Technical File - qPCR

FRIZ Biochem GmbH

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1. 1 Meta Information

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1.1. 1 Purpose

This Summary of Safety and Performance (SSP) is intended to provide public access to an up-to-date summary of the main aspects of the safety and performance of the IVD medical devices res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR.

The SSP is not intended to replace the Instructions For Use (IFU) as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users.

The information in the next section is intended for professional users.

2. 2 Summary of Safety and Performance (SSP) for professional users

2.1. 1 Device identification and general information

Parameter	Value
Device trade name(s)	res5plex *direct* RT-PCR res6plex *direct* RT-PCR res1plex *direct* PCR res2plex *direct* PCR res3plex *direct* PCR
Device reference number	FBC117; FBC118; FBC119; FBC120; FBC121
Manufacturer´s name and address	FRIZ Biochem GmbH Floriansbogen 2-4 82061 Neuried Germany
Manufacturer´s single registration number (SRN)	DE-MF-000017533
Basic UDI-DI	res5plex *direct* RT-PCR: 426075389fbc117U9 res6plex *direct* RT-PCR: 426075389fbc118UB res1plex *direct* PCR: 426075389fbc119UD res2plex *direct* PCR: 426075389fbc120TW res3plex *direct* PCR: 426075389fbc121TY

European Medical Device Nomenclature (EMDN)	• EMDN W0105: infectious diseases (derived based on W010507 multiple parameters) • IVP 3011: In vitro diagnostic devices which require knowledge regarding molecular biological testing including nucleic acid assays and next generation sequencing (NGS)
Risk class of the device	FBC117, FBC118, FBC120 and FBC121: Class B FBC119 : Class C
Indication whether it is a device for near-patient testing and/or a companion diagnostic	☐ Device for near-patient testing ☐ Companion Diagnostic (CDx) ☑ n.a.
Year when the first certificate was issued under Regulation (EU) 2017/746 covering the device	the device has not been certified under IVDR yet
Authorized representative, if applicable; name and the SRN	n.a.
NB's name (the NB that will validate the SSP) and NB's single identification number	Name of NB that will validate the SSP: TÜV SÜD Product Service GmbH NB's single identification number: NB 0123
SSP reference number	FBC119970063874

2.2. 2 Intended use of the device

2.2.1. 1 Intended purpose

DI Intended Purpose res5plex direct RT-PCR

The res5plex *direct* RT-PCR is an assay for *in vitro* examination of viral nucleic acids in nasal/nasopharyngeal and oral/oropharyngeal swabs to provide information to aid to diagnose symptomatic or asymptomatic patients under suspicion of respiratory tract infections with Parainfluenza virus 1/ 2/ 3/ 4, Adenovirus and/or Enterovirus/Rhinovirus.

The IVD medical device detects the RNA or DNA of the aforementioned pathogens by qualitative measurements based on RT-qPCR and is intended for use in medical laboratories or health institutions by laboratory personnel specifically trained in RT-qPCR and *in vitro* diagnostic techniques. It has to be used in combination with conventional nucleic acid extraction systems for DNA/RNA extraction and RT-qPCR cyclers for detection and analysis.

DI Intended Purpose res6plex direct RT-PCR

The res6plex *direct* RT-PCR is an assay for *in vitro* examination of viral nucleic acids in nasal/nasopharyngeal and oral/oropharyngeal swabs to provide information to aid to diagnose symptomatic or asymptomatic patients under suspicion of respiratory tract infections with human Coronavirus (229E/ NL63/ OC43/ HKU1), Metapneumovirus and/or Bocavirus.

The IVD medical device detects the RNA or DNA of the aforementioned pathogens by qualitative measurements based on RT-qPCR and is intended for use in medical laboratories or health institutions by laboratory personnel specifically trained in RT-qPCR and *in vitro* diagnostic techniques. It has to be used in combination with conventional nucleic acid extraction systems for DNA/RNA extraction and RT-qPCR cyclers for detection and analysis.

DI Intended Purpose res1plex direct PCR

The res1plex *direct* PCR is an assay for *in vitro* examination of bacterial nucleic acids in nasal/nasopharyngeal and oral/oropharyngeal swabs to provide information to aid to diagnose symptomatic or asymptomatic patients under suspicion of respiratory tract infections with *Mycoplasma pneumoniae*, *Chlamydia (Chlamydophila) pneumoniae* and/or *Legionella pneumophila*.

The IVD medical device detects the DNA of the aforementioned pathogens by qualitative measurements based on qPCR and is intended for use in medical laboratories or health institutions by laboratory personnel specifically trained in qPCR and *in vitro* diagnostic techniques. It has to be used in combination with conventional nucleic acid extraction systems for DNA extraction and qPCR cyclers for detection and analysis.

