



Rx Only

cobas[®] SARS-CoV-2 Qualitative

**Nucleic acid test for use on the
cobas[®] 5800/6800/8800 Systems**

For in vitro diagnostic use

cobas[®] SARS-CoV-2 Qualitative 192T	P/N: 09446109190
cobas[®] SARS-CoV-2 Qualitative 480T	P/N: 09448870190
cobas[®] SARS-CoV-2 Qualitative Control Kit	P/N: 09446117190
cobas[®] Buffer Negative Control Kit	P/N: 09051953190

Table of contents

Intended use	4
Summary and explanation of the test.....	4
Reagents and materials.....	6
cobas® SARS-CoV-2 Qualitative reagents and controls	6
cobas omni reagents for sample preparation.....	8
Reagent storage requirements.....	9
Reagent handling requirements for the cobas® 5800 System	10
Reagent handling requirements for cobas® 6800/8800 Systems	11
Additional materials required for the cobas® 5800 System.....	12
Additional materials required for cobas® 6800/8800 Systems.....	13
Instrumentation and software required	14
Precautions and handling requirements	15
Warnings and precautions	15
Reagent handling	15
Good laboratory practice.....	16
Sample collection, transport, and storage.....	16
Sample collection – swab specimen types	16
Transport and storage – swab specimen types	17
Instructions for use.....	18
Procedural notes	18
Running cobas® SARS-CoV-2 Qualitative utilizing swab specimens	18
Specimens collected in cobas® PCR Media, 0.9% physiological saline, UTM-RT or UVT	18
Specimens collected using cobas® PCR Media Uni or Dual Swab Sample Kit.....	19
Running cobas® SARS-CoV-2 Qualitative on the cobas® 5800 System.....	20
Running cobas® SARS-CoV-2 Qualitative on cobas® 6800/8800 Systems	21
Results.....	22
Quality control and validity of results on the cobas® 5800 System	22

Control results on the cobas ® 5800 System	22
Interpretation of results on the cobas ® 5800 System.....	23
Quality control and validity of results on the cobas ® 6800/8800 Systems.....	23
Interpretation of results on the cobas ® 6800/8800 Systems.....	24
Procedural limitations.....	26
Non-clinical performance evaluation.....	27
Key performance characteristics performed on the cobas ® 6800/8800 Systems	27
Analytical sensitivity (Limit of Detection)	27
Inclusivity	28
Precision	28
Reproducibility	29
Analytical specificity / cross-reactivity	31
Interference	33
Matrix equivalency	34
Collection media equivalency – UTM-RT, cobas ® PCR Media and 0.9% physiological saline.....	34
Clinical performance evaluation performed on the cobas® 6800/8800 Systems..	35
Performance with clinical specimens	35
System equivalency / system comparison	36
Additional information	36
Key test features	36
Symbols.....	37
Technical support.....	38
Manufacturer and distributor.....	38
Trademarks and patents	38
Copyright.....	38
References.....	39
Document revision.....	40

Intended use

cobas® SARS-CoV-2 Qualitative for use on the cobas® 5800/6800/8800 Systems is a real-time RT-PCR test intended for the qualitative detection of nucleic acids from SARS-CoV-2 in nasal and nasopharyngeal specimens collected from symptomatic individuals suspected of COVID-19 by their healthcare provider.

Results are for the detection of SARS-CoV-2 RNA. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other pathogens.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Results are meant to be used in conjunction with clinical observations, patient history, recent exposures and epidemiological information, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities. cobas® SARS-CoV-2 Qualitative is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and on the use of the cobas® 5800/6800/8800 Systems.

Summary and explanation of the test

Explanation of the test

cobas® SARS-CoV-2 Qualitative is a qualitative nucleic acid test for use on the cobas® 5800/6800/8800 Systems for the detection of the 2019 novel coronavirus (SARS-CoV-2) RNA in individual nasal and nasopharyngeal swab samples collected in transport media (refer to **Sample collection, transport and storage** section for details). The RNA Internal Control, used to monitor the entire sample preparation and PCR amplification process, is introduced into each specimen during sample processing. In addition, the test utilizes external controls (low titer positive control and a negative control).

Principles of the procedure

cobas® SARS-CoV-2 Qualitative is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The cobas® 5800 System is designed as one integrated instrument. The cobas® 6800/8800 Systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the cobas® 5800 or cobas® 6800/8800 Systems software(s), which assigns test results for all tests. Results can be reviewed directly on the system screen, and printed as a report.

Nucleic acid from patient samples and added internal control RNA (RNA IC) molecules are simultaneously extracted. Nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors, are removed with subsequent wash steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature. External controls (positive and negative) are processed in the same way.

Selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for ORF1 a/b non-structural region that is unique to SARS-CoV-2. Additionally, a conserved region in the structural protein envelope E-gene were chosen for pan-Sarbecovirus detection. The pan-Sarbecovirus detection sets will also detect SARS-CoV-2 virus.

