Product Description
SALSA® MLPA® Probemix P275-C4 MAPT-GRN

To be used with the MLPA General Protocol.

Version C4
As compared to version C3, five reference probes have been replaced and one reference probe has been removed. For complete product history see page 8.

Catalogue numbers:
- **P275-025R:** SALSA MLPA Probemix P275 MAPT-GRN, 25 reactions.
- **P275-050R:** SALSA MLPA Probemix P275 MAPT-GRN, 50 reactions.
- **P275-100R:** SALSA MLPA Probemix P275 MAPT-GRN, 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 P275 MAPT-GRN is a **research use only (RUO)** assay for the detection of deletions or duplications in the *MAPT, GRN*, and *CRHR1* genes. This probemix can also be used to detect the presence of wildtype allele of the *MAPT* P301L (c.1853C>T) point mutation.

The *MAPT* gene encodes the microtubule-associated protein tau. Mutations in *MAPT* have been associated with several neurodegenerative disorders, such as frontotemporal dementia with parkinsonism, progressive supranuclear palsy, corticobasal degeneration, Pick disease, and dementia with epilepsy.

The *MAPT* gene (14 exons) spans ~134 kb of genomic DNA and is located on chromosome 17q21.31, 41 Mb from the p-telomere. The region on 17q21, which encompasses the *MAPT* and *CRHR1* genes, is flanked by repeated DNA elements and is often (20% in Europeans) present in inverted position. The Koolen-de Vries syndrome (OMIM 610443), characterized by developmental delay and mild to moderate intellectual disability, can be caused by a microdeletion in this region. Loss of the *KANSL1* gene, which is located 7 kb downstream of the *MAPT* gene, accounts for the features of that syndrome. Duplication of the 17q21 region can result in psychomotor developmental delay (Kirchhoff et al. 2007; Grisart et al. 2009).

The *GRN* (*PGRN*) gene (13 exons), spans ~8 kb of genomic DNA and is located on chromosome 17q21.31, 40 Mb from the p-telomere. Defects in the *GRN* gene cause frontotemporal lobar degeneration.

More information is available at https://www.ncbi.nlm.nih.gov/books/NBK1371/.

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 *MAPT*, *GRN*, and *CRHR1* exon numbering used in this P275-C4 MAPT-GRN product description is the exon numbering from the LRG_660, LRG_661, and NM_001145146.2 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 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 P275-C4 MAPT-GRN contains 41 MLPA probes with amplification products between 148 and 490 nucleotides (nt). This includes 14 probes for the *MAPT* gene, one probe for each exon including one probe specific for the wildtype allele of the P301L (c.1853C>T) point mutation which will only generate a signal when the wildtype allele is present. Furthermore, five probes for the *GRN* gene, five probes for the *CRHR1* gene, seven probes for other genes in the 17q21 region, and one probe each for the 17q11 and 17q12 regions are included in this probemix. 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 neurodegenerative disorders. 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 or in or near the *GRN* gene. 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 *MAPT*, *GRN*, and *CRHR1* genes are small (point) mutations, most of which will not be detected by using SALSA MLPA Probemix P275 MAPT-GRN.
- 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.

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 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 *MAPT* exons 5 and 7 but not exon 6) to MRC Holland: info@mrcholland.com.