DI Intended Purpose res2plex direct PCR

The res2plex *direct* PCR is an assay for *in vitro* examination of bacterial nucleic acids in nasal/nasopharyngeal and oral/oropharyngeal swabs to provide information to aid to diagnose symptomatic or asymptomatic patients under suspicion of respiratory tract infections with *Bordetella pertussis* and/or *Bordetella parapertussis*.

The IVD medical device detects the DNA of the aforementioned pathogens by qualitative measurements based on qPCR and is intended for use in medical laboratories or health institutions by laboratory personnel specifically trained in qPCR and *in vitro* diagnostic techniques. It has to be used in combination with conventional nucleic acid extraction systems for DNA extraction and qPCR cyclers for detection and analysis.

DI Intended Purpose res3plex direct PCR

The res3plex *direct* PCR is an assay for *in vitro* examination of bacterial nucleic acids in nasal/nasopharyngeal and oral/oropharyngeal swabs to provide information to aid to diagnose symptomatic or asymptomatic patients under suspicion of respiratory tract infections with *Haemophilus influenzae* and/or *Streptococcus pneumoniae*.

The IVD medical device detects the DNA of the aforementioned pathogens by qualitative measurements based on qPCR and is intended for use in medical laboratories or health institutions by laboratory personnel specifically trained in qPCR and *in vitro* diagnostic techniques. It has to be used in combination with conventional nucleic acid extraction systems for DNA extraction and qPCR cyclers for detection and analysis.

2.2.2. 2 Indication(s) and target population(s)

The res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR may be applied for symptomatic patients under suspicion of respiratory infection with targets stated in PE Summary of Safety and Performance resXplex. Symptoms may include cough, sneezing, sore throat, nasal congestion, headache, mild body aches and fever. The target population encompasses subjects of all genders and ages. Gastrointestinal infection with the target organisms can affect individuals of any age.

2.2.3. 3 Limitation(s) and/or contra-indication(s)

There are no known contraindications or limitations to the target patient group. For detailed limitation on limitations and/or contra indications arising from associated interferences, cross-reactions, etc. see Instructions for Use IFU FBC117-121 resXplex direct RT-PCR.

2.3. 3 Device description

2.3.1. 1 Description of the device

The res5plex *direct* RT-PCR test is a multiplex RT-qPCR test for the detection and differentiation of the Parainfluenza virus 1, 2, 3, 4, Adenovirus and Rhinovirus/Enterovirus.

The res6plex *direct* RT-PCR test is a multiplex RT-qPCR test for the detection and differentiation of the Human Coronavirus (229E/ NL63/ OC43/ HKU1), Metapneumovirus and Bocavirus.

The res1plex *direct* PCR test is a multiplex qPCR test for the detection and differentiation of the *Mycoplasma pneumoniae, Chlamydia (Chlamydophila) pneumoniae* and *Legionella pneumophila.* The res1plex *direct* PCR test is a part of a resXplex test panel.

The res2plex *direct* PCR test is a multiplex qPCR test for the detection and differentiation of the *Bordetella pertussis* and *Bordetella parapertussis.*

The res3plex *direct* PCR test is a multiplex qPCR test for the detection and differentiation of the *Haemophilus influenzae* and *Streptococcus pneumoniae.*

A separate Internal Control (IC) is added to each sample prior to nucleic acid extraction and serves as control for nucleic acid isolation from the biological specimen as well as for qPCR.

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

The res5plex *direct* RT-PCR, res6plex *direct* RT-PCR test, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR tests contain primers and probes specific for the aforementioned targets as well as 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.

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 are present in the sample, the lower the Ct value.

2.3.2. 2 Description of the components

Each kit contains the following vials which are sufficient for 96 reactions (see *Table 1*). The exact contentrations of the individual components are listed in PD List of Components res5plex direct RT-PCR, PD List of Components res6plex direct RT-PCR, PD List of Components res1plex direct PCR, PD List of Components res2plex direct PCR, PD List of Components res3plex direct PCR.

Table 1: res5plex *direct* RT-PCR /res6plex *direct* RT-PCR/ res1plex *direct* PCR/ res2plex *direct* PCR/ res3plex *direct* PCR package content

Material	Lid colour	#vials; volume	#rxns.	Comment
Solution A	green	1x; 1050 µL	96	Reaction mix (buffer, enzymes, primer and probes)
Internal Control	blue	1x; 400 µL	96	Internal Control (artificial nucleic acid target)
Positive Control	red	1x; 50 µL	4	Nucleic acids of target gene regions

2.3.3. 3 Previous generation(s) or variants

There are no previous generations or variants of the res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR.

2.3.3.1. 4 Accessories

The chapter is not applicable as no accessory is intended to be used in combination with the device.

2.3.3.2. 5 Other devices and products to be used in combination

The res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR are intended to be used in combination with conventional nucleic acid extraction systems for DNA/RNA extraction and qPCR cyclers for detection and analysis.