Selective amplification of RNA Internal Control is achieved by the use of non-competitive sequence specific forward and reverse primers which have no homology with the coronavirus genome. A thermostable DNA polymerase enzyme is used for amplification.

The **cobas**® SARS-CoV-2 Qualitative master mix contains detection probes which are specific for the coronavirus type SARS-CoV-2, members of the Sarbecovirus subgenus, and the RNA Internal Control nucleic acid. The coronavirus and RNA Internal Control detection probes are each labeled with unique fluorescent dyes that act as a reporter. Each probe also has a second dye which acts as a quencher. When not bound to the target sequence, the fluorescent signals of the intact probes are suppressed by the quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage of the probe by the 5' to 3' exonuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye increases concomitantly. Each reporter dye is measured at defined wavelengths, which enables simultaneous detection and discrimination of the amplified coronavirus target and the RNA Internal Control. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythymidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicons from previous PCR runs are destroyed by the AmpErase enzyme [uracil-N-glycosylase], which is included in the PCR mix, when heated in the first thermal cycling step. However, newly formed amplicons are not destroyed since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

Reagents and materials

The materials provided for cobas® SARS-CoV-2 Qualitative can be found in Table 1. Materials required, but not provided can be found in Table 2, Table 3, Table 4, Table 8, Table 9 and Table 11.

Refer to the **Reagents and materials** section and **Precautions and handling requirements** section for the hazard information for the product.

cobas® SARS-CoV-2 Qualitative reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 4.

Table 1 cobas® SARS-CoV-2 Qualitative

cobas® SARS-CoV-2 Qualitative Store at 2-8°C 192 test cassette (P/N 09446109190) 480 test cassette (P/N 09448870190)			
Kit components	Reagent ingredients	Quantity per kit 192 tests	Quantity per kit 480 tests
Proteinase Solution (PASE)	Tris buffer, < 0.05% EDTA, calcium chloride, calcium acetate, 8% proteinase, glycerol EUH210: Safety data sheet available on request. EUH208: Contains Subtilisin from <i>Bacillus subtilis</i> . May produce an allergic reaction.	22.3 mL	38 mL
RNA Internal Control (RNA IC)	Tris buffer, < 0.05% EDTA, < 0.001% non-Sarbecovirus related armored RNA construct containing primer and probe specific primer sequence regions (non-infectious RNA in MS2 bacteriophage), < 0.1% sodium azide	21.2 mL	38 mL
Elution Buffer (EB)	Tris buffer, 0.2% methyl-4 hydroxybenzoate	21.2 mL	38 mL
Master Mix Reagent 1 (MMX-R1)	Manganese acetate, potassium hydroxide, < 0.1% sodium azide	7.5 mL	14.5 mL
SARS-CoV-2 QL Master Mix Reagent 2 (SARS-CoV-2 QL MMX-R2)	Tricine buffer, potassium acetate, < 18% dimethyl sulfoxide, glycerol, < 0.1% Tween 20, EDTA, < 0.12% dATP, dCTP, dGTP, dUTPs, < 0.01% upstream and downstream SARS-CoV-2 and Sarbecovirus primers, < 0.01% Internal Control forward and reverse primers, < 0.01% fluorescent-labeled oligonucleotide probes specific for SARS-CoV-2, Sarbecovirus, and the RNA Internal Control, < 0.01% oligonucleotide aptamer, < 0.1% Z05D DNA polymerase, < 0.10% AmpErase (uracil-N-glycosylase) enzyme (microbial), < 0.1% sodium azide	9.7 mL	17.5 mL

Table 2 cobas® SARS-CoV-2 Qualitative Control Kit


cobas® SARS-CoV-2 Qualitative Control Kit Store at 2–8°C (P/N 09446117190)		
Kit components	Reagent ingredients	Quantity per kit
SARS-CoV-2 QL Positive Control (SARS-CoV-2 QL (+)C)	Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, 0.003% Poly rA, < 0.01% Non-infectious plasmid DNA (microbial) containing SARS-CoV-2 sequence, < 0.01% Non-infectious plasmid DNA (microbial) containing pan-Sarbecovirus sequence	16 mL (16 x 1 mL)

