Instructions for Use

SALSA® MLPA® Probemix P351 PKD1 and SALSA® MLPA® Probemix P352 PKD1-PKD2

See also the MLPA General Protocol, the product description of the SALSA® MLPA® Reagent Kit, and the Coffalyser.Net Reference Manual.

Visit the SALSA® MLPA® Probemix P351 PKD1 and SALSA® MLPA® Probemix P352 PKD1-PKD2 product page on our website to find Certificates of Analysis and a list of related products.

Product Name	SALSA® MLPA® Probemix P351 PKD1
Version	D1
Catalogue numbers	P351-025R (25 reactions) P351-050R (50 reactions) P351-100R (100 reactions)
Basic UDI-DI	872021148P35164
Ingredients	Synthetic oligonucleotides, oligonucleotides purified from bacteria, Tris-HCl, EDTA

Product Name	SALSA® MLPA® Probemix P352 PKD1-PKD2
Version	E1
Catalogue numbers	P352-025R (25 reactions) P352-050R (50 reactions) P352-100R (100 reactions)
Basic UDI-DI	872021148P35266
Ingredients	Synthetic oligonucleotides, oligonucleotides purified from bacteria, Tris-HCl, EDTA

Additional Test Components	Catalogue Numbers
SALSA® MLPA® Reagent Kit	EK1-FAM EK1-CY5 EK5-FAM EK5-CY5 EK20-FAM

Storage and Shelf Life

Recommended conditions		

A shelf life of until the expiry date is guaranteed, also after opening 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.

Regulatory Status	
IVD	EUROPE CE 2797
RUO	ALL OTHER COUNTRIES

Label Symbols			
IVD	In Vitro Diagnostic	RUO	Research Use Only

More Information: www.mrcholland.com	
	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

Any serious incident that has occurred in relation to this product should be reported to MRC Holland and the competent authority of the Member State or country in which the user and/or the patient is located.

Changes in this Product Version

P351 version D1. As compared to version C1, two PKD1 probes have been added, and two PKD1, one TSC2 and four reference probes have been replaced. In addition, three PKD1 probes have been changed in length.

P352 version E1. As compared to version D1, three PKD1 and one PKD2 probe have been added, and one PKD2 and one reference probe have been replaced. In addition, one PKD1 and two PKD2 probes have been changed in length.

1. Intended Purpose

The SALSA MLPA Probemix P351 PKD1 and SALSA MLPA Probemix P352 PKD1-PKD2 are in vitro diagnostic (IVD)[1] or research use only (RUO) semi-quantitative manual assays[2] for the detection of deletions or duplications in the *PKD1* gene and deletions in the *PKD2* gene, in order to confirm a potential cause for or clinical diagnosis of autosomal dominant polycystic kidney disease (ADPKD). P351 PKD1 can also be used to detect deletions in exons 36, 38, and 42 of the *TSC2* gene. Deletions disrupting both *PKD1* and *TSC2* can confirm a potential cause for and clinical diagnosis of *TSC2/PKD1* contiguous gene deletion syndrome. Both assays are for use with genomic DNA isolated from human peripheral whole blood specimens, and are also intended for molecular genetic testing of at-risk family members.

The detection of copy number variations (CNVs) in *PKD1* requires the use of both P351 PKD1 and P352 PKD1-PKD2, whereas the detection of CNVs in *PKD2* only requires the use of P352 PKD1-PKD2. CNVs detected with P351 PKD1 and P352 PKD1-PKD2 should be confirmed with a different technique. In particular, CNVs detected by only a single probe always require confirmation by another method. Most defects in the *PKD1*, *PKD2* and *TSC2* genes are point mutations, none of which will be detected by MLPA. It is therefore recommended to use these assays in combination with sequence analysis.

Assay results are intended to be used in conjunction with other clinical and diagnostic findings, consistent with professional standards of practice, including confirmation by alternative methods, parental evaluation, clinical genetic evaluation, and counselling, as appropriate. The results of these tests should be interpreted by a clinical molecular geneticist or equivalent.

These devices are not intended to be used for standalone diagnostic purposes, pre-implantation or prenatal testing, population screening, or for the detection of, or screening for, acquired or somatic genetic aberrations.