2.4. 4 List of harmonized standards applied

Standard	Title
BS EN ISO 23640:2015	In vitro diagnostic medical devices. Evaluation of stability of in vitro diagnostic reagents
BS EN ISO 17511:2021	In vitro diagnostic medical devices. Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples
BS EN ISO 14971:2019+A11:2021	Medical devices. Application of risk management to medical devices

Standard	Title
BS EN ISO 15223-1:2021	Medical devices. Symbols to be used with information to be supplied by the manufacturer — General requirements
BS EN ISO 13485:2016+A11:2021	Medical devices. Quality management systems. Requirements for regulatory purposes

2.5. 5 Risks and warnings

2.5.1. 1 Residual risks and undesirable effects

We successfully applied risk mitigation strategies. These measures reduced the probability category by at least one level without introducing new risks, thus we positively affected the benefit-risk ratio. After measure implementation all individual residual risks are accepted and consequently the overall residual risk is acceptable.

The res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR fulfil the following parameters:

- compliance with the applicable general safety and performance requirements
- acceptable performance claims according to the state of the art and available diagnostic alternatives
- suitability of the device and its IFU for the intended users and use environment, including usability aspects

The residual risks are unlikely/moderate (probability/severity) or less.

Based on the clinical evidence and in alignment with the state of the art and the common specifications, res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR achieve a clinical benefit by accurately detecting and differentiating DNA/RNA of targets stated in PE Summary of Safety and Performance resXplex, in human clinical specimens (i.e., nasopharyngeal and oropharyngeal swabs) and supporting diagnostic decision-making, taking into account additional clinical and laboratory information.

The clinical benefit is, to provide physicians with useful information with respect to patient management and therapy decisions, if applicable. This may help separate infected people from uninfected people and to isolate them from the rest of the population especially for high-risk patients.

The overall residual risk is in line with the risk policy and acceptable.

2.5.2. 2 Warnings and precautions

The res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR are 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 purpose.

- Before performing the test, read the entire instructions for use and follow them carefully. Deviations from the given test protocols can lead to invalid 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/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 after performing qPCR reaction.
- If contamination of the qPCR cycler is suspected, cleaning and maintenance must be carried out according to the system´s manual.
- Safety Data Sheets (SDS) are available for download via https://frizbiochem.de/downloads/
- Pending EUDAMED entry, the Safety and Performance Summary (SSP) can be downloaded via http://www.frizbiochem.de.

2.5.3. 3 Other relevant aspects of safety

The chapter is not applicable as no field safety corrective actions (FSCA) and field safety notices (FSN) have been taken.

2.6. 6 Summary of performance evaluation and post-market performance follow-up (PMPF)

To demonstrate the scientific validity of res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR, the following data sources are used:

- The State-of-the-Art report (PE SOTA_resXplex) and
- scientific (peer-reviewed) literature.

We selected PubMed (MEDLINE database) as the source for the literature search.

A separate literature search was performed on 14.08.2024-20.09.2024 for each analyte (Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Adenovirus, Enterovirus, Rhinovirus, human Coronavirus 229E, human Coronavirus NL63, human Coronavirus OC43, human Coronavirus HKU1, *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila, Bordetella pertussis, Bordetella parapertussis, Haemophilus influenzae, Streptococcus pneumoniae*) considering the last 20 years (2004 – 2024). Additionally, another literature search is perfomed on 03.09.2025 for Metapneumovirus. We defined the following exclusion criteria:

· Publication investigates only samples from animals.

· Publication does not focus on PCR/NAT-based detection.

· Target organisms and/or analytes differ from the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR.

· Publication focuses on prevalence/characterization of strains and/or antibiotic resistances.

· Sample type does not include swabs.

The following table provides an overview of how many publications were excluded after abstract screening and how many publications were considered for demonstration of scientific validity.

Table 2: Results of the literature searches

Analyte	Literature search results	Excluded after abstract screening	Considered for scientific validity

Parainfluenza virus 1	7	6	1
Parainfluenza virus 2	3	1	2
Parainfluenza virus 3	11	10	1
Parainfluenza virus 4	8	6	2
Adenovirus	51	35	16
Enterovirus	12	7	5
Rhinovirus	16	7	9
Coronavirus 229E	25	20	5
Coronavirus NL63	22	18	4
Coronavirus OC43	23	18	5
Coronavirus HKU1	19	17	2
Metapneumovirus	27	3	24
Bocavirus	1	0	1
M.pneumoniae	7	5	2
C.pneumoniae	1	0	1
L.pneumophila	1	0	1
B.pertussis	34	10	24
B.parapertussis	4	0	4

H.influenzae	6	5	1
S.pneumoniae	17	8	9

The corresponding literature search protocol (PE Literature Search Protocol resXplex) documents the literature searches in more detail.

The applicability and advantages of the real-time PCR method for the viral and bacterial pathogens mentioned above are explained in detail in PE SOTA_resXplex.

