs143838139).
Clinical sensitivity: 95-98 percent in individuals affected with SMA. Detection rate for carrier screening is 90 percent in African Americans, 93 percent in Ashkenazi Jewish, 93 percent in Asians, 95 percent in Caucasians, and 93 percent in Hispanics.
Methodology: Multiplex probe ligation-dependent amplification (MLPA) to detect *SMN1* and *SMN2* copy number and presence or absence of the *SMN1* linked variant c.*3+80T>G (rs143838139).
Analytical sensitivity and specificity: 99 percent.
Limitations: Diagnostic errors can occur due to rare sequence variations. Single base pair substitutions, small deletions/duplications, regulatory region mutations, and deep intronic mutations will not be detected. This test is unable to determine chromosomal phase of *SMN1* or *SMN2* copies. Even if the linked variant associated with *SMN1* duplication is detected, the test cannot definitively differentiate between 1+ copies of *SMN1* on each chromosome from 2+ copies of *SMN1* on one chromosome and none on the other (silent carriers).

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.

Reference Interval:

By report