



December 4, 2023

Roche Molecular Systems, Inc.
Alicja Stradomska
Regulatory Affairs Specialist
4300 Hacienda Drive
Pleasanton, California 94588-2722

Re: K223783

Trade/Device Name: cobas SARS-CoV-2 Nucleic acid test for use on the cobas Liat System

Regulation Number: 21 CFR 866.3982

Regulation Name: Simple Point-Of-Care Device To Detect Sar-Cov-2 Nucleic Acid Targets From
Clinical Specimens In Near-Patient Settings

Regulatory Class: Class II

Product Code: QWR

Dated: September 1, 2023

Received: September 1, 2023

Dear Alicja Stradomska:

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.

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.

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,

Himani Bisht -S

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
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OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K223783

Device Name
cobas SARS-CoV-2 Nucleic acid test for use on the cobas Liat System

Indications for Use (Describe)

The cobas SARS-CoV-2 Nucleic acid test for use on the cobas Liat System (cobas SARS-CoV-2) is an automated, real-time reverse transcriptase polymerase chain reaction (RT-PCR) test intended for the rapid in vitro qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in anterior nasal (nasal) and nasopharyngeal swab specimens collected from individuals with signs and symptoms of respiratory tract infection (i.e., symptomatic). Additionally, this test is intended to be used with nasal and nasopharyngeal swab specimens collected from individuals without signs and symptoms suspected of COVID-19 (i.e., asymptomatic).

The cobas SARS-CoV-2 performed on the cobas Liat System is intended for use as an aid in the diagnosis of COVID-19 if used in conjunction with other clinical, epidemiologic, and laboratory findings. SARS-CoV-2 RNA is generally detectable in nasal and nasopharyngeal swab specimens during the acute phase of infection.

Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not rule out co-infection with other microorganisms.

A negative result from an asymptomatic individual is presumptive. Additionally, a negative result obtained with a nasal swab collected from an asymptomatic patient should be followed up by testing at least twice over three days with at least 48 hours between tests.

Negative results do not preclude SARS-CoV-2 infection.

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

This test is intended for prescription use only and can be used in Point-of-Care settings.

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[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System

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, USA
Contact	Dr. Alicja Stradowska Phone: (+41) 795-177-052 Email: alicja.stradowska@roche.com
Date Prepared	December 1, 2023
Proprietary Name	cobas[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System
Common Name	cobas[®] SARS-CoV-2
Classification Name	Simple Point-of-Care Device to Detect SARS-CoV-2 Nucleic Acid Targets from Clinical Specimens in Near-Patient Settings
Regulation Number	21 CFR 866.3982
Predicate Devices	ID NOW COVID-19 2.0 (K221925)
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

The **cobas[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System (cobas[®] SARS-CoV-2)** uses real-time reverse transcriptase polymerase chain reaction (RT-PCR) technology to rapidly (approximately 20 minutes) detect SARS-CoV-2 virus from nasopharyngeal and nasal swabs. The automation, small footprint, and easy-to-use interface of the **cobas[®] Liat[®] System** enable performance of this test to occur at the POC or in a clinical laboratory setting.

1.1. Principles of the procedure

The **cobas[®] SARS-CoV-2** assay 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 RT-PCR assays. The assay targets both the ORF1 a/b non-structural region and nucleocapsid protein gene that are unique to SARS-CoV-2. An Internal Process

Control (IPC) is also included. The IPC is present to control for adequate processing of the target virus through steps of sample purification, nucleic acid amplification, and to monitor the presence of inhibitors in the RT-PCR processes.

2. INDICATIONS FOR USE

The **cobas**[®] SARS-CoV-2 Nucleic acid test for use on the **cobas**[®] Liat[®] System (**cobas**[®] SARS-CoV-2) is an automated, real-time reverse transcriptase polymerase chain reaction (RT-PCR) test intended for the rapid in vitro qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in anterior nasal (nasal) and nasopharyngeal swab specimens collected from individuals with signs and symptoms of respiratory tract infection (i.e., symptomatic). Additionally, this test is intended to be used with nasal and nasopharyngeal swab specimens collected from individuals without signs and symptoms suspected of COVID-19 (i.e., asymptomatic).

