IVD For *in Vitro* Diagnostic Use

CE

Influenza A B Real-TM

Handbook

Real Time Amplification test for the detection of Influenza A and B Viruses

REF V36-100FRT

REF TV36-100FRT

Σ 100

NAME

Influenza Virus A B Real-TM

INTRODUCTION

Influenza virus infection, one of the most common infectious disease, is a highly contagious airborne disease that causes an acute febrile illness and results in variable degrees of systemic symptoms, ranging from mild fatigue to respiratory failure and death. These symptoms contribute to significant loss of workdays, human suffering, mortality, and significant morbidity. Influenza results from infection with 1 of 3 basic types of influenza virus – A, B, or C – which are classified within the family Orthomyxoviridae. These single stranded RNA viruses are structurally and biologically similar but vary antigenically. The most common prevailing influenza A subtypes that infect humans are H1N1 and H3N2.

INTENDED USE

Influenza Virus A B Real-TM is Real-Time amplification test for the qualitative detection of Influenza A and B RNA in clinical specimens.

PRINCIPLE OF ASSAY

Influenza Virus A B Real-TM Test is based on three major processes: isolation of *virus* RNA from specimens, reverse transcription of the RNA, Real Time amplification of the cDNA. *Influenza virus* A&B detection by the polymerase chain reaction (PCR) is based on the amplification of pathogen genome specific region using specific primers and detection via fluorescent dyes. These dyes are linked with probes of oligonucleotides which bind specifically to the amplified product. The real-time PCR monitoring of fluorescence intensities allows the accumulating product detection without reopening of reaction tubes after the PCR run. **Influenza Virus A B Real-TM** PCR kit is a qualitative test which contain the Internal Control (IC). It must be used in the isolation procedure in order to control the process of each individual sample extraction and serves also to identify possible reaction inhibition.

MATERIALS PROVIDED

Module No.1: Real Time PCR kit (V36-100FRT)

Part N° 2 – **"Reverta-L ":** Reverse transcription of the RNA

- **RT-G-mix-1**, 10 x 0,01 ml;
- **RT-mix,** 10 x 0,125 ml;
- **Reverse transcriptase (M-MLV)**, 2 x 0,03 ml;
- **TE-buffer**, 2 x 1,2 ml.

Contains reagents for 120 tests.

Part N° 3 – **"Influenza A&B ":** Real Time amplification kit

- **PCR-mix-1**, 5 x 0,2 ml;
- **PCR-mix-2-FRT**, 0,6 ml;
- **TaqF Polymerase**, 0,06 ml;
- **Pos cDNA Infl. A** / **Infl. B** / **IC**, 0,2 ml;
- **Negative Control**, 2 x 1,2 ml*;
- **Internal Control RNA**, 10 x 0,12 ml**;
- **DNA buffer**, 0,5 ml;

Contains reagents for 110 tests.

* *must be used in the isolation procedure as Negative Control of Extraction.*
** *add 10 µl of Internal Control RNA during the RNA purification procedure directly to the sample/lysis mixture*

Module No.2: Complete Real Time PCR test with RNA purification kit (TV36-100FRT)

Part N° 1 – **"Ribo-Sorb":** Sample preparation

- **Lysis Solution**, 2 x 22,5 ml;
- **Washing Solution**, 2 x 20 ml;
- **Sorbent**, 2 x 1,25 ml.
- **RNA-eluent**, 10 x 0,5ml;

Contains reagents for 100 tests.

Part N° 2 – **"Reverta-L ":** Reverse transcription of the RNA

- **RT-G-mix-1**, 10 x 0,01 ml;
- **RT-mix,** 10 x 0,125 ml;
- **Reverse transcriptase (M-MLV)**, 2 x 0,03 ml;
- **TE-buffer**, 2 x 1,2 ml.

Contains reagents for 120 tests.

Part N° 3 – **"Influenza A&B ":** Real Time amplification kit

- **PCR-mix-1**, 5 x 0,2 ml;
- **PCR-mix-2-FRT**, 0,6 ml;
- **TaqF Polymerase**, 0,06 ml;
- **Pos cDNA Infl. A** / **Infl. B** / **IC**, 0,2 ml;
- **Negative Control**, 2 x 1,2 ml*;
- **Internal Control RNA**, 10 x 0,12 ml**;
- **DNA buffer**, 0,5 ml;

Contains reagents for 110 tests.