It could be be confirmed that the chosen target genes underlying the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR are appropriate targets for the detection of the pathogens mentioned above. All targets are well described in literature and many of them are also used by similar products. Mutations in the target gene regions that could negatively affect the primer and/or probe binding are analyzed and evaluated in the *in silico* inclusivity report (R&D Report - Inclusivity resXplex). Furthermore, the scientific validity of res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR shall be reviewed and updated regularly (PE PMS and PMPF Plan res1plex direct PCR, PE PMS and PMPF Plan res2plex direct PCR, PE PMS and PMPF Plan res3plex direct PCR, PE PMS and PMPF Plan res5plex direct RT-PCR and PE PMS and PMPF Plan res6plex direct RT-PCR). In our SOTA analysis (PE SOTA_resXplex) it could be shown that qPCR is a powerful method for a fast and comprehensive diagnosis of patients infected with viral and bacterial pathogens mentioned above. Eventually, the scientific validity for the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR was demonstrated as the detection of the target gene regions of DNA/RNA of pathogens mentioned above is verifiably associated with the infection of the respective pathogen.

2.6.1. 1 Summary of performance data from equivalent device(s)

The chapter is not applicable as evidence of the underlying IVD medical device is not based on data from devices claimed to be equivalent to the device.

2.6.2. 2 Summary of performance data from conducted studies prior to CE-marking

The chapter is not applicable as no performance studies have been conducted according to IVDR, Annex I, section 9 prior to CE-marking.

2.6.3. 3 Summary of performance data from other sources

The chapter is not applicable as clinical evidence of the underlying IVD medical device is not based on data from other sources e.g., published experience gained by routine diagnostic testing.

2.6.4. 4 Overall summary of the performance and safety

2.6.4.1. 1 Analytical performance

Analytical performance is described in details in the analytical performance report (PE Analytical Performance Report resXplex).

res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR show analytical specificity, analytical sensitivity, and precision that are similar to competitor devices. All analytical performance claims were able to be proven (**Table 3**).

Table 3: Overview of all applicable analytical performance parameters and the intended claims in comparison to the achieved results.

Analytical performance parameter	Claim	Result/s	Requirement fulfilled
Specimen collection, handling and stability	In general, specimen collection, handling, and stability are applicable for the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR which are performed with nucleic acid that has been extracted from nasopharyngeal and oropharyngeal specimen. Quality and yield of RNA/DNA is highly dependent on the nucleic acid extraction method used. The analytical performance is evaluated based solely on extracted DNA/RNA and thus independent of specimen collection, handling and stability.	N/A	☒ yes ☐ no
Analytical sensitivity	see Limit of Detection		☒ yes ☐ no
Analytical specificity	See Cross-reactivities, Endogenous and exogenous interference, Inclusivity, Competitive interference and physical interaction of primer and probes		☒ yes ☐ no

Cross-reactivities	For the selection of potential cross-reactants, ISO/TS 5798:2022 [1], the Common Specifications for certain class D devices [2] and the FDA Guideline "Respiratory Viral Panel Multiplex Nucleic Acid Assay - Class II Special Controls Guidance for Industry and FDA Staff" [4] were considered. Cross-reactivity is tested with in silico analysis as well as with wet-lab testing. For the in silico analysis, the following acceptance criterion is applied: Cross-reactivity is tested with in silico analysis as well as with wet-lab testing. For the in silico analysis, the following acceptance criterion is applied: According to ISO 5798 [1], the homology between the cross-reactive microorganism and the assay primers and probes is ≤ 80 %. Therefore, if any primer and probe pair or any primer pair within the same master mix show a homology of ≥ 80%, the respective organism is wet-lab tested. Negative samples regarding the test analytes (i.e., human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae*) are tested with the spiked cross-reactant. The following acceptance criteria are applied: · All samples (potential cross reactants) should be negative for all targets. · Internal Control should be positive.	res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR and res3plex *direct* PCR met acceptance criteria. Result details about res2plex *direct* PCR is stated in PE Analytical Performance Report resXplex#4.1.1-Cross-reactivity.	☒ yes ☐ no

Endogenous + exogenous interference	Due to the same chemical composition except oligonucleotides (see PD-List-of-CC-res4plex and (https://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=927826251&draftShareId=347243b2-6258-4224-8641-3a1aef9fb45b, https://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=927826261&draftShareId=7e094545-82b2-49fa-b98a-81e44a068d77, https://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=927858949&draftShareId=694b0ff9-72b5-4146-843c-4f03b5dc9cda, https://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=927858958&draftShareId=ea9d4369-8934-43cb-b5e7-151287e7b5aa, https://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=927858967&draftShareId=c9f3c134-ce2f-4398-8be1-7f37a21d28ba)**,** potential susceptibility against endogenous and exogenous interfering substances between res4plex *direct* RT-PCR test, res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR are considered the same. Endogenous and exogenous interfering substances for res4plex *direct* RT-PCR test could be found in PE_AP-Plan_res4plex.	The analytical specificity concerning interfering substances of the res4plex *direct* RT-PCR test was determined and all acceptance criteria were met. Due to the same chemical composition with res5plex *direct* RT-PCR, res6plex *direct* RT-PCR, res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR except oligonucleotides, potential susceptibility against endogenous and exogenous interfering substances between res4plex *direct* RT-PCR test, res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR are considered the same.	☒ yes ☐ no

