May 1, 2025

Cepheid
Bansari Doshi
Regulatory Affairs Specialist - New Product Development
904 Caribbean Dive
Sunnyvale, California 94089

Re: K250995
Trade/Device Name: Xpert Xpress CoV-2/Flu/RSV plus
Regulation Number: 21 CFR 866.3981
Regulation Name: Device To Detect And Identify Nucleic Acid Targets In Respiratory Specimens From Microbial Agents That Cause The SARS-CoV-2 Respiratory Infection And Other Microbial Agents When In A Multi-Target Test
Regulatory Class: Class II
Product Code: QOF
Dated: March 31, 2025
Received: April 1, 2025

Dear Bansari Doshi:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Joseph Briggs -S

Joseph Briggs, Ph.D.
Deputy Division Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K250995

Device Name
Xpert Xpress CoV-2/Flu/RSV plus

Indications for Use *(Describe)*
The Xpert Xpress CoV-2/Flu/RSV plus test, performed on the GeneXpert Xpress System, 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 test 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 the 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary
for
Xpert Xpress CoV-2/Flu/RSV *plus*

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18 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 541-4191
Contact:	Bansari Doshi, M.S.
Date of Preparation:	April 28, 2025

Device:

Trade name	Xpert® Xpress CoV-2/Flu/RSV *plus*
Common name	Xpert Xpress CoV-2/Flu/RSV *plus*
Type of Test	Qualitative real-time reverse transcription polymerase chain reaction (RT-PCR) and detection test
Regulation number Classification name Product code	21 CFR 866.3981, Multi-Target Respiratory Specimen Nucleic Acid Test Including SARS-CoV-2 and Other Microbial Agents. QOF
Secondary Product Code	OOI
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay:	Xpert Xpress CoV-2/Flu/RSV *plus* (K242071)

18.1 Device Description

The Xpert Xpress CoV-2/Flu/RSV *plus* test is an automated *in vitro* diagnostic test for the simultaneous qualitative detection and differentiation of SARS-CoV-2, Flu A, Flu B, and RSV viral RNA in nasopharyngeal swab (NPS) and anterior nasal swab (NS) specimens collected from individuals showing signs and symptoms of respiratory viral infection.

The Xpert Xpress CoV-2/Flu/RSV *plus* test is performed on GeneXpert Xpress System, which consist of a GeneXpert IV instrument that executes sample preparation, nucleic acid amplification and real-time fluorescent signal detection for the tests, and a GeneXpert Hub with preloaded GeneXpert Xpress software for running the tests and viewing the test results. The GeneXpert Hub accessory integrates the computer, touchscreen monitor and barcode scanner. Each of the GeneXpert modules in the GeneXpert IV instrument can perform independent sample preparation and testing. The GeneXpert Xpress System requires the use of single-use disposable cartridges that hold the RT-PCR reagents and host sample purification, nucleic acid amplification, and detection of the target sequences. Because the cartridges are self-contained, cross-contamination between samples is minimized.

The Xpert Xpress CoV-2/Flu/RSV *plus* test includes reagents for the detection of SARS-CoV-2, Flu A, Flu B and RSV viral RNA from NPS and NS specimens. The primers and probes in the Xpert Xpress CoV-2/Flu/RSV *plus* test are designed to amplify and detect unique sequences in the genes that encode the following proteins: SARS-CoV-2 nucleocapsid (N), SARS-CoV-2 envelope (E), SARS-CoV-2 RNA-dependent RNA polymerase (RdRP), influenza A matrix (M), influenza A basic polymerase (PB2), influenza A acidic protein (PA), influenza B matrix (M), influenza B non-structural protein (NS), and the RSV A and RSV B nucleocapsid.

A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert instrument. The SPC is present to control for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the RT-PCR reaction. The SPC also ensures that the RT-PCR reaction conditions (temperature and time) are appropriate for the amplification reaction and that the RT-PCR reagents are functional. The PCC verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring for probe integrity and dye stability.