* *must be used in the isolation procedure as Negative Control of Extraction.*
** *add 10 µl of Internal Control RNA during the RNA purification procedure directly to the sample/lysis mixture*

MATERIALS REQUIRED BUT NOT PROVIDED

Zone 1: sample preparation (only for Module No. 2):

- RNA extraction kit (Module No. 1)
- Biosafety cabinet
- Desktop microcentrifuge for “eppendorf” type tubes (RCF max. 16,000 x g); Eppendorf 5415D or equivalent
- 60°C ± 2°C dry heat block
- Vortex mixer
- Pipettors (capacity 5-40 µl; 40-200 µl; 200-1000 µl) with aerosol barrier
- 1,5 ml polypropylene sterile tubes (Sarstedt, QSP, Eppendorf)
- Disposable gloves, powderless
- Tube racks
- 70% Ethanol (freshly prepared mixture of reagent grade 96% ethanol and distilled water)
- Acetone
- Refrigerator
- Freezer

Zone 2: RT and amplification:

- Real Time Thermalcycler
- Workstation
- Pipettors (capacity 0,5-10 µl; 5-40 µl) with aerosol barrier
- Tube racks

STORAGE INSTRUCTIONS

Influenza Virus A B Real-TM must be stored at 2-8°C excepting **PCR-mix-1**, **PCR-mix-2-FRT** and **TaqF Polymerase** that must be stored at temperature ≤ -16°C. Store **Ribo-Sorb** kit at 2-25°C.The kits can be shipped at 2-8°C for 3-4 days but should be stored at 2-8°C and ≤ -16°C immediately on receipt.

STABILITY

Influenza Virus A B Real-TM is stable up to the expiration date indicated on the kit label. The product will maintain performance through the control date printed on the label. Exposure to light, heat or humidity may affect the shelf life of some of the kit components and should be avoided. Repeated thawing and freezing of these reagents should be avoided, as this may reduce the sensitivity.

QUALITY CONTROL

In accordance with Sacace’s ISO 13485-Certified Quality Management System, each lot is tested against predetermined specifications to ensure consistent product quality.

WARNINGS AND PRECAUTIONS

IVD

***In Vitro* Diagnostic Medical Device**

For *In Vitro* Diagnostic Use Only

The user should always pay attention to the following:

- ⚠ Lysis Solution contains guanidine thiocyanate*. Guanidine thiocyanate is harmful if inhaled, or comes into contact with skin or if swallowed. Contact with acid releases toxic gas. (Xn; R: 20/21/22-36/37/38; S: 36/37/39).
- Clinical specimens from suspect influenza A (H1N1) cases should be performed in a BSL2 laboratory with BSL3 practices (enhanced BSL2 conditions). Use sterile pipette tips with aerosol barriers and use new tip for every procedure.
- Store extracted positive material (samples, controls and amplicons) away from all other reagents and add it to the reaction mix in a separate area.
- Thaw all components thoroughly at room temperature before starting an assay.
- When thawed, mix the components and centrifuge briefly.
- Use disposable gloves, laboratory coats and eye protection when handling specimens and reagents. Thoroughly wash hands afterwards.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in laboratory work areas.
- Do not use a kit after its expiration date.
- Dispose of all specimens and unused reagents in accordance with local authorities' regulations.
- Specimens should be considered potentially infectious and handled in a biological cabinet in accordance with appropriate biosafety practices.
- Clean and disinfect all sample or reagent spills using a disinfectant such as 0.5% sodium hypochlorite, or other suitable disinfectant.
- Avoid sample or reagent contact with the skin, eyes, and mucous membranes. If skin, eyes, or mucous membranes come into contact, rinse immediately with water and seek medical advice immediately.
- Material Safety Data Sheets (MSDS) are available on request.
- Use of this product should be limited to personnel trained in the techniques of DNA amplification.
- The laboratory process must be one-directional, it should begin in the Extraction Area and then move to the Amplification and Detection Areas. Do not return samples, equipment and reagents to the area in which the previous step was performed.

Some components of this kit contain sodium azide as a preservative. Do not use metal tubing for reagent transfer.