Table 3 cobas® Buffer Negative Control Kit

cobas® Buffer Negative Control Kit Store at 2–8°C (P/N 09051953190)		
Kit components	Reagent ingredients	Quantity per kit
cobas® Buffer Negative Control (BUF (-) C)	Tris buffer, < 0.1% sodium azide, EDTA, 0.002% Poly rA RNA (synthetic)	16 mL (16 x 1 mL)

cobas omni reagents for sample preparation

Table 4 cobas omni reagents for sample preparation*

Reagents	Reagent ingredients	Quantity per kit	Safety symbol and warning**
cobas omni MGP Reagent (MGP) Store at 2–8°C (P/N 06997546190)	Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	480 tests	Not applicable
cobas omni Specimen Diluent (SPEC DIL) Store at 2–8°C (P/N 06997511190)	Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	4 x 875 mL	Not applicable
cobas omni Lysis Reagent (LYS) Store at 2–8°C (P/N 06997538190)	43% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate	4 x 875 mL	 <p>DANGER H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H411: Toxic to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. EUH071: Corrosive to the respiratory tract. P273: Avoid release to the environment. P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. P391: Collect spillage. 593-84-0 Guanidinium thiocyanate 9002-92-0 Polidocanol 3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol</p>
cobas omni Wash Reagent (WASH) Store at 15–30°C (P/N 06997503190)	Sodium citrate dihydrate, 0.1% methyl-4 hydroxybenzoate	4.2 L	Not applicable

*These reagents are not included in the cobas® SARS-CoV-2 Qualitative kits. See listing of additional materials required (Table 8 and Table 9).

**Product safety labeling primarily follows EU GHS guidance.

***Hazardous substance.

Reagent storage requirements

Reagents shall be stored and will be handled as specified in Table 5, Table 6 and Table 7.

When reagents are not loaded on the cobas® 5800 or cobas® 6800/8800 Systems, store them at the corresponding temperature specified in Table 5.

Table 5 Reagent storage (when reagent is not on the system)

Reagent	Storage temperature
cobas® SARS-CoV-2 Qualitative 192T	2–8°C
cobas® SARS-CoV-2 Qualitative 480T	2–8°C
cobas® SARS-CoV-2 Qualitative Control Kit	2–8°C
cobas® Buffer Negative Control Kit	2–8°C
cobas omni Lysis Reagent	2–8°C
cobas omni MGP Reagent	2–8°C
cobas omni Specimen Diluent	2–8°C
cobas omni Wash Reagent	15–30°C

Reagent handling requirements for the cobas® 5800 System

Reagents loaded onto the cobas® 5800 System are stored at appropriate temperatures and their expiration is monitored by the system. The system allows reagents to be used only if all of the conditions shown in Table 6 are met. The system automatically prevents use of expired reagents. Table 6 allows the user to understand the reagent handling conditions enforced by the cobas® 5800 System.

Table 6 Reagent expiry conditions enforced by the cobas® 5800 System

Reagent	Kit expiration date	Open-kit stability	Number of runs for which this kit can be used	On-board stability
cobas® SARS-CoV-2 Qualitative 192T	Date not passed	90 days from first usage	Max 40 runs	Max 36 days ^b
cobas® SARS-CoV-2 Qualitative 480T	Date not passed	90 days from first usage	Max 40 runs	Max 36 days ^b
cobas® SARS-CoV-2 Qualitative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 36 days ^b
cobas® Buffer Negative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 36 days ^b
cobas omni Lysis Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni MGP Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni Specimen Diluent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni Wash Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable

^a Single use reagents.

^b Time is measured from the first time that reagent is loaded onto the cobas® 5800 System.

Reagent handling requirements for cobas® 6800/8800 Systems

Reagents loaded onto the cobas® 6800/8800 Systems are stored at appropriate temperatures and their expiration is monitored by the system. The cobas® 6800/8800 Systems allow reagents to be used only if all of the conditions shown in are met. The system automatically prevents use of expired reagents. Table 7 allows the user to understand the reagent handling conditions enforced by the cobas® 6800/8800 Systems.

Table 7 Reagent expiry conditions enforced by the cobas® 6800/8800 Systems

Reagent	Kit expiration date	Open-kit stability	Number of runs for which this kit can be used	On-board stability (cumulative time on board outside refrigerator)
cobas® SARS-CoV-2 Qualitative 192T	Date not passed	90 days from first usage	Max 40 runs	Max 40 hours
cobas® SARS-CoV-2 Qualitative 480T	Date not passed	90 days from first usage	Max 20 runs	Max 20 hours
cobas® SARS-CoV-2 Qualitative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 8 hours
cobas® Buffer Negative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 10 hours
cobas omni Lysis Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni MGP Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni Specimen Diluent	Date not passed	30 days from loading ^b	Not applicable	Not applicable
cobas omni Wash Reagent	Date not passed	30 days from loading ^b	Not applicable	Not applicable

^a Single use reagents.

^b Time is measured from the first time that reagent is loaded onto the cobas® 6800/8800 Systems.