The **cobas**[®] SARS-CoV-2 performed on the **cobas**[®] Liat[®] System is intended for use as an aid in the diagnosis of COVID-19 if used in conjunction with other clinical, epidemiologic, and laboratory findings. SARS-CoV-2 RNA is generally detectable in nasal and nasopharyngeal swab specimens during the acute phase of infection.

Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not rule out co-infection with other microorganisms.

A negative result from an asymptomatic individual is presumptive. Additionally, a negative result obtained with a nasal swab collected from an asymptomatic patient should be followed up by testing at least twice over three days with at least 48 hours between tests.

Negative results do not preclude SARS-CoV-2 infection.

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

This test is intended for prescription use only and can be used in Point-of-Care settings.

3. TECHNOLOGICAL CHARACTERISTICS

The **cobas**[®] SARS CoV-2 Nucleic acid test for use on the **cobas**[®] Liat[®] System is substantially equivalent to another legally marketed POC test intended for the qualitative detection of SARS-CoV-2 (K221925) as indicated in Table 1.

Table 1: Comparison of the cobas[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System and the predicate device

	Submitted Device: cobas[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System	Predicate Device: ID NOW COVID-19 2.0 (K221925)
Regulation Name	21 CFR 866.3982	21 CFR 866.3982
Product Code	QWR	Same
Intended Use	<p>The cobas[®] SARS-CoV-2 Nucleic acid test for use on the cobas[®] Liat[®] System (cobas[®] SARS-CoV-2) is an automated, real-time reverse transcriptase polymerase chain reaction (RT-PCR) test intended for the rapid <i>in vitro</i> qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in anterior nasal (nasal) and nasopharyngeal swab specimens collected from individuals with signs and symptoms of respiratory tract infection (i.e., symptomatic). Additionally, this test is intended to be used with nasal and nasopharyngeal swab specimens collected from individuals without signs and symptoms suspected of COVID-19 (i.e., asymptomatic).</p> <p>The cobas[®] SARS-CoV-2 performed on the cobas[®] Liat[®] System is intended for use as an aid in the diagnosis of COVID-19 if used in conjunction with other clinical, epidemiologic, and laboratory findings. SARS-CoV-2 RNA is generally detectable in nasal and nasopharyngeal swab specimens during the acute phase of infection.</p> <p>Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not rule out co-infection with other microorganisms.</p> <p>A negative result from an asymptomatic individual is presumptive. Additionally, a negative result obtained with a nasal swab collected from an asymptomatic patient should be followed up by testing at least twice over three days with at least 48 hours between tests.</p> <p>Negative results do not preclude SARS-CoV-2 infection.</p> <p>The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.</p> <p>This test is intended for prescription use only and can be used in Point-of-Care settings.</p>	<p>ID NOW COVID-19 2.0 performed on the ID NOW Instrument is a rapid molecular <i>in vitro</i> diagnostic test utilizing an isothermal nucleic acid amplification technology (NAAT) intended for the qualitative detection of nucleic acid from SARS-CoV-2 in direct anterior nasal (nasal) or nasopharyngeal swabs from individuals with signs and symptoms of respiratory tract infection. ID NOW COVID-19 2.0 performed on the ID NOW Instrument is intended for use as an aid in the diagnosis of COVID-19 if used in conjunction with other clinical, epidemiologic, and laboratory findings. SARS-CoV-2 RNA is generally detectable in nasal and nasopharyngeal swab specimens during the acute phase of infection.</p> <p>Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not preclude co-infection with bacteria or other viruses and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.</p> <p>A negative test result is presumptive, and it is recommended these results be confirmed by another molecular SARS-CoV-2 assay. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. This test is intended for prescription use only and can be used in Point-of-Care settings.</p>

