Product Description SALSA® MLPA® Probemix P219-B4 PAX6

To be used with the MLPA General Protocol.

Version B4. Compared to version B3 two reference probes have been replaced and the length of four probes have been adjusted, no change in sequence detected. For complete product history see page 8.

Catalogue numbers:
- **P219-025R:** SALSA MLPA Probemix P219 PAX6, 25 reactions.
- **P219-050R:** SALSA MLPA Probemix P219 PAX6, 50 reactions.
- **P219-100R:** SALSA MLPA Probemix P219 PAX6, 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.mlpa.com).

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

Precautions and warnings: For professional use only. Always consult the most recent product description AND the MLPA General Protocol before use: www.mlpa.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 P219 PAX6 is a **research use only (RUO)** assay for the detection of deletions or duplications in the 11p13-14 region, which includes the *PAX6* and *WT1* genes, and the *SOX2* gene on 3q26, which are associated with hereditary ocular malformations.

In the human eye morphogenesis a molecular genetic cascade is involved. A number of developmental genes interact in a highly organized process during the embryonic period, to produce functional ocular structures. During the early stages of eye development, *PAX6* induces the differentiation of progenitor cells into neurons in the retina, as well as the expression of crystallins in lens epithelial cells. *PAX6* mutations lead to a variety of hereditary ocular malformations of the anterior and posterior segment that includes aniridia, coloboma of the iris, keratitis, congenital cataracts, Peter's anomaly, and optic nerve defects.

WT1 is required for at least two critical functions during retinogenesis: proliferation of the progenitor cells and development of the retinal ganglion cells. The *WT1* gene is often co-deleted with *PAX6* in patients with Wilms tumor-aniridia-genital anomalies-retardation (WAGR) syndrome. The *SOX2* gene encodes a transcription factor involved in the regulation of embryonic development. Mutations in this gene have been associated with optic nerve hypoplasia and with syndromic microphthalmia, a severe form of structural eye malformation.

More information is available at https://www.ncbi.nlm.nih.gov/books/NBK1360/.

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 *PAX6, WT1* and *SOX2* exon numbering used in this P219-B4 PAX6 product description are the exon numbering from the RefSeq transcripts NM_000280.3, NM_024426.3, and NM_003106.2, which are identical to the LRG_720, LRG_525, and LRG_719 sequences, respectively. The

exon numbering and NM_ sequence used have been retrieved on 09/2019. As changes to the NCBI database can occur after release of this product description, exon numbering may not be up-to-date.
Probemix content: The SALSA MLPA Probemix P219-B4 PAX6 contains 44 MLPA probes with amplification products between 130 and 463 nucleotides (nt). This includes 32 probes for the 11p13-14 region: seven probes downstream of the *PAX6* gene, 13 probes targeting the *PAX6* gene (at least one probe for each exon with the exception of exon 11), six probes located in the region between *PAX6* and *WT1*, three probes for the *WT1* gene, and three probes upstream of the *WT1* gene. Furthermore, three probes are included targeting exon 1 of the *SOX2* gene. In addition, nine 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.mlpa.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, 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.mlpa.com.

Length (nt)	Name
64-70-76-82	Q-fragments (only visible with <100 ng sample DNA)
88-96	D-fragments (low signal of 88 nt and 96 nt fragment 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.mlpa.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 unrelated individuals who are from families without a history of hereditary ocular malformations. More information regarding the selection and use of reference samples can be found in the MLPA General Protocol.

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/home.html) have a diverse collection of biological resources which may be used as a positive control DNA sample 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.mlpa.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 dosage quotient (DQ) 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 DQ of the probes can be used to interpret MLPA results for autosomal chromosomes or pseudo-autosomal regions:

Copy number status	Dosage quotient
Normal	0.80 < DQ < 1.20
Homozygous deletion	DQ = 0
Heterozygous deletion	0.40 < DQ < 0.65
Heterozygous duplication	1.30 < DQ < 1.65
Heterozygous triplication/Homozygous duplication	1.75 < DQ < 2.15
Ambiguous copy number	All other values

- 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. Incomplete DNA denaturation (e.g. due to salt contamination) can 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.
- When running MLPA products, the capillary electrophoresis protocol may need optimization. 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: lower injection voltage / injection time settings, 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 *PAX6, WT1* and *SOX2* gene are small (point) mutations, most of which will not be detected by using SALSA MLPA Probemix P219 PAX6.
- 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. SNPs, point mutations, small indels) in the target sequence detected by a probe can cause false positive results. Mutations/SNPs (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.

