For life science research only. Not for use in diagnostic procedures.

LightCycler® TaqMan® Master

Version: 9

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Ready-to-use hot start reaction mix for PCR on the LightCycler® Carousel-Based System using Hydrolysis TaqMan® Probes.

Cat. No. 04 535 286 001	1 kit 96 reactions of 20 µl final volume each
Cat. No. 04 735 536 001	1 kit 480 reactions of 20 µl final volume each

Store the kit at −15 to −25°C

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1. General Information

1.1. Contents

Vial / Bottle	Cap	Label	Function	Catalog Number	Content
1a	white	Enzyme	After pipetting 10 µl from vial 1a into one vial 1b: ▪ Ready-to-use hot start reaction mix ▪ Contains FastStart Taq DNA Polymerase, reaction buffer, $MgCl_2$ and dNTP mix (with dUTP instead of dTTP).	04 535 286 001	1 vial
				04 735 536 001	5 vials
1b	red	Reaction Mix, 5x conc.		04 535 286 001	3 vials (for 3 × 128 µl)
				04 735 536 001	15 vials (for 15 × 128 µl)
2	colorless	Water, PCR grade	▪ To adjust the final reaction volume.	04 535 286 001	2 vials, 1 ml each
				04 735 536 001	7 vials, 1 ml each

1.2. Storage and Stability

Storage Conditions (Product)

The kit is shipped on dry ice.

Store the unopened kit at −15 to −25°C until the expiration date printed on the label.

Once the kit is opened, store the kit components as described in the following table:

Vial / Bottle	Cap	Label	Storage
1a	white	Enzyme	Store at −15 to −25°C . ⚠ ***Avoid repeated freezing and thawing!*** ⚠ ***Keep vial 1b away from light!***
1b	red	Reaction Mix, 5x conc.	
2	colorless	Water, PCR grade	Store at −15 to −25°C .

Storage Conditions (Working Solution)

After the addition of 1a to 1b:

Vial / Bottle	Cap	Label	Storage
1b	red	Master Mix, 5x conc.	Store at −15 to −25°C for a maximum of three months. After thawing, store at +2 to +8°C for a maximum of one week. ⚠ **Avoid repeated freezing and thawing!**

1.3. Additional Equipment and Reagents Required

Additional reagents and equipment required to perform PCR reactions with the LightCycler® TaqMan® Master, using the LightCycler® Carousel-Based System include:

- LightCycler® Carousel-Based System* (LightCycler® 2.0 Instrument*, LightCycler® 1.5 Instrument, or lower instrument versions)
- LightCycler® Capillaries (20 µl)*
- LightCycler® Centrifuge Adapters (included with the LightCycler® Carousel-Based System) and a standard benchtop microcentrifuge, containing a rotor for 2.0 ml reaction tubes
  or
- LC Carousel Centrifuge 2.0* for use with the LightCycler® 2.0 Sample Carousel (20 µl and 100 µl)
  or
- LC Carousel Centrifuge 2.0 and LC Carousel Centrifuge 2.0 Bucket 2.1*
  or
- LC Carousel Centrifuge and LC Carousel Centrifuge 2.0 Rotor Set*, to centrifuge the LightCycler® Sample Carousel, or the LightCycler® 2.0 Sample Carousel
- LightCycler® Uracil-DNA Glycosylase* (for prevention of carryover contamination)
- Hydrolysis probes (Universal ProbeLibrary assays [1)] or RealTime ready qPCR assays [1)])
- PCR template (genomic DNA or cDNA)
- PCR primers (easiest when designed for amplicons between 50 to 300 bp)
- Nuclease-free, aerosol-resistant pipette tips
- Pipettes with disposable, positive-displacement tips
- Sterile reaction (Eppendorf) tubes for preparing master mixes and dilutions

[1)] for detailed information, please visit universalprobelibrary.com and realtimeready.roche.com.