	Submitted Device: cobas® SARS-CoV-2 Nucleic acid test for use on the cobas® Liat® System	Predicate Device: ID NOW COVID-19 2.0 (K221925)
Sample Types	Healthcare provider-collected nasopharyngeal and nasal swabs, and self-collected nasal swabs	Nasal or nasopharyngeal swab
Analyte Targets	<ul style="list-style-type: none"> • SARS-CoV-2 ORF1 a/b non-structural region • SARS-CoV-2 nucleocapsid protein gene 	RdRp gene of SARS-CoV-2 RNA
Ancillary Collection Kits	<ul style="list-style-type: none"> • Copan FLOQSwabs™ with UTM™, UVT and other swabs with other viral transport media (VTM) e.g., M4RT, M4, M5 and M6 • 0.9% and 0.85% Saline 	UTM
Sample Preparation	Automated	Same
Amplification Technology	Real-time PCR for detecting the presence/absence of viral RNA in clinical specimens	Isothermal nucleic acid amplification for detecting the presence/absence of viral RNA in clinical specimens
Detection Chemistry	Assay using different reporter dyes for target and Internal Control	Fluorescently labeled molecular beacon probes
Controls Used	<ul style="list-style-type: none"> • Internal Control (a process control for sample purification, nucleic acid amplification, and monitoring presence of inhibitors) • External Positive and Negative Controls 	<ul style="list-style-type: none"> • Internal Control (verifying assay reagents) • External Positive and Negative Controls
Result Interpretation	Automated	Same

4. SPECIAL CONTROLS/STANDARDS/GUIDANCE REFERENCED

Class II Special Controls as per 21 CFR 866.3982.

5. NON-CLINICAL PERFORMANCE EVALUATION

5.1.1. Analytical sensitivity (Limit of detection)

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

5.1.1.1. SARS-CoV-2 viral culture

To determine the LoD for SARS-CoV-2, a heat inactivated cultured virus of an isolate from a US patient (USA-WA1/2020, lot number 324047, ZeptoMetrix, NY, USA) was serially diluted in pooled negative nasopharyngeal swab matrix. Five concentration levels were tested with 20 replicates

except for the highest concentration level, which was tested with 10 replicates. Three lots of assay tubes (approximately equal numbers of replicates per lot) and two independent dilution series (equal numbers of replicates per dilution series) were used in the study.

As shown in Table 2, the lowest concentration level with observed hit rates greater than or equal to 95% was 0.012 TCID₅₀/mL (12 copies/mL) for SARS-CoV-2.

Table 2 LoD determination using USA-WA1/2020 strain

Strain - USA-WA1/2020 (stock concentration 3.16E+06 TCID₅₀/mL)

Concentration [TCID ₅₀ /mL]	Concentration [copies/mL]*	Total valid results	Hit rate [%]	Mean Ct**
0.048	49	10	100	33.0
0.024	24	20	100	33.6
0.012	12	20	95	34.7
0.006	6	20	90	35.4
0.003	3	20	55	35.5

*Concentration of each viral stock in copies/mL was quantified using Reverse transcriptase digital PCR with target specific PCR primers and probe sets designed to amplify SARS-CoV-2.

**Calculations only include positive results.

5.1.1.2. WHO International Standard

The LoD using WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146) was determined by reconstituting the WHO Standard to 0.5 mL according to the WHO NIBSC code: 20/146 Instructions for use (Version 1.0, Dated 14/12/2020). Following reconstitution, the WHO Standard was diluted to an intermediate stock (IS) concentration in UTM.

WHO Standard IS was serially diluted in pooled negative clinical nasopharyngeal swabs matrix. Six concentration levels were tested with 24 replicates at each level across three lots of assay tubes (8 replicates per lot). Three independent dilution series were used in the study with approximately equal numbers of replicates per dilution series. The LoD was determined to be 30 IU/mL.