Additional materials required for the cobas® 5800 System

Table 8 Materials and consumables for use on the cobas® 5800 System

Material	P/N
cobas omni Processing Plate 24	08413975001
cobas omni Amplification Plate 24	08499853001
cobas omni Liquid Waste Plate 24	08413983001
Tip CORE TIPS with Filter, 1mL	04639642001
Tip CORE TIPS with Filter, 300µL	07345607001
cobas omni Liquid Waste Container	07094388001
cobas omni Lysis Reagent	06997538190
cobas omni MGP Reagent	06997546190
cobas omni Specimen Diluent	06997511190
cobas omni Wash Reagent	06997503190
Solid Waste Bag or Solid Waste Bag With Insert	07435967001 or 08030073001
cobas omni Secondary Tubes 13x75 (optional)	06438776001
cobas ® PCR Media Tube Replacement Cap Kit	07958056190
cobas ® PCR Media Disposable Tube Stand (Optional)	07958064190
MPA RACK 16 MM LIGHT GREEN 7001-7050 ^{a, b}	03143449001
RD5 RACK – RD Standard rack 0001-0050 LR ^{a, b}	11902997001
16-position tube carrier*	09224319001
5-position rack carrier*	09224475001

*Contact your local Roche representative for a detailed order list for sample racks.

^a RD5 or MPA racks are required in combination with the 5-position Rack Carrier on the cobas® 5800 System.

^b MPA 16mm rack or 16-position tube carrier are the preferred racks for use with samples collected in cobas® PCR Media tubes.

Additional materials required for cobas® 6800/8800 Systems

Table 9 Materials and consumables for use on the **cobas®** 6800/8800 Systems

Material	P/N
cobas omni Processing Plate	05534917001
cobas omni Amplification Plate	05534941001
cobas omni Pipette Tips	05534925001
cobas omni Liquid Waste Container	07094388001
cobas omni Lysis Reagent	06997538190
cobas omni MGP Reagent	06997546190
cobas omni Specimen Diluent	06997511190
cobas omni Wash Reagent	06997503190
Solid Waste Bag and Solid Waste Container or Solid Waste Bag With Insert and Kit Drawer	07435967001 and 07094361001 or 08030073001 and 08387281001
cobas omni Secondary Tubes 13x75 (optional)	06438776001
cobas® PCR Media Tube Replacement Cap Kit	07958056190
cobas® PCR Media Disposable Tube Stand (Optional)	07958064190
MPA RACK 16 MM LIGHT GREEN 7001-7050***	03143449001
RD5 RACK – RD Standard rack 0001-0050 LR***	11902997001

* MPA 16 mm or RD5 racks are required to use **cobas®** SARS-COV-2 Qualitative. Contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack trays accepted on the instruments.

MPA 16 mm rack is the preferred rack for use with samples collected in **cobas® PCR Media tubes.

Instrumentation and software required

The **cobas**® 5800 software and **cobas**® SARS-CoV-2 Qualitative analysis package for the **cobas**® 5800 System must be installed on the **cobas**® 5800 instrument. The Data Manager software and PC for the **cobas**® 5800 System will be provided with the system.

The **cobas**® 6800/8800 Systems software and **cobas**® SARS-CoV-2 Qualitative analysis package for the **cobas**® 6800/8800 Systems must be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

Table 10 Instrumentation

Equipment	P/N
cobas ® 5800 System	08707464001
cobas ® 6800 System (Moveable Platform)	05524245001 or 06379672001
cobas ® 6800 System (Fixed Platform)	05524245001 or 06379664001
cobas ® 8800 System	05412722001
Sample Supply Module	06301037001

Refer to the **cobas**® 5800 System or **cobas**® 6800/8800 Systems – User Assistance and/or User Guides for additional information.

Note: Contact your local Roche representative for a detailed order list for primary and secondary sample tubes, sample racks, racks for clotted tips and rack trays accepted on the instruments.

Precautions and handling requirements

Warnings and precautions

As with any test procedure, good laboratory practice is essential to the proper performance of this assay. Due to the high sensitivity of this test, care should be taken to keep reagents and amplification mixtures free of contamination.

- For in vitro diagnostic use.
- Positive results are indicative of the presence of SARS-CoV-2 RNA.
- All patient samples should be handled as if infectious, using good laboratory procedures as outlined in Biosafety in Microbiological and Biomedical Laboratories and in the CLSI Document M29 -A4.^{1,2} Only personnel proficient in handling infectious materials and the use of **cobas**® SARS-CoV-2 Qualitative and the **cobas**® 5800/6800/8800 Systems should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.5% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10) or follow appropriate site procedures.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.
- Inform your local competent authority about any serious incidents which may occur when using this assay.

Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- **cobas omni** Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- **cobas**® SARS-CoV-2 Qualitative, **cobas**® SARS-CoV-2 Qualitative Control Kit, **cobas**® Buffer Negative Control Kit, **cobas omni** MGP Reagent, and **cobas omni** Specimen Diluent contain sodium azide as a preservative. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur. If these reagents are spilled, dilute with water before wiping dry.
- Do not allow **cobas omni** Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.
- Avoid collecting or handling specimens in areas that are exposed to SARS-CoV-2 vaccine material. Some vaccines may contain PCR-detectable genomic material. Contamination of specimens or testing materials with vaccine can cause false-positive results.