**** Only for Module No.2***

PRODUCT USE LIMITATIONS

All reagents may exclusively be used in in vitro diagnostics. Use of this product should be limited to personnel trained in the techniques of DNA amplification (UNI EN ISO 18113-2:2012). Strict compliance with the user manual is required for optimal PCR results. Attention should be paid to expiration dates printed on the box and labels of all components. Do not use a kit after its expiration date.

SAMPLE COLLECTION, STORAGE AND TRANSPORT

Influenza Virus A B Real-TM can analyze RNA from:

- *nasopharyngeal swabs*: swab area and place in "Eppendorf" tube with 0,5 ml of saline water or PBS sterile (Sacace Transport medium is recommended). Agitate vigorously. Repeat the swab and agitate in the same tube. Centrifuge at 1000g/min for 5 min. Discard the supernatant and leave about 100 µl of solution for RNA extraction.
- *aspirate, bronchial lavage, nasal wash:* centrifuge at 2000 g/min for 10-15 min. If the pellet is not visible add 10 ml of liquid and repeat centrifugation. Remove and discard the supernatant. Resuspend the pellet in 100 µl of Saline water.
- *tissue:* 1,0 gr (parenchimatous organs, trachea, lung, brain) homogenized with mechanical homogenizer or scalpel, glass sticks, teflon pestles and dissolved in 1,0 ml of saline water or PBS sterile. Vortex vigorously and incubate 30 min at room temperature. Transfer the supernatant into a new 1,5 ml tube;

Specimens can be stored at +2-8°C for no longer than 12 hours, or frozen at -20°C to -80°C.
Transportation of clinical specimens must comply with country, federal, state and local regulations for the transport of etiologic agents.

RNA ISOLATION

Any commercial RNA/DNA isolation kit, if IVD-CE validated for the specimen types indicated herein at the "SAMPLE COLLECTION, STORAGE AND TRANSPORT" paragraph, could be used.
Sacace Biotechnologies recommends to use the following kits:

⇒ **Ribo-Sorb-** (Sacace, REF K-2-1);

⇒ **Ribo-Virus** spin column extraction kit (Sacace, REF K-2-C);

⇒ **SaMag Viral Nucleic Acids Extraction kit** (Sacace, REF SM003);

Please carry out the RNA extraction according to the manufacturer's instructions. Add 10 µl of Internal Control during the DNA isolation procedure directly to the sample/lysis mixture.

SPECIMEN AND REAGENT PREPARATION (reagents supplied with the module no.2)

1. **Lysis Solution** and **Washing Solution** (in case of their storage at +2-8ºC) should be warmed up to 60–65 ºC until disappearance of ice crystals. Prepare required quantity of 1.5 ml polypropylene tubes including one tube for **Negative Control of Extraction**.
2. Add to each tube **450 µl Lysis Solution** and **10 µl Internal Control RNA**. Mix by pipetting and incubate 5 min at room temperature.
3. Add **100 µl** of samples to the appropriate tube containing Lysis Solution and IC.
4. Prepare Controls as follows:
   - add **100 µl** of **C– Negative Control** to the tube labeled *Cneg*
5. Vortex the tubes and centrifuge for 5 sec at 5000g. If the sample is not completely dissolved it is recommended to re-centrifuge the tube for 1 min at a maximum speed (12000-16000 g.) and transfer the supernatant into a new tube for RNA extraction
6. Vortex vigorously **Sorbent** and add **25 µl** to each tube.
7. Vortex for 5-7 sec and incubate all tubes for 10 min at room temperature. Vortex periodically.
8. Centrifuge all tubes for 1 min at 10000g and using a micropipette with a plugged aerosol barrier tip, carefully remove and discard supernatant from each tube without disturbing the pellet. Change tips between tubes.
9. Add **400 µl** of **Washing Solution** to each tube. Vortex vigorously, centrifuge for 1 min at 10000g. and using a micropipette with a plugged aerosol barrier tip, carefully remove and discard supernatant from each tube without disturbing the pellet. Change tips between tubes.
10. Add **500 µl** of **Ethanol 70%** to each tube. Vortex vigorously, centrifuge for 1 min at 10000g. and using a micropipette with a plugged aerosol barrier tip, carefully remove and discard supernatant from each tube without disturbing the pellet. Change tips between tubes.
11. Repeat step 10.
12. Add **400 µl** of **Acetone** to each tube. Vortex vigorously , centrifuge for 1 min at 10000g and using a micropipette with a plugged aerosol barrier tip, carefully remove and discard supernatant from each tube without disturbing the pellet. Change tips between tubes.
13. Incubate all tubes with open cap for 10 min at 60°C.
14. Resuspend the pellet in **40 µl** of **RNA-eluent.** Incubate for 10 min at 60°C and vortex periodically. Centrifuge the tubes for 2 min at maximum speed (12000-16000 g).
15. The supernatant contains RNA ready for use. The RT-PCR can be performed the same day. If this is not possible, the RNA preparations can be stored at -80°C for up to one month.