***PAX6*, *WT1* and *SOX2* 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 SNPs and unusual results (e.g., a duplication of *PAX6* exons 5 and 7 but not exon 6) to MRC-Holland: info@mlpa.com.

Table 1. SALSA MLPA Probemix P219-B4 PAX6

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]				
		Reference	11p13-14 region			*SOX2*
			PAX6	*WT1*	Other	
64-105	Control fragments – see table in probemix content section for more information					
130	Reference probe 00797-L00463	5q31				
138	**PAX6 probe** 06026-L07190		**Exon 4**			
142 ¬	**DCDC1 probe** 07076-L07345				**Telomeric**	
148 ¬	**ELP4 probe** 07078-L06707				**Telomeric**	
155	**PAX6 probe** 06025-L07191		**Exon 2**			
160	**SOX2 probe** 07682-L06702					**Exon 1**
166 ¬	**FSHB probe** 07075-L06704				**Telomeric**	
172 ¬	**DCDC1 probe** 07077-L06706				**Telomeric**	
178	**WT1 probe** 05354-L04733			**Exon 5**		
184 *	Reference probe 10973-L11644	14q31				
193 « ¬	**LMO2 probe** 00486-L00083				**Centromeric**	
200 ¬	**HIPK3 probe** 00976-L07192				**Centromeric**	
206 ¬	**BDNF probe** 03089-L07193				**Telomeric**	
214 ¬	**FSHB probe** 07074-L06703				**Telomeric**	
220	**PAX6 probe** 03253-L02690		**Exon 5**			
226 ¬	**RCN1 probe** 07083-L06712				**Intergenic**	
235	Reference probe 14498-L20676	20p12				
240	**PAX6 probe** 03254-L07346		**Exon 7**			
247	**WT1 probe** 02755-L02204			**Exon 1**		
256	**SOX2 probe** 07072-L07347					**Exon 1**
265 ¬	**CD44 probe** 02245-L01731				**Centromeric**	
274	**WT1 probe** 05360-L04739			**Exon 11**		
281	Reference probe 15958-L18610	4q25				
288	**PAX6 probe** 06027-L21437		**Exon 6**			
297	Reference probe 10136-L26376	18q11				
304	**PAX6 probe** 03255-L14006		**Exon 13**			
310 ¬ ¥	**PAX6 probe** 21674-L31791				**Intergenic**	
319	**PAX6 probe** 03748-L03208		**Exon 1**			
328	**PAX6 probe** 07527-L21498		**Exon 8**			
337	**SOX2 probe** 07681-L06700					**Exon 1**
346 ¬	**RCN1 probe** 07082-L06711				**Intergenic**	
357 ¥	**PAX6 probe** 03092-L30095		**Exon 10**			
364 ¬	**WT1-area probe** 07084-L06713				**Intergenic**	
373	Reference probe 13248-L14581	1p21				
383	**PAX6 probe** 03091-L07348		**Exon 3**			
391	**PAX6 probe** 06030-L05486		**Exon 12**			
399 *	Reference probe 21266-L19425	12q13				
409	**PAX6 probe** 03749-L07349		**Exon 1**			
418 ¬	**PAX6 probe** 07081-L06710				**Intergenic**	
431 ¥	**PAX6 probe** 06029-L31897		**Exon 9**			
439 ¥	Reference probe 13058-L31896	15q14				
445 ¬	**WT1-area probe** 07085-L06714				**Intergenic**	
454 ¬	**BDNF probe** 03090-L03996				**Telomeric**	
463	Reference probe 00979-L00568	10p14				

a) See above section on exon numbering for more information.

* New in version B4.

¥ Changed in version B4. Minor alteration, no change in sequence detected.

« 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.

¬ 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.