[1] Please note that these probemixes are for IVD use in the countries specified on page 1 of this product description. In all other countries, these are RUO products.

[2] To be used in combination with a SALSA MLPA Reagent Kit and Coffalyser.Net analysis software.

2. Sample Requirements

Specimen	50-250 ng purified human genomic DNA, free from heparin, dissolved in 5 µl $TE_{0.1}$ buffer, pH 8.0-8.5
Collection Method	Standard methods
Extraction Method	Methods tested by MRC Holland: • QIAGEN Autopure LS (automated) and QIAamp DNA mini/midi/maxi kit (manual) • Promega Wizard Genomic DNA Purification Kit (manual) • Salting out (manual)

Sample Types		
Test Sample	• Provided by user	
Reference Samples (Required)	• Provided by user • Extraction method, tissue type, DNA concentration and treatment as similar as possible in all test and reference samples. • Have a normal copy number and ≤0.10 standard deviation for all probes. • At least three* independent reference samples required in each experiment for proper data normalisation. Derived from unrelated individuals from families without a history of ADPKD or *TSC2/PKD1* contiguous gene deletion syndrome.	
No-DNA Control (Preferably)	• Provided by user • $TE_{0.1}$ buffer instead of DNA • To check for DNA contamination	
Positive Control Samples (Preferably)	• Provided by user, or	
	Available from third parties	See the table of positive samples on the probemix product page on our website.

*When testing >21 samples, include one extra reference for each 7 test samples.

3. Test Procedure

See the MLPA General Protocol.

4. Quality Control, Data Analysis, and Troubleshooting

Quality Control Fragments in the Probemix	
Length (nt)	**Function**
64-70-76-82	DNA quantity control fragments
88-96	DNA denaturation control fragments
92	Benchmark fragment
100	Chromosome X presence control fragment
105	Chromosome Y presence control fragment

Coffalyser.Net should be used for data analysis in combination with the appropriate product and lot-specific Coffalyser sheet. See the Coffalyser.Net Reference Manual for details on data analysis and quality control.

For troubleshooting help, see the additional resources offered on our support portal.

5. Interpretation of Results

Determining Typical Values in Normal and Affected Populations

The typical final ratio (FR) values stated in the copy number tables were determined in a validation study with samples containing abnormal copy numbers. The standard deviation of each individual probe over all the reference samples was ≤0.10.

Expected Results of Reference Probes

Final Ratio (FR)	Copy Number	Description
0.80 – 1.20	2	Normal

Typical Results of Probes Targeting Two Copies (*PKD1/PKD2/TSC2*)

Final Ratio (FR)	Copy Number	Description
0	0	Homozygous deletion
0.40 – 0.65	1	Heterozygous deletion
0.80 – 1.20	**2**	**Normal**
1.30 – 1.65	3	Heterozygous duplication
1.75 – 2.15	4	Homozygous duplication or Heterozygous triplication
All other values	-	Ambiguous

The tables illustrate the relationship between final probe ratio and corresponding copy number. Test results are expected to center around these values. Ambiguous values can indicate a technical problem, but may also reflect a biological cause such as mosaicism or a SNV influencing a single probe. It is important to use Coffalyser.Net to determine the significance of values found.