Table 1. SALSA MLPA Probemix P275-C4 MAPT-GRN

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]				
		Reference	*MAPT*	*GRN*	*CRHR1*	Other
64-105	Control fragments – see table in probemix content section for more information					
148	Reference probe 13257-L14590	1p				
154	**CRHR1 probe** 08369-L08223				**Exon 11**	
160	**MAPT probe** 08355-L08208		**Exon 5**			
165	**MAPT probe** 08357-L08210		**Exon 7**			
175 «	**GRN probe** 10169-L30211			**Exon 3**		
179	**MAPT probe** 16663-L30326		**Exon 1**			
185	**SUZ12 probe** 03786-L14384					17q11
197 «	**GRN probe** 10168-L30212			**Exon 1**		
204	**MAPT probe** 08353-L30327		**Exon 3**			
210	**CRHR1 probe** 08366-L08220				**Exon 1**	
221	**MAPT probe** 08354-L08207		**Exon 4**			
229	**CRHR1 probe** 08367-L08221				**Exon 1**	
238 *	Reference probe 06712-L06298	15q				
245	**MAPT probe** 08364-L08218		**Exon 13**			
253 *	Reference probe 18649-L14074	9q				
260	**JUP probe** 14867-L16591					17q21
266	**MAPT probe** 08365-L19275		**Exon 14**			
279 «	**GRN probe** 10172-L30213			**Exon 12**		
287 «	**GRN probe** 10170-L30214			**Exon 6**		
295	**COL1A1 probe** 07951-L30328					17q21
301	Reference probe 17637-L12634	3q				
310	**IMP5 probe** 08371-L08225					17q21
317	**MAPT probe** 08352-L08205		**Exon 2**			
330 «	**GRN probe** 10171-L30215			**Exon 10**		
337	**MAPT probe** 08359-L20025		**Exon 9**			
346 ∞	**MAPT probe** 08362-L08215		**Exon 11**			
356	**MAPT probe** 08360-L20026		**Exon 10**			
364	**MED1 probe** 09965-L10424					17q12
373 *	Reference probe 21994-L30832	4p				
382	Reference probe 01253-L00801	2p				
391	**SGCA probe** 11378-L12703					17q21
400	**MAPT probe** 08356-L30329		**Exon 6**			
409	**NBR1 probe** 08346-L08278					17q21
418	**MAPT probe** 08358-L21905		**Exon 8**			
427	**CRHR1 probe** 08370-L08224				**Exon 14**	
436	**COL1A1 probe** 07975-L07756					17q21
445 *	Reference probe 15086-L16849	12q				
466	**MAPT probe** 08363-L08217		**Exon 12**			
475	**CRHR1 probe** 07859-L07620				**Exon 8**	
483	**TOP2A probe** 01060-L19458					17q21
490 *	Reference probe 18601-L23958	2q				

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

* New in version C4.
∞ Wild type sequence detected. A lowered probe signal can be due to a P301L mutation. Other variants near the ligation site can also cause a lowered signal. A positive result must be confirmed by another method.
« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading

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. P275-C4 probes arranged according to chromosomal location

