Instructions for Use

In-vitro-Diagnostic

IVD

The res4plex *direct* RT-PCR is a real-time RT-PCR test for simultaneous *in vitro* detection and differentiation of RNA from **SARS-CoV-2**, **Flu A**, **Flu B**, and **RSV** (RSV A and RSV B).

The res4plex *direct* RT-PCR test was validated with the Roche LightCycler® 480 II and with the BioRad CFX Opus 96™. In general, Lab *direct* PCR tests are compatible with other qPCR cyclers (e.g., MIC Cycler, AJ qTOWER, LightCycler® 96 or 480 I).

Content

1. Intended Use

The res4plex *direct* RT-PCR test is an *in vitro* real-time reverse transcription polymerase chain reaction (rRT-PCR) test for the qualitative detection of viral RNA of the pathogens SARS-CoV-2, Influenza A, Influenza B, and Respiratory Syncytial Virus (RSV A and RSV B) from respiratory tract specimens (nasopharyngeal or oropharyngeal swabs) from individuals suspected of having a serious viral cold. The results support the differential diagnosis of infections with SARS-CoV-2, Influenza viruses and RSV. The test is intended for use in qualified laboratories by personnel trained in molecular diagnostic techniques.

2. Pathogen Information

Influenza Viruses belong to the family of Orthomyxoviridae and are the causative agent of 'the flu'. Influenza A and B viruses have a single stranded RNA genome, consisting of 8 RNA segments. The genome of Influenza A Viruses is characterized by a high mutation frequency, the so-called 'antigenic drift'. Numerous subtypes of Influenza A Viruses are known. They can be categorized by their surface antigens H (haemagglutinin) and N (neuraminidase): Influenza A (H1N1) Virus, Influenza A (H5N1) Virus etc.[1] The predominantly affected age groups differ in the severity of influenza. The incidence of physician visits spans the age spectrum. The incidence of influenza-related hospitalizations is highest in young children and in the elderly population. Symptoms typical of influenza are characterized by sudden illness, fever, cough or sore throat, and muscle aches and/or headache. Other symptoms may include general weakness, sweating, rhinorrhea, and rarely nausea/vomiting and diarrhea.[2]

Respiratory Syncytial Viruses are enveloped negative-sense, single stranded RNA Viruses of the Pneumoviridae family, genus Orthopneumovirus. RSV are divided into subgroups A and B. RSV is a virus that causes infections of the lungs and respiratory tract. In adults and older, healthy children, the symptoms of RSV infections are mild and typically mimic the common cold. Infection with RSV can be severe in some cases, especially in premature babies and infants with underlying health conditions. RSV can also become serious in older adults, adults with heart and lung diseases, or anyone with a very weak immune system (immunocompromised).[3][2]

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The novel Coronavirus (SARS-CoV-2) is a new strain within the Sarbecoviruses that has been previously identified in humans and causes the pulmonary disease COVID-19. Coronaviruses are zoonotic, meaning they are transmitted between animals and humans. Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.[4]

3. Testing Principle

The res4plex *direct* RT-PCR test is a multiplex RT-qPCR test for the detection and differentiation of SARS-CoV-2, influenza A, B and RSV (see table 1) including a full process run control from extraction to result.

The separate full process run control is added to each sample prior to RNA extraction and thus serves as internal control for RT-qPCR (Internal Control; IC).

The RNA eluate is added to the ready-to-use reaction solution that contains all reagents necessary for RT-qPCR. RT-qPCR analysis can be performed on any qPCR cycler.

[1] 16 May 2022, https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_Influenza_saisonal.html;jsessionid=0D4B917F987
[2] 17 July 2023 https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_Influenza_saisonal.html
[3] 16 May 2022, https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_RSV.html
[4] 16 May 2022, https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Virologische_Basisdaten.html

The res4plex *direct* RT-PCR test contains primer and probes specific for the targets listed in Table 1 and the Internal Control. The probes are each labelled with fluorescent reporter dyes and a second dye that serves as a quencher and suppresses the fluorescence signals of intact probes.