Good laboratory practice

- Do not pipette by mouth.
- Do not eat, drink, or smoke in designated work areas.
- Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Gloves must be changed between handling samples and cobas® SARS-CoV-2 Qualitative kits, cobas® SARS-CoV-2 Qualitative Control Kit, cobas® Buffer Negative Control Kit and cobas® **omni** reagents to prevent contamination. Avoid contaminating gloves when handling samples and controls.
- Wash hands thoroughly after handling samples and kit reagents, and after removing the gloves.
- Thoroughly clean and disinfect all laboratory work surfaces with a freshly prepared solution of 0.5% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10). Follow by wiping the surface with 70% ethanol.
- If spills occur on the cobas® 5800 or cobas® 6800/8800 instrument, follow the instructions in the cobas® 5800 or cobas® 6800/8800 Systems – User Assistance and/or User Guides to properly clean and decontaminate the surface of instrument(s).
- Laboratory personnel should wear a standard surgical mask (or equivalent) and should avoid touching the mask while handling specimens to mitigate potential specimen contamination.

Sample collection, transport, and storage

Note: Handle all samples and controls as if they are capable of transmitting infectious agents.

Sample collection – swab specimen types

Ensure that the correct collection device is used with the appropriate sample type by referring to the table below:

Table 11 Collection media and sample types evaluated in the analytical and clinical performance studies

Collection Media	Nasopharyngeal	Nasal
Copan Universal Transport Media (UTM-RT®)	√	√
BD™ Universal Viral Transport (UVT)	√	√

The following additional collection media for use with cobas® SARS-CoV-2 Qualitative have been evaluated in analytical studies, and may be acceptable. These media have not been evaluated in the clinical study.

Table 12 Alternative collection media evaluated in the analytical studies

Collection Media	Nasopharyngeal	Nasal
0.9% Physiological saline	√	√
cobas® PCR Media*		√

* **cobas®** PCR Media is a component of the **cobas®** PCR Media Uni Swab Sample Kit and Dual Swab Sample Kits. The performance of the **cobas®** PCR Media Uni Swab Sample Kit (P/N 07958030190) and the **cobas®** PCR Media Dual Swab Sample Kit (P/N 07958021190) for use with **cobas®** SARS-CoV-2 Qualitative on the cobas® 6800/8800 has been evaluated in analytical studies. Clinical performance of the assay with the samples collected using the two kits was not evaluated.

- Collect nasal and nasopharyngeal specimens according to standard collection technique using flocced or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT), cobas PCR media or 0.9% physiological saline.
- Refer to the Instructions for Use of the Collection Devices for hazard information.

Transport and storage – swab specimen types

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- Samples collected in UTM-RT® or UVT,
 - After collection, specimens can be stored for up to 48 hours at 2-25°C followed by up to 3 days at 2-8°C and at ≤ -70°C for up to 30 days.
 - Specimens are stable for up to **two freeze/thaw** cycles when frozen at ≤ -70°C.
- Samples collected in **cobas®** PCR Media,
 - After collection, specimens can be stored for up to 24 hours at 2-25°C followed by up to 3 days at 2-8°C and at ≤ -70°C for up to 30 days.
 - Specimens are stable for up to **one freeze/thaw** cycle when frozen at ≤ -70°C.
- Samples collected in 0.9% physiological saline,
 - After collection, specimens can be stored for up to 48 hours at 2-25°C followed by up to 3 days at 2-8°C and at ≤ -70°C for up to 30 days.
 - Specimens are stable for up to **one freeze/thaw** cycle when frozen at ≤ -70°C.

Instructions for use

Procedural notes

- Do not use cobas® SARS-CoV-2 Qualitative reagent, cobas® SARS-CoV-2 Qualitative Control Kit, cobas® Buffer Negative Control Kit, or cobas omni reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Ensure that specimen barcode labels on sample tubes are visible through the openings on the side of the sample racks. Refer to the cobas® 5800 System or cobas® 6800/8800 Systems User Guide for proper barcode specifications and additional information on loading sample tubes.
- Refer to the cobas® 5800 System or cobas® 6800/8800 Systems – User Assistance and/or User Guides for proper maintenance of instruments.

Running cobas® SARS-CoV-2 Qualitative utilizing swab specimens

For testing swab specimens, cobas® SARS-CoV-2 Qualitative can be run with a minimum required sample volume of 0.6 mL in the cobas omni Secondary Tube for specimens collected in Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT), cobas® PCR Media or 0.9% physiological saline. Specimens collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit can be run in their primary collection tube with a minimum required sample volume of 1.0 mL.

Specimens collected in cobas® PCR Media, 0.9% physiological saline, UTM-RT or UVT

Specimens collected in tubes compatible with the cobas® 5800/6800/8800 Systems may be loaded directly onto the cobas® 5800/6800/8800 Systems. Specimens collected in Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT), cobas® PCR Media or 0.9% physiological saline tubes which are not compatible with the cobas® 5800/6800/8800 Systems must be transferred into a secondary tube prior to processing on the cobas® 5800/6800/8800 Systems. The cobas omni Secondary Tube is the preferred option. Samples should be processed using the 'sample type selection in the user interface (UI) as described in Table 13. Additional tubes for testing cobas® SARS-CoV-2 Qualitative are available. Contact your local Roche representative for detailed testing instructions and an order list of primary tubes and secondary tubes compatible with the instruments.

