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Premarket Registration Full Evaluation Route
Summary Assessment Report for
Cepheid Xpert Xpress CoV-2/Flu/RSV plus

Listing number	MDPR260204X0002
Date of approval	04/02/2026
Product owner	Cepheid
Registrant	Cepheid Singapore Pte Ltd
Risk Class	Class D
Intended use / Indications of use	Xpert® Xpress CoV-2/Flu/RSV plus test, performed on the GeneXpert® Dx and GeneXpert Infinity Systems, is an automated multiplexed real-time reverse transcriptase polymerase chain reaction (RT-PCR) test intended for use in the simultaneous in vitro qualitative detection and differentiation of severe acute respiratory syndrome coronavirus (SARS- CoV-2), influenza A, influenza B, and/or respiratory syncytial virus (RSV) viral RNA in nasopharyngeal swab and anterior nasal swab specimens collected from individuals with signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2, influenza A, influenza B, and RSV can be similar. The Xpert Xpress CoV-2/Flu/RSV plus is intended for use in the differential detection of SARS-CoV-2, influenza A, influenza B and/or RSV RNA and aids in the diagnosis of COVID-19, influenza and/or RSV infections if used in conjunction with other clinical and epidemiological information, and laboratory findings. SARS-CoV-2, influenza A, influenza B, and RSV viral RNA are generally detectable in nasopharyngeal swab and anterior nasal swab specimens during the acute phase of infection. Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other pathogens not detected by the test. The agent(s) detected by the Xpert Xpress CoV-2/Flu/RSV plus test may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A, influenza B and/or RSV infection. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

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1. Device description

The Xpert® Xpress CoV-2/Flu/RSV plus test is an automated multiplexed real-time reverse transcriptase polymerase chain reaction (RT-PCR) test for simultaneous qualitative detection and differentiation of RNA from SARS-CoV-2, Flu A, Flu B and RSV in nasopharyngeal swab and anterior nasal swab specimens collected from individuals with signs and symptoms of respiratory tract infection. The test consists of 10 single use disposable cartridges and is performed on the GeneXpert Instrument Systems, in which sample preparation, nucleic acid extraction and amplification, and detection of the target sequences are integrated.

The assay targets the nucleocapsid (N), envelope (E) and RNA-dependent RNA polymerase (RdRP) genes of the SARS-CoV-2 virus genome, matrix (M), basic polymerase (PB2), and acidic protein (PA) segments of the influenza A genome, matrix (M) and non-structural protein (NS) segments of the influenza B genome and the nucleocapsid genes of RSV A and RSV B. The assay also includes a Sample Processing Control (SPC) and a Probe Check Control (PCC) to ensure adequate sample processing and monitor for the presence of inhibitors in the RT-PCR reaction.

The results are interpreted automatically by the GeneXpert system. Users may select the following tests to run:

- Flu A and Flu B: Select **Xpress Flu plus**
- Flu A, Flu B and RSV: Select **Xpress Flu RSV plus**
- SARS-CoV-2: Select **Xpress SARS-CoV-2 plus**
- SARS-CoV-2, Flu A and Flu B: Select **Xpress SARS-CoV-2 Flu plus**
- SARS-CoV-2, Flu A, Flu B and RSV: Select **Xpress SARS-CoV-2 Flu RSV plus**

The **Xpress SARS-CoV-2 plus and Xpress Flu plus** test modes feature an Early Assay Termination (EAT) function that will provide earlier time to result in high titer specimens when the signal from SARS-CoV-2 or Flu A/B targets reaches a predetermined threshold before completing all PCR cycles. When SARS-CoV-2 or Flu A/B titers are high enough to initiate the EAT function, the SPC and/or other target amplification curves may not be seen, and their results may not be reported.

The format of the test result will depend on the choice of the tests that users have selected to run. When Xpert Xpress SARS-CoV-2 Flu RSV plus test mode is selected, the results may be interpreted as follows:

Result	Interpretation
SARS-CoV-2 POSITIVE	The SARS-CoV-2 target RNA is detected. The SARS-CoV-2 signal has a Ct within the valid range and endpoint above the minimum setting. SPC: NA (not applicable); SPC is ignored because SARS-CoV-2 target amplification occurred. Probe Check: PASS; all probe check results pass.
Flu A POSITIVE	The Flu A target RNA is detected. The Flu A signal for either the Flu A1 RNA target or the Flu A2 RNA target or signals for both RNA targets have a Ct within the valid range and endpoint above the threshold setting. Note: Flu A1 and Flu A2 are in different channels and a Flu A POSITIVE result requires signals from either one, or both, of the channels). SPC: NA; SPC is ignored because Flu A target amplification occurred. Probe Check: PASS; all probe check results pass.
Flu B POSITIVE	The Flu B target RNA is detected. The Flu B signal has a Ct within the valid range and endpoint above the minimum setting. SPC: NA; SPC is ignored because Flu B target amplification occurred. Probe Check: PASS; all probe check results pass.

