MIKROGEN
DIAGNOSTIK

Instruction for Use

*alpha*Cube HSV/VZV

For simultaneous qualitive in vitro detection and differentiation of purified DNA of Herpes Simplex Virus Type 1, Herpes Simplex Virus Type 2 and Varicella Zoster Virus, extracted from biological specimens.

REF	830573	830572
Σ	32	96

- 18°C

IVD

CE

Index

1 Intended Use

*alpha*Cube HSV/VZV real time PCR is an assay for the amplification and differentiation of purified DNA of Herpes Simplex Virus Type 1 (HSV-1), Herpes Simplex Virus Type 2 (HSV-2) and Varicella Zoster Virus (VZV), extracted from biological specimens.

2 Background Information

Herpes Simplex Virus Type 1 and Type 2

The herpes simplex virus, or herpes, is categorized into 2 types: herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). HSV-1 is mainly transmitted by oral-to-oral contact to cause oral herpes (which can include symptoms known as "cold sores"), but can also cause genital herpes. HSV-2 is a sexually transmitted infection that causes genital herpes. Both HSV-1 and HSV-2 infections are lifelong. An estimated 3.7 billion people under age 50 (67%) have HSV-1 infection globally. An estimated 417 million people aged 15-49 (11%) worldwide have HSV-2 infection. Most oral and genital herpes infections are asymptomatic. Symptoms of herpes include painful blisters or ulcers at the site of infection. Herpes infections are most contagious when symptoms are present but can still be transmitted to others in the absence of symptoms. Infection with HSV-2 increases the risk of acquiring and transmitting HIV infection. In immunocompromised people, such as those with advanced HIV infection, HSV-1 can have more severe symptoms and more frequent recurrences. Rarely, HSV-1 infection can also lead to more severe complications such as encephalitis or keratitis (eye infection). Neonatal herpes can occur when an infant is exposed to HSV in the genital tract during delivery. This is a rare condition, occurring in an estimated 10 out of every 100,000 births globally, but can lead to lasting neurologic disability or death. The risk for neonatal herpes is greatest when a mother acquires HSV infection for the first time in late pregnancy. Women who have genital herpes before they become pregnant are at very low risk of transmitting HSV to their infants. Recurrent symptoms of oral herpes may be uncomfortable and can lead to some social stigma and psychological distress. With genital herpes, these factors can have an important impact on quality of life and sexual relationships. However, in time, most people with either kind of herpes adjust to living with the infection. Antiviral medications, such as acyclovir, famciclovir, and valacyclovir, are the most effective medications available for people infected with HSV. These can help to reduce the severity and frequency of symptoms, but cannot cure the infection.

Varicella Zoster Virus

Varicella, also commonly referred to as "chickenpox", is an acute and highly contagious disease. It is caused by primary infection with the varicella-zoster virus (VZV). Varicella occurs worldwide and in the absence of a vaccination programme, affects nearly every person by mid-adulthood. The epidemiology of the disease differs between temperate and tropical climates. The reasons for the differences are poorly understood and may relate to properties of VZV (known to be sensitive to heat), climate, population density and risk of exposure (e.g., attendance at childcare facility or school or the number of siblings in the household).

VZV is highly transmissible via respiratory droplets or direct contact with characteristic skin lesions of the infected person. The first symptoms of clinical varicella generally appear after a 10-21 days incubation period and include fever, malaise and the characteristic itchy rash. Varicella is generally self-limited and vesicles gradually

develop crusts, which disappear over a period of 7-10 days. Individuals remain contagious until all lesions have crusted over. The disease is typically mild, but severe complications may arise, including bacterial infections (e.g. cellulitis, pneumonia) and neurological complications (e.g. encephalitis), and these can be fatal. Disease is associated with higher morbidity and mortality in infants and in individuals with an impaired immune system.
Following infection, the virus remains latent in nerve cells and may be reactivated causing a secondary infection - herpes zoster, commonly referred to as “shingles”. This generally occurs in adults aged >50 years or in the immunocompromised and is associated with a painful rash that may result in permanent nerve damage.
Varicella can be prevented by immunization and multiple vaccine formulations of the live attenuated vaccine, based on the Oka VZV strain, have been available since 1974. Varicella vaccines are available as a single antigen and in combination with measles, mumps and rubella vaccine.