Always use caution when transferring specimens from a primary collection tube to a secondary tube.

Use pipettes with aerosol-barrier or positive-displacement tips to handle specimens.

Always use a new pipette tip for each specimen.

Ensure samples are equilibrated to room temperature prior to transfer into a cobas omni Secondary Tube.

Follow the steps below to transfer patient sample from a primary collection tube into a cobas omni Secondary Tube:

- Unscrew the primary sample tube cap.
- Lift the cap and any attached swab to allow a pipette to be inserted into the sample tube.
- Transfer 0.6 mL into the prepared barcoded secondary tube.
- Transfer secondary tube to a rack. Close the primary sample tube cap.

Specimens collected using cobas® PCR Media Uni or Dual Swab Sample Kit

Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit must be uncapped and can be loaded directly onto racks for processing on the cobas® 5800/6800/8800 Systems. Transfer into a secondary tube is not necessary. cobas® PCR Media tubes fit on to the MPA RACK 16 MM LIGHT GREEN 7001-7050 (P/N 03143449001) can be processed with the swab remaining in the tube. Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kits should be processed using the ‘cobas® PCR Media swab’ sample type selection in the user interface (UI) of cobas® SARS-CoV-2 Qualitative as described in Table 13.

A properly collected swab specimen should have a single swab with the shaft broken at the scoreline. Swab shafts which are broken above the score line will appear longer than normal and may also be bent over to fit into the cobas® PCR Media tube. This may create an obstruction to the pipetting system which might cause the loss of sample, test results and/or mechanical damage to the instrument. In the event that a swab specimen has an improperly broken shaft, remove the swab prior to sample processing on the cobas® 5800/6800/8800 Systems. Use caution when disposing of specimen swabs; avoid splashing or touching swabs to other surfaces during disposal to prevent contamination.

Incoming cobas® PCR Media primary swab specimen tubes with no swabs or with two swabs have not been collected according to the instructions in their respective collection kit instruction for use and should not be tested. If the sample containing two swabs in the cobas® PCR Media primary tubes must be tested, transfer 0.6 mL into the prepared barcoded secondary tube.

Occasionally, incoming swab specimens contain excessive mucus which may induce a pipetting error (e.g., clot or other obstruction) on the cobas® 5800/6800/8800 Systems. Prior to retesting of specimens that exhibited clots during initial processing, remove and discard the swab, then re-cap and vortex these specimens for 30 seconds to disperse the excess mucus.

Swab specimens can be processed twice on the cobas® 5800/6800/8800 Systems while the swab is in the collection tube. If additional testing is required, or if the first test fails due to specimen pipetting error (e.g., clot or other obstruction), the swab must be removed and the remaining fluid must have a minimum volume of 1.0 mL.

Table 13 Sample type selection in the user interface of the cobas® SARS-CoV-2 Qualitative utilizing swab specimens

Collection kit/Matrix type	Minimum volume (mL) Processing tube	Process as Sample Type
Copan Universal Transport Medium BD™ Universal Viral Transport 0.9% Physiological saline	0.6 mL cobas omni Secondary Tube	VTM (on cobas® 6800/8800) Viral transport medium (on cobas® 5800)
cobas® PCR Media Uni or Dual Swab Sample Kit	1.0 mL Primary tube	cobas® PCR media swab

Running cobas® SARS-CoV-2 Qualitative on the cobas® 5800 System

The test procedure is described in detail in the **cobas® 5800 Systems User Assistance and/or User Guide**. Figure 1 below summarizes the procedure.

Figure 1 cobas® SARS-CoV-2 Qualitative procedure on the **cobas® 5800 System**

1	Log onto the system
2	Loading samples onto the system <ul style="list-style-type: none"> • Load sample racks onto the system • The system prepares automatically • Order tests
3	Refill reagents and consumables as prompted by the system <ul style="list-style-type: none"> • Load test specific reagent cassette(s) • Load control mini racks • Load processing tips • Load elution tips • Load processing plates • Load liquid waste plates • Load amplification plates • Load MGP cassette • Refill specimen diluent • Refill lysis reagent • Refill wash reagent
4	Start the run by choosing the Start processing button on the user interface, all subsequent runs will start automatically if not manually postponed
5	Review and export results
6	Remove and cap any sample tubes meeting the minimum volume requirements if needed for future use Clean up the instrument <ul style="list-style-type: none"> • Unload empty control mini racks • Unload empty test specific reagent cassette(s) • Empty amplification plate drawer • Empty liquid waste • Empty solid waste

Running cobas® SARS-CoV-2 Qualitative on cobas® 6800/8800 Systems

The test procedure is described in detail in the **cobas® 6800/8800 Systems – User Assistance and/or User Guide**. Figure 2 below summarizes the procedure.