RSV POSITIVE	The RSV target RNA is detected. The RSV signal has a Ct within the valid range and endpoint above the minimum setting. SPC: NA; SPC is ignored because RSV target amplification occurred. Probe Check: PASS; all probe check results pass.
SARS-CoV-2 NEGATIVE; **Flu A NEGATIVE;** **Flu B NEGATIVE;** **RSV NEGATIVE**	SARS-CoV-2 target RNA is not detected; Flu A target RNA is not detected; Flu B target RNA is not detected; RSV target RNA is not detected. SARS-CoV-2, Flu A, Flu B and RSV target RNAs are not detected. SPC: PASS; SPC has a Ct within the valid range and endpoint above the minimum setting. Probe Check: PASS; all probe check results pass.
INVALID	SPC or other analysis settings do not meet acceptance criteria and all targets are not detected. Repeat test according to the Retest Procedure in the IFU. SPC: FAIL; SPC and SARS-CoV-2, Flu A, Flu B and RSV signals do not have a Ct within valid range and endpoint is below minimum setting. SARS-CoV-2 amplification fails specification Probe Check: PASS; all probe check results pass.
ERROR	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV RNA cannot be determined. Repeat test according to the Retest Procedure in the IFU. • SARS-CoV-2: NO RESULT • Flu A: NO RESULT • Flu B: NO RESULT • RSV: NO RESULT • SPC: NO RESULT • Probe Check: FAIL; all or one of the probe check results fail. If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range, no sample added, or by a system component failure.
NO RESULT	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV RNA cannot be determined. Repeat test according to the Retest Procedure in the IFU. A NO RESULT indicates that insufficient data were collected. For example, the operator stopped a test that was in progress. • SARS-CoV-2: NO RESULT • Flu A: NO RESULT • Flu B: NO RESULT • RSV: NO RESULT • SPC: NO RESULT • Probe Check: NA

Result interpretation for other test modes can be found in the Instructions-for-use.

Negative results do not preclude SARS-CoV-2, influenza A, influenza B and/or RSV infection and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Viral nucleic acid may persist *in vivo*, independent of virus infectivity. Detection of analyte target(s) does not imply that the corresponding virus(es) are infectious or are the causative agents for clinical symptoms. Live attenuated influenza vaccines may cause inaccurate positive influenza results. Additional limitations, warnings and precautions can be found in the labelling.

2. List of standards applied

Standards	Title
ISO 13485	Medical devices – Quality management systems – Requirements for regulatory purposes
ISO 14971	Medical Devices – Application of Risk Management to Medical Devices
EN 13612	Performance evaluation of in vitro diagnostic medical devices
EN ISO 23640	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
EN ISO 20916	In vitro diagnostic medical device -Clinical performance studies using specimens from human subjects – Good study practice
EN ISO 15223-1	Medical devices -Symbols to be used with medical device labels, labelling and information to be supplied.
EN ISO 18113-1	In vitro diagnostic medical devices – Information supplied by the manufacturer (labelling) – Part 1: terms, definitions and general requirements
EN ISO 18113-2	In vitro diagnostic medical devices – Information supplied by the manufacturer (labelling) – Part 2: in vitro diagnostic reagents for professional use.

3. Pre-clinical assessment

(i) Stability

Real-time stability studies were completed on four lots stored for a minimum of 19 months at 2°C and 28°C to support a shelf-life claim of 12 months when stored at 2-28°C.

A transport stability study was conducted on one lot of the assay to stimulate harsh summer or winter conditions for 7 days and thereafter, various transport handling conditions. After which the cartridges were functionally tested until 25 months' time-point when stored at 2°C and 28°C. The product shelf-life is not impacted by the shipping simulation.

