Spinal Muscular Atrophy: **SMN1** Common Deletion Testing

**Test Code:** SM  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81400 x1

### Condition Description

Spinal muscular atrophy (SMA) is the second most common lethal, autosomal recessive disorder in Caucasians. SMA is characterized by anterior horn cell degeneration which causes a symmetrical muscle weakness and wasting. Three types of SMA are described:

- **Type I (Werdnig-Hoffman disease):** most severe form of SMA with an onset of symptoms before 6 months of age; affected individuals usually die by 2 years of age.
- **Type II (intermediate form):** intermediate in severity between Types I and III, with an onset of symptoms between 6 and 18 months of age; death occurs after 2 years of age.
- **Type III (Wohlfart-Kugelberg-Welander disease):** mildest form of childhood onset SMA, with symptoms beginning between 18 months and 17 years of age; affected individuals survive into adulthood.

All three SMA types are linked to chromosome 5q11.2-q13.3. A telomeric gene, known as the **survival motor neuron (SMN1)** gene, was found to be deleted in about 98% of patients. Point mutations are also known in this gene.

**SMN1** is deleted in about 95% of individuals with SMA. This assay tests for the common **SMN1** deletion only; other pathogenic variants will not be detected. Note that approximately 5-8% of individuals that are carriers of SMA carry two copies of **SMN1** on one chromosome with a deletion on the second chromosome, and will not be detected with this assay. This assay will not report **SMN2** copy number.

### 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, according to the SALSA protocol available from MRC Holland. Two copies of the **SMN1** genes most often indicate normal (not affected) status and one copy of a deletion of this region most likely indicates carrier status.

### Detection

Deletions of the **SMN1** gene are found in approximately 95% of individuals with SMA. This carrier assay tests for the common **SMN1** deletion only; other pathogenic variants 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. **SMN2** copy number is not assessed.

### Reference Range

Qualitative assay.

### Specimen Requirements

**Submit only 1 of the following specimen types**

**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 72 hours of collection. Do not freeze.

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

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

Special Instructions
Diagnostic testing only. No prenatal or carrier testing available.

Related Tests
- Congenital Hypotonia Panel