Table 2. P219-B4 probes arranged according to chromosomal location

Table 2a. 11p13-14 region

Length (nt)	SALSA MLPA probe	Gene / exon[a]	Ligation site	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
					Telomere
454 ¬	03090-L03996	*BDNF* Exon 2		CCCAATGAAGAA-AACAATAAGGAC	41.2 kb
206 ¬	03089-L07193	*BDNF* Exon 1		TCCAGGGAAGTT-AAGAGTTTTGAC	2532.6 kb
214 ¬	07074-L06703	*FSHB* Exon 2		GCATCAACACCA-CTTGGTGTGCTG	2.1 kb
166 ¬	07075-L06704	*FSHB* Exon 3		GAACTAACTGCA-GCAGTCTTCTGG	1073.6 kb
172 ¬	07077-L06706	*DCDC1* Exon 4		CAGCAGTATCAG-AAGGGTCAGGAC	61.9 kb
142 ¬	07076-L07345	*DCDC1* Exon 1		TGGAGTGGCGTT-TACTACCAGTAA	280.4 kb
148 ¬	07078-L06707	*ELP4* Exon 9		TCACAGATCAAG-TTATTAAGCCGA	139.8 kb
		***PAX6* gene**	**NM_000280.4**		
		stop codon	*1822-1824 (Exon 13)*		
304	03255-L14006	Exon 13	1761-1762	CCTGGTGTGTCA-GTTCCAGTTCAA	0.7 kb
391	06030-L05486	Exon 12	13 nt after exon 12	TGAGCCACTGCT-TTCTGCAGGCTG	3.0 kb
357	03092-L30095	Exon 10	1413-1414	AGTCATATTCCT-ATCAGCAGTAGT	0.4 kb
431	06029-L31897	Exon 9	1249-1248 reverse	TGGATAATGGGT-TCTCTCAAACTC	0.6 kb
328	07527-L21498	Exon 8	1137-1138	AGTTCCAACGGA-GAAGATTCAGAT	6.1 kb
240	03254-L07346	Exon 7	944-945	TCTTCGCAACCT-GGCTAGCGAAAA	0.8 kb
288	06027-L21437	Exon 6	864-865	TGGGAAATCCGA-GACAGATTACTG	1.2 kb
220	03253-L02690	Exon 5	588-589	GTGAATCAGCTC-GGTGGTGTCTTT	3.6 kb
138	06026-L07190	Exon 4	18 nt after exon 4	GCCTCTGGTCTT-TCTGGGACTTCG	0.5 kb
383	03091-L07348	Exon 3	475-474 reverse	GTCCACTCTCAC-AATAAAAGGCCT	4.1 kb
155	06025-L07191	Exon 2	299-300	AAACTCTCACCA-GCAACTCCTTTA	0.3 kb
319	03748-L03208	Exon 1	108-109	GTTCAGGCGCAG-GAGGAAGTGTTT	0.1 kb
409	03749-L07349	Exon 1	49 nt before exon 1	TCGGCTGGCGCG-AGGCCCCGGCGC	5.2 kb
		start codon	*534-536 (Exon 4)*		
310 ¬	21674-L31791	*PAX6* Upstream	5.2 kb before exon 1	CCTTCTCCTCCA-GTCATAAATCAA	69.1 kb
418 ¬	07081-L06710	*PAX6* Upstream	~74 kb upstream of *PAX6*	TGTGCTAGGGCT-ATCGCGATTTGC	206.9 kb
346 ¬	07082-L06711	*RCN1* Intron 1		GGAGGATTTTGA-CTTGGGCTGTTA	11.3 kb
226 ¬	07083-L06712	*RCN1* Exon 5		GTTGCCCTAGGA-TCAGCTTATTTA	126.5 kb
445 ¬	07085-L06714	*WT1*-area Downstream	158 kb downstream of *WT1*	CCATTCCTTGGT-TACATCATCAAA	88.1 kb
364 ¬	07084-L06713	*WT1*-area Downstream	70 kb downstream of *WT1*	GCTTGTAGATCT-GTCCCTTGGCCT	70.2 kb
		***WT1* gene**	**NM_024426.6**		
		stop codon	*1746-1748 (Exon 11)*		
274	05360-L04739	Exon 11	2276-2277	GTCAGCCAGGCT-GCTAACCTGGAA	29.1 kb
178	05354-L04733	Exon 5	1098-1099	CATCCCAGCTTG-AATGCATGACCT	18.1 kb
247	02755-L02204	Exon 1	217 nt before exon 1	CACCGGCCAGCT-GAGAGCGCGTGT	917.6 kb
		start codon	*180-182 (Exon 1)*		
200 ¬	00976-L07192	*HIPK3* Exon 17		CAGCATCCAACT-TATAATATCTCC	506.2 kb
193 « ¬	00486-L00083	*LMO2* Exon 5		AAGCGGATTCGT-GCCTATGAGATG	1279.8 kb
265 ¬	02245-L01731	*CD44* Exon 1		CCCGCGCCCTCC-GTTCGCTCCGGA	
					Centromere

