Product Description

SALSA® MLPA® Probemix P412-A3 Porphyria mix 2

To be used with the MLPA General Protocol.

Version A3
For complete product history see page 7.

Catalogue numbers:

- **P412-025R:** SALSA MLPA Probemix P412 Porphyria mix 2, 25 reactions.
- **P412-050R:** SALSA MLPA Probemix P412 Porphyria mix 2, 50 reactions.
- **P412-100R:** SALSA MLPA Probemix P412 Porphyria mix 2, 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 P412-A3 Porphyria mix 2 is a **research use only (RUO)** assay for the detection of deletions or duplications in the *FECH*, *UROS*, *UROD* and *CPOX* genes. *FECH*, *UROS* and *UROD* are associated with Erythropoietic porphyria, while *CPOX* is linked to Acute hepatic porphyria. *CPOX* has been included in this probemix instead of the P411-B3 probemix, which contains *ALAD*, *HMBS* and *PPOX*, also linked to Acute hepatic porphyria, due to the limited number of probes which can be included in an MLPA probemix.

Porphyrias are a group of disorders characterised by accumulation of porphyrins and porphyrin precursors owing to enzymatic deficiencies of the haem biosynthetic pathway. They can be divided into acute hepatic porphyrias and erythropoietic porphyrias based on their clinical manifestations. Acute hepatic porphyrias are characterised by abdominal pain, neuropsychiatric symptoms and neuropathy. Erythropoietic porphyrias do not cause neurologic symptoms but are associated with photosensitive dermatologic eruptions and may be associated with additional hepatic injury and/or haemolysis (Simon, N.G et al. 2011).

Acute hepatic porphyrias consist of ALA dehydratase deficiency porphyria (ADP), acute intermittent porphyria (AIP), hereditary coproporphyria (HCP) and variegate porphyria (VP). Erythropoietic porphyrias comprise congenital erythropoietic porphyria (CEP), porphyria cutanea tarda (PCT) and the related hepatoerythropoietic porphyria and erythropoietic protoporphyria (EPP), see Table 1.

Table 1. Genetic classification and clinical manifestations of the porphyrias

Porphyria	Enzyme	Inheritance	Classification	Clinical features
ADP	ALAD	AR	Acute hepatic	Acute neurovisceral
AIP	HMBS	AD	Acute hepatic	Acute neurovisceral
CEP	#UROS	AR	Erythropoietic	Photosensitivity; Liver disease; Haemolytic anaemia
PCT	#UROD	Sporadic 80%, AD 20%	Erythropoietic	Photosensitivity; Liver disease
HCP	#^CPOX	AD	Acute hepatic	Acute neurovisceral (100%); Photosensitivity (20%)
VP	PPOX	AD	Acute hepatic	Acute neurovisceral (50%); Photosensitivity (80%)
EPP	#FECH	AD	Erythropoietic	Photosensitivity; Liver disease

AD = autosomal dominant, AR = autosomal recessive, ADP = ALA dehydratase deficiency porphyria, AIP = acute intermittent porphyria, ALAD = ALA dehydratase, CEP = congenital erythropoietic porphyria, CPOX = coproporphyrinogen oxidase, EPP = erythropoietic protoporphyria, FECH = ferrochetalase, HCP = hereditary coproporphyria, HMBS = hydroxymethylbillane synthase, PCT = porphyria cutanea tarda, PPOX = protoporphyrinogen oxidase, UROD = uroporphyrinogen dehydratase, UROS = uroporphyrinogen synthase, VP = variegate porphyria.
 # FECH, *UROS*, *UROD* and *CPOX* genes are included in SALSA MLPA probemix P412.

The *FECH* gene (11 exons) spans ~42 kb of genomic DNA and is located on 18q21.31, 53 Mb from the p-telomere.
The *UROS* gene (10 exons) spans ~35 kb of genomic DNA and is located on 10q26.2, 127 Mb from the p-telomere.
The *UROD* gene (10 exons) spans ~3.5 kb of genomic DNA and is located on 1p34.1, 45 Mb from the p-telomere.
The *CPOX* gene (7 exons) spans ~14 kb of genomic DNA and is located on 3q11.2, 99 Mb from the p-telomere.

