Spinal Muscular Atrophy: Carrier Screen

**Test Code:** MM490  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81401 x1

**Condition Description**

Spinal muscular atrophy (SMA) is the second most common lethal, autosomal recessive disorder in Caucasians, with an incidence of approximately 1/10,000 and a carrier frequency of 1/50. SMA is characterized by anterior horn cell degeneration which causes a symmetrical muscle weakness and wasting. Other symptoms can include joint contractures, respiratory insufficiency, and feeding and sleep difficulties. Subtypes have been created, although the phenotype can span a broad continuum and subtypes are not clearly delineated. Subtypes of SMA include:

- **Type 0:** prenatal onset of severe joint contractures and weakness at birth; lifespan ranges from days to 2-6 months
- **Type I (Werdnig-Hoffman disease):** most severe form of SMA with an onset of severe weakness before 6 months of age; affected individuals usually die by 2 years of age
- **Type II (Dubowitz disease):** intermediate in severity between Types I and III, with an onset of symptoms after 6 months of age; death occurs in childhood or young adulthood
- **Type III (Kugelberg-Welander disease):** mildest form of childhood onset SMA, with symptoms usually beginning after 10 months; affected individuals can survive into adulthood
- **Type IV:** onset of muscle weakness in second or third decade with normal lifespan

All SMA subtypes are caused by mutations in the survival motor neuron (**SMN1**) gene (5q11.2-q13.3). **SMN1** is deleted in about 95-98% of individuals with SMA. Point mutations are also known in this gene. Approximately 2-5% of affected individuals have one deletion and one point mutation. Approximately 2% of affected individuals have a de novo mutation meaning only one parent is an SMA carrier.

This carrier assay tests for the common **SMN1** deletion only; point mutations will not be detected. Approximately 5-8% of carrier individuals will have a normal **SMN1** copy number of two, but both copies will be on the same chromosome (in cis) with a deletion on the second chromosome. This assay will not detect these carrier individuals. This assay will not report **SMN2** copy number.


**Genes**

**SMN1**

**Indications**

This test is indicated for:

- Carrier testing.
- Individuals or couples seeking to assess reproductive risk.

**Methodology**

**SMN1** gene deletions were quantified by multiplex ligation polymerase chain reaction amplification (MLPA) of exons 7 and 8. Gene dosage ratios of **SMN1** are calculated relative to the average of 16 reference loci and are expressed as gene dosage, and/or copy number. Diploid gene dose or 2 copies of **SMN1** indicates normal (not affected) status, 1x gene dosage or 1 copy of the **SMN1** gene most likely indicates carrier status and deletions (less than 0.1x) of **SMN1** or 0 copies of the **SMN1** gene designates affected status. The SMA component of this assay does not test for point mutations. **SMN2** copy number is not assessed.

**Detection**

Deletions of the **SMN1** gene are found in approximately 95% of SMA patients, but the frequency is less in the milder (type II and III) variants. Affected individuals with 0 copies of **SMN1** seem to have milder form of the disease with increased copy numbers of the **SMN2** gene. Deletions of the **SMN1** gene are the most common pathologic mechanism for SMA, however, other gene rearrangements have been described in affected individuals, including hybrid or fusion **SMN** genes and deleterious point mutations in the **SMN1** gene. Thus, the lack of a deletion does not necessarily rule out this diagnosis, and further testing may be required.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Saliva**

**Specimen Requirements:**

Oragene™ Saliva collection kit

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight
delivery.

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Pan-Ethnic Carrier Screen
- Ashkenazi Jewish Carrier Screen
- Fragile X