Table 1: Detectable genes of res4plex direct RT-PCR test

ANALYTE	GENE(S)
SARS-CoV-2	N gene and E gene
Influenza A	MP gene
Influenza B	NS gene
RSV A/B	N gene

The analysis is performed by determining Ct (cycle threshold) values. The Ct value describes the cycle in which the signal rises above a certain threshold for the first time. The more target copies (here: virus RNA) are present in the sample, the lower the Ct value. The Internal Control serves as control for nucleic acid isolation from the biological specimen and may also indicate individual residual RT-PCR inhibition.

4. Package Content

The reagents of each kit are sufficient for 96 reactions. Each kit contains the following vials which are sufficient for 96 reactions (see Table 2). Additionally, a quick start protocol is provided per packing unit.

Table 2: res4plex direct RT-PCR package content

MATERIAL	LID COLOUR	#VIALS; VOLUME	#RXNS.	COMMENT
Solution A	green	1x; 1.100 µL	96	Reaction mix (buffer, enzymes, primer and probes)
Internal Control	blue	1x; 400 µL	96	Internal Control (artificial nucleic acid target; $1x10^7$ cp/µL)
Positive Control	red	1x; 30 µL	3	Nucleic acids of SARS-CoV-2, Flu A, Flu B and RSV

5. Additional Equipment and Reagents

- qPCR cycler
- disposable protective gloves, powder-free
- PCR reaction tubes/microtiter plate plus lids/adhesive optical film
- Pipettes
- Pipette tips with filter (DNase/RNase-free)
- Table centrifuge
- RNA isolation kit
- Negative Control

RNA Isolation at FRIZ Biochem was performed using the IVD-1033-S chemagic™ Viral DNA/RNA 300 Kit H96 on a chemagic™ 360 instrument (PerkinElmer chemagen Technologie GmbH).

6. Transport, Storage and Stability

The res4plex *direct* RT-PCR test is shipped on dry ice. All components must be stored at -25 °C to -18 °C in the dark immediately after receipt. Reagents should be handled at +2 °C to +8 °C and used within 8 hours. Repeated thawing and freezing of the components – more than once – shall be avoided. If necessary, aliquoting of the test components in RNase-free vials after the first thawing is recommended. The package bears an expiry date, after which no quality guarantee can be given.

7. Warnings and Safety Precautions

The res4plex *direct* RT-PCR test is intended for *in vitro* diagnostic use only. The test should only be performed by personnel trained in molecular diagnostic techniques. If the user makes substantial changes to the product or the application instructions, results may not correlate with the intended use.

- Before performing the test, read the entire instructions for use and follow them carefully. Deviations from the given test protocols can lead to incorrect results.
- All patient samples must be treated as potentially infectious material.
- Discard sample and assay waste (that was in contact with patient material) according to your local, regional, or national safety regulations.
- The concentration specifications and incubation times of the manufacturers must be followed.
- Do not use the test beyond the expiration date.
- Do not use the test with opened or damaged packaging.
- Protect reagents from heat, moisture, and light.
- Do not replace or mix the reagents with reagents from other batches or other chemicals.
- Avoid contamination of the test by microorganisms and nucleases (DNases and RNases).
- Any carry-over of samples during handling and processing of the test may result in false positive test results.
- Good laboratory practice should be followed during the test.
- 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.
- The test kits are intended for single use and must not be reused.
- If contamination of the qPCR device is suspected, cleaning and maintenance must be carried out according to the qPCR system´s manual.
- Safety Data Sheets (SDS) are available on request from FRIZ Biochem GmbH.

8. Important Points before Starting/Sample Material

Follow the procedures in these instructions for use: reliable results can only be guaranteed if proper procedures are used for sampling (according to manufacturer's instructions), transportation, storage, and handling of the samples.

This test is intended for use with samples derived from nasopharyngeal and oropharyngeal swabs. Other specimen types may cause false negative or invalid results.