Inclusivity	For inclusivity analysis, an in silico analysis is performed. For this purpose, all available human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae* sequences in the NCBI GenBank, ATCC Genome Browser and Bacterial and Viral Bioinformatics Resource Center (BV-BRC) are aligned against the assay primers and probes. The following acceptance criterion is applied: · Frequency of sequences with exact match: at least 90% · Frequency of sequences with identical primer 3' end (first 5 nucleotides of 3' end position): at least 97%	The primer and probe sequences are suitable to detect the test analytes.	☒ yes ☐ no

Competitive interference	To analyse competitive interference, one test analyte is applied in a high concentration (e.g., at least 10^5 copies/ mL), whereas the other test analytes are applied in a low concentration (3x LoD). The following acceptance criterion is applied: · No false negative test results for all test analytes.	Parainfluenza virus 2 and Adenovirus 3 at 1000 copies/µl suppressed amplification of Rhinovirus 14 at 3x LoD. Similarly, Adenovirus 3 at 1000 copies/µl suppressed amplification of Enterovirus 68 at 3x LoD. When the concentration of Bocavirus was 1000 copies/µl, all Coronavirus subtypes (229E, NL63, OC43 and HKU1) and Metapneumoviruses (A and B) were suppressed and could not be detected at 3xLoD concentration. Competitive interference was not observed regarding res1plex *direct* PCR, res2plex *direct* PCR and res3plex *direct* PCR.	☒ yes ☐ no (Note in the IFU FBC117 res5plex direct RT-PCR and IFU FBC118 res6plex direct RT-PCR about competitive interference)
Physical Interaction of primers and probes	All assay primers and probes are investigated with the "Multiple Primer Analyzer" tool from ThermoFisher Scientific. Those primer dimer combinations are further investigated with the following underlying acceptance criterion: ΔG (kcal/mol) shall be > -9.0 and > -6.0 at 3´ complementary base pairs	Potential dimers that do not fulfil the acceptance criteria were identified. Other parameters of the analytical performance studies show that potential dimers do not have an effect on the performance of the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR.	☒ yes ☐ no
Accuracy (derived from trueness and precision)	See Trueness and Precision		

Trueness (bias)	The concept of trueness, defined as the closeness of agreement between a measured value and a true value, is not applicable to this qualitative NAT assay, which provides binary results (positive/ negative). Therefore, trueness performance testing has not been performed. Instead, diagnostic sensitivity and specificity will be established through clinical performance studies (PE Clinical Performance Report resXplex), as required under Annex I, Section 9.1(b) of the IVDR.		☒ yes ☐ no
Precision	See Repeatability and Reproducibility		☒ yes ☐ no
Repeatability	For precision estimation, negative and positive samples with different analyte levels (negative, 3x LoD) are used. The agreement between different variation parameters (lot, instruments, operator) is evaluated. For the experiment plan Respiratory Viral Panel Multiplex Nucleic Acid Assay - Class II Special Controls Guidance for Industry and FDA Staff [4] is considered. Following acceptance criteria are considered according to the Common Specifications for certain class D devices [2] and the technical specifications for in vitro diagnostics for SARS-CoV-2 [3]: No false positive test results. Intra-assay precision (repeatability): CV < 3% Inter-assay precision (reproducibility): CV < 5%	Acceptance criteria were met concerning repeatability and reproducibility studies of res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR.	☒ yes ☐ no
Reproducibility			☒ yes ☐ no
Measuring range	As the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR deliver a qualitative result (“detected” or “not detected”), the measuring range is not assessed (see below for details).	N/A	☒ yes ☐ no

Linearity	As the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR deliver a qualitative result ("detected" or "not detected"), the linearity is not assessed (see below for details).	N/A	☒ yes ☐ no
Limit of detection	The limit of detection is determined for each analyte (human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae*), separately. The following acceptance criterion is applied: • The limit of detection for all targets is ≤ 50 copies/reaction. According to CLSI EP17-A2 [5], the Limit of Blank (LoB) is set to zero, as nucleic acid tests using PCR technology "have essentially no distribution of measurement results for negative samples, because all such results are typically reported as zero. In these situations, the 95th percentile of test results on blank samples equals zero" [5]. This is verified by negative samples regarding the test analytes (i.e., human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae*). The following acceptance criterion is applied: • No false positive test results.	Limit of detection is ≤50copies/reaction for all anaytes and acceptance criteria were met.	☒ yes ☐ no