The Xpert Xpress CoV-2/Flu/RSV *plus* test is designed for use with NPS or NS specimens collected with nylon flocked swabs and placed into viral transport medium (VTM), Universal Transport Medium (UTM), or eNAT®. The ancillary specimen collection kits, swabs and transport media validated for use with the Xpert Xpress CoV-2/Flu/RSV *plus* test included:

- **Nasopharyngeal Sample Collection Kit for Viruses**
    - Copan UTM® 3C057N (Flexible Minitip Flocked Swab with UTM® Medium without Beads)
    - Copan eNAT® Molecular Collection and Preservation Medium P/N 6U074S01 (Flexible Minitap Flocked Swab with eNAT® Medium)

- Becton Dickinson Universal Viral Transport Kit P/N 220531 (Flexible Minitip Flocked Swab with UVT Medium)

- **Nasal Sample Collection Kit for Viruses**
  - Copan UTM® 3C064N (Regular Flocked Swab with UTM® Medium without Beads)
  - Copan eNAT® Molecular Collection and Preservation Medium P/N 6U073S01 (Regular Flocked Swab with eNAT® Medium)

- **Alternatively, swabs and transport media can be obtained separately:**
  - Nylon flocked swab (Copan P/N 502CS01, 503CS01)
  - Viral Transport Medium, 3 mL (Copan P/N 330C, 3C047N, BD Universal Transport Medium, Remel M4RT, or Remel M5)

The ancillary reagents allow NPS and NS specimens from patients to be collected, preserved and transported to laboratory prior to analysis with the Xpert Xpress CoV 2/Flu/RSV *plus* test.

18.2 Device Intended Use

The Xpert® Xpress CoV-2/Flu/RSV *plus* test, performed on the GeneXpert® Xpress System, 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* test 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 the 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.

18.3 Technical Characteristics

The Xpert Xpress CoV-2/Flu/RSV *plus* test has the same technological characteristics as the predicate device.

18.4 Substantial Equivalence

The purpose of this Special 510(k) submission is to support design changes to the Xpert Xpress CoV-2/Flu/RSV *plus* test which require modifications of the parameter settings in the Assay Definition File (ADF). These modifications include turning off the Signal Loss Detection (SLD) setting for the Flu B channel and revising the result reporting algorithm for the SARS-CoV-2 only test mode.

Table 18-1 shows the similartities and **Table 18-2** shows the differences between the Xpert Xpress CoV-2/Flu/RSV *plus* test and predicate device. The differences between Xpert Xpress CoV-2/Flu/RSV *plus* test and predicate device do not raise different questions of safety and effectiveness.

Table 18-1. Similarities Between Xpert Xpress CoV-2/Flu/RSV *plus* and the Predicate Device

Similarities		
Attribute	**Subject Device**	**Predicate Device**
	Xpert® Xpress CoV-2/Flu/RSV *plus* (Modified Design)	**Xpert® Xpress CoV-2/Flu/RSV *plus* (K242071)**
Regulation	Same	**21 CFR 866.3981** Devices to detect and identify nucleic acid targets in respiratory samples from microbial agents that cause the SARS-CoV-2 respiratory infection and other microbial agents when in a multi-analyte test
Product Code	Same	QOF Multi-target respiratory specimen nucleic acid test including SARS-CoV-2 and other microbial agents
Device Class	Same	II (Special Controls)
Technology/ Detection	Same	Real-time reverse transcription polymerase chain reaction (RT-qPCR)
Intended Use	Xpert® Xpress CoV-2/Flu/RSV *plus* test, performed on the GeneXpert® Xpress 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)	Xpert® Xpress CoV-2/Flu/RSV *plus* test, performed on the GeneXpert® Xpress 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)

Similarities		
Attribute	**Subject Device**	**Predicate Device**
	Xpert® Xpress CoV-2/Flu/RSV *plus* (Modified Design)	**Xpert® Xpress CoV-2/Flu/RSV *plus* (K242071)**
	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* **test** 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.	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 treatment, or other patient management decisions.
Assay Targets	Same	SARS-CoV-2, Influenza A, Influenza B, RSV viral RNA
Specimen Type	Same	• Nasopharyngeal swab (NPS) • Anterior nasal swab (NS)
Transport Media	Same	• Universal Transport Medium (UTM) / Viral Transport Medium (VTM) • eNAT
Test Format	Same	Single Use
Automation	Same	Automated Nucleic Acid Extraction, Detection and Results Interpretation