In every RT-PCR run one Positive Control and one Negative Control should be included. The Positive Control FBC107-PC consists of nucleic acids of SARS-CoV-2, Flu A, Flu B and RSV. The Negative Control - PCR master mix with e.g., water added instead of sample - must be provided by the user. A failed Positive or Negative Control will invalidate the RT-PCR run and the results must not be reported.

Appropriate nucleic acid extraction methods must be conducted prior to using this assay. RNA extraction reagents are not part of the res4plex *direct* RT-PCR test. Performance evaluation studies have been conducted using the IVD-1033-S chemagic™ Viral DNA/RNA 300 Kit H96 on a chemagic™ 360 instrument (PerkinElmer chemagen Technologie GmbH) for RNA isolation.

9. Test Procedure

Thaw all reagents completely and keep them cool (+2 °C to +8 °C) before starting the test, use within 8 hours.

Table 3: Test procedure res4plex direct RT-PCR

TEST PROCEDURE	
	Sample preparation
1	Thaw all reagents completely.
2	Add Internal Control to the RNA preparation process in accordance to the laboratory´s standard procedure (e.g., add 4µL/sample to lysis buffer).
3	Perform RNA preparation according to your laboratory's standard procedure.
	RT-qPCR
4	Pipette **10 µL/well** of **Solution A** into the PCR microtiter plate/reaction tubes.
5	Add 10 µL/well of eluate from RNA preparation; add 10 µL Positive Control per run; add 10 µL Negative Control per run.
6	Close the microtiter plate with an adhesive optical film or the reaction tubes with the lids provided.
7	Briefly centrifuge the microtiter plate or reaction tubes.
8	Place the filled plate/reaction tubes in the qPCR cycler.
9	Start program.

10. Instrument Settings

The res4plex *direct* RT-PCR test was validated with the Roche LightCycler® 480 II and BioRad CFX Opus 96™. In general, FRIZ Lab *direct* PCR tests are compatible with any qPCR cycler. The following thermal profile is to be used (see Table 4). Channel settings depend on qPCR cycler used. See Table 5 for BioRad CFX Opus 96™ and LightCycler® 480 II channel settings.

Table 4: Instrument Settings res4plex direct RT-PCR

STEPS	TEMPERATURE [°C]	TIME	#CYCLES
Reverse transcription	55	10 min	1
Initial denaturation	95	2 min	1
Denaturation	95	5 sec	45
Amplification/Elongation	61	15 sec	

Table 5: Channel settings

	SARS-CoV-2		Influenza B	RSV (A&B)	Influenza A	Internal Control	
	N-gene	E-gene	NS-gene	N-gene	MP-gene	artificial NA	
Reporter dye	FAM	FAM	HEX	Red 610	Cy5	CY500	Cy5.5
Colour	green	green	red	orange	yellow-green	cyan	far-red
Emission [nm]	520	520	560	610	670	480	700
Quencher	Black Hole Quencher						

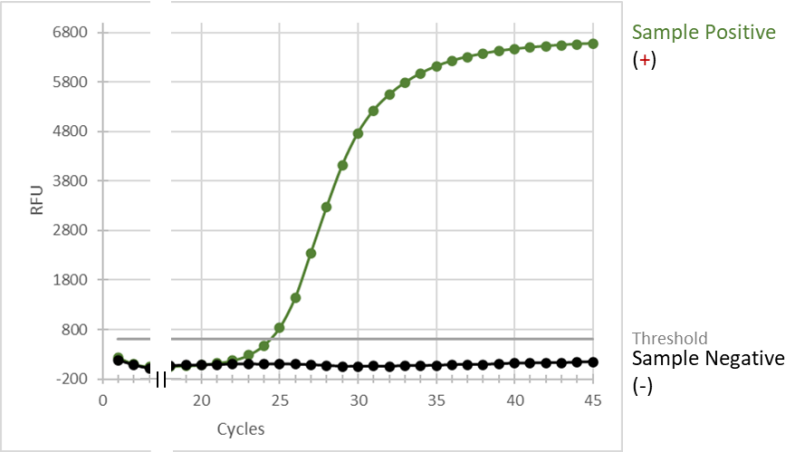
LC 480 II

CFX Opus 96™

11. Results

Positive samples show a qPCR typical amplification curve that crosses a certain threshold generating the Ct value (see Table 6).