6. Performance Characteristics

Study	Description
Expected values for copy number in normal and affected populations	To determine the expected values in normal and affected populations a study was conducted on over 1500 MLPA reactions using samples with and without abnormal copy numbers. When the standard deviation of each individual probe over all the reference samples is ≤0.10, the ranges stated in the copy number table in the product description can be used. Cut-off values for copy number determination were verified with P351 PKD1 in 42 samples from healthy individuals with normal copy number and five control plasmid samples with known CNVs. At most six deviating measurements per control plasmid sample were obtained. This was expected due to the artificial nature of the control plasmid DNA used as positive samples. FRs corresponding to the expected copy number were still obtained in the large majority of measurements. For P352 PKD1-PKD2, 38 samples from healthy individuals with normal copy number and five samples with known CNVs were tested. FRs corresponding to the expected number were obtained in all but five ambiguous measurements.
Limit of Detection	A study using representative probemixes was conducted to evaluate the minimum and maximum amount of DNA acceptable as the assay input. Results support the use of 50-250 ng of human DNA as the recommend input amount. The use of insufficient or too much sample DNA can affect performance. These lower and higher limits of detection were verified using P351 PKD1 on one sample without any aberration and expected results were obtained using both the lower and upper input amount of DNA. For P352 PKD1-PKD2, two samples with known CNVs and one sample without any aberration were tested and expected results were obtained using both the lower and upper input amount of DNA.
Interfering substances	SNVs or other polymorphisms (e.g. indels) in the DNA target sequence and impurities in the DNA sample (e.g. NaCl or KCl, EDTA and hemoglobin) can affect the MLPA reaction. A study using P351 PKD1 and P352 PKD1-PKD2 was performed to assess the potential for interference of endogenous and exogenous substances on genomic DNA on samples with known CNVs. For most probes, expected FRs (FRs within the expected cut-off category) were obtained even in the presence of potential interferents at concentrations shown in the table below.

Interferent	Source	Testing Concentration	P351 PKD1 Results*	P352 PKD1-PKD2 Results**
EDTA	Exogenous – specimen	1.5 mM	Expected FR for 480/480 measurements	Expected FR for 273/288 measurements

Study	Description
	<table><tr><td></td><td>collection tubes</td><td></td><td></td><td></td></tr><tr><td>NaCl</td><td>Exogenous – DNA extraction</td><td>40 mM</td><td>Expected FR for 479/480 measurements</td><td>Expected FR for 252/288 measurements</td></tr><tr><td>Fe^{3+} ($FeCl_3$)</td><td>Exogenous – DNA extraction</td><td>1 µM</td><td>Expected FR for 475/480 measurements</td><td>Expected FR for 280/288 measurements</td></tr><tr><td>Heparin</td><td>Exogenous – specimen collection tubes</td><td>0.02 U/mL</td><td>Expected FR for 479/480 measurements</td><td>Expected FR for 285/288 measurements</td></tr><tr><td>Hemoglobin</td><td>Endogenous – blood sample</td><td>0.02 µg/µl</td><td>Expected FR for 126/480 measurements</td><td>Expected FR for 188/288 measurements</td></tr></table> * Results are summarised for all probes across all five samples tested. ** Results are summarised for all probes across all three samples tested. An effect on the FRs was observed for a low number of probes with NaCl, $FeCl_3$, and heparin for both P351 PKD1 and P352 PKD1-PKD2. EDTA also had an effect on a low number of P352 PKD1 probes. Hemoglobin had the largest effect in both Probemixes. Coffalyser.Net issues warnings for the samples in which hemoglobin showed an effect, as well as lowered quality scores, leading to the samples needing a re-test. To minimise variability across samples, 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.
Cross-reactivity	Cross-reactivity is the potential for probes to bind to homologous regions (e.g. pseudogenes) or other cross-reactive sequences. Quality tests were carried out to determine whether probes are specific to their target sequence and all probes met the quality criteria for specificity.
Accuracy	Results of accuracy are derived from trueness and precision studies. For trueness, 24 wildtype samples were tested using P351 PKD1 and five samples with CNVs were tested using P352 PKD1-PKD2 and found to have the expected results, with the exception of a five deviating measurements for P352 PKD1-PKD2. Assay precision was tested by repeatedly testing samples with known copy number over multiple days, and by multiple operators. Results showed a correct call in 2251/2304 data points for P351 PKD1, leading to a precision of 98%, and in 1405/1408 data points for P352 PKD1-PKD2, leading to a precision of 99%.
Clinical validity*	*PKD1:* around 2% of ADPKD cases are explained by CNVs in *PKD1 (GeneReviews)* *PKD2:* 0.45% of ADPKD cases are explained by deletions in *PKD2 (GeneReviews)* *TSC2/PKD1:* 100% of *TSC2/PKD1* contiguous gene deletion syndrome cases are explained by deletions involving *PKD1* and the adjacent *TSC2 (GeneReviews)* *(Based on a 2008-2025 literature review)

Summary of Safety and Performance (SSP)
The SSP is available in the European database on medical devices (Eudamed), https://ec.europa.eu/tools/eudamed, or upon request.