1.4. Application

The LightCycler® TaqMan® Master is designed for life science research. In combination with the LightCycler® Carousel-Based System, the kit enables high sensitive detection and quantification of defined DNA sequences (with suitable PCR primers and detection probes). It can also be used to detect and quantify defined RNA sequences in a two-step RT-PCR (with additional reagents for reverse transcription).

1.5. Preparation Time

Procedure	Assay Time
PCR Set-up	20 min
LightCycler® Carousel-Based System run (incl. Melting Curve)	40 min
Total assay time	**60 min**

2. How to Use this Product

2.1. Before you Begin

Sample Materials

- Use any template DNA (*e.g.*, genomic or plasmid DNA, cDNA) suitable for PCR in terms of purity, concentration and absence of inhibitors.
- Use up to 500 ng complex genomic DNA or 10^1 to 10^{10} copies plasmid DNA.

When using a non-purified cDNA sample from reverse transcription, especially if it contains high background concentrations of RNA and oligonucleotides, use 2 µl or less of that sample for each capillary.

For reproducible isolation of nucleic acids, use one of the following:
- Either a MagNA Pure System together with a dedicated nucleic acid isolation kit (for automated isolation)
- or a High Pure nucleic acid isolation kit (for manual isolation)

For further information, consult the Roche Life Science catalog or homepage: lifescience.roche.com

Control Reactions

Always run a negative and a positive control with the samples.

To prepare a negative control, replace the template DNA with Water, PCR grade (vial 2, colorless cap).

To use a positive control, prepare a plasmid DNA of the sequence of interest and if desired, run a dilution series to produce a standard curve for qPCR.

Primers

Use PCR primers at a final concentration of 0.1 – 1.0 µM. The recommended starting concentration is 0.5 µM in each case.

Probe

Use Hydrolysis probes at a final concentration of 0.05 – 0.1 µM. In some cases the fluorescence signal may be increased with a higher probe concentration of up to 0.2 µM.

Mg^{2+} Concentration

All components in the reaction mix of the LightCycler® TaqMan® Master are optimized for almost all primer combinations. You do not need to add additional $MgCl_2$ to the mix to produce an efficient and specific PCR.

General Considerations

In principle, the kit can be used for the amplification and detection of any DNA or cDNA target. However, you would have to adapt each amplification protocol to the reaction conditions of the LightCycler® Carousel-Based System and design a pair of specific PCR primers and a Hydrolysis probe for each target.

⚠ ***The amplicon size should not exceed 1 kb in length. For optimum results, select a product length of 700 bp or less.***

⚠ ***The performance of the kit described in this Instruction for Use is warranted only when it is used with the LightCycler® Carousel-Based System.***

Two-Step RT-PCR

The LightCycler® TaqMan® Master can also be used to perform two-step RT-PCR.
In two-step RT-PCR, the reverse transcription of RNA into cDNA is separated from the other reaction steps and is performed outside the LightCycler® Carousel-Based System. Subsequent amplification and online monitoring is performed according to the standard LightCycler® Carousel-Based System procedure, using cDNA as starting sample material.
One of the following reagents is required for reverse transcription of RNA into cDNA:

- Transcriptor Reverse Transcriptase
- Transcriptor First Strand cDNA Synthesis Kit, Transcriptor High Fidelity cDNA Synthesis Kit, Transcriptor Universal cDNA Master
- First Strand cDNA Synthesis Kit for RT-PCR (AMV)

Synthesis of cDNA is performed according to the detailed instructions provided with the cDNA synthesis reagent.

⚠ ***Do not use more than 8 µl of undiluted cDNA template per 20 µl final reaction volume, because greater amounts may inhibit PCR. For initial experiments, Roche recommends running undiluted, 1:10 diluted and 1:100 diluted cDNA templates, in parallel to determine the optimal template amount.***

2.2. Protocols

The following procedure is optimized for use with the LightCycler® Carousel-Based System.