Table 6: Exemplary amplification curves



- The Negative Control must not show amplification curves in all channels except for the IC channel.
- The Positive Control must show amplification curves in all channels. The Ct value of the Positive Control must be < 36. A Positive Control with a higher Ct value indicates procedural problems.
- The IC for negative samples must show a positive amplification curve with a Ct value comparable to the IC Ct value in the Negative Control.
- The IC for positive samples should show a positive amplification curve with a Ct value comparable to the IC Ct value in the Negative Control.
- A significantly higher IC Ct value in samples compared to the IC Ct value in the Negative Control indicates procedural problems (e.g. purification problems or RT-PCR inhibition).
- A high concentration of detectable viral RNA in the sample can lead to reduced or absent IC signals. In such cases the result for the IC can be neglected.

The results support the differential diagnosis of infections with SARS-CoV-2, Influenza viruses and RSV. The viral RNA is generally detectable in respiratory samples during the acute phase of the infection. Positive results indicate the presence of the respective pathogen, but do not exclude a co-infection with other pathogens. Co-infections of two or more viruses are possible, (see Appendix; page 13).

A negative result does not exclude the presence of SARS-CoV-2, Influenza viruses or RSV, as results depend on correct sampling, the absence of inhibitors and sufficient RNA to be detected. Invalid results may be obtained if the sample contains inhibitors that prevent lysis, extraction, transcription and/or amplification or detection of the target nucleic acids. For information on tested interfering substances, please refer to section "Interfering Substances".

Table 7: Results of res4plex direct RT-PCR

SARS-CoV-2		Influenza B	RSV (A&B)	Influenza A	Internal Control			
N-gene	E-gene	NS-gene	N-gene	MP-gene	artificial NA			
FAM		HEX	Red 610	Cy5	CY500	Cy5.5	**Result**	**Interpretation**
+		–	–	–	+/–		Valid	SARS-CoV-2 detected.
–		+	–	–	+/–		Valid	Influenza B detected.
–		–	+	–	+/–		Valid	RSV detected.
–		–	–	+	+/–		Valid	Influenza A detected.
–		–	–	–	+/–		Valid	No SARS-CoV-2, Influenza B, RSV or Influenza A detecte
–		–	–	–	–		Invalid	The test result can not be evaluated.

LC480II

CFX Opus 96™

12. Limitations of the Method

Test results should always be seen in the context of the clinical findings. Therapeutic consequences of the diagnostic results must be drawn in relation to the clinical findings.

The detection of analyte target does not mean that they are the causative agents of clinical symptoms.

Mutations or polymorphisms in primer and probe binding regions can interfere with the detection of new variants that may result in false negative results.

13. Analytical Performance

13.1 Analytical Sensitivity

The limit of detection (LoD) was determined with serial dilutions of synthetic target-specific RNA. The analytes were tested in 24 replicates per concentration on a Bio-Rad CFX Opus 96™. The 95% detection limit (95 CI) was determined using Logistic Regression (Logit) with the GraphPad Prism 9.3.1 software (see table 7).

