Product Description
SALSA® MLPA® Probemix P197-A4 KCNQ3

To be used with the MLPA General Protocol.

Version A4
As compared to version A3, two reference probes have been replaced and a small change in length of two target probes. For complete product history see page 8.

Catalogue numbers
- **P197-025R:** SALSA® MLPA® Probemix P197 KCNQ3, 25 reactions
- **P197-050R:** SALSA® MLPA® Probemix P197 KCNQ3, 50 reactions
- **P197-100R:** SALSA® MLPA® Probemix P197 KCNQ3, 100 reactions

SALSA® MLPA® Probemix P197 KCNQ3 (hereafter: P197 KCNQ3) is to be used in combination with:

1. SALSA® MLPA® Reagent Kit (Cat. No: EK1-FAM, EK1-CY5, EK5-FAM, EK5-CY5, EK20-FAM),
2. Data analysis software Coffalyser.Net™ (Cat. No: n.a.)

Volumes and ingredients

Volumes			Ingredients
P197-025R	**P197-050R**	**P197-100R**	
40 µl	80 µl	160 µl	Synthetic oligonucleotides, oligonucleotides purified from bacteria, Tris-HCl, EDTA

The MLPA probemix is not known to contain any harmful agents. Based on the concentrations present, none of the ingredients are hazardous as defined by the Hazard Communication Standard. A Safety Data Sheet (SDS) is not required for this product: none of the ingredients contain dangerous substances at concentrations requiring distribution of an SDS (as per Regulation (EC) No 1272/2008 [EU-GHS/CLP] and 1907/2006 [REACH] and amendments).

Storage and handling

Recommended storage conditions		

A shelf life of until the expiry date is guaranteed, when stored in the original packaging under recommended conditions. For the exact expiry date, see the label on the vial. This product should not be exposed to more than 25 freeze-thaw cycles. Do not use the product if the packaging is damaged or opened. Leave chemicals in original containers. Waste material must be disposed of in accordance with the national and local regulations.

Certificate of Analysis
Information regarding 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
SALSA® MLPA® Probemix P197 KCNQ3 is a **research use only (RUO)** assay for the detection of deletions or duplications in the *KCNQ3*, *CHRNA4*, *EPM2A*, *NHLRC1* (also known as *EPM2B*), *KCNQ1* and *CHRNB2* genes, which are associated with Epilepsy.

Defects in the *KCNQ3* gene can cause benign familial neonatal convulsions type 2 (BFNC2) or benign neonatal epilepsy type 2 (EBN2), which is also known as epilepsy. The *KCNQ3* gene comprises 15 exons and spans ~360 kb of genomic DNA on chromosome 8q24.22. The *CHRNA4* gene comprises 6 exons spanning ~18 kb of genomic DNA on chromosome 20q13.33. Mutations in this gene appear to account for a small proportion of the cases of nocturnal frontal lobe epilepsy. Mutations in the *EPM2A* gene have been associated with myoclonic epilepsy of Lafora. The *EPM2A* gene encodes the laforin protein, comprises 4 exons, and spans ~111 kb of genomic DNA on chromosome 6q24.3. The *NHLRC1* (*EPM2B*) gene encoding the malin protein, comprises 1 exon and spans ~1.2 kb of genomic DNA on chromosome 6p22.3. Mutations in *NHLRC1* cause progressive myoclonus epilepsy and are also associated with autosomal dominant nocturnal frontal lobe epilepsy. The *CHRNB2* gene comprises 6 exons spanning ~12.2 kb of genomic DNA on chromosome 1q21.3. Finally, the *KCNQ1* gene comprises 17 exons and spans ~404 kb of genomic DNA on chromosome 11p15.5-4.

This product is not CE/FDA registered for use in diagnostic procedures. The SALSA® MLPA® technique is covered by US patent 6,955,901 and corresponding patents outside the US. The purchase of this product includes a license to use only this amount of product solely for the purchaser's own use.

Gene structure and transcript variants:
Entrez Gene shows transcript variants of each gene: https://www.ncbi.nlm.nih.gov/gene
For NM_ mRNA reference sequences: https://www.ncbi.nlm.nih.gov/nuccore?db=nucleotide
Matched Annotation from NCBI and EMBL-EBI (MANE): https://www.ncbi.nlm.nih.gov/refseq/MANE