Length (nt)	SALSA MLPA probe	Gene / exon[a]	Ligation site	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
185	03786-L14384	*SUZ12*		CAATGATAAATC-TACGGCTCCTAT	7.5 **Mb**
364	09965-L10424	*MED1*		GCATCAGTGACA-ATTGAAGGAACA	1.0 **Mb**
483	01060-L19458	*TOP2A*		AAGCCCTTCAAT-GGAGAAGATTAT	1.4 **Mb**
260	14867-L16591	*JUP*		ACGCTCAAGAAA-ACCACCACTTAC	1.4 **Mb**
409	08346-L08278	*NBR1*		AACAGGTTGATA-AGAACTTTCTTA	1.2 **Mb**
			GRN		
			NM_002087.2		
		start codon	*220-222 (Exon 2)*		
197 «	10168-L30212	Exon 1	38-39	ATTTGAGTAGAA-AAGAAACACAGC	4.3 kb
175 «	10169-L30211	Exon 3	382-383	CAACACTGAGCA-GGCATCTGGGTG	1.1 kb
287 «	10170-L30214	Exon 6	740-741	CTGCGACCTGGT-TCACACCCGCTG	1.2 kb
330 «	10171-L30215	Exon 10	1292-1293	GCCAGACCCACA-AGCCTTGAAGAG	0.8 kb
279 «	10172-L30213	Exon 12	1795-1796	GGGAAGGACACT-TCTGCCATGATA	1.4 **Mb**
		stop codon	*1999-2001 (Exon 13)*		
			CRHR1		
			NM_001145146.2		
		start codon	*226-228 (Exon 1)*		
210	08366-L08220	Exon 1	627 nt before exon 1	CTTGCAGAGCGT-TCGCGTCTCAGC	0.9 kb
229	08367-L08221	Exon 1	242-241, reverse	CGAGACGGAGCT-GCGGGTGCCCTC	45.9 kb
475	07859-L07620	Exon 8	922-923	TGACCAACTTCT-TCTGGATGTTCG	3.0 kb
154	08369-L08223	Exon 11	1216-1215, reverse	CTCAGACGTGGT-GGATGCCCGGAG	1.4 kb
427	08370-L08224	Exon 14	1652-1653	AGGTGACCTGTT-AGGTCTCATGCC	10.5 kb
		stop codon	*1558-1560 (Exon 14)*		
310	08371-L08225	*IMP5*		CACCATCCCTGT-GGCTATGCTCCA	49.3 kb
			MAPT		
			NM_016835.4		
		start codon	*323-325 (Exon 2)*		
179	16663-L30326	Exon 1	294-295	TCCTCGCCTCTG-TCGACTATCAGG	67.8 kb
317	08352-L08205	Exon 2	413-414	GGGGCTACACCA-TGCACCAAGACC	9.4 kb
204	08353-L30327	Exon 3	456-457	ATGTGTTCCAGA-ATCTCCCCTGCA	2.5 kb
221	08354-L08207	Exon 4	544-545	TGGTTTCTAGAT-GTGACAGCACCC	4.0 kb
160	08355-L08208	Exon 5	645-646	AGAAGCAGGCAT-TGGAGACACCCC	5.2 kb
400	08356-L30329	Exon 6	1144-1145	TTCCTCTCCAAA-GTTTCCACAGAG	3.4 kb
165	08357-L08210	Exon 7	1470-1471	CAGTAAAAGCAA-AGACGGGACTGG	2.8 kb
418	08358-L21905	Exon 8	1536-1537	TAAAACCTTGAA-AAATAGGCCTTG	1.5 kb
337	08359-L20025	Exon 9	11 nt before exon 9	CCTCTATCATGT-TTCATTTACAGG	4.9 kb
356	08360-L20026	Exon 10	1 nt before exon 10	CCTTCCTTCCCA-GGTGAACCTCCA	14.0 kb
346 ∞	08362-L08215	Exon 11	2175-2174, reverse	TGCCGCCTCCCG-GGACGTGTTTGA	3.9 kb
466	08363-L08217	Exon 12	2194-2195	CTCCAGGTGCAA-ATAGTCTACAAA	4.4 kb
245	08364-L08218	Exon 13	2333-2334	TCCAGTCGAAGA-TTGGGTCCCTGG	5.4 kb
266	08365-L19275	Exon 14	2469-2470	GTCGCCAGTGGT-GTCTGGGGACAC	4.2 **Mb**
		stop codon	*2597-2599 (Exon 14)*		
391	11378-L12703	*SGCA*		GAGAAGGGAGGA-TGAAGTCAGGGC	13.0 kb
436	07975-L07756	*COL1A1* Exon 42		GCAACACTCCAT-GACCACAGCCTT	11.2 kb
295	07951-L30328	*COL1A1* Exon 2		ACGGCCTCAGGT-ACCATGACCGAG	

[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.

∞ Wild type sequence detected. A lowered probe signal can be due to a P301L mutation. Other variants near the ligation site can also cause a lowered signal. A positive result must be confirmed by another method.
« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading

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.

Complete probe sequences are available at www.mrcholland.com.

Related SALSA MLPA probemixes

P245 Microdeletion-1	Primary screening for microdeletion syndromes.
P443 KANSL1	Contains probes for *KANSL1*, which is also present in the 17q21.31 region. Loss of the gene results in Koolen-de Vries syndrome.