RT AND AMPLIFICATION

Reverse Transcription:

1. Prepare Reaction Mix: for 12 reactions, **add 5,0 µl RT-G-mix-1** into the tube containing **RT-mix** and vortex for at least 5-10 seconds, centrifuge briefly. This mix is stable for 1 month at -20°C. Add **6 µl M-MLV** into the tube with Reagent Mix, mix by pipetting, vortex for 3 sec, centrifuge for 5-7 sec (must be used immediately after the preparation).
   *(If it is necessary to test less than 12 samples add for each sample (N) in the new sterile tube **10*N µl** of **RT-G-mix-1 with RT-mix** and **0,5*N µl** of **M-MLV**).*
2. Add **10 µl** of **Reaction Mix** into each sample tube.
3. Pipette **10 µl RNA** samples to the appropriate tube. (*If the Ribo-Sorb isolation kit is used as a RNA extraction kit, re-centrifuge all the tubes with extracted RNA for 2 min at maximum speed (12000-16000 g) and take carefully supernatant. N.B. don't disturb the pellet, sorbent inhibit reaction).*Carefully mix by pipetting.
4. Place tubes into thermalcycler and incubate at 37ºC for 30 minutes.
5. Dilute 1: 2 each obtained cDNA sample with TE-buffer (add **20 µl TE-buffer** to each tube).

cDNA specimens could be stored at -20ºC for a week or at -70ºC during a year.

Real Time amplification:

Reaction Mix 25 µl

1. Prepare required quantity of tubes or PCR plate.
2. Prepare for each sample in the new sterile tube **10*N µl** of **PCR-mix-1**, **5*N µl** of **PCR-mix-2-FRT** and **0,5*N** of **TaqF Polymerase.**
3. Add **15 µl** of **Reaction Mix** into each tube.
4. Add **10 µl** of **cDNA** sample to appropriate tube with Reaction Mix.
5. Prepare for each panel 2 controls:
   - add **10 µl** of **DNA-buffer** to the tube labeled Amplification Negative Control;
   - add **10 µl** of **Pos cDNA Infl. A** / **Infl. B** / **IC** to the tube labeled C_{pos};

Amplification

1. Create a temperature profile on your instrument as follows:

	Rotor type instruments[1]			Plate type instruments[2]		
Step	**Temperature, °C**	**Time**	**Cycles**	**Temperature, °C**	**Time**	**Cycles**
1	95	15 min	1	95	15 min	1
2	95	10 s	10	95	10 s	10
	54	20 s		54	25 s	
	72	10 s		72	25 s	
3	95	10 s	35	95	10 s	35
	54	20 s Fluorescence detection		54	25 s Fluorescence detection	
	72	10 s		72	25 s	

[1] Rotor-Gene™ 3000/6000/Q (Corbett Research, Qiagen);
[2] For example SaCycler-96™ (Sacace), CFX/iQ5™ (BioRad); Mx3005P™ (Agilent), ABI® 7300/7500/StepOne Real Time PCR (Applied Biosystems), LineGeneK® (Bioer);

Modular type instruments			
Step	**Temperature, °C**	**Time**	**Cycles**
Hold	**95**	**900 s (variant FRT-100 F)**	**1**
Stage1	**95**	**15 s**	**42**
	54	25 s Fluorescence acquiring	
	72	25 s	

For example, SmartCycler® (Cepheid)

Influenza Virus A is detected on the Rox (Orange) channel, *Influenza Virus B* is detected on the JOE (Yellow) channel, *IC* on the FAM (Green) channel.

