Product Description
SALSA® MLPA® Probemix P350 CLCN1-KCNJ2

To be used with the MLPA General Protocol.

Version C1
For complete product history see page 8.

Catalogue numbers:
- **P350-025R:** SALSA MLPA Probemix P350 CLCN1-KCNJ2, 25 reactions.
- **P350-050R:** SALSA MLPA Probemix P350 CLCN1-KCNJ2, 50 reactions.
- **P350-100R:** SALSA MLPA Probemix P350 CLCN1-KCNJ2, 100 reactions.

To be used in combination with a SALSA MLPA reagent kit and Coffalyser.Net data analysis software. MLPA reagent kits are either provided with FAM or Cy5.0 dye-labelled PCR primer, suitable for Applied Biosystems and Beckman/SCIEX capillary sequencers, respectively (see www.mrcholland.com).

Certificate of Analysis
Information regarding storage conditions, quality tests, and a sample electropherogram from the current sales lot is available at www.mrcholland.com.

Precautions and warnings
For professional use only. Always consult the most recent product description AND the MLPA General Protocol before use: www.mrcholland.com. It is the responsibility of the user to be aware of the latest scientific knowledge of the application before drawing any conclusions from findings generated with this product.

General information
The SALSA MLPA Probemix P350 CLCN1-KCNJ2 is a **research use only (RUO)** assay for the detection of deletions or duplications in the *CLCN1* and *KCNJ2* genes, which are associated with Becker disease, Thomsen disease, and Andersen-Tawil syndrome (ATS).

Myotonia congenita is characterised by muscle stiffness and delayed relaxation after muscle contraction (myotonia). Myotonia congenita is inherited in either an autosomal recessive (Becker disease) or an autosomal dominant manner (Thomsen disease). Thomsen disease is less common and less severe than Becker disease. Defects in the *CLCN1* gene on chromosome 7 are the main cause of myotonia congenita. The protein encoded by this gene is a chloride voltage-gated channel, important in controlling the influx of chloride ions into skeletal muscle cells.

ATS is an autosomal dominant multisystem channelopathy characterised by periodic paralysis, ventricular arrhythmias and dysmorphic facial or skeletal features. Defects in the *KCNJ2* gene on chromosome 17 are the main cause of ATS. The protein encoded by this gene is inward rectifier potassium channel 2 (Kir2.1), important in controlling the (in)flux of potassium ions into skeletal and cardiac muscle cells.

More information is available at https://www.ncbi.nlm.nih.gov/books/NBK1355/ and https://www.ncbi.nlm.nih.gov/books/NBK1264/.

This SALSA MLPA probemix is not CE/FDA registered for use in diagnostic procedures. Purchase of this product includes a limited license for research purposes.

Gene structure and transcript variants:
Entrez Gene shows transcript variants of each gene: http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene
For NM_ mRNA reference sequences: http://www.ncbi.nlm.nih.gov/sites/entrez?db=nucleotide
Locus Reference Genomic (LRG) database: http://www.lrg-sequence.org/

Exon numbering
The *CLCN1* and *KCNJ2* exon numbering used in this P350-C1 CLCN1-KCNJ2 product description is the exon numbering from the NG_009815.2 and LRG_328 sequences respectively. The exon numbering of the NM_ sequence that was used for determining a probe's ligation site does not always correspond to the exon numbering obtained from the LRG/NG sequences. As changes to the databases can occur after release of this product description, the NM_ sequence and exon numbering may not be up-to-date.

Probemix content
The SALSA MLPA Probemix P350-C1 CLCN1-KCNJ2 contains 39 MLPA probes with amplification products between 130 and 472 nucleotides (nt). This includes 24 probes for the *CLCN1* gene, one probe for each exon and two probes for exon 17, and two flanking probes, one upstream and one downstream of the *CLCN1* gene. Furthermore, five probes for the *KCNJ2* gene are included, two probes for exon 1 and three probes for exon 2. In addition, eight reference probes are included that detect autosomal chromosomal locations. Complete probe sequences and the identity of the genes detected by the reference probes are available online (www.mrcholland.com).