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

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 *FECH*, *UROS*, *UROD* and *CPOX* exon numbering used in this P412-A3 Porphyria mix 2 product description is the exon numbering of NM_000140.5 (*FECH*), NM_000375.3 (*UROS*), NM_000097.7 (*CPOX)* and NM_000374.5 (*UROD)* sequences. The *UROS* exon numbering has changed from description version A3-02 onwards. The exon numbering used in previous version of this product description can be found in between brackets in Table 3b. 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 P412-A3 Porphyria mix 2 contains 46 MLPA probes with amplification products between 130 and 489 nucleotides (nt). This P412-A3 includes the *FECH, UROS* , *UROD* and *CPOX* genes. 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.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 Erythropoietic porphyria. 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 *FECH*, *UROS*, *UROD* and *CPOX* genes are small (point) mutations, none of which will be detected by using SALSA MLPA Probemix P412-A3 Porphyria mix 2.
- 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.

***FECH*, *UROS*, *UROD* and *CPOX* genes 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 *FECH* exons 5 and 7 but not exon 6) to MRC Holland: info@mrcholland.com.

Table 2. SALSA MLPA Probemix P412-A3 Porphyria mix 2

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]				
		Reference	*FECH*	*CPOX*	*UROS*	*UROD*
64-105	Control fragments – see table in probemix content section for more information					
130	Reference probe 14118-L15719	7p				
136	Reference probe 03972-L19682	9q				
142	**FECH probe** 14811-L16519		**Exon 9**			
148	**UROS probe** 14812-L16520				**Exon 8**	
154	**UROD probe** 14813-L16521					**Exon 1**
160	**UROD probe** 15983-L18138					**Exon 9**
166	**CPOX probe** 14815-L16523			**Exon 1**		
172	**FECH probe** 14816-L16524		**Exon 7**			
178	Reference probe 17900-L07550	8p				
184	**UROD probe** 14817-L16525					**Exon 7**
190	**CPOX probe** 14818-L16526			**Exon 7**		
197	**UROS probe** 14819-L16527				**Exon 3**	
203	**FECH probe** 14820-L18793		**Exon 1**			
211	**UROD probe** 14821-L18794					**Exon 10**
218	**FECH probe** 14822-L17166		**Exon 4**			
226	**UROS probe** 14900-L16644				**Exon 6**	
232	**FECH probe** 14823-L18796		**Exon 8**			
238	**UROD probe** 14824-L16532					**Exon 3**
246	**FECH probe** 14825-L16533		**Exon 6**			
256	**UROS probe** 14826-L16534				**Exon 4**	
265	**CPOX probe** 14827-L16535			**Exon 4**		
274	Reference probe 10708-L11290	6p				
283	**CPOX probe** 14828-L18795			**Exon 2**		
289	**CPOX probe** 14830-L17168			**Exon 5**		
295	**UROS probe** 14829-L17169				**Exon 9**	
309	**UROD probe** 14831-L16539					**Exon 2**
319	**UROS probe** 14832-L16540				**Exon 2**	
328	**FECH probe** 15984-L18139		**Exon 2a**			
340	Reference probe 21099-L30929	11p				
348	**FECH probe** 14833-L21742		**Exon 10**			
355	**UROS probe** 14834-L16542				**Exon 5**	
363	**UROD probe** 14835-L29122					**Exon 6**
373	**CPOX probe** 14836-L16544			**Exon 3**		
391	**UROD probe** 15986-L18141					**Exon 5**
400	**UROD probe** 14839-L16547					**Exon 8**
409	**UROS probe** 14840-L29123				**Exon 7**	
415	Reference probe 18255-L22981	12q				
426	Reference probe 10465-L29125	2p				
430	**UROS probe** 14841-L29126				**Exon 1**	
440	**FECH probe** 14842-L29127		**Exon 11**			
449	**UROS probe** 14843-L29128				**Exon 10**	
454	**FECH probe** 14844-L29129		**Exon 5**			
463	**FECH probe** 15987-L18142		**Exon 3**			
472	**CPOX probe** 14846-L16554			**Exon 6**		
481	Reference probe 08586-L13087	17q				
489	Reference probe 10236-L14068	20q				

