Spinal muscular atrophy (SMA; OMIM 253300) is an autosomal recessive disorder caused by mutations in the SMN1 gene (OMIM 600354). SMA is characterized by progressive, symmetric proximal muscle weakness and respiratory failure. Muscle atrophy is due to degeneration of lower motor neurons of the spinal cord and lower brainstem. It is now recognized that SMA includes a spectrum of phenotypes without a clear delineation of subtypes. Nonetheless, classification by age of onset and severity can be useful for prognosis and management. Clinically defined subtypes include SMA of prenatal onset, with arthrogryposis multiplex congenital and facial weakness; SMA type I (Werdnig-Hoffmann disease), with onset before 6 months of age; SMA type II, with onset between 6 and 12 months of age; SMA type III, with onset in childhood after 12 months; and SMA type IV, with adult onset.

Testing:

Deletion analysis:
In approximately 95% of cases, SMA is caused by homozygous deletion of SMN1. Deletion testing is performed to detect the presence or absence of SMN1. This can detect a homozygous deletion of SMN1, which is consistent with a diagnosis of SMA.

Testing also includes semi-quantitative dosage analysis to determine number of SMN1 and SMN2, performed by multiplex PCR. This test can detect heterozygous carriers of an SMN1 deletion who have only one copy of SMN1. This test can not distinguish between individuals who have two copies of SMN1 with one on each chromosome (1+1) and individuals who have two copies of SMN1 on a single chromosome and a deletion on the other chromosome (2+0). About 4% of the general population are thought to be carriers with a “2+0” configuration.

Indications:
- Confirm or rule out a suspected diagnosis of SMA
- Determine SMN1 copy number in a symptomatic individual with negative deletion testing
- Determine SMN2 copy number in an affected individual for prognostic information
- Carrier testing in an adult for family members of an affected individual
  
(Please note: Our laboratory does not offer carrier screening for the general population.)

Sequence analysis:
About 5% of the time, SMA is caused by a deletion of SMN1 on one allele in combination with an intragenic mutation on the other allele. Gene sequencing can be performed for individuals who test negative by deletion testing. The entire coding regions of SMN1 and SMN2 are sequenced. Large duplications and deletions within the gene may not be detected.

Indications:
- Confirm or rule out a suspected diagnosis of SMA after negative deletion testing (deletion testing must be completed prior to the sequencing test, either in our lab or another facility)
- Carrier testing in an adult for a known familial intragenic mutation
  
(Please note: Our laboratory does not offer sequence analysis for general population carrier screening.)
Sensitivity:
*SMN1* is the only gene known to be associated with this form of SMA. These assays will detect mutations in greater than 99% of individuals with this form of SMA. There are other disorders that include muscular atrophy and loss of lower motor neurons. A negative *SMN1* test does not rule out a genetic cause of muscle weakness, and additional testing may be indicated.

**Turnaround time:**
Deletion testing: 7-10 days  
Sequence analysis: 10-14 days

**BILLING:** We do not bill third party payers (insurance companies) for samples received from external sources. The person or institution (e.g., Clinical Lab; Send-out Lab; Physician Office) sending the sample is responsible for full payment of the invoices within 30 days of receipt of the invoice. If the patient is on Medical assistance, please contact the lab prior to sample submission. Direct patient billing will be accepted only when a valid credit card form is received with the patient sample.

**CPT codes and cost:**
Deletion testing and dosage analysis: 83891 x 1  83900 x 1  83894 x 2  83912 x 1  $475  
Sequence analysis: 83891 x 1  83898 x 2  83900 x 1  83901 x 1  83904 x 22  83912 x 1  $890  
Deletion testing and sequence analysis:  $1310

**Online resources:**
Families of SMA - [http://www.fsma.org](http://www.fsma.org)  
Claire Altman Heine Foundation, Inc. - [http://www.clairealtmanheinefoundation.org](http://www.clairealtmanheinefoundation.org)  
International SMA Patient Registry - [http://smaregistry.iu.edu](http://smaregistry.iu.edu)  
SMA Foundation - [http://www.smafoundation.org](http://www.smafoundation.org)  
FightSMA - [http://www.fightsma.org](http://www.fightsma.org)  

Facsimile Verification Form

Name of Facility receiving Fax: ____________________________________________

Name of Physician/Lab receiving Fax: ____________________________________________

Street Address: _____________________________________________________________

City_________________________ State: _____

Fax Number: ______________________________ (to which lab results and/or patient information may be sent)

Phone Number: ______________________________

By signing this Facsimile Verification Form, I validate the accuracy of the above information and assume responsibility for assuring that the Fax machine is in a location which will maintain confidentiality of all reports transmitted by the Molecular Diagnostics Laboratory of the Nemours/Alfred I. duPont Hospital for Children, to the above fax number.

Authorized Contact Person: ________________________________________________

Signature: _______________________________ Date: ______________

Title: ________________________________________________________________

In our continuing efforts to maintain patient confidentiality, the Molecular Diagnostics Laboratory of the Nemours/Alfred I. duPont Hospital for Children requests you to verify the fax number only once from your medical practice or institution and to assure that all faxes regarding patient information are received in a secure location in accordance with HIPAA regulations.

Please complete this Facsimile Verification Form and fax back to 302.651.6795. If you have any questions regarding this form please contact Susan Kirwin, Assistant Director of the Molecular Diagnostics Laboratory, at 302.651.6777.

This is a confidential document that is being sent from a fax machine in a secure location. This fax is covered by the Electronic Communications Privacy Act 18 U.S.C. 2510-521. The information contained in this fax is considered privileged, is otherwise confidential and is intended only for the use of the individual or entity named above. Dissemination, distribution, or copying of this communication is strictly prohibited. If you have received this communication in error please notify us immediately by telephone, and return the original message to us at the above address via the U.S. Postal Service.
### For Direct Patient Billing

Prepayment for the testing services is required prior to beginning our testing. Please complete this form and include this paperwork with the shipment of the patient sample.

Billing questions can be addressed to: Denise Axsmith  
Senior Budget/Financial Analyst  
Nemours/A.I. duPont Hospital for Children  
[daxsmith@nemours.org](mailto:daxsmith@nemours.org)  
Phone: 302.651.6802  
Fax: 302.651.6881

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<th>Credit Card Billing Information</th>
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| **Patient Name:** | **Credit Card:**  
| | MasterCard  
| | Visa  
| | American Express  
| | Discover  
| | **Other:** ________  |
| **Name of Card holder:** | **Credit Card Number:** |  |
| **Card holder address:** | **Expiration Date:** |  |
| | **Credit Card Number:** |  |
| | **Security Code:**  
| | **(on back of card)** |  |
| **Card holder phone:**  
| | **Authorized payment amount:** |  
| | **Home:** |  |
| | **Work:** |  |