Limit of quantitation	As the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR deliver a qualitative result (“detected” or “not detected”), a limit of quantitation cannot be determined (see below for details).	N/A	☒ yes ☐ no
Assay cut-off	As the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR deliver a qualitative result (“detected” or “not detected”), a limit of quantitation cannot be determined (see below for details).	N/A	☒ yes ☐ no
Metrological traceability	The res1plex direct PCR, res2plex direct PCR, res3plex direct PCR, res5plex direct RT-PCR and res6plex direct RT-PCR contain an internal control which is based on an artificial sequence (seehttps://frizbiochem.atlassian.net/wiki/pages/resumedraft.action?draftId=336363521&draftShareId=7f4a3e91-f24c-4c96-8eea-94adc74092f3). No suitable reference materials or reference measurement procedures of higher metrological order are available.	N/A	☒ yes ☐ no
Stability	See Transport stability, Shelf life, and In-use stability		☒ yes ☐ no

Transport stability	Before and after the transport simulation, negative and positive samples regarding the test analytes (i.e., human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae*) are tested. The following acceptance criteria are applied: · No false positive test results. · The agreement of the test results before and after the transport simulation is ≤ 10% for each test analyte.	In accordance with the acceptance criteria, Ct values deviated ≤ 10% for each test analyte, Positive Control and the Internal Control.	☒ yes ☐ no

Shelf life	The res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR shall have a shelf life of 12 months when stored between temperatures from -25 °C to -18 °C. Within the shelf-life study, positive and negative samples regarding the test analytes (i.e., human Parainfluenza 1-4, Adenovirus, Enterovirus/Rhinovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Metapneumovirus, Bocavirus, *Bordetella pertussis, Bordetella parapertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Streptococcus pneumoniae and Haemophilus influenzae*) are tested up to 13 months. The following acceptance criteria are applied: No false positive test results. The agreement of the test results between T0 and a measurement test point is ≤ 10% for each test analyte. According to CLSI EP25-A, “the stability claim may be established as duration up to the last time point at which acceptance criteria had been met” [6].	The shelf life study is still ongoing.	☒ yes ☐ no

In-use stability	The res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR should be able to be thawed and refrozen 4 times. The following acceptance criteria are applied: · No false positive test results · The agreement of test results between thawing cycle 1 and a later thawing cycle is ≤ 10% for each test analyte. Moreover, the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR shall have an in-use stability up to 8 hours in a temperature range from 2°C to 8°C. 3 positive samples (1000 copies/ reaction) regarding the representative test analytes and positive controls in three replicates are tested with the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR before and after storage for 2, 4, and 8 hours at 4°C. The following acceptance criteria are applied: · No false negative test results with positive samples regarding the test analytes. The agreement of test results before and after storage at 4°C is ≤ 10% for each test analyte, positive controls and the internal control.	In accordance with the acceptance criteria, Ct values deviated ≤ 10% for each test analyte, Positive Control and the Internal Control.	☒ yes ☐ no

2.6.4.2. 2 Clinical performance

For the evidence of clinical performance of the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR, we evaluated the parameters according to Annex I, section 9.1 b) of the IVDR. Diagnostic sensitivity and specificity data of the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR fulfill acceptance criteria (**Table 3**). In conclusion, clinical performance data demonstrate clinical evidence of res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR.

Table 4: Overview of applicable clinical performance parameters and the intended claims in comparison to the achieved results.

Clinical Performance Parameter	**Acceptance criteria**	**Results**
Diagnostic sensitivity	For each analyte, the diagnostic sensitivity is ≥ 90%	For parainfluenza virus the diagnostic sensitivity is 100.0% (78.2-100.0) For adenovirus the diagnostic sensitivity is 100.0% (66.4-100.0) For enterovirus/rhinovirus the diagnostic sensitivity is 100.0% (87.2-100.0) For coronavirus the diagnostic sensitivity is 100.0% (83.9-100.0) For metapneumovirus the diagnostic sensitivity is 100.0% (66.4-100.0) For bocavirus the diagnostic sensitivity is 100.0% (29.2-100.0) For *Mycoplasma pneumoniae* the diagnostic sensitivity is 98.04% (89.5-99.9) For *Chlamydia pneumoniae* the diagnostic sensitivity is 100.0% (63.1-100.0) For *Legionella pnuemophila* the diagnostic sensitivity is 100.0% (71.5-100.0) For *Bordetella pertussis* the diagnostic sensitivity is 100.0% (66.4-100.0) For *Bordetella parapertussis* the diagnostic sensitivity is 100.0% (39.8-100.0) For *Haemophilus influenzae* the diagnostic sensitivity is 100.0% (88.4-100.0) For *Streptococcus pneumoniae* the diagnostic sensitivity is 100.0% (85.2-100.0)