Program the LightCycler® Instrument before preparing the reaction mixes.

A LightCycler® Carousel-Based System protocol that uses LightCycler® TaqMan® Master contains the following programs:

- **Pre-Incubation** (activation of FastStart DNA polymerase and denaturation of the DNA)
- **Amplification** of the target DNA
- **Cooling** the rotor and thermal chamber

For details on how to program the experimental protocol, see the LightCycler® 2.0 Instrument Operator's Manual.

Set all other protocol parameters not listed in the tables below to '0'.

The following table shows the PCR parameters that must be programmed for a LightCycler® Carousel-Based System PCR run with the LightCycler® TaqMan® Master.

LightCycler® Software Version 4.1				
Programs				
Setup		Setting		
Default Channel		Fluorescence Channel		
Seek Temperature		30°C		
Max Seek Pos.		Enter the total number of sample positions for which the instrument should look for.		
Instrument Type		"6 Ch." for LightCycler® 2.0 Instrument or "3 Ch." for LightCycler® 1.5 Instrument and lower instrument versions		
Capillary Size		Select "20 µl" as the capillary size for the experiment. (available only for LightCycler® 2.0 Instrument (6 channels))		
Programs				
Program Name		Cycles	Analysis Mode	
Initial Denaturation		1	None	
Amplification		45 [1]	Quantification	
Cooling		1	None	
Temperature Targets				
	Target [°C]	Hold [hh:mm:ss]	Ramp Rate [°C/s]	Acquisition Mode [per °C]
Initial Denaturation	95	00:10:00 [2]	20	None
Amplification	95	00:00:10	20	None
	60 (primer dependent [3])	00:00:20 - 00:00:40 [4]	20	None
	72	00:00:01	20	Single
Cooling	40	00:00:30	20	None

1) 45 cycles are suitable for most of the assays. Nevertheless, for a well optimized assay with steep amplification curves and early crossing points, even with low target concentrations, 40 cycles should be sufficient (resulting in a reduced assay time!).
2) If high polymerase activity is needed in early cycles, you can sometimes improve results by extending the initial denaturation to 15 min.
3) For initial experiments, set the target temperature 5°C below the calculated primer melting temperatures.
4) For higher precision in target quantification experiments, in some cases it can be advantageous to choose relatively long annealing times, up to 45 s when amplifying sequences > 500 bp.

Color Compensation

When using TaqMan® probes that contain different fluorophore labels in the same capillary, a (previously generated) color compensation file must be used to compensate for the crosstalk between the individual channels. A previously stored color compensation file can be activated during the LightCycler® Instrument run, or during data analysis, after the run.

ⓘ *Although the optical filters of each detection channel of the LightCycler® Carousel-Based Instrument are optimized for the different emission maxima of the fluorescent dyes, some residual crosstalk will occur, unless corrected for with a color compensation file.*

ⓘ *Color Compensation is instrument-specific. Therefore, a color compensation file must be generated for each LightCycler® Carousel-Based Instrument.*

ⓘ *No universal color compensation set is available for 6-channel applications on the LightCycler® 2.0 Instrument. All multicolor assays must use a specific color compensation protocol. A new color compensation object must be generated for each set of parameters.*

For more information on the generation and use of a color compensation file for TaqMan® probes, please see the LightCycler® Technical Note 21/2007 "Color Compensation for Hydrolysis Probe Assays" (Online Technical Support), or www.lightcycler.com.

Preparation of the Master Mix

Prepare the 5x conc. Master Mix as described below.

1. Thaw one vial of "Reaction Mix" (vial 1b, red cap)
2. Briefly centrifuge one vial 1a ("Enzyme", white cap) and one thawed vial 1b ("Reaction Mix", red cap, from Step1).
3. Pipet 10 µl from vial 1a (white cap) into vial 1b (red cap).
   ⓘ *Each vial 1a contains enough enzyme for three vials of Reaction Mix.*
4. Mix gently by pipetting up and down.
   ⚠ ***Do not vortex.***
5. Re-label vial 1b (red cap) with the new label (vial 1: Master Mix) provided with the kit.
   ⓘ *The volume of the resulting Master Mix (5x conc.) is sufficient for 32 reactions with a final reaction volume of 20 µl in each case.*

Preparation of the PCR Mix

Proceed as described below for a 20 µl standard reaction.

