Spinal Muscular Atrophy: \textit{SMN1} Common Deletion Testing

\textbf{Test Code:} SM  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81400 x1

\section*{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 \textit{survival motor neuron (SMN1)} gene, was found to be deleted in about 98% of patients. Point mutations are also known in this gene.

\textit{SMN1} is deleted in about 95% of individuals with SMA. This assay tests for the common \textit{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 \textit{SMN1} on one chromosome with a deletion on the second chromosome, and will not be detected with this assay. This assay will not report \textit{SMN2} copy number.

Please click here for the GeneReviews clinical summary on this condition.  
Visit \url{www.ThinkGenetic.com} for patient-friendly information on spinal muscular atrophy.

\section*{Genes}

\textbf{SMN1}

\section*{Indications}

\section*{Methodology}

\textit{SMN1} gene deletions were quantified by multiplex ligation polymerase chain reaction amplification (MLPA) of exons 7 and 8. Gene dosage ratios of \textit{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 \textit{SMN1} genes most often indicate normal (not affected) status and one copy of a deletion of this region most likely indicates carrier status.

\section*{Detection}

Deletions of the \textit{SMN1} gene are found in approximately 95% of individuals with SMA. This carrier assay tests for the common \textit{SMN1} deletion only; other pathogenic variants will not be detected. Approximately 5-8% of carrier individuals will have a normal \textit{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. \textit{SMN2} copy number is not assessed.

\section*{Reference Range}

Qualitative assay.

\section*{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\textbf{Type: Whole Blood (EDTA)}

\textbf{Specimen Requirements:}

\begin{itemize}
  \item EDTA (Purple Top)  
  \item Infants and Young Children (2 years of age to 10 years old): 3-5 ml  
  \item Older Children & Adults: 5-10 ml  
  \item Autopsy: 2-3 ml unclotted cord or cardiac blood
\end{itemize}

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

\textbf{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:
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