The results of the LoD study are shown in Table 3 below.

Table 3 Hit rate and mean Ct results of SARS-CoV-2 LoD determination

Strain - WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)

Concentration [IU/mL]	Valid Positive Results	Total Valid Results	Hit Rate [%]	Mean Ct*
120	24	24	100	32.74
60	24	24	100	33.81
30	24	24	100	34.28
20	21	24	88	34.97
15	19	24	79	35.48
7.5	9	24	38	36.05

*Calculations only include positive results

5.1.2. Reactivity/inclusivity

The inclusivity study evaluates the assay ability to detect SARS-CoV-2 isolates/variants. In this study, sixteen (16) SARS-CoV-2 isolates/variants were tested. The isolates/variants were tested as inactivated viruses diluted into pooled clinical negative nasopharyngeal swab matrices. The isolates/variants tested in the study and the concentrations that they can be detected at 100%, i.e., in 3 out of 3 replicates are listed in Table 4. In silico analysis of the oligo sets for SARS-CoV-2 (taxonomy ID 2697049) have been continuously performed since the onset of the pandemic and **cobas**[®] SARS-CoV-2 test will detect all analyzed SARS-CoV-2 sequences in the GISAID (>14 M) database (as of 15th November, 2023).

Table 4 Summary of SARS-CoV-2 inclusivity testing

Isolate/Variant	Pango Lineage	WHO Label	Lowest Concentration Detected (cp/mL)
Italy-INMI1	not listed	N/A	5.0E+00
Hong Kong/VM20001061/2020	A	N/A	2.0E+01
UK variant	B.1.1.7	Alpha	5.0E+00
South Africa Variant	B.1.351	Beta	2.0E+01
USA/COR-22-063113/2022	BA5.5	Omicron	6.0E+00
USA/GA-EHC-2811C/2021	BA.1	Omicron	1.5E+00
hCoV-19/USA/MD-HP40900/2022	B.1.1.529, XBB.1.5	Omicron	6.0E+00
hCoV-19/USA/MD-HP38861/2022	B.1.1.529, BQ.1.1	Omicron	1.2E+01
hCoV-19/USA/MD-HP38288/2022	B.1.1.529, BF.7	Omicron	1.2E+01
hCoV-19/USA/MD-HP30386/2022	B.1.1.529, BA.4	Omicron	6.0E+00
USA/MD-HP24556/2022	BA.2.3	Omicron	1.2E+01

Isolate/Variant	Pango Lineage	WHO Label	Lowest Concentration Detected (cp/mL)
USA/MD-HP20874/2021	B.1.1.529	Omicron	6.0E+00
USA/CA-Stanford-15_S02/2021	B.1.617.1	Kappa	1.2E+01
USA/NY-Wadsworth-21025952/2021	B.1.526	Iota	1.2E+01
USA/PHC658/2021	B.1.617.2	Delta	3.6E+01
Japan/TY7-503/2021 (Brazil P.1)	P.1	Gamma	3.6E+01

5.1.3. Cross- reactivity and microbial interference

Cross-reactivity and microbial interference of **cobas**[®] SARS-CoV-2 were evaluated by testing a panel of multiple unique sub-species of microorganisms. High titer stocks of the potentially cross-reacting microorganisms were spiked into pooled negative nasopharyngeal swab clinical matrix and tested for cross-reactivity with **cobas**[®] SARS-CoV-2, and into pooled negative nasopharyngeal swab clinical matrix spiked with 3x LoD concentrations of SARS-CoV-2 and tested for microbial interference. The testing concentrations for potentially interfering microorganisms are $\geq 1.0E+05$ units/mL for viruses and $\geq 1.0E+06$ units/mL for other microorganisms unless otherwise noted (Table 5).