The protocol is designed for a final reaction volume of 20 µl. For volumes < 20 µl, the reaction and cycle conditions must be optimized.

Do not touch the surface of the capillaries. Always wear gloves when handling the capillaries.

1. Depending on the total number of reactions, place the required number of LightCycler® Capillaries in precooled centrifuge adapters or in a LightCycler® Sample Carousel in a precooled LightCycler® Centrifuge Bucket.
2. Prepare a 10x conc. solution that contains PCR primers and Hydrolysis probe.
3. Thaw the LightCycler® TaqMan® Master, 5x conc. (vial 1, red cap), mix gently and store on ice.
4. In a 1.5 ml reaction tube on ice, prepare one reaction by adding the following components in the order listed below, then mix gently by pipetting up and down:

Component	Volume
Water, PCR grade (vial 2, colorless cap)	9 µl
Primers/Probe, 10x conc.	2 µl
Master Mix, 5x conc.	4 µl
Final Volume	**15 µl**

To prepare the PCR Mix for more than one reaction, multiply the amount in the “Volume” column above by the number of reactions to be run plus one additional reaction.

5. – Pipet 15 µl PCR mix into each precooled LightCycler® Capillary.
– Add 5 µl of the DNA template.

Use up to 500 ng complex genomic DNA or 10^1 – 10^{10} copies of plasmid DNA.

6. – Seal each capillary with a stopper and place the adapters (containing the capillaries) in a standard benchtop microcentrifuge.

Place the centrifuge adapters in a balanced arrangement in the centrifuge.
– Centrifuge at 700 × *g* for 5 s (3,000 rpm in a standard benchtop microcentrifuge). Alternatively, use the LC Carousel Centrifuge for spinning the capillaries.

7. Transfer the capillaries to the sample carousel of the LightCycler® Instrument.
8. Cycle the samples as described above.

2.3. Other Parameters

Prevention of Carryover Contamination

Uracil DNA N-Glycosylase (UNG) is suitable for preventing carryover contamination in PCR. This carryover prevention technique involves incorporating deoxyuridine triphosphate (dUTP, a component of the Master Mix in this kit) into amplification products, then pretreating later PCR mixtures with UNG. If a dUTP-containing contaminant is present in the later PCRs, it will be cleaved by a combination of the UNG and the high temperatures of the initial denaturation step; it will not serve as a PCR template.

Since your target DNA template contains thymidine rather than uridine it is not affected by this procedure.

Refer to the package insert of LightCycler® Uracil-DNA Glycosylase for details on application.

3. Results

The following amplification curves were obtained with dilutions of human genomic DNA in 1:10 steps and a set of primers and a FAM/TAMRA-labeled probe, specific for a fragment of 442 bp of the Cyclophilin A gene.