INSTRUMENT SETTINGS

Rotor-type instruments

Channel	Calibrate/Gain Optimisation…	Threshold	More Settings/ Outlier Removal	Slope Correct
FAM/Green	*from 5 Fl to 10 Fl*	0.1	0 %	off
JOE/Yellow	*from 5 Fl to 10 Fl*	0.1	5 %	off
Rox/Orange	*from 5 Fl to 10 Fl*	0.1	5 %	off

Plate- or modular type instruments

The threshold line should cross only sigmoid curves of signal accumulation of positive samples and should not cross the baseline; otherwise, the threshold level should be raised. Set the threshold at a level where fluorescence curves are linear and do not cross curves of the negative samples.

RESULTS ANALYSIS

Analysis of results is performed by the software of the real-time PCR instrument used by measuring fluorescence signal accumulation in three channels:

– The signal of the IC cDNA amplification product is detected in the channel for the FAM fluorophore.
– The signal of the Influenza virus B cDNA amplification product is detected in the channel for the JOE fluorophore.
– The signal of the Influenza virus A cDNA amplification product is detected in the channel for the ROX fluorophore.

1. The sample is considered to be positive for *Influenza Virus A* if in the channel Rox (Orange) the value of **Ct** is different from zero and is less than the boundary value specified in the table below.
2. The sample is considered to be positive for *Influenza Virus B* if in the channel Joe (Yellow) the value of **Ct** is different from zero and is less than the boundary value specified in the table below.
3. The sample is considered to be negative *for* Influenza A/B if Ct value is not determined (absent) in ROX and JOE channels, whereas the Ct value is determined in FAM channel and is less than the value specified in the table below.

Boundary values for rotor type intruments:

Sample	Stage for control	Ct channel Fam (Green)	Ct channel Joe (Yellow)	Ct channel Rox (Orange)	Result
NCE	RNA isolation	< 28	Neg	Neg	Valid result
NCA	PCR	Neg	Neg	Neg	Valid result
Pos cDNA Infl. A / Infl. B / IC	PCR	< 25	< 25	< 25	Valid result
Clinical samples	RNA isolation	< 28	< 33	< 33	Valid result

Boundary values for plate type intruments:

Sample	Stage for control	Ct channel Fam (Green)	Ct channel Joe (Yellow)	Ct channel Rox (Orange)	Result
NCE	RNA isolation	< 30	Neg	Neg	Valid result
NCA	PCR	Neg	Neg	Neg	Valid result
Pos cDNA Infl. A / Infl. B / IC	PCR	< 28	< 28	< 28	Valid result
Clinical samples	RNA isolation	< 30	< 33	< 33	Valid result

Boundary values for modular type intruments:

Sample	Stage for control	Ct channel Fam (Green)	Ct channel Joe (Yellow)	Ct channel Rox (Orange)	Result
NCE	RNA isolation	< 36	Neg	Neg	Valid result
NCA	PCR	Neg	Neg	Neg	Valid result
Pos cDNA Infl. A / Infl. B / IC	PCR	< 37	< 37	< 37	Valid result
Clinical samples	RNA isolation	< 37	< 40	< 40	Valid result

The result of the analysis is considered reliable only if the results obtained for Positive and Negative Controls of amplification as well as for the Negative Control of extraction are correct (see the table below).

Results for controls:

Control	Stage for control	Ct channel Fam (Green)	Ct channel Joe (Yellow)	Ct channel Rox (Orange)
NCE	RNA isolation	< boundary value	Neg	Neg
NCA	PCR	Neg	Neg	Neg
Pos cDNA Infl. A / Infl. B / IC	PCR	< boundary value	< boundary value	< boundary value

PERFORMANCE CHARACTERISTICS

Sensitivity

The kit **Influenza A B Real-TM** allows to detect *Influenza A&B viruses* in 100% of the tests with a sensitivity of not less than 1 x 10^3 GE/ml*.

* Genome equivalents (GE) of the pathogen agent per 1 ml of a sample.

Specificity

The analytical specificity of **Influenza A B Real-TM** PCR kit is ensured by the selection of specific primers and probes as well as stringent reaction conditions. The primers and probes have been checked for possible homologies to all sequences published in gene banks by sequence comparison analysis.

