April 25, 2025

Roche Molecular Systems, Inc.
Sumedha Sinha
Clinical Development Lead
4300 Hacienda Drive
Pleasanton, California 94588

Re: K243400
Trade/Device Name: cobas liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test
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: October 30, 2024
Received: October 31, 2024

Dear Sumedha Sinha:

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)*
K243400

Device Name
cobas liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test

Indications for Use *(Describe)*

The cobas liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test is an automated rapid multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus and influenza B virus nucleic acids in anterior nasal (nasal) and nasopharyngeal swab specimens from individuals exhibiting signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2 and influenza can be similar. This test is intended to aid in the differential diagnosis of SARS-CoV-2, influenza A and influenza B infections in humans and is not intended to detect influenza C virus infections.

Nucleic acids from the viral organisms identified by this test are generally detectable in nasopharyngeal and nasal swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus, and aid in diagnosis if used in conjunction with other clinical and epidemiological information and laboratory findings.

The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Positive results do not rule out coinfection with other organisms. The organism(s) detected by the cobas liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus or influenza B virus infections.

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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cobas® **liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive, Pleasanton, CA 94588-2722
Contact	Sumedha Sinha Phone: 925-366-0146 Email: sumedha.sinha@roche.com
Date Prepared	14 April 2025
Proprietary Name	**cobas**® **liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test
Common Name	**cobas**® **liat** SARS-CoV-2 & Influenza A/B v2
Classification	21 CFR 866.3981 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
Product Codes	QOF
Predicate Devices	HOLOGIC Panther Fusion® SARS-CoV-2/Flu A/B/RSV Assay (K241240)
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

The **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test is performed on the **cobas® liat** analyzer which automates and integrates sample purification, nucleic acid amplification, and detection of the target sequence in biological samples using real-time PCR assays. The assay targets both the ORF1 a/b non-structural region and membrane protein gene that are unique to SARS-CoV-2, a well-conserved region of the matrix gene of influenza A (Flu A target), and the nonstructural protein 1 (NS1) gene of influenza B (Flu B target). An Internal Control (IC) is included to control for adequate processing of the target virus through all steps of the assay process and to monitor the presence of inhibitors in the RT-PCR processes.

2. INDICATIONS FOR USE

The **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test is an automated rapid multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus and influenza B virus nucleic acids in anterior nasal (nasal) and nasopharyngeal swab specimens from individuals exhibiting signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2 and influenza can be similar. This test is intended to aid in the differential diagnosis of SARS-CoV-2, influenza A and influenza B infections in humans and is not intended to detect influenza C virus infections.

Nucleic acids from the viral organisms identified by this test are generally detectable in nasopharyngeal and nasal swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus, and aid in diagnosis if used in conjunction with other clinical and epidemiological information and laboratory findings.

The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Positive results do not rule out coinfection with other organisms. The organism(s) detected by the **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus or influenza B virus infections.

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the Roche **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of SARS-CoV-2 & Influenza A/B.

As indicated in Table 1, the Roche **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test is substantially equivalent to the identified predicate device, the cleared HOLOGIC Panther Fusion® SARS-CoV-2/Flu A/B/RSV Assay (K241240).

Table 1: Comparison of the cobas® liat SARS-CoV-2 & Influenza A/B v2 test and the Predicate Device

	Submitted Device: **cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test**	**Predicate Device:** **Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (K241240)**
Regulation Name	21 CFR 866.3981	21 CFR 866.3981
Product Code	QOF	QOF
Intended Use	The **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test is an automated rapid multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus and influenza B virus nucleic acids in anterior nasal (nasal) and nasopharyngeal swab specimens from individuals exhibiting signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2 and influenza can be similar. This test is intended to aid in the differential diagnosis of SARS-CoV-2, influenza A and influenza B infections in humans and is not intended to detect influenza C virus infections. Nucleic acids from the viral organisms identified by this test are generally detectable in nasopharyngeal and nasal swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of	The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a fully automated multiplexed real-time polymerase chain reaction (RT-PCR) in vitro diagnostic test intended for the qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (Flu A), influenza B virus (Flu B), and respiratory syncytial virus (RSV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens and anterior nasal (AN) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza, and RSV can be similar. This assay is intended to aid in the differential diagnosis of SARS-CoV-2, Flu A, Flu B, and RSV infections in humans and is not intended to detect influenza C virus infections. Nucleic acids from the viral organisms identified by this test are generally detectable in NP and AN swab specimens during the acute phase of infection. The