3 Principle of the Test

*alpha*CubeHSV/VZV contains specific primers and dual-labeled probes for the amplification and detection of the DNA of HSV-1, HSV-2 and VZV. The presence of nucleic acids is detected by an increase in fluorescence due to hydrolysis of the probes during amplification. The fluorescence signals of the specific probes are measured in the FAM (HSV-1), ROX (HSV-2) and Cy5 (VZV) channels.
Furthermore, *alpha*CubeHSV/VZV real time PCR contains a Control DNA, which is added during DNA extraction and detected in the same reaction by a differently labeled probe.
The Control DNA allows the detection of PCR inhibition and acts as control, that the nucleic acid was isolated from the clinical specimen. The fluorescence of the Control DNA is measured in the HEX channel.

4 Package Contents

The reagents supplied are sufficient for 32 or 96 reactions respectively.

Table 1: Components of alphaCube HSV/VZV.

Label	Lid Colour	Content	
		32	96
Reaction Mix	yellow	1 x 512 µl	2 x 768 µl
Positive Control	red	1 x 50 µl	1 x 100 µl
Negative Control	green	1 x 50 µl	1 x 100 µl
Control DNA	colourless	1 x 160 µl	2 x 240 µl

5 Equipment and Reagents to be Supplied by User

- DNA isolation kit (e.g. *alpha*Clean Pure RNA/DNA or *alpha*Clean Mag RNA/DNA)
- PCR grade Water
- Sterile microtubes
- Pipets (adjustable volume)
- Sterile pipet tips with filter

- Table centrifuge
- Vortexer
- Real time PCR instrument
- If using LightCycler® 480 (Roche) alphaCube Colour Compensation (831009) is required.
- Optical PCR reaction tubes with lid
- Optional: Liquid handling system for automation

6 Transport, Storage and Stability

*alpha*Cube HSV/VZV is shipped on dry ice or cool packs. All components must be stored at maximum -18°C in the dark immediately after receipt. Do not use reagents after the date of expiry printed on the package. Up to 20 freeze and thaw cycles are possible.
For convenience, opened reagents can be stored at +2-8°C for up to 6 months.
Protect kit components from direct sunlight during the complete test run.

7 Important Notes

Read the Instructions for Use carefully before using the product.
Before first use check the product and its components for:

- Use of this product is limited to personnel specially instructed and trained in the techniques of real-time PCR procedures.
- Specimens should always be treated as infectious and/or biohazardous in accordance with safe laboratory procedures.
- Avoid microbial and nuclease (DNase/RNase) contamination of the eluates and the components of the kit.
- Always use DNase/RNase-free disposable pipette tips with aerosol barriers.
- Always wear protective disposable powder-free gloves when handling kit components.
- Use separated and segregated working areas for (1) sample preparation, (2) reaction setup and (3) amplification/detection activities. The workflow in the laboratory should proceed in unidirectional manner. Always wear disposable gloves in each area and change them before entering a different area.
- Dedicate supplies and equipment to the separate working areas and do not move them from one area to another.
- Store positive and/or potentially positive material separated from all other components of the kit.
- Do not open the reaction tubes/plates post amplification, to avoid contamination with amplicons.
- Additional controls may be tested according to guidelines or requirements of local, state and/or federal regulations or accrediting organizations.
- Do not autoclave reaction tubes after the PCR, since this will not degrade the amplified nucleic acid and will bear the risk to contaminate the laboratory area.
- Discard sample and assay waste according to your local safety regulations.

8 Sample Preparation

Purified DNA is suitable for downstream processing in real time PCR. For the extraction and purification of DNA from various biological materials, commercial kits are available. The operator needs to evaluate the suitability of respective DNA extraction kit. Commercial kits for DNA isolation such as the following are recommended:

- *alpha*Clean Pure RNA/DNA
- *alpha*Clean Mag RNA/DNA

Important:
In addition to the samples always run a ‚water control' in your extraction. Treat this water control analogous to a sample.
Comparing the amplification of the Control DNA in the samples to the amplification of the internal control in the water control will give insights on possible inhibitions of the real time PCR. Furthermore, possible contaminations during DNA extraction will be detectable.

Please note the chapter ‚Control DNA'.

If the real time PCR is not performed immediately, store extracted DNA according to the instructions given by the manufacturer.