This probemix contains nine quality control fragments generating amplification products between 64 and 105 nt: four DNA Quantity fragments (Q-fragments), two DNA Denaturation fragments (D-fragments), one Benchmark fragment, and one chromosome X and one chromosome Y-specific fragment (see table below). More information on how to interpret observations on these control fragments can be found in the MLPA General Protocol and online at www.mrcholland.com.

Length (nt)	Name
64-70-76-82	Q-fragments (only visible with <100 ng sample DNA)
88-96	D-fragments (low signal indicates incomplete denaturation)
92	Benchmark fragment
100	X-fragment (X chromosome specific)
105	Y-fragment (Y chromosome specific)

MLPA technique
The principles of the MLPA technique (Schouten et al. 2002) are described in the MLPA General Protocol (www.mrcholland.com).

MLPA technique validation
Internal validation of the MLPA technique using 16 DNA samples from healthy individuals is required, in particular when using MLPA for the first time, or when changing the sample handling procedure, DNA extraction method or instruments used. This validation experiment should result in a standard deviation ≤0.10 for all probes over the experiment.

Required specimens
Extracted DNA free from impurities known to affect MLPA reactions. For more information please refer to the section on DNA sample treatment found in the MLPA General Protocol.

Reference samples
A sufficient number (≥3) of reference samples should be included in each MLPA experiment for data normalisation. All samples tested, including reference DNA samples, should be derived from the same tissue type, handled using the same procedure, and prepared using the same DNA extraction method when possible. Reference samples should be derived from different unrelated individuals who are from families without a history of Becker disease, Thomsen disease, and Andersen-Tawil syndrome. More information regarding the selection and use of reference samples can be found in the MLPA General Protocol (www.mrcholland.com).

Positive control DNA samples

MRC Holland cannot provide positive DNA samples. Inclusion of a positive sample in each experiment is recommended. Coriell Institute (https://catalog.coriell.org) and Leibniz Institute DSMZ (https://www.dsmz.de/) have diverse collections of biological resources which may be used as positive control DNA samples in your MLPA experiments. The quality of cell lines can change; therefore samples should be validated before use.

Data analysis

Coffalyser.Net software should be used for data analysis in combination with the appropriate lot-specific MLPA Coffalyser sheet. For both, the latest version should be used. Coffalyser.Net software is freely downloadable at www.mrcholland.com. Use of other non-proprietary software may lead to inconclusive or false results. For more details on MLPA quality control and data analysis, including normalisation, see the Coffalyser.Net Reference Manual.

Interpretation of results

The standard deviation of each individual probe over all the reference samples should be ≤0.10 and the final ratio (FR) of each individual reference probe in the patient samples should be between 0.80 and 1.20. When these criteria are fulfilled, the following cut-off values for the FR of the probes can be used to interpret MLPA results for autosomal chromosomes or pseudo-autosomal regions:

Copy number status	Final ratio (FR)
Normal	0.80 < FR < 1.20
Homozygous deletion	FR = 0
Heterozygous deletion	0.40 < FR < 0.65
Heterozygous duplication	1.30 < FR < 1.65
Heterozygous triplication/homozygous duplication	1.75 < FR < 2.15
Ambiguous copy number	All other values

Note: The term “dosage quotient”, used in older product description versions, has been replaced by “final ratio” to become consistent with the terminology of the Coffalyser.Net software. (Calculations, cut-offs and interpretation remain unchanged.) Please note that the Coffalyser.Net software also shows arbitrary borders as part of the statistical analysis of results obtained in an experiment. As such, arbitrary borders are different from the final ratio cut-off values shown here above.

- Arranging probes according to chromosomal location facilitates interpretation of the results and may reveal more subtle changes such as those observed in mosaic cases. Analysis of parental samples may be necessary for correct interpretation of complex results.
- False positive results: Please note that abnormalities detected by a single probe (or multiple consecutive probes) still have a considerable chance of being a false positive result. Sequence changes (e.g. SNVs, point mutations) in the target sequence detected by a probe can be one cause. Incomplete DNA denaturation (e.g. due to salt contamination) can also lead to a decreased probe signal, in particular for probes located in or near a GC-rich region. The use of an additional purification step or an alternative DNA extraction method may resolve such cases. Additionally, contamination of DNA samples with cDNA or PCR amplicons of individual exons can lead to an increased probe signal (Varga et al. 2012). Analysis of an independently collected secondary DNA sample can exclude these kinds of contamination artefacts.
- Normal copy number variation in healthy individuals is described in the database of genomic variants: http://dgv.tcag.ca/dgv/app/home. Users should always consult the latest update of the database and scientific literature when interpreting their findings.
- Not all abnormalities detected by MLPA are pathogenic. In some genes, intragenic deletions are known that result in very mild or no disease (as described for *DMD* by Schwartz et al. 2007). For many genes, more than one transcript variant exists. Copy number changes of exons that are not present in all transcript variants may not have clinical significance. Duplications that include the first or last exon of a gene (e.g. exons 1-3) might not result in inactivation of that gene copy.