	Submitted Device: **cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test**	**Predicate Device:** **Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (K241240)**
	the presence of the identified virus, and aid in diagnosis if used in conjunction with other clinical and epidemiological information and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms. The organism(s) detected by the **cobas® liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus or influenza B virus infections.	detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus and aids in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms. The organism(s) detected by the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections. This assay is designed for use on the Panther Fusion system. The Hologic RespDirect Collection Kit is cleared for NP swab specimens only for testing with the Panther Fusion SARSCoV-2/Flu A/B/RSV assay.
Sample Type	Nasopharyngeal and anterior nasal swabs	Nasopharyngeal and anterior nasal swabs
Analyte	SARS-CoV-2, Flu A, Flu B RNA	SARS-CoV-2, Flu A, Flu B, RSV RNA
Ancillary Collection Kits	• Copan FLOQSwabs™ with UTM™ • BD UVT with flocked swabs • Sterile flocked swabs with a synthetic tip with other viral transport media (VTM) – Remel™M4RT, M4, M5 and M6 • 0.9% Saline	• RespDirect Swab, intended for collection of NPS specimens with UTM™/ VTM or eSTM • Enhanced Direct Load Tube (eDLT), containing enhanced specimen transport media (eSTM).
Time to result	About 15 minutes	~ 2.5 hours
Amplification Technology	Real-time PCR	Real-time PCR
Detection Chemistry	Assay using different reporter dyes for target and control	Assay using different reporter dyes for target and control
Controls Used	Sample processing control (IC), Positive and negative control	Sample processing control (IC), Positive and negative control
Instrumentation	**cobas® liat** System	Panther Fusion System

4. SPECIAL CONTROLS/STANDARDS/GUIDANCE REFERENCED

Class II Special Controls as per 21 CFR 866.3981.

5. NON-CLINICAL PERFORMANCE EVALUATION

5.1. Analytical sensitivity (Limit of Detection)

Limit of detection (LoD) studies determine the lowest detectable concentration of SARS-CoV-2, influenza A, and influenza B at which equal to or greater than 95% of all replicates test positive.

Two strains for each target (SARS-CoV-2, influenza A, influenza B) were evaluated. To determine the LoD for each target, co-spiked panels were formulated using cultured or inactivated viral material diluted in pooled negative nasopharyngeal swab matrix. Twenty-one replicates per lot of assay tubes per dilution were tested for five or six 2-fold dilutions using three lots of assay tubes. Each strain evaluated as well as the corresponding LoD are shown in Table 2.

Table 2: LoD determination for SARS-CoV-2, influenza A & influenza B strains

Virus	Strain	Concentration at LoD	Hit rate (Mean Ct)
SARS-CoV-2*	USA-WA1/2020	0.0350 $TCID_{50}$/mL	20/21 (35.5)
SARS-CoV-2*	WHO International Standard 20/146, v3, 11/2021	65.1 IU/mL	21/21 (34.9)
Influenza A	Darwin/6/2021	0.295 $TCID_{50}$/mL	21/21 (35.0)
Influenza A	Brisbane/02/2018	0.00325 $TCID_{50}$/mL	21/21 (36.4)
Influenza B	B/Austria/1359417/2021	0.979 $TCID_{50}$/mL	20/21 (34.6)
Influenza B	Phuket/3073/2013	0.183 $TCID_{50}$/mL	21/21 (34.1)

* Inactivated virus

A separate study was performed to demonstrate that the LoD of each strain individually was equivalent to the co-spiked LoD.

5.2. Reactivity/Inclusivity

The inclusivity study evaluates the ability of the test to detect SARS-CoV-2, influenza A and influenza B isolates/variants. The reactivity/inclusivity was evaluated with 10 SARS-CoV-2, 28 influenza A (15 H1N1 & 10 H3N2, 1 H5N1, 1 H5N2 and 1 H7N9), and ten (10) influenza B (5 Victoria and 5 Yamagata) variants. All strains were individually tested at 3x LoD in 3 replicates

to evaluate inclusivity. If < 100% hit rate was observed, the concentration was doubled until 3/3 replicates were detected.