Clinical Performance Parameter	Acceptance criteria	Results
Diagnostic specificity	For each analyte, the diagnostic specificity is ≥ 95%	For parainfluenza virus the diagnostic specificity is 100.0% (98.3-100.0) For adenovirus the diagnostic specificity is 100.0% (98.4-100.0) For enterovirus/rhinovirus the diagnostic specificity is 100.0% (98.2-100.0) For coronavirus the diagnostic specificity is 100.0% (98.3-100.0) For metapneumovirus the diagnostic specificity is 100.0% (98.4-100.0) For bocavirus the diagnostic specificity is 100.0% (98.4-100.0) For *Mycoplasma pneumoniae* the diagnostic specificity is 100.0% (98.4-100.0) For *Chlamydia pneumoniae* the diagnostic specificity is 100.0% (98.7-100.0) For *Legionella pnuemophila* the diagnostic specificity is 100.0% (98.7-100.0) For *Bordetella pertussis* the diagnostic specificity is 100.0% (96.6-100.0) For *Bordetella parapertussis* the diagnostic specificity is 100.0% (96.8-100.0) For *Haemophilus influenzae* the diagnostic specificity is 100.0% (94.9-100.0) For *Streptococcus pneumoniae* the diagnostic specificity is 100.0% (95.4-100.0)

2.6.5. 5 Ongoing or planned post-market performance follow-up (PMPF)

We use a Post-Market Performance Follow-Up (PMPF) Plan to define PMPF measures to be taken for the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR in order to keep the performance evaluation continually updated. The results of the PMPF activities are summarized and evaluated in the post-market performance follow-up report.

The following PMPF activities are planned:

- Research customer feedback, if applicable evaluate for trends and initiate action.
- Compile information from in-house quality control tests. If applicable, evaluate for trends and initiate action.
- Search for information on equivalent/comparative products and alternative procedures:
    - Review the scientific literature and other sources for relevant (clinical) performance and scientific data
    - Monitor relevant clinical guidelines from professional (medical) societies

    - Verify the performance data of equivalent and similar products, including searches in safety databases
- Search for changes in regulations, laws, initiate action if necessary
- Regular check of primer/probe sequences against sequence data bank entries
- Interlaboratory comparisons; further quality assurance programs

2.7. 7 Metrological traceability of assigned values

The res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR kits contain an internal control which is based on an artificial sequence. No suitable reference materials or reference measurement procedures of higher metrological order are available.

2.7.1. 1 Explanation of the unit of measurement

The chapter is not applicable as no suitable reference materials or reference measurement procedures of higher metrological order are available.

2.7.2. 2 Applied reference materials and/or reference measurement procedures

The chapter is not applicable as no suitable reference materials or reference measurement procedures of higher metrological order are available.

2.8. 8 Suggested profile and training for users

We define the following user groups:

Table 5: User Groups

No.	Name of the User Group	Short Description
1	Healthcare Professional	tertiary/indirect user: collects and handles specimen, uses the results to derive an organizational and/or patient management decision
2	Laboratory Personnel	primary user: uses the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR for in vitro diagnostic analysis in a medical laboratory.
3	Laboratory Specialist	primary user: responsible for evaluation and release of the results

Table 6: User Group 1 “Healthcare Professional” as tertiary user

User group:	**Healthcare Professional**
Typical job title(s):	Physician, nurse, caregiver, pharmacist, pharmaceutic-technical assistant

Demographic characteristics (age, sex, language, specific physical attributes):	no specific gender typical age: between 20 and 67 years not necessarily a native speaker, but knows the required technical terminology
Expected qualification (education, degree, training):	medical or pharmaceutical education
Expected job experience (related to the product, similar products or IT in general):	No specific job experience related to the product required
Typical work environment (physical and organizational/social):	clinical environment (e.g. reception area), doctors' office
Core tasks:	1. Register a patient/specimen
	2. Collect a specimen
	3. Ship the collected specimen
	4. Interpret results to make an organizational and/or patient management decision
Typical equipment (used during performance of the tasks):	Swab and transport medium for specimen collection
Expected product training (with regard to the medical device)	no training required

Table 7: User Group 2 "Laboratory Personnel" as primary user

User group:	**Laboratory Personnel**
Typical job title(s):	medical/biological-laboratory assistant, laboratory technician
Demographic characteristics (age, sex, language, specific physical attributes):	no specific gender typical age: between 20 and 67 years not necessarily a native speaker, but knows the required technical terminology
Expected qualification (education, degree, training):	education as medical/biological-laboratory assistant or laboratory technician