9 Control DNA

A Control DNA is supplied and can be used as extraction control or only as inhibition control. This allows the user to control the DNA isolation procedure and to check for possible real time PCR inhibition.

DNA isolation from biological specimens
a) Control DNA used as Extraction Control:
*alpha*Cube HSV/VZV Control DNA is added to the DNA extraction.
Add 5 µl Control DNA per extraction (5 µl x (N+1)). Mix well. Perform the DNA isolation according to the manufacturer's instructions. Please follow protocol A.

The Control DNA must be added to the Lysis Buffer of the extraction kit.

b) Control DNA used as Internal Control of the real time PCR:
If only inhibition will be checked please follow protocol B.

10 Real time PCR

10.1 Important Points Before Starting:

- Please pay attention to the chapter ‚Important Notes'.
- Before setting up the real time PCR familiarise yourself with the real time PCR instrument and read the user manual supplied with the instrument.
- The programming of the thermal profile should take place before the PCR set up.
- In every PCR run one Positive Control and one Negative Control should be included.
- Before each use, all reagents should be thawed completely at room temperature, thoroughly mixed (do NOT vortex the Reaction Mix but mix by pipetting up and down repeatedly), and centrifuged very briefly.

10.2 Procedure

If the Control DNA is used to control both, the real time PCR and the DNA isolation procedure, please follow protocol A. If the Control DNA is solely used to detect possible inhibition of the real time PCR, please follow protocol B.

Protocol A

The Control DNA was added during DNA extraction (see chapter ‚Control DNA'). In this case, prepare the Master Mix according to Table 2.
The Master Mix contains all of the components needed for PCR except the sample. Prepare a volume of Master Mix for at least one sample more than required, in order to compensate for pipetting inaccuracy.

Table 2: Preparation of the Master Mix (Control DNA was added during DNA extraction)

Volume per Reaction	Volume Master Mix
16.0 µl Reaction Mix	16.0 µl x (N+1)

Protocol B
The Control DNA is used for the control of the real time PCR only (see chapter 9 ‚Control DNA'). In this case, prepare the Master Mix according to Table 3.
The Master Mix contains all of the components needed for real time PCR except the sample. Prepare a volume of Master Mix for at least one sample more than required, in order to compensate for pipetting inaccuracy.

Table 3: Preparation of the Master Mix (Control DNA is added directly to the Master Mix)

Volume per Reaction	Volume Master Mix
16.0 µl Reaction Mix	16.0 µl x (N+1)
0.5 µl Control DNA*	0.5 µl x (N+1)*

*The increase in volume caused by adding the Control DNA is not taken into account when preparing the PCR assay.

Protocol A and B: real time PCR set up
- Place the number of optical PCR reaction tubes needed into the respective tray of the real time PCR instrument.
- Pipet **16 µl** of the Master Mix into each optical PCR reaction tube.
- Add **4 µl** of the eluates from the DNA isolation (including the eluate of the water control), the Positive Control and the Negative Control to the corresponding optical PCR reaction tube (Table 4).
- Close the optical PCR reaction tubes immediately after filling in order to reduce the risk of contamination.

Table 4: Preparation of the real time PCR

Component	Volume
Master Mix	16.0 µl
Sample	4.0 µl
Total Volume	20.0 µl

10.3 Instrument Settings

For the real time PCR use the thermal profile in the table shown below.

Table 5: real time PCR thermal profile

Description	Time	Temperature	Number of Cycles
Reverse Transcription	10 min	45°C	1
Initial Denaturation	5 min	95°C	1
Amplification			
Denaturation	10 sec	95°C	45
Annealing and Extension	40 sec Aquisition at the end of this step	60°C	

The real time PCR thermal profile mentioned represents the universal settings for *alpha*Cube real time PCR and real time RT-PCR kits. Therefore, different kits can be used in the same run. For *alpha*Cube real time PCR kits used for amplification of DNA, the reverse transcription can be omitted. Dependent on the real time PCR instrument used, further instrument settings have to be adjusted according to the table below.

Table 6: Overview of the instrument settings required for *alpha*Cube HSV/VZV.