Exon numbering
The *CHRNB2, NHLRC1, EPM2A, KCNQ3,* and *CHRNA4* exon numberings used in this P197-A4 KCNQ3 product description are the exon numberings from the RefSeq transcripts NM_000748.3, NM_198586.3, NM_005670.4, NM_004519.4, and NM_000744.6, which are identical to the NG_008027.1, NG_016750.1, NG_012832.2, NG_008854.2, and NG_011931.1 sequences, respectively. The *KCNQ1* exon numbering used in this product description is the exon numbering derived from MANE project based on MANE Select transcript NM_000218.3. The *KCNQ1* exon numbering has changed; the exon numbering used in previous versions of this product description can be found in between brackets in Table 2. 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
P197-A4 KCNQ3 contains 39 MLPA probes with amplification products between 137 and 463 nucleotides (nt). This includes 15 probes for the *KCNQ3* gene, six probes for the *CHRNA4* gene, four probes for the *EPM2A* gene, two probes for *NHLRC1* gene, two probes for the *CHRNB2* gene, and finally two probes for the *KCNQ1* gene. 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 MLPA (Schouten et al. 2002) are described in the MLPA General Protocol (www.mrcholland.com).

MLPA technique validation
Internal validation using 16 different DNA samples from healthy individuals is required, in particular when using MLPA for the first time, or when changing the sample type or 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. MRC Holland has tested and can recommend the following extraction methods:

- QIAGEN Autopure LS (automated) and QIAamp DNA mini/midi/maxi kit (manual)
- Promega Wizard Genomic DNA Purification Kit (manual)
- Salting out (manual)

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. 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 different reference samples from unrelated individuals should be included in each MLPA experiment for data normalisation. Reference samples should be derived from individuals who are from families without a history of epilepsy. 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 deviations to the indicated copy number alteration (CNA) findings might occur.

Data analysis
Coffalyser.Net should be used for data analysis in combination with the appropriate lot-specific Coffalyser sheet. For both, the latest version should be used. Coffalyser.Net 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/gain	1.30 < FR < 1.65
Heterozygous triplication/homozygous duplication/gain	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 Coffalyser.Net (Calculations, cut-offs and interpretation remain unchanged.) Please note that Coffalyser.Net 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. single nucleoide variants (SNVs), point mutations) in the target sequence detected by a probe can be one cause. Incomplete DNA denaturation (e.g. due to salt contamination in the DNA sample) 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: https://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 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 *KCNQ3*, *CHRNA4*, *EPM2A*, *NHLRC1*, *KCNQ1* and *CHRNB2* genes are small (point) mutations, none of which will be detected by using P197 KCNQ3.
- 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 in sequence data 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.

LOVD mutation database
https://databases.lovd.nl/shared/genes. 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 https://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 *KCNQ3* exons 4 and 6 but not exon 5) to MRC Holland: info@mrcholland.com.

Table 1. P197 KCNQ3

Length (nt)	MLPA probe	Chromosomal position (hg18)[a]				
		Reference	*KCNQ3*	*EPM2A*	*CHRNA4*	Other
64-105	Control fragments – see table in probemix content section for more information					
137	Reference probe 03797-L04594	21q22				
142	**KCNQ3 probe** 06595-L06153		**Exon 3**			
154	Reference probe 20337-L27719	1p36				
160 Δ	**EPM2A probe** 06617-L29224			**Exon 1**		
166	**KCNQ3 probe** 06596-L06154		**Exon 4**			
172	**KCNQ3 probe** 06603-L06161		**Exon 11**			
178	**CHRNB2 probe** 06616-L06174					**Exon 6**
184	**KCNQ3 probe** 06601-L06159		**Exon 9**			
190 *	Reference probe 22509-L31658	14q32				
198	**KCNQ3 probe** 06604-L29191		**Exon 12**			
205	**NHLRC1 probe** 06621-L07195					**Exon 1**
214	**CHRNA4 probe** 06609-L06167				**Exon 2**	
220	**CHRNA4 probe** 06613-L06171				**Exon 6**	
228 ¥	**EPM2A probe** 06619-L32046			**Exon 3**		
234 *	Reference probe 11156-L16377	5q31				
240 ¥	**CHRNA4 probe** 06610-L10371				**Exon 3**	
247	**EPM2A probe** 06618-L06176			**Exon 2**		
256	**EPM2A probe** 06620-L07196			**Exon 4**		
265	Reference probe 03241-L02678	13q14				
274 «	**KCNQ3 probe** 06593-L06151		**Upstream**			
283	**KCNQ3 probe** 06600-L29155		**Exon 8**			
293 «	**CHRNB2 probe** 06615-L06173					**Exon 2**
301	**KCNQ1 probe** 03551-L02917					**Exon 13**
310	**KCNQ3 probe** 06597-L06155		**Exon 5**			
320	**KCNQ3 probe** 06602-L06160		**Exon 10**			
328	**NHLRC1 probe** 06622-L06180					**Exon 1**
337	Reference probe 04097-L02899	7q36				
346	**CHRNA4 probe** 06611-L07197				**Exon 4**	
364	**CHRNA4 probe** 06612-L06170				**Exon 5**	
378	Reference probe 05921-L05366	17q11				
388	**KCNQ3 probe** 06594-L29158		**Exon 2**			
394	**KCNQ3 probe** 06606-L29192		**Exon 14**			
400	**CHRNA4 probe** 06608-L06166				**Upstream**	
409	**KCNQ1 probe** 03555-L02921					**Exon 16**
418	**KCNQ3 probe** 06598-L06156		**Exon 6**			
427	**KCNQ3 probe** 06607-L07198		**Exon 15**			
436	**KCNQ3 probe** 07315-L06163		**Exon 13**			
454 «	**KCNQ3 probe** 08195-L08089		**Exon 1**			
463	Reference probe 11713-L12484	10q22				