Expected job experience (related to the product, similar products or IT in general):	Experience in molecular diagnostic techniques, i.e. nucleic acid extraction and qPCR
Typical work environment (physical and organizational/social):	medical laboratory
Core tasks:	1. Receive the specimen
	2. Register the patient/specimen
	3. Perform nucleic acid extraction according to the laboratory's standard
	4. Perform the res1plex *direct* PCR, res2plex *direct* PCR, res3plex *direct* PCR, res5plex *direct* RT-PCR and res6plex *direct* RT-PCR using a qPCR cycler
Typical equipment (used during performance of the tasks):	RT-qPCR cycler disposable protective gloves PCR reaction tubes/microtiter plate plus lids/adhesive optical film Pipettes Pipette tips with filter (DNase/RNase-free) Table centrifuge Nucleic acid extraction kit
Expected product training (with regard to the medical device)	Training in RT-qPCR and *in vitro* diagnostic techniques

Table 8: User Group 3 "Laboratory Specialist" as primary user

User group:	**Laboratory Specialist**
Typical job title(s):	specialist in laboratory medicine
Demographic characteristics (age, sex, language, specific physical attributes):	no specific gender typical age: between 30 and 67 years not necessarily a native speaker, but knows the required technical terminology

Expected qualification (education, degree, training):	university degree, specialist training for laboratory medicine
Expected job experience (related to the product, similar products or IT in general):	specialist training in infectious respiratory diseases
Typical work environment (physical and organizational/social):	medical laboratory
Core tasks:	Analyze and release the diagnostic report
Typical equipment (used during performance of the tasks):	RT-qPCR cycler with corresponding software LIMS software
Expected product training (with regard to the medical device)	Analysis and interpretation of the results

3. 3 Annex

3.1. 1 Terms and abbreviations

The following table lists document-specific abbreviations and definitions:

Term	Description	Reference
CDx	Companion diagnostic	n. a.
Companion diagnostic	Device which is essential for the safe and effective use of a corresponding medicinal product to: • identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or • identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product	IVDR, Art. 2
Contra-indication	Specific medical reasons for not using a particular IVD medical device in the usual way (e. g. a virus infection that interferes with the biomarker analysis, a urinary tract infection that affects the results of a urine test).	internal definition
DI	Device Identifier	n. a.
EMDN	European Medical Device Nomenclature	n.a.

EUDAMED	European Database on Medical Devices	n.a.
FSCA	Field Safety Corrective Action; Corrective action taken by a manufacturer for technical or medical reasons to prevent or reduce the risk of a serious incident in relation to a device made available on the market	IVDR, Art. 2
FSN	Field Safety Notice; Communication sent by a manufacturer to users or customers in relation to a field safety corrective action	IVDR, Art. 2
IFU	Instructions For Use; Information provided by the manufacturer to inform the user of a device's intended purpose and proper use and of any precautions to be taken	IVDR, Art. 2
Intended purpose	Use for which the IVD medical device is intended according to the data supplied by the manufacturer on the label, the IFU, or in promotional and sales materials and as specified by the performance evaluation.	IVDR, Art. 2
IVD	In Vitro Diagnostic	n. a.
IVDD	Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices	n. a.
IVDR	European Regulation 2017/476 on in vitro diagnostic medical devices	n. a.
Kit	Set of components that are packaged together and intended to be used to perform a specific in vitro diagnostic examination, or a part thereof	IVDR, Art. 2
Lay person	Individual who does not have formal education in a relevant field of healthcare or medical discipline	IVDR, Art. 2
Limitation	A situation/factor that (may) affect the results of an in-vitro diagnostic test (e.g. running a marathon before Ca^{2+}-measurement due to untypically high Ca^{2+}-level) or for which the test has not been clinically validated (e.g. usage for children, usage during pregnancy).	internal definition
MDSW	Medical device software	MDCG 2019-11
n. a.	not applicable	n. a.

NB	Notified Body; conformity assessment body designated in accordance with this Regulation	IVDR, Art. 2
Near-patient testing	Any device that is not intended for self-testing but is intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient by a health professional	IVDR, Art. 2
PEP	Performance evaluation plan	n. a.
PER	Performance evaluation report	n. a.
Performance of a device	Ability of a device to achieve its intended purpose as claimed by the manufacturer. It consists of the analytical and, where applicable, the clinical performance supporting that intended purpose	IVDR, Art. 2
PMPF	Post-Market Performance Follow-up	n. a.
Scientific validity	Association of an analyte with a clinical condition or a physiological state	IVDR, Art. 2
Self-testing	Any device intended by the manufacturer to be used by lay persons, including devices used for testing services offered to lay persons by means of information society services	IVDR, Art. 2
SRN	Single Registration Number	n. a.
SSP	Summary of Safety and Performance	n. a.
SVR	Scientific validity report	n. a.
TD	Technical documentation	n. a.
UDI	Unique Device Identification; Series of numeric or alphanumeric characters that is created through internationally accepted device identification and coding standards and that allows unambiguous identification of specific devices on the market	IVDR, Art. 2

3.2. 2 Revision history

SSP revision number	Date issued	Change description	Revision validated by the Notified Body

1	2026-07-22	Initial creation	☐	Yes Validation language: ENG