

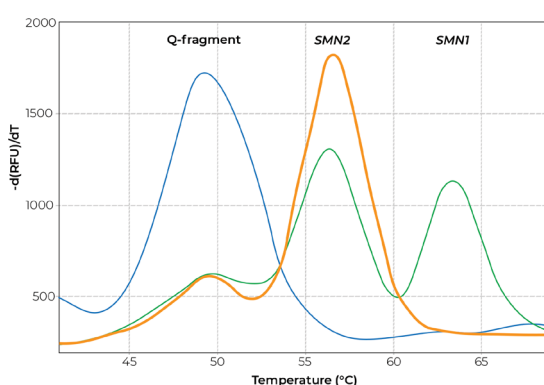
Meeting your SMA newborn screening needs

- ✓ **Reliable and robust:** high sensitivity and specificity for SMA patient detection.
- ✓ **Fast and simple:** results in 4 hours from DBS punch — no DNA purification needed.
- ✓ **Cost-effective:** low start-up costs — only thermocycler with melt curve required.
- ✓ **Built-in controls:** DNA quantity, threshold DNA and positive DNA controls in every kit.
- ✓ **Ideal for newborn screening programs:** only patient detection, no carrier identification.

MRC Holland's Solution for SMA Neonatal Screening

MRC Holland's MC002 SMA Newborn Screen is based on melt curve analysis – a simple and affordable technique which utilizes the fact that different genetic sequences targeted by the same probe will display different DNA melting temperatures. Following a PCR amplification and a probe binding step, peaks specific for *SMN1* and *SMN2* are generated. The method is highly sequence-specific, sensitive, and easy to perform. Requiring only a dried blood spot (DBS) card as input, the assay accurately determines the presence or absence of the *SMN1* and *SMN2* gene, reliably identifying SMA patients (0 *SMN1* copies) - but not carriers (1 *SMN1* copy).

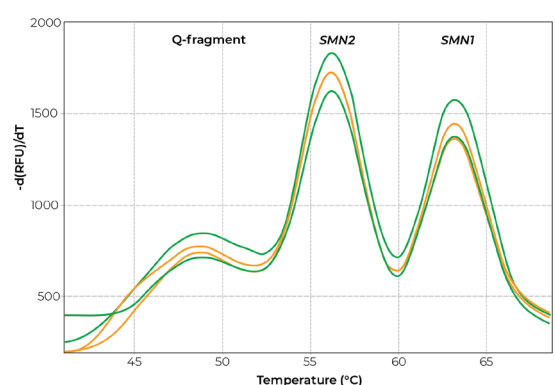
Easy Patient Identification



SMA patient: $SMN1=0, SMN2 \geq 1$
Normal sample: $SMN1 \geq 1, SMN2 \geq 1$
No DNA control: Prominent Quantity fragment peak (49°C) only

Fig. 1. MC002 SMA Newborn Screen results obtained on a **patient sample**, a **healthy control** and a **no DNA control** reaction. The absence of the *SMN1* exon 7 target in the patient is clearly discernible by the complete absence of a peak for *SMN1*. Q-fragment: internal control for DNA quantity; high peak indicating insufficient DNA.

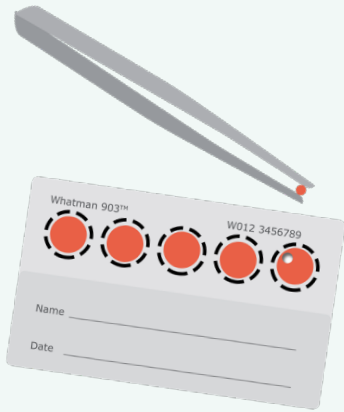
No Carrier Detection



Carrier example: $SMN1=1, SMN2=1$
Non-Carrier: $SMN1=2, SMN2=2$

Fig. 2. MC002 SMA Newborn Screen results only show the *SMN1*:*SMN2* ratio, not absolute copy numbers. MC002 SMA Newborn Screen can therefore not be used to detect SMA carriers.

"The MC002 SMA Newborn Screen showed the feasibility and accuracy of SMA screening in a neonatal screening program"



A clinical performance study by national neonatal screening lab Isala (The Netherlands) using SALSA® MC002 SMA Newborn Screen on anonymised dried blood spot (DBS) cards (47 SMA patients; 375 controls) found 100% diagnostic sensitivity and specificity. MC002 SMA Newborn Screen was able to detect the absence of the *SMN1* exon 7 DNA sequence, thereby reliably discriminating *SMN1* from the highly homologous *SMN2* gene. Furthermore, the assay did not detect asymptomatic carriers — an added advantage in newborn screening. The test's concordance with the second-tier 'gold standard' SALSA® MLPA® Probemix P021 SMA was 100%.

Strunk et al. (2019). Validation of a Fast, Robust, Inexpensive, Two-Tiered Neonatal Screening Test algorithm on Dried Blood Spots for Spinal Muscular Atrophy. Int. J. Neonatal Screen 5, 2

MRC Holland: Market Leader in SMA Testing

As the market leader in SMA tests, MRC Holland offers five different assays for SMA that cover the complete range of genetic analysis needs.

Unsure about which test is right for your lab?

We are here to help you,
email us at info@mrcholland.com.



		SALSA® MC002 SMA Newborn Screen	SALSA® MLPA® Probemix P021 SMA	SALSA® MLPA® Probemix P060 SMA Carrier	SALSA® MLPA® Probemix P460 SMA (Silent) Carrier	NXtec™ D028 Carrier Panel 1
<ul style="list-style-type: none"> ● Primary test ○ Secondary test 						
Properties	CE-marked	yes	yes	yes [†]	yes	no
	Technique	Melt Assay	MLPA	MLPA	MLPA	digitalMLPA
Used for	Neonatal Screening	●	○	○		
	Patient Detection		●	○	○	
	Carrier Detection		○	●	●	●
	Silent Carrier Detection				● [#]	● [#]
Coverage	<i>SMN1</i> exon 7	✓ ^Δ	✓	✓	✓	✓
	<i>SMN1</i> exon 8		✓	✓	✓	✓
	<i>SMN2</i> exon 7	✓ ^Δ	✓	✓ [†]	✓	
	<i>SMN2</i> exon 8		✓	✓ [†]		
	<i>SMN1+2</i> exon 1-8		✓			
	Silent Carrier SNP probe(s)				✓	✓

[#] P460 and D028: Increased detection of silent carriers: individuals with 2 *SMN1* copies on one allele + 0 on the other.

^Δ MC002: no absolute copy numbers aside from 0 determined.

[†] P060: cannot be used to determine *SMN2* copy numbers for diagnostic purposes. The *SMN2* probes in P060 can only be used as an interpretation aid for *SMN1* copy number determination. *SMN2* copy number determination for diagnostic purposes can only be done with P021.