SARS-CoV-2

The SARS-CoV-2 isolates/variants were tested as inactivated viruses in the study and the lowest concentrations detected are listed in Table 3.

In silico analysis on January 15, 2025 indicates 99.9% detection of all available SARS-CoV-2 sequences in the GISAID (>7.94M sequences) and NCBI (>15.04M sequences) databases.

Table 3: Results of Testing SARS-CoV-2 Isolate/Variants

Lineage/Subtype*	Isolate/Variant	Test Concentration ($TCID_{50}$/mL)	Relative to LoD
Alpha	Hong Kong/VM20001061/2020	0.105	3x
Beta, B.1.595_2020 (was B.1.2)	NY-Wadsworth-33126-01/2020	0.105	3x
Delta, B.1.617.2	USA/MD-HP05285/2021	0.105	3x
Epsilon, B.1.427	USA/CA/VRLC009/2021	0.105	3x
Gamma, P.1	Japan/TY7-503/2021	0.105	3x
Iota, B.1.526_2021	USA/NY-Wadsworth-21025952-01/2021	0.105	3x
Kappa, B.1.617.1	USA/CA-Stanford-15_S02/2021	0.105	3x
Omicron, B.1.1.529, CH.1.1	USA/MD-HP41275/2022	0.105	3x
Omicron, B.1.1.529, XBB.1.5	USA/MD-HP40900/2022	0.105	3x
Zeta, P2_2021	USA/NY-Wadsworth-21006055-01/2021	0.105	3x

*These strains are in addition to the SARS-CoV-2 USA-WA1/2020 and WHO Standard 20/146, v3, 11/2021 used in the analytical sensitivity study.

Influenza A

The influenza A isolates/variants tested in the study and the lowest concentrations detected are listed in Table 4.

Table 4: Results of Testing Influenza A Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL) [ä]	Relative to LoD
H1N1	A/Brisbane/59/07	0.885	3x

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL) [ä]	Relative to LoD
H1N1	A/Christ Church/16/2020	1.77 EID_{50}/mL	6x
H1N1	A/Denver/01/57	0.885	3x
H1N1	England/221740513/2022**	75 copies/mL [‡]	1x
H1N1	A England/224020815/2022**	91.5 copies/mL [‡]	1x
H1N1	A/Fort Monmouth/01/47	0.885	3x
H1N1	A/Malaya/302/54	0.885	3x
H1N1	A/New Caledonia/20/99	0.885	3x
H1N1	A/Swine/Iowa/15/30	1.77 $CEID_{50}$/mL	6x
H1N1	A/Sydney/5/2021[β]	1.77	6x
H1N1	A/Victoria/2570/2019	3.54 EID_{50}/mL	12x
H1N1	A/WS/33	0.885	3x
H1N1	A/Brisbane/14/2023	75 copies/mL [‡]	1x
H1N1	A/Townsville/1A/2023	75 copies/mL [‡]	1x
H1N1	A/ Townsville/2A/2023	75 copies/mL [‡]	1x
H3N2	A/Aichi/2/68	0.885 $CEID_{50}$/mL	3x
H3N2	A/Brisbane/10/07	0.885	3x
H3N2	A/Cambodia/E0826360/2020	0.885	3x
H3N2	A/Darwin/9/2021	1.77	6x
H3N2	A/Hong Kong/8/68	0.885	3x
H3N2	A/H3/Perth/16/09	0.885	3x
H3N2	A/Tasmania/503/2020	0.885 EID_{50}/mL	3x
H3N2	A/Victoria/3/75	0.885 $CEID_{50}$/mL	3x
H3N2	A/Wisconsin/67/2005	0.885	3x
H3N2	A/Singapore/INFIMH-16-0019/2016	0.885	3x
H5N1	A/mallard/Wisconsin/2576/2009	0.885 $CEID_{50}$/mL	3x
H5N2	A/ruddy turnstone/New Jersey/828212/2001	0.885 $CEID_{50}$/mL	3x
H7N9	A/northern shoveler/ Mississippi/ 11OS145/2011	3.54 $CEID_{50}$/mL	12x

*These strains are in addition to the influenza A Darwin/6/2021 and Brisbane/02/2018 strains used in the analytical sensitivity study.