Table 8: Limit of Detection

ANALYTICAL SENSITIVITY	RNA (COPIES/REACTION)
SARS-CoV-2 LoD (95 CI)	8.17 (6.55 – 10.16)
Influenza A LoD (95 CI)	26.61 (24.31– 28.99)
Influenza B LoD (95 CI)	13.82 (13.41 – 14.24)
RSV A LoD (95 CI)	7.78 (7.24 – 8.32)
RSV B LoD (95 CI)	9.18 (6.84 – 12.22)

13.2 Analytical Specificity

In silico analyses for potential cross-reactivities was performed with potentially co-sampled organisms using BLAST Alignment with the sequences stored in the NCBI database (see Appendix; page 15). Identities of the primers and probes of less than 80% to the target sequence were considered not significant. The *in silico* analyses showed an identity of more than 80% in some organisms: RSV B primers and probe showed a sequence

identity of more than 80% to RSV A and vice versa, RSV A primers and probe are more than 80% identical to RSV B. Since the res4plex *direct* RT-PCR test does not differentiate between RSV A and RSV B, the sequence homologies can be neglected. All other sequence identities of more than 80% were verified in an *in vitro* cross-reactivity study, that included a panel of 28 organisms consisting of 15 viral, 9 bacterial and 4 yeast strains. These organisms encompassed some of the most common respiratory viruses required from the common specifications for SARS-CoV-2 in vitro diagnostics (IVDs), as well as all organisms exhibiting a minimum of 80% homology to one of the primer or probe sequences utilized in res4plex *direct* RT-PCR test (see Appendix; page 13). Six replicates of each strain with highest possible concentrations were tested as spiked and unspiked group. In the spiked group, positive signals were observed for all five targets in each set of triplicate samples. In contrast, unspiked samples displayed positive signals only for the Internal Control, while the rest of the targets showed negative signals. In conclusion, the analytical specificity was 100%.

13.3 Interfering Substances

To investigate the effect of potentially interfering substances on the performance of the res4plex *direct* RT-PCR testing, the highest concentration of the substance potentially present in naso-/oropharyngeal samples was added to a negative clinical matrix with and without heat-inactivated SARS-CoV-2, Influenza A, Influenza B and RSV.

In addition, a control sample with clinical matrix and heat-inactivated virus, but without potentially interfering substance was used as reference. Each condition was tested in triplicates. Potentially interfering substances, their active ingredient, the amount of medication applied as well as the res4plex *direct* RT-PCR test results are summarised. Viral RNA of all targets was clearly identified in the presence of the tested potentially interfering substances at relevant concentrations (see Appendix; page 17).

13.4 Competitive Interference

The competitive interference study evaluated the effects of clinically relevant co-infections with any of the analytes probed by the assay. The study assessed whether a high concentration of one virus in the specimen could potentially affect assay performance for another target present at low levels in the multiplex assay. High concentrations of 10^6 copies/mL (1000 cp/µL) were first tested and if these produced negative results for the 3x LoD analyte lower concentrations of 10^5 copies/mL (100 cp/µL) were tested. High concentrations of SARS-CoV-2 may interfere with Influenza A and RSV B detection and high RSV A concentrations may interfere with Influenza A detection (see Appendix; page 14).

14. Diagnostic Performance

For clinical performance evaluation RNA was extracted by using the IVD-1033-S chemagic™ Viral DNA/RNA 300 Kit H96 on a chemagic™ 360 instrument (PerkinElmer chemagen Technologie GmbH). Eluates were tested with the res4plex *direct* RT-PCR test and a CE certified test from another manufacturer in direct comparison on a LightCycler® 480 (Roche) in a laboratory where tests are conducted on (clinical) specimens to obtain information about the health of a patient to aid in diagnosis, treatment, and prevention of disease (clinical laboratory).

SARS-CoV-2 samples

		positive	negative	
res4plex	positive	101	1	Sensitivity: 100.0% (96.4 - 100.0)
	negative	0	738	Specificity: 99.9% (99.3 - 100.0)

Influenza A samples

		positive	negative	
res4plex	positive	73	1	Sensitivity: 94.8% (87.2 - 98.6)
	negative	4	680	Specificity: 99.9% (99.2 - 100.0)

Influenza B samples

		positive	negative	
res4plex	positive	54	0	Sensitivity: 100.0% (93.4 - 100.0)
	negative	0	725	Specificity: 100.0% (99.5 - 100.0)

RSV samples

		positive	negative	
res4plex	positive	83	1	Sensitivity: 100.0% (95.7 - 100.0)
	negative	0	667	Specificity: 99.9% (99.2 - 100.0)

The diagnostic sensitivity of the res4plex *direct* RT-PCR test using RNA extraction is dependent on the RNA extraction method used to isolate RNA from biological specimens. It is the responsibility of the user to qualify the extraction methods used for RNA isolation from biological samples.