Real time PCR Instrument	**Parameter Reaction Mix**	**Detection Channel**	**Notes**		
LightCycler 480II			*alpha*Cube 480 Colour Compensation (831009) required		
			Melt Factor	Quant Factor	Max Integration Time (sec)
	HSV-1	465-510	1	10	1
	HSV-2	533-610	1	10	2
	Control DNA	533-580	1	10	2
	VZV	618-660	1	10	3
Stratagene Mx3000P / Mx3005P	HSV-1	FAM	Gain 8		
	HSV-2	ROX	Gain 1		Reference Dye: None
	Control DNA	HEX	Gain 1		
	VZV	Cy5	Gain 4		
Agilent Aria Mx BioRad CFX 96	HSV-1	FAM			
	HSV-2	ROX			Reference Dye: None
	Control DNA	HEX			
	VZV	Cy5			
ABI 7500	HSV-1	FAM	Option Reference Dye ROX: NO		
	HSV-2	ROX			
	Control DNA	JOE			
	VZV	Cy5			
Rotor-Gene Q, Rotor-Gene 3000 Rotor-Gene 6000	HSV-1	Green	Gain 5		
	HSV-2	Orange	Gain 5		
	Control DNA	Yellow	Gain 5		
	VZV	Red	Gain 5		
mic qPCR Cycler	HSV-1	Green	Gain 8		
	HSV-2	Orange	Gain 10		
	Control DNA	Yellow	Gain 10		
	VZV	Red	Gain 10		

11 Data Analysis

The specific amplifications are measured in the FAM, ROX, and Cy5 channel. The amplification of the Control DNA is measured in the HEX channel. The Positive Control contains nucleic acid target sequences of HSV-1, HSV-2 and VZV. For the Positive Control, signals in the FAM, ROX, and Cy5 channels must be detected.

Table 7: Interpretation of results

Signal/Ct Values				**Interpretation**
FAM HSV-1	**ROX** HSV-2	**Cy5** VZV	**HEX** Control DNA	
positive	negative	negative	positive or negative*	Positive result, the eluate contains HSV-1 DNA.
negative	**positive**	negative	positive or negative*	Positive result, the eluate contains HSV-2 DNA.
negative	negative	**positive**	positive or negative*	Positive result, the eluate contains VZV DNA.
negative	negative	negative	≤ 34**	Negative result, the eluate contains no HSV-1, HSV-2 and VZV DNA.
negative	negative	negative	negative or > 34**	No diagnostic statement can be made. The real time PCR is either inhibited or errors occurred while DNA extraction.

* A strong positive signal in the FAM, ROX and/or Cy5 can inhibit the amplification of the Control DNA. In such cases the result for the Control DNA can be neglegted.

** Depending on the PCR instrument and/or the chosen extraction method, the Ct values might be shifted. The water control can be used as reference. If the HEX Ct value of a sample differs a lot from the water control, partial inhibition has occurred, leading to false negative results in case of weak positive samples.

Figure 1 and **Figure 2** show examples for positive and negative real time PCR results.

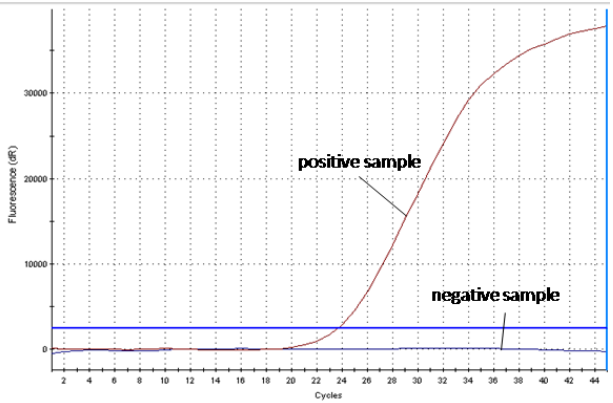


Figure 1: The positive eluate shows specific amplification in the FAM channel, whereas no fluorescence signal is detected in the negative sample.