The PCR kit allows detection of cDNA fragments of *Influenza virus* A and *Influenza virus* B. The specific activity of the PCR kit was proven in detection of reference strains and isolates of epidemic *Influenza viruses* A/H1N1 and A/H3N2 extracted in the period from 1977 to 2011 from clinical samples, *Influenza viruses* A extracted from animals (H1N1, H2N2, H2N3, H2N9, H3N2, H3N8, H4N6, H5N1, H5N3, H5N2, H5N3, H6N2, H7N1, H8N4, H9N2, H10N7, H11N6, H12N5, H13N2), *Influenza viruses* B lineages Yamagata and Victoria as well as A/California/07/2009 strain of pandemic *Influenza virus* A/H1N1pdm2009.

The absence of nonspecific reactions of the kit components was shown for cDNA/DNA of other viral (*Human Respiratory-Syncytial virus* “Long” strain, *Human Rhinoviruses* (types 13, 15, 16,

17, 21, 26, and 29), *Herpes viruses*, *Cytomegalovirus*, *Enteroviruses* (types Echo9, Echo30) and bacterial (*Streptococcus* spp., *Staphylococcus aureus*, *Mycoplasma pneumoniae*, *Chlamydophila pneumonia*, *Haemophilus influenzae, Moraxella catarrhalis, Legionella pneumophila*) causative agents of acute respiratory disease; normal microflora of human nasal cavity and oropharynx; and human cDNA/DNA as well as analysis of clinical material containing nucleic acids of *Respiratory Syncytial viruses* (types A and B), *Parainfluenza viruses* (types 1-4), *Human Coronavirus* OC43, E229, NL63, HKUI, *Human Adenoviruses* groups B, C, and E, *Human Metapneumovirus,* and *Human Bocavirus.*

The clinical specificity of **Influenza A B Real-TM** PCR kit was confirmed by laboratory clinical trials.

TROUBLESHOOTING

1. Weak or absent signal of the IC (Fam (Green) channel): retesting of the sample is required.
    - The PCR was inhibited.
        - ⇒ Make sure that you use a recommended RNA extraction method and follow the manufacturer's instructions.
        - ⇒ Re-centrifuge all the tubes before pipetting the extracted RNA for 2 min at maximum speed (12000-16000 g) and take carefully supernatant. Don't disturb the pellet, sorbent inhibit reaction.
    - The reagents storage conditions didn't comply with the instructions.
        - ⇒ Check the storage conditions
    - The PCR conditions didn't comply with the instructions.
        - ⇒ Check the PCR conditions and for the IC detection select the fluorescence channel reported in the protocol.
    - The IC was not added to the sample during the pipetting of reagents.
        - ⇒ Make attention during the RNA extraction procedure.
2. Weak signal on the Joe (Yellow)/Cy3/HEX and Rox/TexasRed channels: retesting of the sample is required.
3. Joe (Yellow)/Cy3/HEX or Rox/TexasRed signal with Negative Control of extraction.
    - Contamination during RNA extraction procedure. All samples results are invalid.
        - ⇒ Decontaminate all surfaces and instruments with sodium hypochlorite and ethanol.
        - ⇒ Use only filter tips during the extraction procedure. Change tips among tubes.
        - ⇒ Repeat the RNA extraction with the new set of reagents.
4. Any signal with Negative PCR Control.
    - Contamination during PCR preparation procedure. All samples results are invalid.
        - ⇒ Decontaminate all surfaces and instruments with sodium hypochlorite and ethanol or special DNA decontamination reagents.
        - ⇒ Pipette the Positive controls at the end.
        - ⇒ Repeat the PCR preparation with the new set of reagents.

KEY TO SYMBOLS USED

REF	List Number		Caution!
LOT	Lot Number		Contains sufficient for <n> tests
IVD	For *in Vitro* Diagnostic Use	VER	Version
	Store at	**NCA**	Negative Control of Amplification
	Manufacturer	**NCE**	Negative control of Extraction
	Consult instructions for use	**C+**	Positive Control of Amplification
	Expiration Date	**IC**	Internal Control

* SaCycler™ is a registered trademark of Sacace Biotechnologies
* CFX™ and iQ5™ are registered trademarks of Bio-Rad Laboratories
* Rotor-Gene™ is a registered trademark of Qiagen
* MX3005P® is a registered trademark of Agilent Technologies
* ABI® is a registered trademark of Applied Biosystems
* LineGeneK® is a registered trademark of Bioer
* SmartCycler® is a registered trademark of Cepheid

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