EGL Genetics | Eurofins Clinical Diagnostics
2460 Mountain Industrial Boulevard | Tucker, Georgia 30084
Phone: 470-378-2200 or 855-831-7447 | Fax: 470-378-2250
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# 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.

Visit www.ThinkGenetic.com for patient-friendly information on spinal muscular atrophy.

## 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: DNA, Isolated

**Specimen Requirements:**
Microtainer
3µg
Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

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Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

### Type: Whole Blood (EDTA)

**Specimen Requirements:**
EDTA (Purple Top)
Infants and Young Children ( 2 years of age to 10 years old: 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

## Related Tests

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