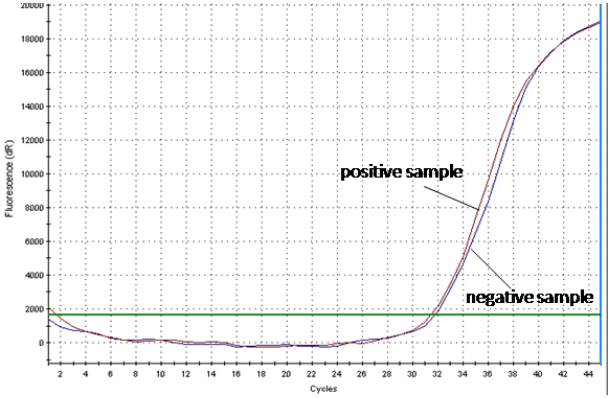


Figure 2: The positive eluate as well as the negative eluate show a signal in the Control DNA specific HEX channel. The amplification signal of the Control DNA in the negative eluate shows, that the missing signal in the specific FAM channel is not due to PCR inhibition or failure of DNA isolation, but that the eluate is a true negative.

12 Assay Validation

Set a threshold as follows:

Negative Controls
All negative controls should be below the threshold. If there is a potential contamination (appearance of a curve in the negative control or a cluster of curves in specimens at high C_T – for example above 36), results obtained are not interpretable and the whole run (including extraction) has to be repeated.

Positive Controls
All the positive controls must show a positive (i.e. exponential) amplification curve. The positive controls must fall below a C_T of 30.

Internal Controls
All internal controls must show a positive (i.e. exponential) amplification curve. The internal control must fall below a C_T of $\leq$34. If the internal control is above C_T 34, this points to a purification problem or a strong positive eluate that can inhibit the IC. In the latter case, the assay is valid. If a water control run is performed, the IC must fall below a C_T of $\leq$34.

13 Limitations of the Method

- Strict compliance with the Instructions for Use is required for optimal results.
- Use of this product is limited to personnel specially instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures.
- Good laboratory practice is essential for proper performance of this assay.
- All reagents should be closely monitored for impurity and contamination. Any suspicious reagents should be discarded.
- This assay must not be used on a biological specimen directly. Appropriate nucleic acid extraction methods have to be conducted prior to using this assay.
- The presence of PCR inhibitors may cause false negative or invalid results.
- Potential mutations within the target regions of the HSV-1, HSV-2 or VZV genome covered by the primers and/or probes used in the kit may result in failure to detect the respective DNA.
- As with any diagnostic test, results of the alphaCube HSV/VZV kit need to be interpreted in consideration of all clinical and laboratory findings.

14 Troubleshooting

The following troubleshooting guide is included to help you with possible problems that may arise when performing a real time PCR.

No fluorescence signal in the specific channels of the Positive Control	
The selected channel for analysis does not comply with the protocol	Select the channel according to chapter ‚Instrument Settings'.
Incorrect configuration of the real time PCR	Check your work steps and compare with chapter ‚Procedure'.

The programming of the thermal profile is incorrect	Compare the thermal profile with chapter ‚Instrument Settings'.
Incorrect storage conditions for one or more kit components or kit expired	Check the storage conditions and the date of expiry printed on the kit label. If necessary, use a new kit and make sure kit components are stored as described in chapter ‚Transport, Storage and Stability'.
Weak or no signal of the Control DNA and simultaneous absence of a signal in the specific channels	
real time PCR conditions do not comply with the protocol	Check the real time PCR conditions (chapter ‚Real time PCR').
real time PCR inhibited	Make sure that you use an appropriate isolation method (see chapter ‚Sample Preparation') and follow the manufacturer's instructions. Make sure that the ethanol-containing washing buffers have been completely removed. An additional centrifugation step at high speed is recommended before elution of the DNA.
DNA loss during isolation process	In case the Control DNA was added before extraction, the lack of an amplification signal can indicate that the DNA isolation was not successful. Make sure that you use an appropriate isolation method (commercial kits are recommended) and stick to the manufacturer's protocol.
Incorrect storage conditions for one or more components or kit expired	Check the storage conditions and the date of expiry printed on the kit label. If necessary, use a new kit and make sure kit components are stored as described in chapter ‚Transport, Storage and Stability'.
Detection of a fluorescence signal in the specific channels of the Negative Control	
Contamination during preparation of the PCR	Repeat the real time PCR in replicates. If the result is negative in the repetition, the contamination occured when the samples were pipetted into the optical PCR reaction tubes. Make sure to pipet the Positive Control last and close the optical PCR reaction tube immediately after adding the sample. If the same result occurs, one or more of the kit components might be contaminated. Make sure that work space and instruments are decontaminated regularly. Use a new kit and repeat the real time PCR.