References

- Grisart B et al. (2009). 17q21. 31 microduplication patients are characterised by behavioural problems and poor social interaction. *J Med Genet*, 46(8), 524-530.
- Kirchhoff M et al. (2007). A 17q21. 31 microduplication, reciprocal to the newly described 17q21. 31 microdeletion, in a girl with severe psychomotor developmental delay and dysmorphic craniofacial features. *Eur J Med Genet*, 50(4), 256-263.
- 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 P275 MAPT-GRN

- Chiang HH et al. (2013). Novel progranulin mutations with reduced serum-progranulin levels in frontotemporal lobar degeneration. *Eur J Hum Genet*, 21(11), 1260-1265.
- Das G et al. (2013). Genetic study on frontotemporal lobar degeneration in India. *Parkinsonism Relat Disord*, 19(4), 487-489.
- Karch CM et al. (2016). Missense mutations in progranulin gene associated with frontotemporal lobar degeneration: study of pathogenetic features. *Neurobiol aging*. 38: 215-e1.
- McCarthy A et al. (2015). Closing the tau loop: the missing tau mutation. *Brain*. 138:3100-9.
- Clot F et al. (2014). Partial deletions of the GRN gene are a cause of frontotemporal lobar degeneration. *Neurogenetics.* 15:95-100.
- Ogaki K et al. (2013). Analyses of the MAPT, PGRN, and C9orf72 mutations in Japanese patients with FTLD, PSP, and CBS. *Parkinsonism Relat Disord*. 19:15-20.
- Rohrer JD et al. (2013). Exome sequencing reveals a novel partial deletion in the progranulin gene causing primary progressive aphasia. *J Neurol Neurosurg Psychiatry*. 85:1411-2.
- Rossi G et al. (2014). Different mutations at V363 MAPT codon are associated with atypical clinical phenotypes and show unusual structural and functional features. *Neurobiology of aging*, 35(2), 408-417.
- Saracino D et al. (2020). The missense p. Trp7Arg mutation in GRN gene leads to progranulin haploinsufficiency. *Neurobiol Aging*, 85, 154-e9.

P275 product history	
Version	*Modification*
C4	Five reference probes have been replaced and one reference probe has been removed.
C3	Compared to previous version, two reference probes have been replaced and one removed. Also, the length of several probes have been adjusted.
C2	One flanking probe has been removed.
C1	New control fragments and exon one probe for *MAPT* gene. Replacement of three flanking and seven reference probes.
B1	Various changes compared to lot 1107.
A1	First release.

Implemented changes in the product description

Version C4-01 – 5 July 2021 (04P)
- 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 *CRHR1* gene updated according to new version of the NM_ reference sequence.
- Small changes of probe lengths in Table 1 and 2 in order to better reflect the true lengths of the amplification products.
- Warnings removed in and below Tables 1 and 2.

Version 09 – 24 November 2017 (55)
- Product description adapted to a new product version (version number changed, lot number added, small changes in Table 1 and Table 2, new picture included).
- New reference added on page 1.
- Ligation sites of the probes targeting the MAPT gene updated according to the NM_016835.3_reference sequence.
- Various minor textual changes.

Version 08 – 29 September 2016 (55)
- Product description adapted to a new lot (lot number added, small changes in Table 1 and Table 2, new picture included).
- Address Manufacturer changed.
- Exon numbering of the MAPT and CRHR1 genes changed.
- Introduction updated.
- References added on page 2.
- New related SALSA MLPA probemixes added on page 1.
- Probe numbers of the 185 nt, 283 nt and 483 nt probes corrected in Table 2.
- Various minor textual changes.

Version 07 (50)
- Product description adapted to a new lot (lot number added, small changes in Table 1 and Table 2, new picture included).

Version 06 (48)
- Electropherogram pictures using the new MLPA buffer (introduced in December 2012) added.

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