- Copy number changes detected by reference probes or flanking probes are unlikely to have any relation to the condition tested for.
- False results can be obtained if one or more peaks are off-scale. For example, a duplication of one or more exons can be obscured when peaks are off-scale, resulting in a false negative result. The risk on off-scale peaks is higher when probemixes are used that contain a relatively low number of probes. Coffalyser.Net software warns for off-scale peaks while other software does not. If one or more peaks are off-scale, rerun the PCR products using either: a lower injection voltage or a shorter injection time, or a reduced amount of sample by diluting PCR products.

Limitations of the procedure

- In most populations, the major cause of genetic defects in the *CLCN1* and *KCNJ2* genes are small (point) mutations, none of which will be detected by using SALSA MLPA Probemix P350 CLCN1-KCNJ2.
- MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect copy number neutral inversions or translocations. Even when MLPA did not detect any aberrations, the possibility remains that biological changes in that gene or chromosomal region *do* exist but remain undetected.
- Sequence changes (e.g. SNVs, point mutations) in the target sequence detected by a probe can cause false positive results. Mutations/SNVs (even when >20 nt from the probe ligation site) can reduce the probe signal by preventing ligation of the probe oligonucleotides or by destabilising the binding of a probe oligonucleotide to the sample DNA.

Confirmation of results

Copy number changes detected by only a single probe always require confirmation by another method. An apparent deletion detected by a single probe can be due to e.g. a mutation/polymorphism that prevents ligation or destabilises the binding of probe oligonucleotides to the DNA sample. Sequence analysis can establish whether mutations or polymorphisms are present in the probe target sequence. The finding of a heterozygous mutation or polymorphism indicates that two different alleles of the sequence are present in the sample DNA and that a false positive MLPA result was obtained.

Copy number changes detected by more than one consecutive probe should be confirmed by another independent technique such as long range PCR, qPCR, array CGH or Southern blotting, whenever possible. Deletions/duplications of more than 50 kb in length can often be confirmed by FISH.

***CLCN1* and *KCNJ2* mutation database**

https://databases.lovd.nl/shared/genes/CLCN1 and https://databases.lovd.nl/shared/genes/KCNJ2. We strongly encourage users to deposit positive results in the Leiden Open Variation Database (LOVD). Recommendations for the nomenclature to describe deletions/duplications of one or more exons can be found on http://varnomen.hgvs.org/.

Please report copy number changes detected by the reference probes, false positive results due to SNVs and unusual results (e.g., a duplication of *CLCN1* exons 5 and 7 but not exon 6) to MRC Holland: info@mrcholland.com.

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Table 1. SALSA MLPA Probemix P350-C1 CLCN1-KCNJ2