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

* New in version A4.
¥ Changed in version A4. Minor alteration, no change in sequence detected.
Δ More variable. This probe may be sensitive to certain experimental variations. Aberrant results should be treated with caution.
« 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.

The probe lengths in the table above may vary slightly depending on the capillary electrophoresis machine settings. Please see the most up-to-date Coffalyser sheet for exact probe lengths obtained at MRC Holland.

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

Table 2. Target and flanking probes arranged according to chromosomal location

Table 2a. *CHRNB2*

Length (nt)	MLPA probe	CHRNB2 exon[a]	Ligation site[b] NM_000748.3	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*268-270 (Exon 1)*		
293 «	06615-L06173	Exon 2	440-441	GCTGGTGACAGT-ACAGCTTATGGT	6.4 kb
178	06616-L06174	Exon 6	1844-1845	TTGGGTGGAGGA-TGGACGAGTGAG	
		stop codon	*1774-1776 (Exon 6)*		

Table 2b. *NHLRC1*

Length (nt)	MLPA probe	NHLRC1 exon[a]	Ligation site[b] NM_198586.3	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*72-74 (Exon 1)*		
205	06621-L07195	Exon 1	712-713	CATTGGAGGCCA-ATTCTCCTTACC	0.4 kb
328	06622-L06180	Exon 1	1065-1066	ATCACCAGGGAA-ATGTGATTGTTG	
		stop codon	*1257-1259 (Exon 1)*		

Table 2c. *EPM2A*

Length (nt)	MLPA probe	EPM2A exon[a]	Ligation site[b] NM_005670.4	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*23-25 (Exon 1)*		
160 Δ	06617-L29224	Exon 1	121 nt before exon 1	GATGCATCCCAA-AGAAGGCGCAGA	49.4 kb
247	06618-L06176	Exon 2	388-389	GATGGTGTGTAT-TGTCTCCCAATA	50.9 kb
228	06619-L32046	Exon 3	644-645	GCTGTAACCGCT-ACCCAGAGCCCA	7.8 kb
256	06620-L07196	Exon 4	942-943	CTACATTGACGA-AGAGGCCTTGGC	
		stop codon	*1016-1018 (Exon 4)*		

Table 2d. *KCNQ3*

Length (nt)	MLPA probe	KCNQ3 exon[a]	Ligation site[b] NM_004519.4	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*564-566 (Exon 1)*		
274 «	06593-L06151	Upstream (Exon 1)	961 nt before exon 1	TTGGAGGGCTCT-CTGGACATTTAC	1.8 kb
454 «	08195-L08089	Exon 1	871-872	AAACAACGCCAA-GTACCGGCGCAT	294.1 kb
388	06594-L29158	Exon 2	973-974	CCTGGGGTGCTT-GATTCTGGCTGT	1.8 kb
142	06595-L06153	Exon 3	1104-1105	CTGCTGGATGTT-GCTGCCGATACA	4.1 kb
166	06596-L06154	Exon 4	1280-1281	CGCATGCTGCGG-ATGGACCGGAGA	4.7 kb
310	06597-L06155	Exon 5	1438-1439	GGTGGATGCACA-AGGAGAGGAGAT	1.2 kb
418	06598-L06156	Exon 6	1497-1498	TCTCTCTTCAGA-TCACACTGGCCA	3.9 kb
283	06600-L29155	Exon 8	1719-1720	CCTGGAGGTATT-ATGCTACCAACC	7.0 kb
184	06601-L06159	Exon 9	15 nt after exon 9	AGTTTCTGATTA-TGAATTCCCTTC	22.3 kb
320	06602-L06160	Exon 10	2026-2027	GCAGAGTTCTGA-AGGTAATGCCTT	1.0 kb
172	06603-L06161	Exon 11	2074-2075	GGGCTATGGGAA-TGACTTCCCCAT	2.2 kb
198	06604-L29191	Exon 12	2191-2192	GCCTTACGATGT-GAAGGATGTGAT	3.6 kb
436	07315-L06163	Exon 13	2334-2335	AAGGGTCAGCAT-TCACCTTCCCAT	2.1 kb
394	06606-L29192	Exon 14	2393-2394	AGACCATCCACA-TCAGAAATCGAA	2.4 kb
427	06607-L07198	Exon 15	2622-2623	TCATCTGCAACT-ATTCTGAGACAG	
		stop codon	*3180-3182 (Exon 15)*		