**A/England/221740513/2022 GISAID ID is EPI_ISL_14387941 and for A/England/224020815/2022 GISAID ID is EPI_ISL_15803829.

[‡] The concentrations tested are near the 1x LOD value (69 copies/mL) determined by digital PCR for the influenza A/Darwin/6/2021 strain in Table 8.

[ä] Concentrations are shown in $TCID_{50}$/mL unless otherwise indicated.

[β] Inactivated virus

Influenza B

The influenza B isolates/variants tested in the study and the lowest concentrations detected are listed in Table 5.

Table 5: Results of Testing Influenza B Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL) [ä]	Relative to LoD
Victoria	B/Brisbane/60/2008	2.937	3x
Victoria	B/Colorado/06/2017	2.937	3x
Victoria	B/Malaysia/2506/04	2.937	3x
Victoria	B/Michigan/09/2011	2.937 EID_{50}/mL	3x
Victoria	B/Washington/02/2019	2.937	3x
Yamagata	B/Florida/04/06	2.937	3x
Yamagata	B/Massachusetts/2/2012	2.937	3x
Yamagata	B/Texas/6/2011	2.937	3x
Yamagata	B/Texas/81/2016	2.937 EID_{50}/mL	3x
Yamagata	B/Wisconsin/1/2010	2.937	3x

*These strains are in addition to the influenza B Austria/1359417/2021 and Phuket/3073/2013 strains used in the analytical sensitivity study.

[ä] Concentrations are shown in $TCID_{50}$/mL unless otherwise indicated.

5.3. Cross reactivity and microbial interference

Cross-reactivity and microbial interference were evaluated by testing a panel of microorganisms (Table 6). High titer stocks of the potentially cross-reacting microorganisms were tested for cross-reactivity, and also in the presence of SARS-CoV-2, influenza A and influenza B at 3x LoD concentrations for microbial interference. Three (3) replicates in target negative background and three (3) replicates in target positive background were tested for each non-target microorganism. The testing concentrations for potentially interfering viruses are ≥1.0E+05 units/mL except for three viruses (SARS Coronavirus, Urbani, Human Rhinovirus Type 1A, and Human Parainfluenza Virus Type 4A) which were tested at a concentration less than 1.0e+5, but higher than 1.0e+4 units/mL due to their low stock concentration. Other microorganisms (non virus) were tested at ≥1.0E+06 units/mL. Clinical specimens containing Human Coronavirus HKU1 and *Pneumocystis jirovecii* were also tested (concentration was unknown). None of the organisms tested cross reacted or interfered with **cobas® liat** SARS-CoV-2 & Influenza A/B v2 performance at the concentrations tested.

Table 6: Microorganisms tested for cross-reactivity and microbial interference

Adenovirus Type 1 [β]	MERS-Coronavirus [β]	*Mycobacterium tuberculosis*
Adenovirus Type 7	Measles	*Mycoplasma genitalium* [β]
Cytomegalovirus	Mumps	*Mycoplasma pneumoniae*
Epstein-Barr virus [β]	RSV (Long/Subtype A)	*Neisseria elongata*
Human Coronavirus OC43	RSV (9320/Subtype B)	*Neisseria flava*
Human Coronavirus 229E	SARS Coronavirus, Urbani* [β]	*Neisseria meningitidis*
Human Coronavirus HKU [ł]	*Bordetella parapertussis*	*Pneumocystis jirovecii* [ł]
Human Coronavirus NL63 [β]	*Bordetella pertussis*	*Pseudomonas aeruginosa*
Human Enterovirus 68	*Chlamydophila pneumoniae*	*Staphylococcus aureus*
Human Metapneumovirus 27	*Corynebacterium flavescens*	*Staphylococcus epidermidis*
Human Parainfluenza Virus Type 1 [β]	*Escherichia coli*	*Streptococcus pneumoniae*
Human Parainfluenza Virus Type 2	*Fusobacterium necrophorum subsp. necrophorum*	*Streptococcus pyogenes*
Human Parainfluenza Virus Type 3	*Haemophilus influenzae*	*Streptococcus salivarius*
Human Parainfluenza Virus Type 4A* [β]	*Lactobacillus crispatus*	*Aspergillus flavus var. flavus*
Human Rhinovirus Type 1A* [β]	*Legionella pneumophila*	*Candida albicans*
Human Rhinovirus B	*Moraxella catarrhalis*	-

* Tested at highest concentration available

[β] Inactivated virus

[ł] Clinical specimens at unknown concentrations were tested.