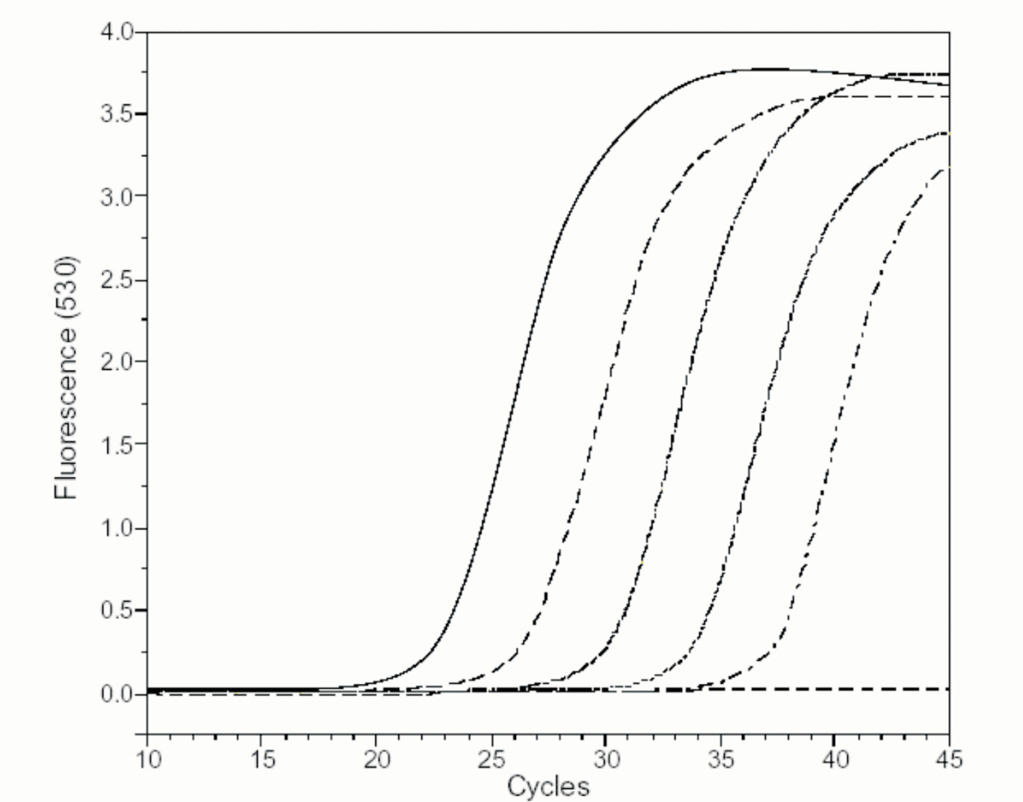

Fig. 1: Cyclophilin A amplification curves in the analysis module for absolute quantification in the LightCycler® Software 4.0.
Serially diluted samples containing DNA starting from 30 ng (far left) to 3 pg (far right) were amplified; as a negative control, template DNA was replaced by Water, PCR grade (flat line).

4. Troubleshooting

	Possible cause	Recommendation
Fluorescence curves reach maximum long before cycling is finalized.	Starting amount of nucleic acid is very high.	Stop the program by clicking the **End Program** button. The next cycle program will start automatically.
	Number of cycles is too high.	Reduce the number of cycles in the protocol.
Log-linear phase of amplification just starts as the amplification program finishes.	Number of cycles is too low.	Increase the number of cycles in the protocol.
		Use the **+ 10 cycles** button to increase the number of cycles in the program.
No amplification occurs.	Using wrong channel to display amplification on screen.	Change the channel setting on the programming screen. (All data from all channels are always saved.)
	Inhibitory effects of the sample material due to insufficient purification.	Try a 1 to 10 fold dilution of your sample.
		Isolate the nucleic acids of your sample material to ensure removal of inhibitory agents.
	FastStart Taq DNA polymerase is not fully activated.	Make sure PCR included a pre-incubation step at 95°C for 10 min.
		Make sure denaturation time during cycles is about 10 s.
	Pipetting errors or omitted reagents.	Check for missing or defective reagents.
	Amplicon length is >1 kb	Do not use primers for amplicons >1 kb. Optimal results are obtained with a product length less than 700 bp.
	Difficult template (*e.g.,* unusual GC-rich sequence).	Optimize temperatures and times in the amplification cycles.
		Optimize primer/probe sequences.
		Repeat PCR with increasing content of DMSO, up to 10% final concentration.
Fluorescence intensity varies.	Some of the reagent is still in the upper vessel of the capillary, or an air bubble is trapped in the capillary tip.	Ensure the centrifugation step was properly performed.
	Skin oils or dirt are on the surface of the capillary tip.	Always wear gloves when handling the capillaries.
	Pipetting inaccuracy	Repeat run under same conditions.
Fluorescence intensity is too low.	Low concentration or deterioration of dyes in reaction mixtures; dyes not stored properly.	Store the dye containing reagents at −15 to −25°C, and keep them away from light.
		Avoid repeated freezing and thawing.
		After thawing, store the Master Mix at +2 to +8°C for a maximum of 1 week.
	Reaction conditions are not optimized, leading to poor PCR efficiency.	Primer concentration should be between 0.1 and 1.0 µM.
		Check annealing temperature of primers.
		Check experimental protocol.
		Always run a positive control along with your samples.