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]		
		Reference	*CLCN1*	*KCNJ2*
64-105	Control fragments – see table in probemix content section for more information			
130	Reference probe 00797-L13645	5q		
138	**CLCN1 probe** 22157-L31185		**Exon 1**	
144	**CLCN1 probe** 13959-L31798		**Exon 4**	
151 «	**CLCN1 probe** 13978-L31548		**Exon 23**	
154	Reference probe 18714-L31549	2q		
160	**CLCN1 probe** 22158-L31550		**Exon 7**	
166 ◎	**KCNJ2 probe** 17294-L21186			**Exon 1**
172	**CLCN1 probe** 22295-L31411		**Exon 17**	
184 ◎	**KCNJ2 probe** 13979-L15548			**Exon 1**
190	Reference probe 12422-L13423	14q		
196 ¬	CASP2 probe 17295-L20777		**Upstream**	
202	**CLCN1 probe** 22159-L31187		**Exon 21**	
210	**CLCN1 probe** 13957-L15526		**Exon 2**	
220	**CLCN1 probe** 22160-L31188		**Exon 12**	
238	**CLCN1 probe** 13964-L15533		**Exon 9**	
248	**KCNJ2 probe** 13980-L15549			**Exon 2**
256	Reference probe 09380-L17664	6q		
265	**CLCN1 probe** 22161-L31189		**Exon 5**	
274	**CLCN1 probe** 13968-L15537		**Exon 13**	
283	**CLCN1 probe** 22296-L31412		**Exon 17**	
292	**CLCN1 probe** 13975-L15544		**Exon 20**	
301	**CLCN1 probe** 13958-L15527		**Exon 3**	
310	Reference probe 21216-L29591	16p		
317 Ж	**CLCN1 probe** 17298-SP0474-L21318		**Exon 18**	
328 ¬ «	FAM131B probe 17297-L20779		**Downstream**	
337	**CLCN1 probe** 22162-L31190		**Exon 6**	
346	**CLCN1 probe** 13965-L15534		**Exon 10**	
355	**CLCN1 probe** 13971-L15540		**Exon 16**	
364	Reference probe 19502-L26792	15q		
373	**CLCN1 probe** 14538-L15538		**Exon 14**	
382	**CLCN1 probe** 13974-L15543		**Exon 19**	
401	Reference probe 13343-L14769	18q		
419 ±	**CLCN1 probe** 13963-L21284		**Exon 8**	
427	**KCNJ2 probe** 13981-L15550			**Exon 2**
434 ±	**CLCN1 probe** 13966-L15535		**Exon 11**	
445	**KCNJ2 probe** 17300-L20782			**Exon 2**
454 «	**CLCN1 probe** 13977-L15546		**Exon 22**	
463	**CLCN1 probe** 13970-L15539		**Exon 15**	
472	Reference probe 12761-L13877	4q		

[a] See section Exon numbering on page 2 for more information.

± SNP rs118066140 (419 nt) could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.; SNP rs764936586 (c.1183_1187delGGAAT; 434 nt) could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.
« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading to incomplete DNA denaturation, especially of GC-rich regions.
Ж This probe consists of three parts and has two ligation sites. A low signal of this probe can be due to depurination of the sample DNA, e.g. due to insufficient buffering capacity or a prolonged denaturation time. When this occurs in reference samples, it can look like an increased signal in the test samples.
¬ Flanking probe. Included to help determine the extent of a deletion/duplication. Copy number alterations of only the flanking or reference probes are unlikely to be related to the condition tested.

ɷ The significance of exon 1 deletions is not clear as this exon is non-coding and alternative transcript variants using other transcription start sites are known.

SNVs located in the target sequence of a probe can influence probe hybridization and/or probe ligation. Single probe aberration(s) must be confirmed by another method.

