Penn Medicine

Hospital *of the* University *of* Pennsylvania

THE DIVISION OF Precision & Computational Diagnostics

To: UPHS Physicians and Staff

From: Department of Pathology and Laboratory Medicine, Division of Precision and Computational Diagnostics
Vivianna Van Deerlin, MD, PhD, Interim Director
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Date: September 9, 2024

Re: **NEW GENETIC ASSAY**: *SMN1* and *SMN2* Analysis for Spinal Muscular Atrophy (SMA)
METHOD CHANGE: *CFTR* Analysis for Cystic Fibrosis (CF)

In September, *CFTR* variant analysis and *SMN1* and *SMN2* copy number and variant testing, which are currently being sent to a reference laboratory, will be available in the Molecular Pathology Laboratory at HUP. The American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG) recommend carrier screening for CF and SMA be offered to all women who are pregnant or considering pregnancy, regardless of ethnicity.

***SMN1/SMN2* analysis**

- Methodology: PCR and capillary electrophoresis (Asuragen AmplideX SMN1/2).
- Detection: Determines *SMN1* and *SMN2* copy number and can identify potential silent carriers who have two *SMN1* copies in cis (2+0) through evaluation of two variants associated with the gene duplication haplotype (c.*3+80G>T and c.*211_*212delA). Can also identify the disease modifying variant *SMN2* c.859G>C.
- Reporting: *SMN1* and *SMN2* copy number (0, 1, 2, 3, and 4 or more) and present or not detected for variants.
- Limitations: Does not identify rare causes of SMA, including pathogenic variants in *SMN1.*

***CFTR* analysis**

- Methodology: FDA-cleared, next generation sequencing (TruSight Cystic Fibrosis 139 – Variant Assay).
- Detection: 134 CF disease-associated variants, 1 variant of varying clinical consequence (R117H), 1 disease modifying variant (intron 8 PolyTG/PolyT, conditionally reported if R117H is positive), and 3 benign variants (I506V, I507V and F508C, conditionally reported only in the context of deltaI507 or deltaF508 homozygosity).
- Reporting: Positive (heterozygous or homozygous) or not detected for variants.
- Limitations: Phasing of the PolyTG/PolyT and R117H (i.e., cis/trans determination) is not performed by this assay. The assay is designed to identify a specific subset of known variants in *CFTR*.

Testing Information

	SMN1/SMN2	***CFTR***
PennChart Ordering:	"Spinal muscular atrophy(SMA) copy number analysis" (PxCode SMACN)	"Cystic Fibrosis – CFTR 139 Variant Analysis" (PxCode C2008401)
Turnaround Time:	7-10 days	
Acceptable Specimen:	Only peripheral blood collected in an EDTA (lavender) tube (1 tube) will be accepted	

Contact Information: Call the Molecular Pathology Laboratory (215-615-3094) on weekdays during regular business hours. For information on ordering and specimen requirements, kindly consult the Lab Tests Services Guide.

References

1. Deignan, *et al*. Updated recommendations for CFTR carrier screening: A position statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 25(8): 100867, 2023.
2. Committee Opinion: Carrier Screening for Genetic Conditions. American College of Obstetricians and Gynecologists. Opinion Number 691, March 2017: 1-15.