	Possible cause	Recommendation
Negative control samples give a positive signal.	Contamination	Remake all critical solutions.
		Pipet reagents on a clean bench.
		Close lid of the negative control reaction immediately after pipetting it.
		Use LightCycler® UNG to eliminate carryover contamination.
High background.	Fluorescence signals are very low, therefore the background seems relatively high.	Follow general optimization strategies for PCR with the LightCycler® Carousel-Based System.
	Insufficient quality of Hydrolysis probes.	Prepare a new solution of probes.

5. Additional Information on this Product

5.1. Test Principle

How this Product Works

Hot start PCR has been shown to significantly improve the specificity and sensitivity of PCR by minimizing the formation of non-specific amplification products during the first PCR cycles. LightCycler® TaqMan® Master is an easy-to-use hot start reaction mix using the FastStart enzyme. This chemically modified form of thermostable recombinant Taq DNA polymerase is inactive at room temperature and becomes activated at very high temperatures. The FastStart enzyme is activated at the onset of real time PCR, in a 10 minute pre-incubation step of +95°C.

LightCycler® TaqMan® Master is a ready-to-use reaction mix designed for the TaqMan® detection format using the LightCycler® Carousel-Based System.
It contains FastStart polymerase for a "Hot Start" PCR, which has been shown to significantly improve the specificity and sensitivity of PCR by minimizing the formation of non-specific amplification products [Chou Q, et al, 1992) and (Kellogg DE, et al, 1994). FastStart Taq DNA Polymerase is a chemically modified form of thermostable recombinant Taq DNA polymerase that is inactive at +15 to +25°C and below. The enzyme is active only at high temperatures, where primers no longer bind non-specifically. The enzyme is completely activated (by removal of blocking groups) in a single pre-incubation step (95°C, 10 minutes) before cycling begins. Activation does not require the extra handling steps typical of other "Hot Start" techniques.
The LightCycler® TaqMan® Master provides convenience, excellent performance, reproducibility, and minimal contamination risk. All you have to supply is PCR primers, a detection probe and your template DNA.

The reaction mix in this kit is optimized for a fixed $MgCl_2$ concentration, which works with nearly all primer combinations. You do not need to adjust the $MgCl_2$ concentration to amplify different sequences.

The performance of the kit described in this Instruction Manual is guaranteed only when it is used with the LightCycler® Carousel-Based System.

Hydrolysis probe assays, also called TaqMan® Assays, use a single probe containing two labels, a fluorescent reporter dye and a fluorescent quencher. While the probe is intact, the quencher is close to the reporter dye and suppresses the reporter fluorescence via fluorescence resonance energy transfer (FRET). When the probe is hybridized to the target sequence, the 5'-nuclease activity of the polymerase can cleave the hydrolysis probe, separating the reporter and the quencher. With a rising amount of target sequence during PCR, more probe is cleaved and the fluorescence signal of the unquenched reporter dye increases.

As the principle of Hydrolysis probe assays is probe cleavage during PCR, Hydrolysis probes cannot be used to perform a melting curve analysis. In contrast, HybProbe probes which consist of two specially designed, sequence-specific oligonucleotide probes labeled N with different dyes, are still intact at the end of amplification, and thus may be used in a subsequent melting curve experiment (e.g., for mutation detection or SNP analysis).