None of the organisms tested interfered with **cobas**[®] SARS-CoV-2 performance.

Results show that the presence of the microorganisms at the concentrations tested did not interfere with the detection of SARS-CoV-2 by generating false negative results. Note that in presence of SARS-coronavirus (SARS-CoV-1) at $1e5$ pfu/mL, 3x LoD concentrations of SARS-CoV-2 was not detected, when SARS-CoV-1 was at $1e4$ pfu/mL, 3x LoD of SARS-CoV-2 can be detected indicating SARS CoV-1 at $1e5$ pfu/mL or higher may interfere with SARS-CoV-2 detection. However, the likelihood of a co-infection with SARS CoV-1 is remote as the last confirmed case of SARS-CoV-1 was reported in 2004.

Table 5 Cross-reactivity/Microbial interference: list of organisms tested

Description	Concentration Tested*	Description	Concentration Tested*
Human coronavirus 229E	2.80E+05	<i>Aspergillus Flavus var. flavus</i>	1.00E+06
Human Coronavirus HKU1	1.38E+07	<i>Bordetella parapertussis</i>	1.00E+06
Human coronavirus OC43	3.16E+05	<i>Bordetella pertussis</i>	1.74E+06
Human Coronavirus, NL63	1.38E+06	<i>Candida albicans</i>	1.58E+07
SARS Coronavirus**	1.00E+05	<i>Chlamydia pneumoniae</i>	6.88E+06
SARS Coronavirus**	1.00E+04	<i>Corynebacterium flavescens</i>	1.00E+06

Description	Concentration Tested*	Description	Concentration Tested*
MERS Coronavirus	1.50E+07	<i>Escherichia coli</i>	1.00E+06
Adenovirus	2.88E+05	<i>Fusobacterium necrophorum subsp. necrophorum</i>	1.00E+06
Cytomegalovirus	1.00E+05	<i>Haemophilus influenzae</i>	2.00E+06
Enterovirus Type 71	1.05E+05	<i>Lactobacillus crispatus</i>	1.00E+06
Epstein-Barr virus	1.00E+05	<i>Legionella pneumophila</i>	1.38E+08
Human Metapneumovirus (hMPV)	1.60E+05	<i>Moraxella catarrhalis</i>	1.00E+06
Influenza A (Brisbane 59/07) H1N1	1.00E+05	<i>Mycobacterium tuberculosis</i>	5.75E+06
Influenza A (Kansas-14/2017)	1.99E+07	<i>Mycoplasma genitalium</i>	1.00E+06
Influenza B (Colorado-06/2017)	6.10E+08	<i>Mycoplasma pneumoniae</i>	3.45E+06
Influenza B (Florida/04/06)	1.00E+05	Nasal Wash	1:10
Measles	1.00E+05	<i>Neisseria flava</i>	1.00E+06
Mumps	1.00E+05	<i>Neisseria meningitidis</i>	1.00E+06
Parainfluenza Virus (hPIV)	1.60E+05	<i>Pneumocystis jirovecii</i>	1.59E+07
Parainfluenza Virus Type 1	1.26E+05	<i>Pneumocystis jirovecii</i> (Clinical sample)	1:10
Parainfluenza Virus Type 3	3.45E+05	<i>Pseudomonas aeruginosa</i>	2.03E+07
Parainfluenza Virus Type 4A	2.88E+05	<i>Staphylococcus aureus</i>	1.00E+06
Respiratory Syncytial Virus Type A	1.26E+05	<i>Staphylococcus epidermis</i>	1.20E+07
Rhinovirus	5.50E+05	<i>Streptococcus pneumoniae</i>	1.22E+06
		<i>Streptococcus pyogenes</i>	6.25E+06
		<i>Streptococcus salivarius</i>	6.63E+06

* TCID50/mL, EID50/mL, cp/mL PFU/mL, genome equiv/mL for viruses; CFU/mL, IFU/mL for bacteria and fungi.