14. Note to the User

All serious incidents relating to the kit must be notified to the manufacturer and the national competent authority of the EU Member State where the laboratory and/or patient is located.

CE This product complies with the requirements of the European Directive 98/79/EC for in vitro diagnostics.

15. Symbols

IVD	For use in in vitro diagnostics	REF	Item number
	Manufacturer		Content sufficient for XY provisions
	Temperature limitation		Biological risk
	Can be used until	LOT	Batch designation
	Follow instructions for use	CONT	Content

Document Version:

FBC107_IFU_EN	
Version 1.0 Date: 19.05.2022	First publication 19.05.2022
Version 2.0 Date: 16.11.2022	Revised Version Adjustment of Test Configurations
Version 3.0 Date: 08.03.2022	Revised Version Adjustment of Test Configurations
Version 4.0 Date: 08.03.2022	Revised Version Adjustment of Test Configuration; Correction of tipping errors

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16. Appendix

18.1 Microorganisms tested for cross-reactivity

VIRUSES	FINAL CONC.	UNIT
Adenovirus 1	3,72E+07	TCID50/ml
Adenovirus 7	1,26E+05	TCID50/ml
Enterovirus D	5,01E+04	TCID50/ml
Human coronavirus 229E	1,29E+04	TCID50/ml
Human coronavirus HKU1	1,00E+06	genome copies/ml
Human coronavirus OC43	1,70E+04	TCID50/ml
Human coronavirus NL63	3,55E+04	TCID50/ml
Human cytomegalovirus	5,62E+03	TCID50/ml
Human metapneumovirus	1,41E+04	TCID50/ml
MERS coronavirus	1,00E+05	genome copies/ml
Parainfluenza virus 1	1,38E+06	TCID50/ml
Parainfluenza virus 2	1,41E+04	TCID50/ml
Parainfluenza virus 3	3,39E+06	TCID50/ml
Rhinovirus A	1,41E+04	TCID50/ml
SARS-CoV-1	1,00E+05	genome copies/ml

BACTERIA	FINAL CONC.	UNIT
Chlamydia pneumoniae	1,00E+06	genome copies/ml
Escherichia coli	1,00E+06	genome copies/ml
Haemophilus influenzae	1,00E+06	genome copies/ml
Klebsiella pneumoniae	1,00E+06	genome copies/ml
Neisseria meningitidis	1,00E+06	genome copies/ml
Pseudomonas aeruginosa	1,00E+06	genome copies/ml
Corynebacterium diphtheriae subsp. Diphtheriae	1,00E+06	genome copies/ml
Legionella pneumophila	1,00E+06	genome copies/ml
Streptococcus pyogenes	1,00E+06	genome copies/ml

YEAST	FINAL CONC.	UNIT
Aspergillus fumigatus	1,32E+06	genome copies/ml
Candida albicans	4,45E+07	genome copies/ml
Candida glabrata	1,31E+08	genome copies/ml
Cryptococcus neoformans	3,99E+07	genome copies/ml