Table 2e. *KCNQ1*

Length (nt)	MLPA probe	KCNQ1 exon[a]	Ligation site[b] NM_000218.3	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*92-94 (Exon 1)*		
301	03551-L02917	Exon 13 (14)	1749-1750	CCTCAACCTCAT-GGTGCGCATCAA	72.8 kb
409	03555-L02921	Exon 16 (17)	2908-2909	CCAAACACACAG-AAGGGGACTGCC	
		stop codon	*2120-2122 (Exon 17)*		

Table 2f. *CHRNA4*

Length (nt)	MLPA probe	CHRNA4 exon[a]	Ligation site[b] NM_000744.6	Partial sequence[c] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*232-234 (Exon 1)*		
400	06608-L06166	Upstream (Exon 1)	666 nt before exon 1	CTGCACACGAGA-TTCAGCCGCACA	2.4 kb
214	06609-L06167	Exon 2	364-365	TGAAGAAACTCT-TCTCCGGTTACA	3.3 kb
240	06610-L10371	Exon 3	486-487	ATGATGACCACG-AACGTATGGGTG	0.4 kb
346	06611-L07197	Exon 4	562-563	ATGTCACCTCCA-TCCGCATCCCCT	5.2 kb
364	06612-L06170	Exon 5	794-795	CGACAAGGCCAA-GATCGACCTGGT	4.3 kb
220	06613-L06171	Exon 6	2314-2315	TGTGGAGCTGCT-TCCAGTTGGACT	
		stop codon	*2113-2115 (Exon 6)*		

[a] See section Exon numbering on page 2 for more information.
[b] Ligation sites are relative to the start of the NM_ sequence, and not relative to the coding sequence.
[c] Complete probe sequences are available at www.mrcholland.com. Please notify us of any mistakes: info@mrcholland.com.

Δ More variable. This probe may be sensitive to certain experimental variations. Aberrant results should be treated with caution.
« 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.

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

Related products
For related products, see the product page on our website.

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 P197 KCNQ3

- Grinton et al. (2015). Familial neonatal seizures in 36 families: Clinical and genetic features correlate with outcome. *Epilepsia* 56:1071-80.
- Soldovieri et al. (2014). Novel KCNQ2 and KCNQ3 Mutations in a Large Cohort of Families with Benign Neonatal Epilepsy: First Evidence for an Altered Channel Regulation by Syntaxin-1A. *Hum Mut.* 35:356-67.

P197 product history	
Version	*Modification*
A4	Two reference probes have been replaced and a small change in length of two target probes.
A3	Two reference probes are replaced and the length of several probes adjusted.
A2	QDX2 fragments have been added.
A1	First release.

Implemented changes in the product description
Version A4-03 — 24 December 2025 (05P) - Product description adapted to a new template. - Related SALSA MLPA products section replaced with reference to product page on website. - MANE link added and LRG link removed from section: Gene structure and transcript variants. - Adjusted the exon numbering in Table 1 and 2e for the KCNQ1 probes according to the MANE transcript and added old exon numbering between brackets to Table 2e. - Updated section “Exon numbering” on page 2. Version A4-02 — 05 July 2022 (02P) - Corrected the exon numbering for the KCNQ1 probes according to LRG_287 and added old exon numbering between brackets to Table 2e. - Various minor textual or layout changes. Version A4-01 — 24 March 2020 (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). - Ligation sites of the probes targeting the *CHRNB2*, *NHLRC1*, *EPM2A*, *KCNQ3*, and *KCNQ1* genes updated according to new versions of the NM_ reference sequences. - Warning removed in Tables for 214 nt probe 06609-L06167, 240 nt probe 06610-L10371 and 400 nt probe 06608-L06166. - Exon numbering has been adjusted for 274 nt KCNQ3 probe and 400 nt CHRNA4 probe from exon 1 to Upstream.

More information: www.mrcholland.com; www.mrcholland.eu	
	MRC Holland BV; Willem Schoutenstraat 1 1057 DL, Amsterdam, The Netherlands
E-mail	info@mrcholland.com (information & technical questions) order@mrcholland.com (orders)
Phone	+31 888 657 200