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

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 3. P412-A3 probes arranged according to chromosomal location

Table 3a. *FECH* gene

Length (nt)	SALSA MLPA probe	*FECH* Exon[a]	Ligation site NM_000140.5	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		Start Codon	*83-85 (exon 1)*		
203	14820-L18793	Exon 1	88-89	CAGGCAATGCGT-TCACTCGGCGCA	6.6 kb
328	15984-L18139	Exon 2a	72 nt after exon 2a	ACACAAGCTGCC-TGGGAGGAAAGG	6.6 kb
463	15987-L18142	Exon 3	10 nt before exon 3	CGTTGTATTTTA-TTTTATATAGGA	1.8 kb
218	14822-L17166	Exon 4	403-404	TTTAGTAAGCTG-GCACCATTCATC	5.1 kb
454	14844-L29129	Exon 5	653-654	CTTTCACACAGT-ATCCACAGTACA	3.6 kb
246	14825-L16533	Exon 6	745-746	ACGATGAAGTGG-AGCACTATTGAC	3.7 kb
172	14816-L16524	Exon 7	10 nt before exon 7	TCCTTTCTTGTT-ACTCACTCAGTG	4.3 kb
232	14823-L18796	Exon 8	920-921	ATCCTCAGGAGG-TAAGCGCCACTG	0.6 kb
142	14811-L16519	Exon 9	1079-1080	ATATCCTCTTGG-TTCCGATAGCAT	3.0 kb
348	14833-L21742	Exon 10	1208-1209	ATGGAAATCCAT-TGTTCTCTAAGG	0.5 kb
440	14842-L29127	Exon 11	1274-1275	TGTGTTCCAAGC-AGCTGACCCTGA	
		Stop Codon	*1352-1354 (exon 11)*		

Table 3b. *UROS* gene

Length (nt)	SALSA MLPA probe	*UROS* Exon[a]	Ligation site NM_000375.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		Start Codon	*257-259 (exon 2)*		
430	14841-L29126	Exon 1 (1b)	120-121	GGAGGGGGCTTC-CGCCCCTGTTGT	6.7 kb
319	14832-L16540	Exon 2	267-268	AATGAAGGTTCT-TTTACTGAAGGA	0.3 kb
197	14819-L16527	Exon 3	366-367	CCCTGTTTTATC-GTTTGAGTTTTT	1.2 kb
256	14826-L16534	Exon 4	495-496	AAACAATAAAAC-TGAAGGTGAGGG	2.8 kb
355	14834-L16542	Exon 5	552-553	AGTGTATGTGGT-TGGAAATGCTAC	5.0 kb
226	14900-L16644	Exon 6	214 nt after exon 6	CCCCTGTACCAA-AGAACTTGACTT	9.1 kb
409	14840-L29123	Exon 7 (8)	708-709	AAGAGAAATCCT-GCCAAAAGCGCT	2.0 kb
148	14812-L16520	Exon 8 (9)	792-793	AATCCAAGGGAA-CCTGAACAGCTA	1.2 kb
295	14829-L17169	Exon 9 (10)	856-857	AGTCCCTCTGGC-CTCACATACAGT	6.3 kb
449	14843-L29128	Exon 10 (12a)	1271-1272	AGCTTAAACCCT-AGCCCTGTGAGA	
		Stop Codon	*1052-1054 (exon 10)*		