** SARS CoV-1 at 1e5 pfu/mL or higher may interfere with SARS-CoV-2 detection. It did not interfere with the SARS-CoV-2 detection at 1e4 pfu/mL.

5.1.4. Endogenous and exogenous interference

Potentially interfering substances that may be commonly encountered in respiratory specimens were evaluated. Medically and/or physiologically relevant concentrations of potential interferents were tested with **cobas**[®] SARS-CoV-2. Each substance was tested, by introducing potential interferents into pooled negative nasopharyngeal swab specimens (NNPS) in UTM and tested with and without 3x LOD of SARS-CoV-2 target. As shown in Table 6 substances at the concentrations tested did not interfere in the detection of SARS-CoV-2.

Table 6 Endogenous and exogenous interference

Potential Interferent	Active Ingredient	Concentration Tolerated
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Potential Interferent	Active Ingredient	Concentration Tolerated
Mucin	Purified mucin protein	5 mg/mL
Human Whole Blood	-	5% (v/v)
Peripheral blood mononuclear cell (PBMC)	-	1.0E+06 cells/mL
Nasal spray - Afrin / Anefrin	Oxymetazoline	5% (v/v)
Nasal corticosteroids - Flonase	Fluticasone	5% (v/v)
Nasal gel - Zicam	Galphimia glauca, Histaminum hydrochloricum, Luffa operculata, Sulphur	5% (v/v)
Throat lozenges, oral anesthetic and analgesic - Cepacol	Benzocaine, Menthol	5 mg/mL
Antibiotic, nasal ointment - Bactroban	Mupirocin	5 mg/mL
Antiviral drug - Relenza	Zanamivir	5 mg/mL
Antiviral drug - Tamiflu	Oseltamivir	7.5 mg/mL
Antimicrobial, systemic	Tobramycin	4 µg/mL
Influenza vaccine - FluMist	Live Quadrivalent 2022-2023 A/Victoria/1/2020 (H1N1) (an A/Victoria/2570/2019 (H1N1) pdm09 - like virus), A/Norway/16606/2021 (H3N2) (an A/Darwin/9/2021 (H3N2) - like virus), B/Phuket/3073/2013 (B/Yamagata lineage), and B/Austria/1359417/2021 (B/Victoria lineage) lineage)	5.93E+06 FFU/mL

6. REPRODUCIBILITY

Reproducibility study assesses the total variability of the assay in detecting SARS-CoV-2 across operators, study sites, testing days, Analyzers, and assay tube lots. The reproducibility was evaluated at 3 study sites representative of CLIA-waived intended use settings. Two operators at each of the 3 sites tested a 3-member reproducibility panel in triplicate on 5 different days, for a total of ~270 runs (3 panel members x 3 replicates x 2 operators x 5 days x 3 sites). Nine Analyzers and 3 assay tube lots were used. The reproducibility panel comprises a low positive and a moderate positive for SARS-CoV-2, in addition to a negative sample. The expected result for the true negative panel member is “Not Detected,” while the expected result for the low positive and moderate positive panel member is “Detected.” Percent agreement with expected result, mean Ct, Ct SD, and Ct %CV are shown in Table 7.

Table 7 SARS-CoV-2 reproducibility

Panel Member	Total number of valid test runs	Site 1	Site 2	Site 3	All sites	All sites
-	-	Agreement with Expected Results	Agreement with Expected Results	Agreement with Expected Results	Avg. Ct ± SD (%CV)	Agreement (n/N) and (95% CI)
Negative	268	100.0% (90/90)	100.0% (88/88)	98.9% (89/90)	-	99.6% (267/268) (97.9%-99.9%)
SARS-CoV-2 Low Positive	266	100.0% (89/89)	100.0% (90/90)	97.7% (85/87)	33.4±0.96 (2.9%)	99.2% (264/266) (97.3%-99.8%)
SARS-CoV-2 Moderate Positive	268	100.0% (88/88)	100.0% (90/90)	100.0% (90/90)	32.5±0.54 (1.7%)	100.0% (268/268) (98.6%-100.0%)