(ii) IVD specific studies

- Analytical sensitivity

  Studies provided supported the following limit of detection (LoD) for the viruses tested in nasopharyngeal swab (NPS) matrix:

Virus strain	LoD
USA-WA1/2020 (NATtrol)	138 copies/mL
1st WHO International Standard	94 IU/mL
Flu A/Idaho/07/2018	0.007 $TCID_{50}$/mL
Flu A/California/07/2009	0.0022 $TCID_{50}$/mL
Flu A/Hong Kong/45/2019	0.34 FFU/mL
Flu A/Victoria/361/2011	0.05 $TCID_{50}$/mL
Flu B/Washington/2/2019	12.9 $CEID_{50}$/mL
Flu B/Wisconsin/10/2016	2.4 $TCID_{50}$/mL
RSV A/2/Australia/61	0.33 $TCID_{50}$/mL
RSV A/Long/MD/56	0.17 $TCID_{50}$/mL
RSV B/9320/MA/77	0.37 $TCID_{50}$/mL
RSV B/Wash/18537/62	0.2 $TCID_{50}$/mL

Studies provided supported the following limit of detection (LoD) for the viruses tested in anterior nasal swab (NS) matrix:

Virus strain	LoD
USA-WA1/2020 (NATtrol)	50 copies/mL

1st WHO International Standard	99 IU/mL
Flu A/Idaho/07/2018	0.0058 $TCID_{50}$/mL
Flu A/California/07/2009	0.0028 $TCID_{50}$/mL
Flu A/Hong Kong/45/2019	0.38 FFU/mL
Flu A/Victoria/361/2011	0.065 $TCID_{50}$/mL
Flu B/Washington/2/2019	18.9 $CEID_{50}$/mL
Flu B/Wisconsin/10/2016	2.41 $TCID_{50}$/mL
RSV A/2/Australia/61	0.28 $TCID_{50}$/mL
RSV A/Long/MD/56	0.22 $TCID_{50}$/mL
RSV B/9320/MA/77	0.27 $TCID_{50}$/mL
RSV B/Wash/18537/62	0.24 $TCID_{50}$/mL

- Inclusivity

  In silico analysis of assay amplicons of SARS-CoV-2 in GISAID database showed that for the E amplicon, 99.5% of GISAID sequences were an exact match to the reference amplicon, for the N2 amplicon, 98.1% of GISAID sequences were an exact match to the reference amplicon and for the RdRP amplicon, 99.2% of GISAID sequences were an exact match to the reference amplicon. *In silico* analysis further support the detection of SARS-CoV-2 variants including Alpha, Beta, Eta, Iota, Kappa, Delta, Mu. Lambda, Gamma, Zeta, Theta, Omicron, Nimbus and Stratus variants.

  In silico analysis was supported by inclusivity wet-testing which tested 18 SARS-CoV-2 strains, 48 influenza A viruses, 21 influenza B viruses and 15 RSV strains. All SARS-CoV-2, Flu and RSV strains tested positive in all 3 replicates. Information on the strains tested is available in the instructions-for-use.

- Analytical specificity

  In silico exclusivity analysis of assay amplicons and oligonucleotides of SARS-CoV-2 against sequences in GISAID database indicates that the E gene primers and probes may amplify and detect bat and human SARS coronavirus. The RdRP primers may amplify human SARS coronavirus but this is not detected by the RdRP probe.

  In silico exclusivity analysis of assay amplicons and oligonucleotides of Flu A and Flu B against the GenBank database indicates that there were no genomic fragments from any organism where an amplicon could be generated and detected. For RSV A primer and probe may amplify and detect pangolin RSV while for RSV B amplicon, there were no matches to RSV isolates from other species or to genomic sequences from non-RSV species.

  In addition to *in silico* exclusivity analysis, cross-reactivity study was conducted on 48 microorganisms as documented in the table below. Viruses were tested at concentrations of ≥ 10^5 $TCID_{50}$/ml. The bacterial and yeast strains were tested at concentrations of ≥ 10^6 CFU/ml (except for Lactobacillus reuteri tested at 5 x 10^7 copies/ml of genomic DNA). No cross-reactivity was observed.