Figure 2 cobas® SARS-CoV-2 Qualitative procedure on the **cobas® 6800/8800 Systems**

1	Log onto the system Press Start to prepare the system Order tests
2	Refill reagents and consumables as prompted by the system <ul style="list-style-type: none">• Load test specific reagent cassette• Load control cassettes• Load pipette tips• Load processing plates• Load MGP reagent• Load amplification plates• Refill specimen diluent• Refill lysis reagent• Refill wash reagent
3	Loading samples onto the system <ul style="list-style-type: none">• Load sample racks and clotted tip racks onto the sample supply module• Confirm samples have been accepted into the transfer module
4	Start the run by choosing the Start manually button on the user interface or have it start automatically after 120 minutes or if the batch is full
5	Review and export results
6	Remove and cap any sample tubes meeting the minimum volume requirements if needed for future use Clean up the instrument <ul style="list-style-type: none">• Unload empty control cassettes• Empty amplification plate drawer• Empty liquid waste• Empty solid waste

Results

The cobas® 5800/6800/8800 Systems automatically detect the SARS-CoV-2, for each individually processed sample and control, displaying individual target results for samples as well as test validity and overall results for controls.

Quality control and validity of results on the cobas® 5800 System

- One cobas® Buffer Negative Control [Ctrl (-)] and one Positive Control [SARS-CoV-2 QL (+) C] are processed at least every 72 hours and with every new kit lot. Positive and/or negative controls can be scheduled more frequently based on laboratory procedures and/or local regulations.
- In the cobas® 5800 software and/or report, check for flags and their associated results to ensure the result validity.
- Invalidation of results is performed automatically by the cobas® 5800 software based on negative or positive control failures.

NOTE: The cobas® 5800 System will be delivered with the standard setting of running a set of controls (positive and negative) with every run, but can be configured to a less frequent scheduling up to every 72 hours based on laboratory procedures and/or local regulations. Please contact your Roche service engineer and/or Roche customer technical support for more information.

Control results on the cobas® 5800 System

The results of the controls are shown in the cobas® 5800 software in the “Controls” app.

- Controls are marked with “Valid” in the column “Control result” if all Targets of the control are reported valid. Controls are marked with “Invalid” in the column “Control result” if all or one Target of the control are reported invalid.
- Controls marked with “Invalid” show a flag in the “Flags” column. More information on why the control is reported invalid including flag information is shown in the detail view
- If one of the controls is invalid, repeat testing of all controls and all associated samples is required.

Interpretation of results on the cobas® 5800 System

The results of the samples are shown in the cobas® 5800 software in the “Results” app.

For a valid control batch, check each individual sample for flags in the cobas® 5800 software and/or report. The result interpretation should be as follows:

- Samples associated with a valid control batch are shown as ‘Valid’ in the “Control result” column if all Control Target Results reported valid. Samples associated with a failed control batch are shown as ‘Invalid’ in the “Control result” column if all Control Target Results reported invalid.
- If the associated controls of a sample result are invalid, a specific flag will be added to the sample result as follows:
 - Q05D : Result validation failure because of an invalid positive control
 - Q06D :Result validation failure because of an invalid negative control
- The values in “Results” column for individual sample target result should be interpreted as shown in Table 15 below.
- If one or more sample targets are marked with “Invalid” the cobas® 5800 software shows a flag in the “Flags” column. More information on why the sample target(s) is reported invalid including flag information is shown in the detail view.

Quality control and validity of results on the cobas® 6800/8800 Systems

- One cobas® Buffer Negative Control [Ctrl (-) C] and one Positive Control [SARS-CoV-2 QL (+) C] are processed with each batch.
- In the cobas® 6800/8800 Systems software and/or report, check for flags and their associated results to ensure the batch validity.
- All flags are described in the cobas® 6800/8800 Systems User Guide.
- The batch is valid if no flags appear for any controls. If the batch is invalid, repeat testing of the entire batch.

Validation of results is performed automatically by the cobas® 6800/8800 Systems software based on negative and positive control performance.

Interpretation of results on the cobas® 6800/8800 Systems

For a valid batch, check each individual sample for flags in the cobas® 6800/8800 Systems software and/or report. The result interpretation should be as follows:

- A valid batch may include both valid and invalid sample results.
- Results display examples for cobas® SARS-CoV-2 Qualitative are shown in Table 14.
- The “Valid” and “Overall Result” columns are not applicable to sample results for cobas® SARS-CoV-2 Qualitative.
- Invalid results for one or more target combinations are possible and are reported out specifically for each target. If any individual target result is invalid, the presence or absence of that individual target cannot be determined.
- Other initial valid target results can be interpreted as described in Table 15.