Content – Probe Details Sorted by Chromosomal Position

SALSA MLPA Probemix P351-D1 PKD1

Chr. position	Target	Exon	Distance to next probe	Length (nt)	Probe number	Warnings
16p13.3	*TSC2*	Exon 36	1.5 kb	424	01842-L24628	«
16p13.3	*TSC2*	Exon 38	1.7 kb	441	01843-L24629	«
16p13.3	*TSC2*	Exon 42	0.9 kb	209	22214-L31268	«
16p13.3	*PKD1*	Exon 46	0.9 kb	232	14095-L24702	«
16p13.3	*PKD1*	Exon 45	0.4 kb	472	21755-L30421	«
16p13.3	*PKD1*	Exon 44	0.4 kb	335	10964-L27363	«
16p13.3	*PKD1*	Exon 43	0.4 kb	184	10963-L24700	«
16p13.3	*PKD1*	Exon 42	0.3 kb	202	10962-L24699	«
16p13.3	*PKD1*	Exon 41	0.3 kb	160	10961-L31500	«
16p13.3	*PKD1*	Exon 40	0.5 kb	148	10960-L16105	«
16p13.3	*PKD1*	Exon 39	0.4 kb	379	10959-L24697	«
16p13.3	*PKD1*	Exon 38	1.3 kb	178	10958-L24696	«
16p13.3	*PKD1*	Exon 35	5.4 kb	450	19918-L24695	« +
16p13.3	*PKD1*	Exon 30	0.4 kb	258	21758-L31693	« #
16p13.3	*PKD1*	Exon 29	0.6 kb	322	10955-L24693	« #
16p13.3	*PKD1*	Exon 27	1.9 kb	274	10954-L24692	« + #
16p13.3	*PKD1*	Exon 25	1.3 kb	414	10953-L24691	« #
16p13.3	*PKD1*	Exon 23	2.0 kb	226	10952-L24690	« #
16p13.3	*PKD1*	Exon 20	0.7 kb	154	10950-L24689	« + #
16p13.3	*PKD1*	Exon 18	1.4 kb	290	10949-L24688	« #
16p13.3	*PKD1*	Exon 16	0.7 kb	238	21754-L31494	« #
16p13.3	*PKD1*	Exon 15	1.5 kb	251	14096-L24686	« #
16p13.3	*PKD1*	Exon 15	2.3 kb	343	14097-L24685	« #
16p13.3	*PKD1*	Exon 14	0.4 kb	196	10946-L27456	« #
16p13.3	*PKD1*	Exon 13	0.4 kb	361	19919-L24683	« #
16p13.3	*PKD1*	Exon 12	1.0 kb	307	10944-L31694	« #
16p13.3	*PKD1*	Exon 11	1.0 kb	371	22348-L29683	« #
16p13.3	*PKD1*	Exon 10	0.9 kb	266	10942-L27362	« + #
16p13.3	*PKD1*	Exon 9	1.9 kb	394	10941-L24679	« + #
16p13.3	*PKD1*	Exon 5	1.1 kb	297	10940-L24678	« #
16p13.3	*PKD1*	Exon 3	17.0 kb	141	10938-L24677	« #
16p13.3	*PKD1*	Upstream (Exon 1)		172	22347-L30144	« Ø #
1p	Reference			316	18924-L25193	
1q	Reference			244	20757-L28659	
2q	Reference			431	15541-L25346	
5q	Reference			135	00797-L26847	
6q	Reference			352	13400-L20982	
9p	Reference			190	08528-L24624	
12q	Reference			281	08887-L24627	
13q	Reference			459	01799-L23610	
15q	Reference			481	15738-L11546	
19p	Reference			166	02310-L24631	
20p	Reference			387	07925-L21227	