Human coronavirus NL63	Human parainfluenza Type 4	*Moraxella catarrhalis*
MERS-coronavirus	Measles	*Mycoplasma pneumoniae*
Human coronavirus 229E	Mumps virus	*Neisseria meningitides*
Human coronavirus OC43	Rhinovirus Type 1A	*Neisseria mucosa*
Human coronavirus HKU1*	*Acinetobacter baumannii*	*Propionibacterium acnes*
Adenovirus Type 1	*Bordetella pertussis*	*Pseudomonas aeruginosa*
Adenovirus Type 7	*Burkholderia cepacia*	*Staphylococcus haemolyticus*
Cytomegalovirus	*Candida albicans*	*Staphylococcus aureus*
Echovirus	*Candida parapsilosis*	*Staphylococcus epidermidis*
Enterovirus	*Citrobacter freundii*	*Streptococcus agalactiae*
Epstein Barr Virus	*Corynebacterium sp.*	*Streptococcus pneumoniae*
HSV	*Enterococcus faecalis*	*Streptococcus pyogenes*
Human metapneumovirus	*Escherichia coli*	*Streptococcus salivarius*
Human parainfluenza Type 1	*Hemophilus influenzae*	*Streptococcus sanguinis*

Human parainfluenza Type 2	*Lactobacillus reuteri***	*Chlamydia pneumoniae*
Human parainfluenza Type 3	*Legionella pneumophila*	*Mycobacterium tuberculosis (avirulent)*

* Synthetic RNA used
** Genomic DNA used

In the microbial interference study, 10 potentially interfering microorganisms were investigated for potential to interfere with the detection of SARS-CoV-2, Flu A, Flu B, RSV A or RSV B. There was no interference by potentially interfering viral or bacterial strains tested.

Potential interfering microbes	Concentration
Adenovirus Type 1C	$1x10^5$ $TCID_{50}$/ml
Human Coronavirus OC43	$1x10^5$ $TCID_{50}$/ml
Rhinovirus Type 1A	$1x10^5$ $TCID_{50}$/ml
Human metapneumovirus	$1x10^5$ $TCID_{50}$/ml
Human parainfluenza Types 1, 2, and 3	$1x10^5$ $TCID_{50}$/ml
Hemophilus influenzae	$1x10^6$ CFU/ ml
Staphylococcus aureus	$1x10^7$ CFU/ ml
Staphylococcus epidermidis	$1x10^7$ CFU/ ml

Competitive inhibition studies were conducted to assess the potential interference between co-infections amongst the target analytes. Competitive inhibitory effects were observed when high concentrations of certain pathogens were present. Specifically, Flu A concentrations above 1.7×10^5 RNA copies/ml inhibited the detection of Flu B, whilst concentrations above 1.7×10^6 RNA copies/ml interfered with RSV A detection. Additionally, SARS-CoV-2 concentrations exceeding 1×10^5 RNA copies/ml demonstrated inhibitory effects on Flu B detection. No other competitive interference was observed amongst the remaining analyte combinations.

Potential interference from endogenous and exogenous substances was assessed under conditions with and without the target analytes present. The substances listed in the table below showed no interference at the stated concentrations.

Potential interferent	Concentration Tested
Beta-adrenergic bronchodilator – Albuterol Sulfate	0.83 mg/mL (equivalent to 1 dose per day)
Nasal Spray- Afrin	15% (v/v)
Transport media	100% (v/v)
Blood	2% (v/v)
Vaccine – Live attenuated influenza vaccine (FluMist)*	6.7×10^{-7}% (v/v).
Nasal corticosteroid	5 µg/ml
Human peripheral blood mononuclear cells (PBMC)**	2.5×10^5 cells/ml
Ibuprofen	5% w/v
Throat lozenges, oral anesthetic and analgesic – Menthol	1.7 mg/ml
Mucin	0.1 (w/v)
Mupirocin	10 mg/ml
Nasal Drops – Phenylephrine 1%	15% (v/v)
Saline nasal spray	15% (v/v)
Tobacco product, Snuff***	0.1% (w/v)
Tamiflu	7.5 mg/ml
Tobramycin	4 µg/ml
Zicam****	7.5% (w/v).
Zinc	0.1 µg/ml

* Interfering effects were observed at 6.7×10^{-4}% (v/ v) FluMist for SARS-CoV-2, RSV A and RSV B strains and at 6.7×10^{-6}% (v/v) for RSV A/Long/MD/56
** Interfering effects were observed at 1×10^6 cells/ml for Flu B/Washington /2/2019.