7. CLINICAL PERFORMANCE EVALUATION

The clinical performance of the **cobas**[®] SARS-CoV-2 test was evaluated using prospectively collected fresh paired clinical nasopharyngeal swab (NPS) and nasal swab (NS) specimens and unpaired frozen specimens collected from either symptomatic individuals suspected of respiratory viral infection consistent with COVID-19 or asymptomatic individuals. Testing of clinical samples was performed with the **cobas**[®] SARS-CoV-2 test at 10 point-of-care healthcare facilities (e.g., emergency rooms, outpatient clinics, and physician offices). Results from clinical specimens tested with **cobas**[®] SARS-CoV-2 were compared to results from three highly sensitive FDA-EUA-authorized laboratory-based RT-PCR assays (composite comparator method).

Prospective clinical specimens were tested February–June 2022. In total, 1874 evaluable NPS samples and 1872 evaluable NS samples were included in the analysis for the performance evaluation of the **cobas**[®] SARS-CoV-2 assay. Of these, 673 NPS specimens were collected from individuals with signs and symptoms of respiratory tract infection and 1201 were from asymptomatic individuals (413 suspected of SARS-CoV-2 infection due to recent exposure or other reasons and 788 from individuals without symptoms or other reasons to suspect COVID-19). Among the NS specimens tested in the study, 674 were collected from individuals with signs and symptoms of respiratory tract infection and 1198 were from asymptomatic individuals (411 suspected of SARS-CoV-2 infection due to recent exposure or other reasons and 787 from individuals without symptoms or other reasons to suspect COVID-19).

For each specimen type (NPS and NS), 23 each frozen SARS-CoV-2-positive and -negative specimens from 92 symptomatic individuals earlier during the COVID-19 pandemic (March–June

2021) were distributed to 3 of the 10 sites and worked into the daily workflow of sites for testing.

7.1. Clinical performance evaluation using nasopharyngeal swab specimens

The clinical performance of the **cobas**[®] SARS-CoV-2 test for the detection of SARS-CoV-2 from healthcare-provider collected NPS specimens collected in UTM/UVT was evaluated based on test results from a total of 1876 individual fresh and frozen (23 prospective frozen SARS-CoV-2-positive NPS specimens were tested at sites; one frozen negative specimen was included for each frozen positive specimen) NPS specimens. Of these, 2 NPS specimens were non-evaluable due to invalid/failed tests. The remaining 1874 NPS specimens were evaluable and included in the clinical performance evaluation of **cobas**[®] SARS-CoV-2.

As shown in Table 8 for symptomatic individuals, 125 NPS specimens tested positive for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test on **cobas**[®] Liat[®] System and the composite comparator; six SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test. A total of 539 NPS specimens tested negative for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test and the composite comparator; three SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test.

For NPS specimens prospectively collected from symptomatic individuals, **cobas**[®] SARS-CoV-2 demonstrated 95.4% PPA (125/131; 95% score CI: 90.4%-97.9%) and 99.5% NPA (539/542; 95% score CI: 98.4%-99.8%).

Table 8 Clinical performance comparison with the composite comparator method – NPS specimens from symptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas [®] SARS-CoV-2 on cobas [®] Liat [®] System Nasopharyngeal Swab	Positive	125	3
	Negative	6	539

PPA 95.4% (95% CI: 90.4% - 97.9%)
 NPA 99.5% (95% CI: 98.4% - 99.8%)

As shown in Table 9 for asymptomatic individuals, 52 NPS specimens tested positive for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test on **cobas**[®] Liat[®] System and the composite comparator; two SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test. A total of 1142 NPS specimens tested negative for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test and the composite comparator; five SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test. For NPS specimens prospectively collected from asymptomatic individuals, **cobas**[®] SARS-CoV-2 demonstrated 96.3% PPA (52/54; 95% score CI: 87.5%-99.0%) and 99.6% NPA (1142/1147; 95% score CI: 99.0%-99.8%).