15 Kit Performance

15.1 Analytical Sensitivity

The limit of detection (LoD) of *alpha*Cube HSV/VZV was determined using serial dilutions of synthetic target DNA-sequences in a Stratagene Mx3005 real time PCR instrument. The LoD of *alpha*Cube HSV/VZV for HSV-1 is ≤10 target copies per reaction each for HSV-2 ≤10 target copies per reaction each and for VZV ≤10 target copies per reaction each.

Table 8: Determination of the LoD for the detection of HSV-1 DNA.

	copies per reaction	**HSV-1** **FAM channel Ct-values**
gBlock Mix HSV-1; HSV-2; VZV	10000000	14,49 14,46 14,66
gBlock Mix HSV-1; HSV-2; VZV	1000000	18,00 17,99 18,16
gBlock Mix HSV-1; HSV-2; VZV	100000	21,76 21,97 21,48
gBlock Mix HSV-1; HSV-2; VZV	10000	25,28 25,52 25,77
gBlock Mix HSV-1; HSV-2; VZV	1000	29,32 29,32 29,14
gBlock Mix HSV-1; HSV-2; VZV	100	32,91 33,16 32,98
gBlock Mix HSV-1; HSV-2; VZV	10	36,72 38,84 35,95

Table 9: Determination of the LoD for the detection of HSV-2 DNA.

	copies per reaction	HSV-2 ROX channel Ct-values
gBlock Mix HSV-1; HSV-2; VZV	10000000	14,44 14,30 14,21
gBlock Mix HSV-1; HSV-2; VZV	1000000	17,72 17,72 17,65
gBlock Mix HSV-1; HSV-2; VZV	100000	20,88 21,06 20,96
gBlock Mix HSV-1; HSV-2; VZV	10000	24,45 24,59 24,60
gBlock Mix HSV-1; HSV-2; VZV	1000	27,96 28,15 27,98
gBlock Mix HSV-1; HSV-2; VZV	100	31,04 31,21 31,64
gBlock Mix HSV-1; HSV-2; VZV	10	34,33 34,26 34,89

Table 10: Determination of the LoD for the detection of VZV DNA.

	copies per reaction	VZV Cy5 channel Ct-values
gBlock Mix HSV-1; HSV-2; VZV	10000000	13,90 13,10 13,71
gBlock Mix HSV-1; HSV-2; VZV	1000000	16,91 16,43 16,69
gBlock Mix HSV-1; HSV-2; VZV	100000	20,08 20,02 20,36
gBlock Mix HSV-1; HSV-2; VZV	10000	23,67 23,76 23,36
gBlock Mix HSV-1; HSV-2; VZV	1000	26,69 26,84 27,25
gBlock Mix HSV-1; HSV-2; VZV	100	30,67 30,16 30,18
gBlock Mix HSV-1; HSV-2; VZV	10	32,99 33,08 33,43

15.2 Analytical Specificity

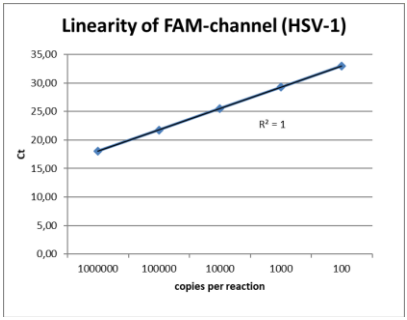
The specificity of the *alpha*Cube HSV/VZV real time PCR was evaluated by testing a panel of RNA/DNA extracted from viruses and bacteria.
The *alpha*Cube HSV/VZV real time PCR kit did not cross-react with the DNA and RNA from the following viruses and bacteria.

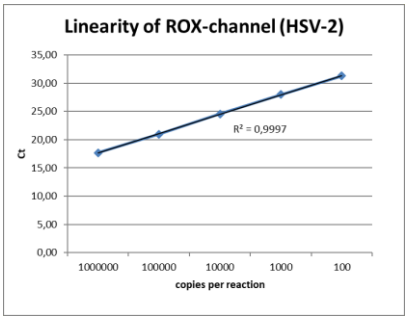
Table 11: Determination of the analytical specificity of *alpha*Cube HSV/VZV.