Table 2. P350-C1 probes arranged according to chromosomal location

Table 2a. *CLCN1*

Length (nt)	SALSA MLPA probe	*CLCN1* exon[a]	Ligation site NM_000083.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
196 ¬	17295-L20777	Upstream	*CASP2* gene	ACTTATCAAGGA-TCGGGAAGGTTA	11.4 kb
		start codon	*103-105 (Exon 1)*		
138	22157-L31185	Exon 1	271-270, reverse	CTGTGTGGGGTG-GACGTTGTGGCG	3.4 kb
210	13957-L15526	Exon 2	306-307	CACAAAGAACAA-TTCTCAGACAGG	1.0 kb
301	13958-L15527	Exon 3	518-519	GGACTACGTCAG-TGCCAAAAGCCT	0.7 kb
144	13959-L31798	Exon 4	662-663	TCCCCAGGCTGT-TGGTGAGAACTT	0.4 kb
265	22161-L31189	Exon 5	796-797	CCGTGGGGAAAG-AGGTAGGCCTGG	1.5 kb
337	22162-L31190	Exon 6	871-870, reverse	CCTTACCTCATA-TACCCCGCAGAA	1.0 kb
160	22158-L31550	Exon 7	890-891	GCCATACTACTA-CTCTGATATCCT	6.4 kb
419 ±	13963-L21284	Exon 8	1014-1015	AACTACTGGAGA-GGATTCTTTGCA	0.4 kb
238	13964-L15533	Exon 9	1109-1110	GTTCAGAACCAA-TTTCCGAATGGA	0.3 kb
346	13965-L15534	Exon 10	1203-1202, reverse	TGGCGATGCAGA-TACACAAATACA	0.9 kb
434 ±	13966-L15535	Exon 11	1300-1301	TTGTTACCTTTG-TCATTGCCTCAT	0.3 kb
220	22160-L31188	Exon 12	1392-1393	TTGTTTGACAAC-AATACATGGGTG	6.5 kb
274	13968-L15537	Exon 13	1563-1562, reverse	CCTAGCACAAAC-ACAGGCATGAAG	0.2 kb
373	14538-L15538	Exon 14	1604-1605	GGTAGGAGAAAT-CATGGCCATGCT	2.4 kb
463	13970-L15539	Exon 15	1737-1736, reverse	AATTCGAAGCAA-ATCACAGCTGTG	0.4 kb
355	13971-L15540	Exon 16	1967-1966, reverse	GCAACTCCCCAT-ATGTGTAAGAAG	3.1 kb
172	22295-L31411	Exon 17	2039-2040	CTCAGATTCAAT-GATCCTGCTGGG	0.3 kb
283	22296-L31412	Exon 17	40 nt after exon 17	GGGATAGATCAG-GAGCAAAGGGAA	0.3 kb
317 Ж	17298-SP0474-L21318	Exon 18	2304-2303 and 24 nt before exon 18; reverse	GGGGCAGTAGTA-53 nt spanning oligo-AGCCTGGGAGCA	0.5 kb
382	13974-L15543	Exon 19	6 nt before exon 19, reverse	TTTGACCTGAGA-GGACAGGTGAGT	0.4 kb
292	13975-L15544	Exon 20	2503-2504	TGTCACCTGAAG-AGGTGAGTAAGG	3.5 kb
202	22159-L31187	Exon 21	2603-2602, reverse	TCACCTTGTGCA-GGGTTGTCTGCT	0.1 kb
454 «	13977-L15546	Exon 22	2650-2651	TCCACCTCGCTT-ACGTGACCAGCA	1.2 kb
151 «	13978-L31548	Exon 23	2870-2869, reverse	GGGAGGCAGCAA-TCACATCCCCTG	5.1 kb
		stop codon	*3067-3069 (Exon 23)*		
328 ¬ «	17297-L20779	Downstream	*FAM131B* gene	AGAGTATCCTGA-AGCTGGTTGGGA	

Table 2b. *KCNJ2*

Length (nt)	SALSA MLPA probe	*KCNJ2* exon[a]	Ligation site NM_000891.3l	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*387-389 (Exon 2)*		
184 ɷ	13979-L15548	Exon 1	93-92, reverse	AGTGGTTTGTAA-AAAGCGAGTGAG	0.1 kb
166 ɷ	17294-L21186	Exon 1	163-164	GCTCCTGCGCCA-GCAACAGGTAAG	5.5 kb
248	13980-L15549	Exon 2	527-526, reverse	TCTTTCTTCACA-AAGCGGCTCCTG	0.2 kb
427	13981-L15550	Exon 2	765-766	TGTCCGAGGTCA-ACAGCTTCACGG	0.6 kb
445 #	17300-L20782	Exon 2	1363-1364	GGGCCACCGCTA-TGAGCCTGTGCT	
		stop codon	*1668-1670 (Exon 2)*		

[a] See section Exon numbering on page 2 for more information.
[b] Only partial probe sequences are shown. Complete probe sequences are available at www.mrcholland.com. Please notify us of any mistakes: info@mrcholland.com.