Table 3c. *CPOX* gene

Length (nt)	SALSA MLPA probe	*CPOX* Exon[a]	Ligation site NM_000097.7	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		Start Codon	*108-110 (exon 1)*		
166	14815-L16523	Exon 1	529-530	CCTGGGCGAGCT-GCGAAGGAGGCC	2.0 kb
283	14828-L18795	Exon 2	692-693	TGTGTACTTCAA-GATGGGTGTGTT	0.4 kb
373	14836-L16544	Exon 3	834-835	GTGCTATGGGCG-TGAGCTCTGTTA	1.9 kb
265	14827-L16535	Exon 4	946-947	GTTTGGTGGTGG-ATGTGACCTCAC	3.3 kb
289	14830-L17168	Exon 5	1199-1200	GTAGTTCCTTCT-TACATTCCCCTT	4.1 kb
472	14846-L16554	Exon 6	1354-1355	CAGAATTGAAAG-TATCTTGATGTC	0.7 kb
190	14818-L16526	Exon 7	1476-1477	TGCGTTGATGCA-GGCAGAATGGCT	
		Stop Codon	*1470-1472 (exon 7)*		

Table 3d. *UROD* gene

Length (nt)	SALSA MLPA probe	*UROD* Exon[a]	Ligation site NM_000374.5	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		Start Codon	*13-15 (exon 1)*		
154	14813-L16521	Exon 1	0-1	GCTCGCAGTTAC-AGACAGCTGACC	0.7 kb
309	14831-L16539	Exon 2	118-119	CCGTTTGGTGCA-TGCGCCAGGCAG	0.2 kb
238	14824-L16532	Exon 3	198-199	TGTCGCTCTCCT-GAGGCCTGCTGT	0.5 kb
	No probe	Exon 4			
391	15986-L18141	Exon 5	395-396	AGAAGTGGTAGC-CTCTGAGCTAGG	0.2 kb
363	14835-L29122	Exon 6	536-537	AAGCACCATGGC-TCAGGCCAAGCG	0.6 kb
184	14817-L16525	Exon 7	729-730	TACATCCGTGAT-GTGGCCAAGCAA	0.3 kb
400	14839-L16547	Exon 8	849-850	GGCTATGAGGTG-GTTGGGCTTGAC	0.1 kb
160	15983-L18138	Exon 9	10 nt before exon 9	GTGGCGCTGGCT-TTGCTTCCAGGG	0.4 kb
211	14821-L18794	Exon 10	979-980	AGTTGGTGAAGC-AGATGCTGGATG	
		Stop Codon	*1114-1116 (exon 10)*		

[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.

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

- P411 Porphyria mix 1: Contains probes for the *ALAD*, *HMBS* and *PPOX* genes linked to Acute hepatic porphyria.

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.

P412 product history	
Version	*Modification*
A3	One additional reference probe has been added and three reference probes have been replaced.
A2	One reference probe has been removed and the length of several probes have been adjusted.
A1	First release.

Implemented changes in the product description

Version A3-02 – 06 July 2023 (04P)
- Product description rewritten and adapted to a new template.
- Ligation sites of the probes targeting the *FECH* gene updated according to new version of the NM_ reference sequence.
- Exon numbering of the probes targeting the *UROS* gene updated.

Version A3-01 – 11 June 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 *UROS*, *UROD* and *CPOX* genes are updated according to new versions of the NM_ reference sequence.
- Exon numbering of the *UROS* gene has been changed due to updating the exon numbering to the LRG_1081 sequence.
- Ligation sites of the probes targeting the *FECH* gene are updated according to new NM_ reference sequence, from NM_001012513 to NM_000140.

Version 04 – 24 March 2016 (55)

- Product description is adapted to a new product version (version number changed, lot number added, tables 1 and 2 adapted and new pictures included).
- Various textual changes on page 1 and 2.
- Product name has been adjusted in product description from P412 Porphyria-2 Erythopoietic to P412 Porphyria mix 2.

Version 03 – 06 July 2015 (54)

Electropherogram picture of the old buffer (introduced Dec. 2012) removed.

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