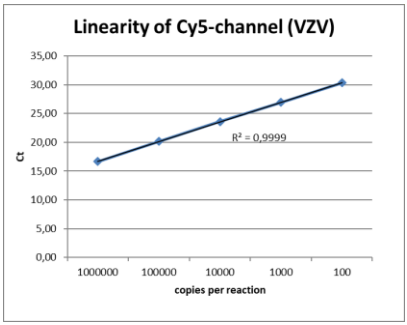
Strain	**Expected Result**	**Result *alpha*Cube HSV/VZV**
Influenza Virus A	negative	negative
Influenza Virus B	negative	negative
RSV Strain A2 ATCC-VR-1540	negative	negative
RSV Strain B WV/14617/85 ATCC-VR-1400	negative	negative
Parainfluenzavirus Typ 3 Str. C243 VR93	negative	negative
Mycoplasma pneumoniae ATCC 15531	negative	negative
Chlamydophila pneumoniae Str. CM-1, ATCC-VR-1360	negative	negative
Adenovirus	negative	negative
Legionella pneumophila Serogroup 2	negative	negative
Tick Borne Encephalitis Virus	negative	negative
Epstein-Barr Virus	negative	negative
Cytomegalovirus	negative	negative
Human Herpesvirus 6	negative	negative
Human Herpesvirus 8	negative	negative
HSV-1	positive	positive (FAM)
HSV-2	positive	positive (ROX)
VZV	positive	positive (Cy5)

15.3 Linear Range

The linear range of the *alpha*Cube HSV/VZV was evaluated by analyzing logarithmic dilution series of synthetic DNA fragments.







15.4 Precision

The precision of the *alpha*Cube HSV/VZV was determined as intra-assay variability, inter-assay variabilitity and inter-lot variability.
Variability data are expressed by standard deviation and coefficient of variation. The data are based on quantification analyses of defined concentrations of HSV-1, HSV-2 and VZV specific DNA and on the threshold cycle of the Control-DNA.

Table 12: Precision of alphaCube HSV/VZV

HSV-1	copies/µl	Standard Deviation	Coefficient of Variation [%]
Intra-Assay Variability	25	0.19	0.56
Inter-Assay-Variability	25	0.30	0.91
Inter-Lot Variability	25	0.15	0.47

HSV-2	copies/µl	Standard Deviation	Coefficient of Variation [%]
Intra-Assay Variability	25	0.30	0.97
Inter-Assay-Variability	25	0.22	0.70
Inter-Lot Variability	25	0.14	0.44

VZV	copies/µl	Standard Deviation	Coefficient of Variation [%]
Intra-Assay Variability	25	0.32	1.05
Inter-Assay-Variability	25	0.08	0.26
Inter-Lot Variability	25	0.19	0.63

Control DNA	copies/µl	Standard Deviation	Coefficient of Variation [%]
Intra-Assay Variability	25	0.11	0.36
Inter-Assay-Variability	25	0.26	0.85
Inter-Lot Variability	25	0.11	0.36

16 Abbreviations and Symbols

DNA	Deoxyribonucleid Acid
PCR	Polymerase Chain Reaction
HSV-1	Herpes Simplex Virus Type 1
HSV-2	Herpes Simplex Virus Type 2
VZV	Varicella Zoster Virus
REACTION MIX	Reaction Mix
CONTROL +	Positive Control
CONTROL −	Negative Control
CONTROL DNA IC	Control DNA
REF	Catalog number

Σ	Contains sufficient for <n> test
-18°C	Upper limit of temperature
	Manufacturer
	Use by YYYY-MM-DD
LOT	Batch code
CONT	Content
	Consult instructions for use
IVD	*In vitro* diagnostic medical device
CE	European Conformity

gerbion GmbH & Co. KG
Remsstr. 1
70806 Kornwestheim
Germany
phone: +49 7154 806 20 0
fax: +49 7154 806 20 29
e-mail: info@gerbion.com
www.gerbion.com

Distributor
Mikrogen GmbH
Floriansbogen 2-4
D-82061 Neuried
Germany
phone: +49 (0) 89-54801-0
fax: +49 (0) 89-54801-100
e-mail: mikrogen@mikrogen.de
www.mikrogen.de

17 Literature

[1] WHO, https://www.who.int/news-room/fact-sheets/detail/herpes-simplex-virus.
[2] WHO, https://www.who.int/immunization/diseases/varicella/en/