SALSA MLPA Probemix P352-E1 PKD1-PKD2

Chr. position	Target	Exon	Distance to next probe	Length (nt)	Probe number	Warnings
4q22.1	*PKD2*	Exon 1	0.2 kb	388	14740-L24646	
4q22.1	*PKD2*	Exon 1	11.6 kb	297	10994-L24647	
4q22.1	*PKD2*	Exon 2	0.1 kb	142	10995-L24648	
4q22.1	*PKD2*	Exon 2	16.7 kb	463	14741-L24649	
4q22.1	*PKD2*	Exon 3	2.0 kb	370	21760-L30426	
4q22.1	*PKD2*	Exon 4	5.0 kb	342	10997-L24651	
4q22.1	*PKD2*	Exon 5	3.4 kb	220	10998-L24652	
4q22.1	*PKD2*	Exon 6	0.1 kb	263	14738-L20398	
4q22.1	*PKD2*	Exon 6	5.3 kb	233	14739-L24653	
4q22.1	*PKD2*	Exon 7	4.1 kb	202	11000-L24654	
4q22.1	*PKD2*	Exon 8	1.9 kb	178	21417-L11672	
4q22.1	*PKD2*	Exon 9	3.9 kb	325	11002-L24656	
4q22.1	*PKD2*	Exon 10	3.5 kb	352	11003-L24657	
4q22.1	*PKD2*	Exon 11	0.4 kb	166	11004-L24658	
4q22.1	*PKD2*	Exon 12	2.2 kb	148	11005-L24659	
4q22.1	*PKD2*	Exon 13	6.9 kb	478	21578-L30146	
4q22.1	*PKD2*	Exon 14	0.7 kb	381	22213-L24661	
4q22.1	*PKD2*	Exon 15		425	11008-L24662	
16p13.3	*PKD1*	Exon 37	0.4 kb	405	14087-L24675	«
16p13.3	*PKD1*	Exon 36	3.2 kb	159	10992-L24674	«
16p13.3	*PKD1*	Exon 34	0.2 kb	208	21759-L30691	«
16p13.3	*PKD1*	Exon 33	0.5 kb	416	10990-L24673	«
16p13.3	*PKD1*	Exon 31	4.2 kb	191	11011-L27419	Δ « #
16p13.3	*PKD1*	Exon 26	0.8 kb	315	11009-L24671	◊ « #
16p13.3	*PKD1*	Exon 24	1.7 kb	226	21756-L30692	« #
16p13.3	*PKD1*	Exon 22	0.9 kb	452	14094-L24670	« #
16p13.3	*PKD1*	Exon 21	0.7 kb	270	10986-L24669	« + #
16p13.3	*PKD1*	Exon 19	5.3 kb	291	10984-L32624	◊ « #
16p13.3	*PKD1*	Exon 15	5.3 kb	248	10983-L24667	Δ « #
16p13.3	*PKD1*	Exon 7	0.7 kb	153	14100-L24666	« #
16p13.3	*PKD1*	Exon 6	2.0 kb	185	19917-L11651	« #
16p13.3	*PKD1*	Intron 1 (Exon 2)	17.9 kb	240	21752-L30143	« Ø #
16p13.3	*PKD1*	Upstream	0.5 kb	257	14102-L24664	« Ø
16p13.3	*PKD1*	Upstream		444	14103-L24663	« Ø
1q	Reference			334	01918-L24637	
2q	Reference			280	10799-L24638	
4p	Reference			490	20096-L27538	
5q	Reference			136	00797-L24120	
7q	Reference			433	00680-L24640	
8p	Reference			362	06383-L24641	
13q	Reference			172	03245-L24643	
15q	Reference			471	07607-L24644	
17q	Reference			307	18034-L22721	
19q	Reference			396	00713-L24645	
21q	Reference			214	18153-L22663	

Probe lengths may vary slightly depending on capillary electrophoresis instrument settings. Please see the most up to date Coffalyser sheet for exact probe lengths obtained at MRC Holland.
The *PKD1, PKD2,* and *TSC2* exon numbers are derived from MANE project and are based on MANE Select transcript. For more information, see the probe sequences document available on the product page at www.mrcholland.com. Annotations of several probes with targets at the edge of or slightly outside the coding region were altered. The exon numbering from the previous version of this product description is disclosed between brackets.
Chromosomal bands are based on: hg18.