5.4. Competitive inhibition

To assess competitive inhibition between SARS-CoV-2, influenza A and influenza B, each target prepared at high concentration with the other targets at low concentrations (approximately three times the respective LoD) was tested to evaluate any potential impact by the high concentration target on the detection of the other targets (Table 7). Five (5) replicates were tested for each concentration combination.

Testing results indicated that when one viral target was present at high concentration, no interference was observed for the other viral targets that were present at low concentrations (~3x LoD).

Table 7: Competitive inhibition strains and concentrations tested with the cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test

Assay Target	Strain	3x LoD Concentration ($TCID_{50}$/mL)	High Concentration Used in Combination with other Low Concentration Targets ($TCID_{50}$/mL)
SARS-CoV-2*	SARS WA 1/2020	0.105	1.14E+05
Influenza A	A/Darwin/6/2021	0.885	1.48E+06
Influenza B	B/Austria/1359417/2021	2.937	9.79E+06

***** Inactivated virus

5.5. Endogenous and exogenous interference

Potentially interfering substances that may be commonly encountered in respiratory specimens were evaluated. Each substance was tested, by introducing potential interferents. Five (5) replicates were tested with and five (5) replicates were tested without 3x LoD SARS-CoV-2, influenza A and influenza B targets. The substances listed in Table 8 at the concentrations tested did not interfere with the detection of SARS-CoV-2, influenza A or influenza B nor did they produce invalid results in negative samples.

Table 8: Endogenous and Exogenous Interference

Potential Interferent	Concentration Tested
Peripheral blood mononuclear cell (PBMC)	1.00E+06 cell/mL
Mucin: bovine submaxillary gland, type I-S	5 mg/mL
Human Whole Blood	5% v/v
Nasal spray - Afrin / Anefrin	15% v/v
Nasal corticosteroids - Flonase	5% (v/v)
Nasal gel - Zicam	5% (v/v)
Throat lozenges, oral anesthetic and analgesic – Cepacol**	5 mg/mL
Antibiotic, nasal ointment - Bactroban mupirocin ointment	5 mg/mL
Antiviral drug – Relenza	5 mg/mL
Antiviral drug - Tamiflu	7.5 mg/mL
Antimicrobial, systemic- Tobramycin	4 µg/mL
Intranasal Vaccine – FluMist*	6.25% (v/v)

*FluMist® contains influenza A and B virus and will test positive if present in the sample. See Procedural limitations.

**One invalid result was obtained in the presence of target analytes. Repeat testing was performed and all targets were detected. The one invalid result was most likely caused by other factors such as general tube processing error, lot variation, etc. that are not related to the interference test condition.

5.6. Reproducibility study

A reproducibility study assessed the total variability of the assay in detecting SARS-CoV-2, influenza A and influenza B across operators, study sites, testing days, analyzers, and assay tube lots. The reproducibility was evaluated at three (3) study sites representative of intended use settings. Two (2) operators at each of the three sites tested a 3-member reproducibility panel in triplicate on five different days for three assay tube lots. The reproducibility panel comprises a low positive (1-2x LoD) and a moderate positive (3-5x LoD) co-formulated for SARS-CoV-2, influenza A and influenza B in addition to negative samples. The expected result for the true negative panel member is "Not Detected," while the expected result for the low positive and moderate positive panel members is "Detected." Percent agreement with expected result is shown in Table 9.

Table 9: Reproducibility Results for the cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test

Target Analyte	Expected Panel Member Concentration	Valid Tests (N)	Results in Agreement with Target Analyte (n)	Percent Agreement n/N x 100	95% Score CI
Negative	0	265	265	100.0	(98.6, 100.0)
SARS-CoV-2	1x-2x LoD	270	270	100.0	(98.6, 100.0)
SARS-CoV-2	3x-5x LoD	267	267	100.0	(98.6, 100.0)
Influenza A	1x-2x LoD	269	268	99.6	(97.9, 99.9)
Influenza A	3x-5x LoD	267	267	100.0	(98.6, 100.0)
Influenza B	1x-2x LoD	269	268	99.6	(97.9, 99.9)
Influenza B	3x-5x LoD	267	267	100.0	(98.6, 100.0)

Note: Results were in agreement when a positive panel member had a valid result of "Detected" for the analyte or when the negative panel member had a valid result of "Not Detected" for the analyte.