Table 2b. *SOX2* gene

Length (nt)	SALSA MLPA probe	*SOX2* exon[a]	Ligation site NM_003106.2	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*428-430 (Exon 1)*		
337	07681-L06700	Exon 1	56-55 reverse	CCCCCTTTTGCA-AACACTCTCTTC	0.7 kb
256 #	07072-L07347	Exon 1	751-752	CACCCGGATTAT-AAATACCGGCCC	0.2 kb
160 #	07682-L06702	Exon 1	909-910	GGACAGTTACGC-GCACATGAACGG	
		stop codon	*1379-1381 (Exon 1)*		

a) See above section on exon numbering for more information.

b) Only partial probe sequences are shown. Complete probe sequences are available at www.mlpa.com. Please notify us of any mistakes: info@mlpa.com.

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.
« 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.
¬ 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.

Related SALSA MLPA probemixes

P229 OPA1	Contains probes for *OPA1*, involved in optic atrophy type 1.
P118 WT1	Contains more probes for the *WT1* gene.

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 P219 PAX6

- Blanco-Kelly F et al. (2017). Improving molecular diagnosis of aniridia and WAGR syndrome using customized targeted array-based CGH. *PloS one*, *12*(2), e0172363.
- de Castro-Miró M et al. (2018). Novel mutation in the choroideremia gene and multi-Mendelian phenotypes in Spanish families. *Br J Ophthalmol*, *102*(10), 1378-1386.
- Franzoni A et al. (2017). A CGH array procedure to detect PAX6 gene structural defects. *Mol cell probe*, *32*, 65-68.
- Haer-Wigman L et al. (2017). Diagnostic exome sequencing in 266 Dutch patients with visual impairment. *Eur J Hum Genet*, *25*(5), 591.
- Hernández-Martínez N et al. (2018). Molecular characterization of Axenfeld-Rieger spectrum and other anterior segment dysgeneses in a sample of Mexican patients. *Ophthalmic genet*, *39*(6), 728-734.
- Plaisancié J et al. (2018). Implication of non-coding PAX6 mutations in aniridia. *Hum genet*, *137*(10), 831-846.
- Souzeau E et al. (2018). PAX6 molecular analysis and genotype–phenotype correlations in families with aniridia from Australasia and Southeast Asia. *Mol vis*, *24*, 261.
- Syrimis A et al. (2018). Molecular analysis of Cypriot families with aniridia reveals a novel PAX6 mutation. *Mol med rep*, *18*(2), 1623-1627.

P219 Product history	
Version	*Modification*
B4	Two reference probes have been replaced and the length of four probes have been adjusted, no change in sequence detected.
B3	Two reference probes have been replaced and one added. One flaking probe has been removed.
B2	One reference probe has been added and two reference probes have been replaced, QDX2 fragments have been added
B1	The reference probes at 160 and 337 nt have been replaced by two extra *SOX2* probes.
A1	First release.

Implemented changes in the product description

Version B4-01 — 19 September 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).
- Ligation sites of the probes targeting the *WT1* and *PAX6* 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.
- Warning added to Table 2 for probe specificity relying on a single nucleotide difference between target gene and related gene or pseudogene.

Version 12 – 13 January 2017 (55)
- Warning added in Table 1 and Table 2, 383 nt probe 03091-L07348 and 193 nt probe 00486-L00083.
- Several minor textual changes on page 1.

Version 11 – 11 December 2015 (55)
- Product description adapted to a new product version (version number changed, lot number added, changes in Table 1 and Table 2, new picture included).
- Exon numbering of PAX6 and BDNF adjusted according to RefSeq sequence.
- Ligation sites of PAX6 and SOX2 adjusted according to RefSeq sequence.
- "Peak area" replaced with "peak height".
- Update link for "Database of Genomic Variants".
- Manufacturer's address adjusted.

Version 10 – 22 June 2015 (48)
- Electropherogram pictures of the old buffer (introduced Dec. 2012) removed.

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