5.2. References

- Chou Q, Russell M, Birch DE, Raymond J, Bloch W (1992) Prevention of pre-PCR mis-priming and primer dimerization improves low-copy-number amplifications Nucleic Acids Research 7 1717-1723
- Kellogg DE, Rybalkin I, Chen S, Mukhamedova N, Vlasik T, Siebert PD, Chenchika A (1994) TaqStart antibody : hot start PCR facilitated by a neutralizing monoclonal antibody directed against Taq DNA polymerase BioTechniques 6 1134-1137

5.3. Quality Control

The LightCycler® TaqMan® Master is function tested using the LightCycler® Carousel-Based System.

6. Supplementary Information

6.1. Conventions

To make information consistent and easier to read, the following text conventions and symbols are used in this document to highlight important information:

Text convention and symbols	
ℹ	*Information Note: Additional information about the current topic or procedure.*
⚠	**Important Note: Information critical to the success of the current procedure or use of the product.**
① ② ③ etc.	Stages in a process that usually occur in the order listed.
❶ ❷ ❸ etc.	Steps in a procedure that must be performed in the order listed.
* (Asterisk)	The Asterisk denotes a product available from Roche Diagnostics.

6.2. Changes to Previous Version

Layout changes
Editorial changes
Information about LightCycler® Software 3.5 has been deleted.

6.3. Ordering Information

Roche offers a large selection of reagents and systems for life science research. For a complete overview of related products and manuals, please visit and bookmark our homepage lifescience.roche.com.

Product	Pack Size	Cat. No.
Accessories general (hardware)		
LightCycler® Software 4.1	1 software package	04 898 915 001
LC Carousel Centrifuge 2.0	1 centrifuge plus rotor and rotor bucket (115 V)	03 709 507 001
	1 centrifuge plus rotor and rotor bucket (230 V)	03 709 582 001
LC Carousel Centrifuge 2.0 Rotor Set	1 rotor + 2 rotor buckets for the earlier model LC Carousel Centrifuge	03 724 697 001
LC Carousel Centrifuge 2.0 Bucket 2.1	1 rotor bucket for LC Carousel Centrifuge 2.0	03 724 689 001
Consumables		
LightCycler® Capillaries (20 µl)	1 pack, containing 5 boxes, each with 96 capillaries and stoppers	04 929 292 001
Instruments		
LightCycler® 2.0 Instrument	1 instrument, plus related products and data station	03 531 414 001
Reagents , kits		
LightCycler® Uracil-DNA Glycosylase	50 µl, 100 U (2 U/µl)	03 539 806 001

6.4. Trademarks

LIGHTCYCLER, MAGNA PURE, HIGH PURE, FASTSTART, HYBPROBE, and TAQMAN are trademarks of Roche.
Exiqon and ProbeLibrary are registered trademarks of Exiqon A/S Vedbaek, Denmark.
Other brands or product names are trademarks of their respective holders.

6.5. License Disclaimer

For patent license limitations for individual products please refer to: http://technical-support.roche.com.

6.6. Regulatory Disclaimer

For life science research only. Not for use in diagnostic procedures.

6.7. Safety Data Sheet

Please follow the instructions in the Safety Data Sheet (SDS).

6.8. Contact and Support

If you have questions or experience problems with this or any Roche product for Life Science, please contact our Technical Support staff. Our scientists are committed to providing rapid and effective help.
Please also contact us if you have suggestions for enhancing Roche product performance or using our products in new or specialized ways. Such customer information has repeatedly proven invaluable to the research community worldwide.

To ask questions, solve problems, suggest enhancements or report new applications, please visit our **Online Technical Support** Site.

Visit **lifescience.roche.com**, to download or request copies of the following **Materials**:
- Instructions for Use
- Safety Data Sheets
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- Information Material

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