The means, standard deviations, and coefficients of variation (%) for cycle threshold (Ct) values by target analyte and expected concentration (Positive Panel Members) are shown in Table 10.

Table 10: Overall Mean Estimate, Standard Deviations, and Coefficients of Variation (%) for Cycle Threshold Values by Target Analyte and Expected Concentration (Positive Panel Members) for the cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test

Target Analyte	Expect-ed Concen-tration	n/N[a]	Mean Ct	Site SD	Site CV%	Lot SD	Lot CV %	Day SD	Day CV %	Run SD[b]	Run CV%	Within-Run (Residu-al) SD	Within-Run (Resid u-al) CV%	Total SD	Total CV%
SARS-CoV-2	1x-2x LoD	270/270	33.8	0.00	0.0	0.38	1.1	0.17	0.5	0.36	1.1	1.03	3.0	1.16	3.4
SARS-CoV-2	3x-5x LoD	267/267	32.4	0.13	0.4	0.54	1.7	0.27	0.8	0.00	0.0	1.00	3.1	1.18	3.6
Influenza A	1x-2x LoD	268/269	34.8	0.11	0.3	0.08	0.2	0.13	0.4	0.00	0.0	0.62	1.8	0.65	1.9
Influenza A	3x-5x LoD	267/267	33.8	0.00	0.0	0.05	0.2	0.00	0.0	0.11	0.3	0.39	1.2	0.41	1.2
Influenza B	1x-2x LoD	268/269	33.8	0.04	0.1	0.29	0.9	0.00	0.0	0.13	0.4	0.66	2.0	0.73	2.2
Influenza B	3x-5x LoD	267/267	32.8	0.05	0.2	0.47	1.4	0.12	0.4	0.00	0.0	0.52	1.6	0.71	2.2

Note: Ct = cycle threshold; LoD = Limit of Detection; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; SD = standard deviation; CV% = percent coefficient of variation.

[a] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member by target analyte.

[b] In the reproducibility study, each panel member was tested in triplicate, defining one run.

6. CLINICAL PERFORMANCE EVALUATION

6.1. Prospective Study

The clinical performance of **cobas® liat** SARS-CoV-2 & Influenza A/B v2 for the detection of SARS-CoV-2, influenza A and influenza B was evaluated using paired prospective fresh nasopharyngeal swab (NPS) and anterior nasal swab (ANS) specimens collected in Universal Viral Transport medium (UVT) or Universal Transport Medium (UTM) from individuals with signs and symptoms of respiratory viral infection. For prospectively enrolled subjects an NPS specimen was collected from each subject along with either a self-collected or a healthcare-provider collected ANS specimen. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were determined by comparing the results of **cobas® liat** SARS-CoV-2 & Influenza A/B v2 to the results of an FDA-cleared Nucleic Acid Amplification Test (NAAT).

Prospective clinical (Category I) specimens were collected and tested in a non-interventional study between September 2023 and March 2024 at 14 point of care testing sites in the United States (US). Of the 1729 prospective symptomatic subjects enrolled, 1705 NPS specimens were evaluable for analyses, 19 were non-evaluable due to missing or invalid **cobas® liat** test results, and 5 were non-evaluable due to specimen handling issues. Of the 1729 prospective symptomatic subjects enrolled, 1706 ANS specimens were evaluable in the SARS-CoV-2 and influenza B analyses, 22 were non-evaluable due to missing or invalid **cobas® liat** test results, and 1 was non-evaluable due to specimen handling issues. Two (2) additional ANS specimens obtained inconclusive comparator results for influenza A, leaving 1704 ANS specimens in the influenza A analysis. Available demographic data regarding the individuals from whom specimens were obtained are presented in Table 11.