*** Interfering effects were observed at 1% (w/v) for Flu A /California/07/2009 and Flu B/Washington/2/2019.
**** Interfering effects were observed at 15% (w/v) for Flu A, Flu B and RSV A strains.

- Precision

  Precision and reproducibility validation was conducted using negative, low positive (1.5× LoD), and moderate positive (3× LoD) specimens. The precision study was performed at a single site using one assay kit lot, with one operator conducting two runs containing two replicates per run. The reproducibility study was conducted over six days across three sites, utilising three assay kit lots and two operators per site. Each operator performed two runs with two replicates per panel per run.

  The validation demonstrated acceptable performance with no significant variance. Low positive samples achieved ⩾95% positivity, whilst both moderate positive and negative samples achieved 100% positivity.

- Specimen stability

  Specimen stability study validated the claims that specimens in VTM/UTM may be stored at room temperature (15°C to 30°C) for 48 hours, refrigerated (2°C to 8°C) for seven days or stored frozen at -20°C to -80°C and undergo 1 freeze/thaw cycle.

- Carry-over

  No carryover contamination was observed when alternate high positive and negative specimens were run on the compatible instrument.

4. Clinical assessment

(i) Evaluation of Clinical Investigations

IVD Specific Requirements

Clinical performance

The clinical performance of Cepheid Xpert Xpress CoV-2/Flu/RSV plus was established through a multi-site study conducted across 21 geographically diverse locations in the United States. The study utilised both prospective specimens and archived specimens collected and tested between January 2022 and October 2022, and August 2024 and September 2024, respectively. Trained users performed all testing on the GeneXpert Dx Instrument in laboratory settings. The specimen types included clinical nasopharyngeal swabs (NPS) and nasal swabs (NS) collected from individuals presenting with signs and symptoms of respiratory viral infection.

For SARS-CoV-2 evaluation, a total of 2,794 specimens were analysed, comprising 1,385 NPS and 1,409 NS specimens. For the evaluation of Influenza A, Influenza B, and RSV targets, 2,891 specimens were used, consisting of 1,439 NPS and 1,452 NS specimens. Clinical studies demonstrated the following performance compared against the method comparator. Performance data stratified by prospective and archived specimens are available in the instructions for use.

Specimen type NPS

Pathogens	Specimen Size	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
SARS-CoV-2	1385	97.0% (95%CI: 94.4%-98.4%)	98.3% (95%CI: 97.3%-98.9%)
Flu A	1439	97.5% (95%CI: 91.3%-99.3%)	99.6% (95%CI: 99.1%-99.8%)
Flu B	1439	100.0% (95%CI: 95.2%-100.0%)	100.0% (95%CI: 99.7%-100.0%)
RSV	1439	96.7% (95%CI: 90.7%-98.9%)	100.0% (95%CI: 99.7%-100.0%)

Specimen type NS

Pathogens	Specimen Size	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
SARS-CoV-2	1409	98.4% (95%CI: 96.3%-99.3%)	98.5% (95%CI: 97.7%-99.1%)
Flu A	1452	100.0% (95%CI: 95.3%-100.0%)	99.9% (95%CI: 99.5%-100.0%)
Flu B	1452	100.0% (95%CI: 96.2%-100.0%)	99.9% (95%CI: 99.6%-100.0%)
RSV	1452	97.9% (95%CI: 92.6%-99.4%)	100.0% (95%CI: 99.7%-100.0%)

5. Assessment of device quality

The assay is manufactured in Sweden and United States at Cepheid AB and Cepheid, respectively. Both manufacturing sites conform to ISO 13485:2016 quality management system.

6. Conclusion

The Cepheid Xpert Xpress CoV-2/Flu/RSV plus demonstrates acceptable safety and performance for its intended use of qualitative detection and differentiation of SARS- CoV-2, Flu A, Flu B, and RSV viral RNA in NPS and NS specimens collected from individuals with signs and symptoms of respiratory tract infection.

The benefits of this device outweigh the associated risks, as it enables healthcare providers to simultaneously test for multiple respiratory pathogens when patients present with upper respiratory tract infection symptoms. This multiplex capability streamlines diagnostic workflows and supports timely clinical decision-making.

All foreseeable risks have been systematically identified and mitigated through appropriate design controls, comprehensive labelling, and detailed user instructions. The preclinical and clinical validation data substantiate the device's safety and effectiveness for the intended patient population and clinical environment.