18.2 Competitive Interference

SAMPLE	ANALYTE	POSITIVE CALLS	TOTAL	% POSITIVITY
SARS-CoV-2 at 1000 cp/µL with 3x LoD Influenza B	FluB	3	3	100,0
SARS-CoV-2 at 1000 cp/µL with 3x LoD Influenza A	FluA	0	3	0,0
SARS-CoV-2 at 100 cp/µL with 3x LoD Influenza A	FluA	3	3	100,0
SARS-CoV-2 at 1000 cp/µL with 3x LoD RSV B	RSVB	0	3	0,0
SARS-CoV-2 at 100 cp/µL with 3x LoD RSV B	RSVB	3	3	100,0
SARS-CoV-2at 1000 cp/µL with 3x LoD RSV A	RSVA	3	3	100,0
Influenza A at 1000 cp/µL with 3x LoD RSV B	RSVB	3	3	100,0
Influenza A at 1000 cp/µL with 3x LoD SARS-CoV-2	SARS-CoV-2	3	3	100,0
Influenza A at 1000 cp/µL with 3x LoD RSV A	RSVA	3	3	100,0
Influenza A at 1000 cp/µL with 3x LoD Influenza B	FluB	3	3	100,0
Influenza B at 1000 cp/µL with 3x LoD SARS-CoV-2	SARS-CoV-2	3	3	100,0
Influenza B at 1000 cp/µL with 3x LoD Influenza A	FluA	3	3	100,0
Influenza B at 1000 cp/µL with 3x LoD RSV A	RSVA	3	3	100,0
Influenza B at 1000 cp/µL with 3x LoD RSV B	RSVB	3	3	100,0
RSVA at 1000 cp/µL with 3x LoD SARS-CoV-2	SARS-CoV-2	3	3	100,0
RSVA at 1000 cp/µL with 3x LoD Influenza A	FluA	0	3	0,0
RSVA at 100 cp/µL with 3x LoD Influenza A	FluA	3	3	100,0
RSVA at 1000 cp/µL with 3x LoD Influenza B	FluB	3	3	100,0
RSVB at 1000 cp/µL with 3x LoD Influenza B	FluB	3	3	100,0
RSVB at 1000 cp/µL with 3x LoD Influenza A	FluA	3	3	100,0
RSVB at 1000 cp/µL with 3x LoD SARS-CoV-2	SARS-CoV-2	3	3	100,0

18.3 In silico analyses for cross-reactivity and inclusivity of the used primers and probes

Identities of primers and probes of less than 80% to the target sequence were considered not significant.

Organism (identity)	SARS	Flu A	Flu B	RSV A	RSV B	IC
Human coronavirus 229E	-	-	-	-	-	-
Human coronavirus OC43	-	-	-	-	-	-
Human coronavirus HKU1	-	-	-	-	-	-
Human coronavirus NL63	-	-	-	-	-	-
SARS-CoV	100%	-	81% to fw primer	-	-	-
MERS-CoV	-	-	-	-	-	-
Adenovirus	-	-	-	-	-	-
Humanes metapneumovirus	-	-	-	-	-	-
HPIV1	-	-	-	-	-	-
HPIV2	-	-	-	-	-	-
HPIV3	-	-	-	-	-	-
HPIV4	-	-	-	-	-	-
Influenza A Virus	-	100%	-	-	-	-
Influenza B Virus	-	-	100%	-	-	-
Influenza C Virus	-	-	-	-	-	-
Enterovirus/Rhinovirus	-	-	-	-	-	-
RSV A	-	-	-	100%	> 80%	-
RSV B	-	-	-	> 80%	100%	-
Rubella Virus	-	-	-	-	-	-
Parechovirus	-	-	-	-	-	-
Chlamydia pneumoniae	-	-	-	-	-	86% to rev primer
Haemophilus influenzae	83% to E-gene primer	-	-	-	-	-
Legionella pneumophila	-	-	-	-	-	-
Mycobacterium bovis subsp. Bovis	-	-	-	-	-	-
Streptococcus pneumoniae	-	-	-	-	-	-
Streptococcus pyogenes	-	-	-	-	-	-
Bordetella pertussis	-	-	-	-	-	-
Mycoplasma pneumoniae	-	-	-	-	-	-
Pneumocystis jirovecii	-	-	-	-	-	-
Candida albicans	-	-	90% to rev primer	-	-	-
Corynebacterium diphtheriae	-	90% to probe	-	-	-	-
Bacillus anthracis	-	-	-	-	-	-
Moraxella catarrhalis	-	-	-	-	-	-
Neisseria elongata	-	-	-	-	-	-
Neisseria meningitidis	86% to N-gene primer	-	-	-	-	-
Pseudomonas aeruginosa	89% to E-gene primer	-	-	-	-	-
Staphylococcus aureus	-	-	-	-	-	-
Staphylococcus epidermidis	-	-	-	-	-	-
Streptococcus salivarius	-	-	-	-	-	-
Leptospiraceae	-	-	-	-	-	-