Table 11: Demographics of Prospectively Enrolled Individuals

Characteristics	Overall N(%) (N=1729)
Sex at Birth	-
Male	681 (39.4%)
Female	1048 (60.6%)
Age Group (Years)	-
<1	33 (1.9%)
1 - <18	434 (25.1%)
18 - <30	381 (22.0%)
30 - <40	246 (14.2%)
40 - <50	200 (11.6%)
50 - <60	181 (10.5%)
>=60	254 (14.7%)
Ethnicity	-
Hispanic / Latino	244 (14.1%)
Not Hispanic / Latino	1478 (85.5%)
Not Reported	4 (0.2%)
Unknown	3 (0.2%)
Race	-
American Indian / Alaska Native	8 (0.5%)
Asian	24 (1.4%)
Black / African American	212 (12.3%)
Native Hawaiian / Other Pacific Islander	3 (0.2%)
White	1413 (81.7%)

Characteristics	Overall N(%) (N=1729)
Other Race	52 (3.0%)
Not Reported	17 (1.0%)

For the NPS specimens , **cobas® liat** SARS-CoV-2 & Influenza A/B v2 demonstrated a PPA and NPA of 94.5% and 97.6% for SARS-CoV-2, respectively; 100.0% and 99.3% for influenza A, respectively; 100.0% and 99.3% for influenza B, respectively (Table 12)). For the ANS specimens, **cobas® liat** SARS-CoV-2 & Influenza A/B v2 demonstrated a PPA and NPA of 96.7% and 97.2% for SARS-CoV-2, respectively; 100.0% and 99.3% for influenza A, respectively; 100.0% and 99.5% for influenza B, respectively (Table 12). The initial invalid rate of **cobas® liat** SARS-CoV-2 & Influenza A/B v2 on NPS and ANS specimens was 0.5% and 0.7% respectively. Upon repeat testing, the final assay invalid rate on NPS and ANS specimens was 0% and 0.1% respectively.

Table 12: Clinical Performance of cobas® liat SARS-CoV-2 & Influenza A/B v2 relative to the comparator by Specimen Type and Target

Target	Specimen Type	a/ (a+c)	PPA (%)	PPA 95% CI	d/ (b+d)	NPA (%)	NPA 95% CI
SARS-CoV-2*	NPS	207/219	94.5	90.7-96.8	1451/1486	97.6	96.7-98.3
SARS-CoV-2**	ANS	208/215	96.7	93.4-98.4	1449/1491	97.2	96.2-97.9
Influenza A#	NPS	54/54	100.0	93.4-100.0	1640/1651	99.3	98.8-99.6
Influenza A##	ANS	53/53	100.0	93.2-100.0	1640/1651	99.3	98.8-99.6
Influenza B&	NPS	22/22	100.0	85.1-100.0	1671/1683	99.3	98.8-99.6
Influenza B&&	ANS	24/24	100.0	86.2-100.0	1673/1682	99.5	99.0-99.7

Abbreviations: PPA = Positive Percent Agreement; CI = Confidence Interval; NPA = Negative Percent Agreement; NPS = Nasopharyngeal swab; ANS = Anterior Nasal Swab; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2.

Note: N = Total number of specimens; a = number of specimens where both **cobas® liat** and the comparator are positive; b = number of specimens where **cobas® liat** is positive and the comparator is negative; c = number of specimens where **cobas® liat** is negative and the comparator is positive; d = number of specimens where both **cobas® liat** and the comparator are negative.

* SARS-CoV-2 NPS discrepant NAAT results: Of 12 specimens negative on **cobas® liat** and positive on the comparator, 8 were positive and 4 were negative. Of 35 specimens positive on **cobas® liat** and negative on the comparator, 12 were positive and 23 were negative .

Influenza A NPS discrepant NAAT results: Of 11 specimens positive on **cobas® liat** and negative on the comparator, 2 were positive and 9 were negative.

& Influenza B NPS discrepant NAAT results: Of 12 specimens positive on **cobas® liat** and negative on the comparator, all 12 were negative.

** SARS-CoV-2 ANS discrepant NAAT results: Of 7 specimens negative on **cobas® liat** and positive on the comparator, 6 were positive and 1 was negative. Of 42 specimens positive on **cobas® liat** and negative on the comparator, 8 were positive and 34 were negative.

Target	Specimen Type	a/ (a+c)	PPA (%)	PPA 95% CI	d/ (b+d)	NPA (%)	NPA 95% CI

[##] Influenza A ANS discrepant NAAT results: Of 11 specimens positive on **cobas® liat** and negative on the comparator, 1 was positive and 10 were negative.
[&&] Influenza B ANS discrepant NAAT results: Of 9 specimens positive on **cobas® liat** and negative on the comparator, all 9 were negative.