± SNP rs118066140 (419 nt) could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.; SNP rs764936586 (c.1183_1187delGGAAT; 434 nt) could influence the probe signal. In case of apparent deletions, it is recommended to sequence the region targeted by this probe.
« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading to incomplete DNA denaturation, especially of GC-rich regions.
Ж This probe consists of three parts and has two ligation sites. A low signal of this probe can be due to depurination of the sample DNA, e.g. due to insufficient buffering capacity or a prolonged denaturation time. When this occurs in reference samples, it can look like an increased signal in the test samples.
¬ Flanking probe. Included to help determine the extent of a deletion/duplication. Copy number alterations of only the flanking or reference probes are unlikely to be related to the condition tested.
ѡ The significance of exon 1 deletions is not clear as this exon is non-coding and alternative transcript variants using other transcription start sites are known.
This probe's specificity relies on a single nucleotide difference compared to a related gene or pseudogene. As a result, an apparent duplication of only this probe can be the result of a non-significant single nucleotide sequence change in the related gene or pseudogene.

SNVs located in the target sequence of a probe can influence probe hybridization and/or probe ligation. Single probe aberration(s) must be confirmed by another method.

Related SALSA MLPA probemixes

P114 Long-QT	Contains probes for the *KNCQ1*, *KCNH2*, *KCNE1* and *KCNE2* genes, involved in Congenital long QT syndrome.
P397 SCN4A-CACNA1S	Contains probes for the *SCN4A* and *CACNA1S* genes, involved in hypokalemic periodic paralysis.

References

- Schouten JP et al. (2002). Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. *Nucleic Acids Res.* 30:e57.
- Schwartz M et al. (2007). Deletion of exon 16 of the dystrophin gene is not associated with disease. *Hum Mutat.* 28:205.
- Varga RE et al. (2012). MLPA-based evidence for sequence gain: pitfalls in confirmation and necessity for exclusion of false positives. *Anal Biochem.* 421:799-801.

Selected publications using SALSA MLPA Probemix P350 CLCN1-KCNJ2

- Brugnoni R et al. (2021). Next-generation sequencing application to investigate skeletal muscle channelopathies in a large cohort of Italian patients. *Neuromuscul Disord*, 31(4), 336-347.
- Dabby R et al. (2014). Myotonia in DNM2-related centronuclear myopathy. *J Neural Transm*. 121(5), 549-553.
- Lehmann-Horn F et al. (2011). A novel N440K sodium channel mutation causes myotonia with exercise-induced weakness-exclusion of CLCN1 exon deletion/duplication by MLPA. *Acta Myol*. 30(2), 133.
- Mazón M et al. (2012). Screening for mutations in Spanish families with myotonia. Functional analysis of novel mutations in CLCN1 gene. *Neuromuscul Disord*. 22(3), 231-243.
- Palma Milla C et al. (2019). Myotonia congenita: mutation spectrum of CLCN1 in Spanish patients. *J Genet*, 98(3), 1-10.
- Rayan DR et al. (2012). A new explanation for recessive myotonia congenita: exon deletions and duplications in CLCN1. *Neurology*. 78(24), 1953-1958.
- Skálová D et al. (2013). CLCN1 Mutations in Czech Patients with Myotonia Congenita, In Silico Analysis of Novel and Known Mutations in the Human Dimeric Skeletal Muscle Chloride Channel. *PLoS ONE*. 8(12), e82549.

P350 product history	
Version	*Modification*
C1	Seven probes for *CLCN1* have been replaced and one added, four reference probes have been replaced and three removed, two probe lengths have been adjusted.
B2	One reference probe has been removed.
B1	Two *CLCN1* probes, one *KJCNJ2* probe and four reference probes have been replaced, one new *KCNJ2* probe, and two flanking probes for *CLCN1* have been included and the 88 and 96 nt control fragments have been replaced (QDX2 fragments).
A1	First release.

Implemented changes in the product description
Version C1-02 – 04 October 2022 (04P) - Product description rewritten and adapted to a new template. - Ligation sites of the probes targeting the *CLCN1* and *KJCNJ2* genes updated according to new version of the NM_ reference sequence. - Two warnings added to the Table 1 and Table 2a for 151 nt probe 13978-L31548 and 434 nt probe 13966-L15535. - Publication list updated. *Version C1-01 — 18 July 2019 (02P)* - Product description rewritten and adapted to a new template. - Product description adapted to a new product version (version number changed, changes in Table 1 and Table 2). - Warning added to Table 2 for probe specificity relying on a single nucleotide difference between target gene and related gene or pseudogene.

More information: www.mrcholland.com; www.mrcholland.eu	
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