Organism (identity)	SARS	Flu A	Flu B	RSV A	RSV B	IC
Chlamydia psittaci	-	-	-	-	-	-
Coxiella burnetii	-	-	-	-	-	-
Mycobacterium tuberculosis	-	-	-	-	-	-
Epstein Barr virus	-	-	-	-	-	-
Human cytomegalovirus	-	-	81% to fw primer	-	-	-
Measles virus	-	-	-	-	-	-
Mumps virus	-	-	-	-	-	-
Norovirus	-	-	-	-	-	-
Rotavirus	-	-	-	-	-	-
Escherichia coli	83% to E-gene primer	-	81% to fw primer	-	-	-
Klebsiella pneumoniae	-	-	85% to rev primer	-	-	-
Aspergillus fumigatus	-	-	86% to fw primer	83% to rev primer	-	-
Candida glabrata	-	-	81% to fw primer	-	-	81% to rev primer
Cryptococcus neoformans	82% to E-gene primer	-	90% to fw primer	-	-	-
Lactobacillus	-	-	-	-	-	-

18.3 Potentially interfering substances

			RESULTS				
MEDICATION (TRADE NAME)	**ACTIVE INGREDIENT PER UNIT**	**% (V/V)***	**SARS-COV-2**	**FLU A**	**FLU B**	**RSV**	**IC**
ratioAllerg® Hay fever spray	50 µg Beclomethasone dipopionate	20	3/3	3/3	3/3	3/3	3/3
Otri-Allergie Hay fever spray	50 µg Fluticasone propionate	20	3/3	3/3	3/3	3/3	3/3
MometaHEXAL® Hay fever spray	50 µg Mometasone Fuorate	35	3/3	3/3	3/3	3/3	3/3
NASACORT® Nasal Spray	55 µg triamcinolone acetonide	30	3/3	3/3	3/3	3/3	3/3
Vividrin® akut Nasal Spray	140 µg Azelastine hydrochloride	30	3/3	3/3	3/3	3/3	3/3
Nasivin® Nasal Spray	22.5 µg Oxymetazoline hydrochloride	10	3/3	3/3	3/3	3/3	3/3
NASENSPRAY Heumann	90 µg Xylometazolinhydrochlorid	20	3/3	3/3	3/3	3/3	3/3
Syntaris® Nasal Spray	25 µg Flunisolide	20	3/3	3/3	3/3	3/3	3/3
Rhinocort Topinasal Nasal Spray	64 µg Budesonide	10	3/3	3/3	3/3	3/3	3/3
CromoHEXAL® Eye drops	ca 400 µg Sodium agglomoglicate	5	3/3	3/3	3/3	3/3	3/3
Tobrex® Eye drops	ca 60 µg Tobramycin	5	3/3	3/3	3/3	3/3	3/3
LISTERINE® Cool Mint Mouthwash	Ethanol (n.a.)	25**	3/3	3/3	3/3	3/3	3/3
Chlorhexamed® FLUID 0.1%	15 µg Chlorhexidine bis (D-gluconate)	50	3/3	3/3	3/3	3/3	3/3
Dequonal® Solution	1.5 mg Dequalinium chloride, 3.5 mg Benzalkonium chloride	50	3/3	3/3	3/3	3/3	3/3
Octenident® Mouth rinse solution	Octenidine (n.a.)	25**	3/3	3/3	3/3	3/3	3/3

* Concentration of medication in the medication-matrix mixture. It is assumed that the volume of one application is completely transferred into the sample.

** Higher concentrations of medication are prone to cause invalid or false negative results

18.4 List of tables