6.2. Retrospective Study

Influenza B was of lower prevalence and was not encountered in sufficiently large numbers during the prospective clinical study to adequately demonstrate assay performance. To supplement the results of the prospective clinical study, retrospective frozen clinical NPS and ANS specimens collected in Universal Viral Transport medium (UVT) or Universal Transport Medium (UTM) from individuals with signs and symptoms of respiratory viral infection were tested. Frozen archived (Category III) influenza B positive and negative NPS (n=223) and ANS (n=206) specimens obtained between 2019 and 2023 were distributed to 6 sites and tested in the course of the daily workflow. One NPS sample pre-characterized as positive for influenza B was non-evaluable due to missing/invalid results on the comparator method. The comparator method was an acceptable FDA-cleared molecular assay. Available demographic data regarding the individuals from the retrospective study are shown in Table 13.

Table 13: Demographics of Subjects from Retrospective Population

Characteristics	Overall N(%) (N=429)
Sex at Birth	-
Male	151 (35.20%)
Female	226 (52.68%)
Not Reported	52 (12.12%)
Age Group (Years)	-
<1	0 (0.00%)
1 - <18	129 (30.07%)
18 - <30	77 (17.95%)
30 - <40	79 (18.41%)
40 - <50	28 (6.53%)
50 - <60	14 (3.26%)
>=60	23 (5.36%)
Not Reported	79 (18.41%)
Ethnicity	-
Hispanic / Latino	98 (22.84%)

Characteristics	Overall N(%) (N=429)
Not Hispanic / Latino	112 (26.11%)
Not Reported	213 (49.65%)
Other	5 (1.17%)
Unknown	1 (0.23%)
Race	-
American Indian / Alaska Native	2 (0.47%)
Asian	3 (0.70%)
Black / African American	12 (2.80%)
White	196 (45.69%)
Other Race	3 (0.70%)
Unknown	5 (1.17%)
Not Reported	208 (48.48%)

For the retrospective NPS specimens, **cobas® liat** SARS-CoV-2 & Influenza A/B v2 demonstrated a PPA and NPA of 100.0% and 97.9% for influenza B, respectively (Table 14). For the retrospective ANS specimens, **cobas® liat** SARS-CoV-2 & Influenza A/B v2 demonstrated a PPA and NPA of 100.0% and 98.3% for influenza B, respectively (Table 14). No invalid results were observed for the **cobas® liat** SARS-CoV-2 & Influenza A/B v2 with retrospective NPS or ANS specimens for an invalid rate of 0.0%.

Table 14: Agreement of cobas® liat SARS-CoV-2 & Influenza A/B v2 nucleic acid test and Comparator Test for influenza B in Retrospective Samples

Target	Specimen Type	a/(a+c)	PPA (%)	PPA 95% CI	d/(b+d)	NPA (%)	NPA 95% CI
Influenza B*	NPS	34/34	100.0	89.8-100.0	184/188	97.9	94.7-99.2
Influenza B**	ANS	34/34	100.0	89.8-100.0	169/172	98.3	95.0-99.4

Abbreviations: PPA = Positive Percent Agreement; CI = Confidence Interval; NPA = Negative Percent Agreement; NPS = Nasopharyngeal swab; ANS = Anterior Nasal Swab; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2.

Note: N = Total number of specimens; a = number of specimens where both **cobas® liat** and the comparator are positive; b = number of specimens where **cobas® liat** is positive and the comparator is negative; c = number of specimens where **cobas® liat** is negative and the comparator is positive; d = number of specimens where both **cobas® liat** and the comparator are negative.

* Influenza B NPS discrepant NAAT results: Of 4 specimens positive on **cobas® liat** and negative on the comparator, all 4 were negative.

** Influenza B ANS discrepant NAAT results: Of 3 specimens positive on **cobas® liat** and negative on the comparator, 1 was positive and 2 were negative.

7. CONCLUSIONS

A comparison of the intended use, technological characteristics, and the results of non-clinical analytical and clinical performance studies demonstrate that **cobas**® **liat** SARS-CoV-2 & Influenza A/B v2 nucleic acid test is **substantially equivalent** to the predicate device.