Similarities		
Attribute	**Subject Device**	**Predicate Device**
	Xpert® Xpress CoV-2/Flu/RSV *plus* (Modified Design)	**Xpert® Xpress CoV-2/Flu/RSV *plus* (K242071)**
Combinatorial Assay Definition Files (ADFs)	Same	• Xpress SARS-CoV-2 Flu RSV plus • Xpress SARS-CoV-2 Flu plus • Xpress SARS-CoV-2 plus • Xpress Flu plus • Xpress Flu RSV plus Additionally, a video to guide user through ordering and running the test
Assay Results	Same	Qualitative
Non-Determinate Results Text	Same	NO RESULTS – REPEAT TEST INSTRUMENT ERROR
Internal Control	Same	Sample Processing Control (SPC) Probe Check Control (PCC)
Instrument Systems	Same	Cepheid GeneXpert® Xpress System
GeneXpert Software	Same	GeneXpert Xpress software
Time to Result	Same	≤ 36 min for sample preparation and RT-PCR

Table 18-2. Differences Between Xpert Xpress CoV-2/Flu/RSV *plus* and the Predicate Device

Differences		
Attribute	**Subject Device**	**Predicate Device**
	Xpert® Xpress CoV-2/Flu/RSV *plus* (Modified Design)	**Xpert® Xpress CoV-2/Flu/RSV *plus* (K242071)**
Assay Definition File	• Signal Loss Detection (SLD) Turned off in the Flu B channel	• Signal Loss Detection (SLD) Turned on in the Flu B channel
	• The rules table for Xpress SARS-CoV-2 only test mode reports a NO RESULT – REPEAT TEST GeneXpert test result if the analyte result for SARS-CoV-2 is INVALID and for SPC is FAIL (i.e., the SPC does not have a valid Ct)	• The rules table for Xpress SARS-CoV-2 only test mode reports a SARS-CoV-2 NEGATIVE GeneXpert test result if the analyte result for SARS-CoV-2 is INVALID and for SPC is FAIL (*i.e.,* the SPC does not have a valid Ct)

18.5 Summary of Performance Data

The performance of the Xpert Xpress CoV-2/Flu/RSV *plus* with the updated ADF was assessed by re-analyzing verification, validation and flex studies data from the original studies. The analytical, clinical and flex studies data generated with the original design (K242071), were reanalyzed and compared to data generated using the updated ADF with the SLD setting for the Flu B channel turned off. The comparison of 16264 test results demonstrated that the numbers of valid test runs and non-determinate (ND) test results were the same between the original ADF

and the updated ADF with Flu B SLD Off. All non-determinate GeneXpert ERROR test results with error code 5011 (SLD) were changed to NO RESULT. For the specific tests in the flex study where the Xpress SARS-CoV-2 plus only test mode of the ADF was used, the original data were reanalyzed and compared to the data generated using the updated Xpress SARS-CoV-2 plus only test mode. The comparison of 25 test results demonstrated that the number of valid test runs and ND test results were the same between the original and the updated ADF.

Additionally, a study was conducted to verify the revised algorithm for the Xpress SARS-CoV-2 plus only test mode. Test cartridges were simulated to generate SARS-CoV-2 INVALID and SPC FAIL conditions. The revised algorithm produced the expected NO RESULT – REPEAT TEST GeneXpert test results for the Xpress SARS-CoV-2 plus test mode.

The assessment of the re-analysis results determined that the performance claims of the Xpert Xpress CoV-2/Flu/RSV *plus* test were not impacted by the modifications made to the predicate device.

18.6 Conclusion

The results of the re-analysis of verification and validation studies demonstrated that the Xpert Xpress CoV-2/Flu/RSV *plus* test when performed with an updated ADF is substantially equivalent to the original design of the Xpert Xpress CoV-2/Flu/RSV *plus* (K242071, the predicate device).