7. Precautions and Warnings

Probe warnings

◊ If the ligation reaction is performed at room temperature, these probes are more prone to binding to homologous sequences. Aberrant results should always be verified.

Δ These probes may be sensitive to certain experimental variations. Aberrant results should be treated with caution.

« Probes detecting *PKD1* and *TSC2*, in particular those detecting the region between *PKD1* exon 31 and *TSC2* exon 42, are 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.

Ø These probes target sequences outside of the known coding region. Copy number alterations of only one of these probes are of unknown clinical significance.

The specificity of these probes relies on a single nucleotide difference compared to a related gene or pseudogene. As a result, an apparent duplication of only these probes can be the result of a non-significant single nucleotide sequence change in the related gene or pseudogene.

\+ The ligation site of these probes is >20 nt away from the nearest exon. For more information, download the probe sequences document available on the product page at www.mrcholland.com.

Probemix-specific precautions

1. This product 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).
2. Sample or technical artefacts may appear as a (mosaic) copy number change of the whole/partial gene. Whole/partial gene deletions or duplications should therefore be confirmed by analysis of an independent DNA sample, to exclude false positive results.
3. Small changes (e.g. SNVs, small indels) in the sequence targeted by a probe can cause false positive results, even when >20 nt from the probe ligation site. Sequence changes 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. Deviations detected by this product should be confirmed, and single-probe deviations always require confirmation. Sequencing of the target region is recommended. Please contact MRC Holland for more information: info@mrcholland.com.
4. Copy number alterations of reference probes are unlikely to be related to the condition tested.
5. No probes are present for *PKD1* exons 4, 8, 17, 28 and 32. This is due to the existence of several *PKD1* pseudogenes that are almost identical to the actual gene. These pseudogenes are also present on chromosome 16.
6. Probes detecting *PKD1* exons 1-31 rely for their specificity on a single nucleotide difference between the *PKD1* gene and its pseudogenes. For these probes, an apparent duplication can be the result of a clinically non-significant single nucleotide sequence change in one of the pseudogenes.
7. The complete *PKD1* gene is difficult to denature, and the region between *PKD1* exon 31 and *TSC2* exon 42 is even more difficult to denature due to an extremely high GC content. This may cause false results in DNA samples containing salt that can lead to incomplete DNA denaturation. A low signal of the 88 nt and 96 nt D-fragments provides a warning for incomplete DNA denaturation.
8. MLPA may not be able to detect deletions or duplications in the *PKD1* gene, deletions in the *PKD2* gene, or deletions in the *TSC2* gene in the cases in which mosaicism is considered.

Technique-specific precautions
See the MLPA General Protocol.

8. Limitations

Technique-specific limitations
See the MLPA General Protocol.

Implemented changes in the product description

Version D1/E1-04 – 03 February 2026 (03S)

- Product description adapted to new template.
- Intended purpose updated specifying assay is manual. The specification of the detection of duplications in the *PKD2* and *TSC2* genes has been removed due to limited clinical evidence. The function of the device for ADPKD has been specified: the device can be used to confirm a potential cause for *or* confirm a clinical diagnosis of ADPKD. It has been added that assay results should be used in conjunction with parental evaluation (this is in case of mosaicism).
- Warnings for probes with a ligation site >20nt from the nearest exon added for probes 10941-L24679, 10942-L27362, 10950-L24689, 10986-L24669, 10954-L24692, and 19918-L24695. No change in actual target sites.
- Warnings for target sequences outside the known coding region added for probes 22347-L30144, 21752-L30143, 14102-L24664, and 14103-L24663.
- Warnings for salt contamination removed for probes 14740-L24646 and 10994-L24647.
- Description of probe targets at the edge of or slightly outside the coding region has been adjusted. No change in actual target sites.
- SNVs rs528103165, rs147464577, rs151157369, and rs139573366 can affect the probe signal. However, the warnings for these SNVs present in previous product description versions have been replaced by a general warning for small sequence changes, included in section Precautions and Warnings.
- The term 'rare' has been removed from the probemix-specific precaution on mosaicism.
- Probemix is now IVDR certified.