Table 9 Clinical performance comparison with the composite comparator method – NPS specimens from asymptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas [®] SARS-CoV-2 on cobas [®] Liat [®] System Nasopharyngeal Swab	Positive	52	5
	Negative	2	1142

PPA 96.3% (95% CI: 87.5% - 99.0%)
 NPA 99.6% (95% CI: 99.0% - 99.8%)

7.2. Clinical performance evaluation using nasal swab specimens

The clinical performance of the **cobas**[®] SARS-CoV-2 test for the detection of SARS-CoV-2 from nasal (NS) specimens collected in UTM/UVT was evaluated from a total of 1950 individual fresh and frozen (twenty-three prospective frozen SARS-CoV-2-positive NS specimens were tested at sites; one frozen negative specimen was included for each frozen positive specimen) NS specimens; NS specimens were comprised of either healthcare provider-collected (49.6%) or self-collected swabs (50.4%). Overall, 77 NS specimens were non-evaluable due to not being tested, protocol deviation, or invalid/failed tests. The remaining 1873 NS specimens (including 1 indeterminate result) were evaluable and included in the clinical performance evaluation of **cobas**[®] SARS-CoV-2.

As shown in Table 10 for symptomatic individuals, 129 NS specimens tested positive for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test on **cobas**[®] Liat[®] System and the composite

comparator; five SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test. A total of 539 NS specimens tested negative for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test and the composite comparator; one SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test.

Overall, for NS specimens prospectively collected from symptomatic individuals, **cobas**[®] SARS-CoV-2 demonstrated 96.3% PPA (129/134; 95% score CI: 91.6%-98.4%) and 99.8% NPA (539/540; 95% score CI: 99.0%-100.0%).

Table 10 Clinical performance comparison with the composite comparator method – NS specimens from symptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas [®] SARS-CoV-2 on cobas [®] Liat [®] System Nasal Swab	Positive	129	1
	Negative	5	539

PPA 96.3% (95% CI: 91.6% - 98.4%)

NPA 99.8% (95% CI: 99.0% - 100.0%)

Note: The nasal swabs were comprised of healthcare provider-collected nasal swab specimens and nasal swab specimens self-collected on-site with healthcare provider instructions.

As shown in Table 11 for asymptomatic individuals, 45 NS specimens tested positive for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test on **cobas**[®] Liat[®] System and the composite comparator; five SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test. A total of 1147 NS specimens tested negative for SARS-CoV-2 with both the **cobas**[®] SARS-CoV-2 test and the composite comparator; one SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**[®] SARS-CoV-2 test.

Overall, for NS specimens prospectively collected from asymptomatic individuals, **cobas**[®] SARS-CoV-2 demonstrated 90.0% PPA (45/50; 95% score CI: 78.6%-95.7%) and 99.9% NPA (1147/1148; 95% score CI: 99.5%-100.0%).

Table 11 Clinical performance comparison with the composite comparator method – NS specimens from asymptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on cobas® Liat® System Nasal Swab	Positive	45	1
	Negative	5	1147

PPA 90.0% (95% CI: 78.6% - 95.7%)

NPA 99.9% (95% CI: 99.5% - 100.0%)

Note: The nasal swabs were comprised of healthcare provider-collected nasal swab specimens and nasal swab specimens self-collected on-site with healthcare provider instructions.

8. CONCLUSIONS

A comparison of the intended use, technological characteristics, and the results of non-clinical analytical and clinical performance studies demonstrate that **cobas® SARS-CoV-2 Nucleic acid test** for use on the **cobas® Liat® System** is substantially equivalent to the predicate device.