Table 14 Example of cobas® SARS-CoV-2 Qualitative results display

Test*	Sample ID	Valid**	Flags	Sample type	Overall result*	Target 1	Target 2
SCoV2- QL 400 µL	Sample _01	NA		VTM	NA	SCoV2 Negative	PanSarB Negative
SCoV2- QL 400 µL	Sample _C1	NA	Y40T	VTM	NA	Invalid	Invalid
SCoV2- QL 400 µL	Sample _B1	NA		VTM	NA	SCoV2 Negative	PanSarB Positive
SCoV2- QL 400 µL	Sample _B2	NA		VTM	NA	SCoV2 Positive	PanSarB Positive
SCoV2- QL 400 µL	Sample _D1	NA		VTM	NA	SCoV2 Negative	PanSarB Negative
SCoV2- QL 400 µL	Sample _A6	NA		VTM	NA	SCoV2 Positive	PanSarB Negative
SCoV2- QL 400 µL	Sample _E1	NA	C01H2	VTM	NA	SCoV2 Positive	Invalid
SCoV2- QL 400 µL	Sample _A2	NA	C01H1	VTM	NA	Invalid	PanSarB Positive
SCoV2- QL	C161420284090428828404	Yes		(-) Ctrl	Valid	Valid	Valid
SCoV2- QL	C161420284093009580264	Yes		SCoV2-QL (+) C	Valid	Valid	Valid

* Depends on sample type used.

**The “Valid” and “Overall Result” columns are not applicable to sample results for the cobas® SARS-CoV-2 Qualitative. Values reported in these columns are not applicable and do not impact the validity of results reported within individual Target Result columns. Refer to Table 15, cobas® SARS-CoV-2 Qualitative results interpretation, for specific instructions on test results interpretation.

Results and their corresponding interpretation for detecting SARS-CoV-2 are shown below (Table 15).

Table 15 cobas® SARS-CoV-2 Qualitative results interpretation

Target 1 (SCoV2)	Target 2 (PanSarb)	Interpretation
Positive	Positive	All Target Results were valid. Result for SARS-CoV-2 RNA is Detected.
Positive	Negative	All Target Results were valid. Result for SARS-CoV-2 RNA is Detected. A positive Target 1 result and a negative Target 2 result is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the Target 2, target region, or 3) other factors.
Negative	Positive	All Target Results were valid. Result for SARS-CoV-2 RNA is Presumptive Positive. A negative Target 1 result and a positive Target 2 result is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the Target 1 target region in the oligo binding sites, or 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Negative	Negative	All Target Results were valid. Result for SARS-CoV-2 RNA is Not Detected.
Positive	Invalid	Not all Target Results were valid. Result for SARS-CoV-2 RNA is Detected.
Invalid	Positive	Not all Target Results were valid. Result for SARS-CoV-2 RNA is Presumptive Positive. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Negative	Invalid	Not all Target Results were valid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	Negative	Not all Target Results were valid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	Invalid	All Target Results were invalid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.

Procedural limitations

- For prescription use only.
- A negative Test result does not exclude the possibility of viral or bacterial infection.
- Results from this test must be used in conjunction with the clinical history, epidemiological data, or laboratory data available to the clinician evaluating the patient.
- Positive and negative predictive values are highly dependent on disease prevalence.
- The performance of this device has not been specifically assessed in individuals without signs or symptoms of respiratory infection.
- FluMist was not evaluated to assess potential interference.
- Test results may also be affected by concurrent antiviral/antibacterial therapy or levels of organism in the specimen that are below the limit of detection for the test.
- **cobas® SARS-CoV-2 Qualitative** has been evaluated only for use in combination with the **cobas® SARS-CoV-2 Qualitative Control Kit**, **cobas® Buffer Negative Control Kit**, **cobas omni MGP Reagent**, **cobas omni Lysis Reagent**, **cobas omni Specimen Diluent**, and **cobas omni Wash Reagent** for use on the **cobas® 5800/6800/8800 Systems**.
- Reliable results depend on proper sample collection, storage and handling procedures. Failure to observe proper procedures in any one of these steps can lead to incorrect results.
- This test is intended to be used for the detection of SARS-CoV-2 RNA in nasal and nasopharyngeal swab samples collected in a Copan UTM-RT System (UTM-RT), BD™ Universal Viral Transport System (UVT) or 0.9% physiological saline and nasal swab samples collected in **cobas® PCR Media**. Testing of other sample types with **cobas® SARS-CoV-2 Qualitative** may result in inaccurate results.
- Detection of SARS-CoV-2 RNA may be affected by sample collection methods, patient factors (e.g., presence of symptoms), and/or stage of infection.
- As with any molecular test, mutations within the target regions of **cobas® SARS-CoV-2 Qualitative** could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. One hundred percent agreement between the results should not be expected due to aforementioned differences between technologies. Users should follow their own specific policies/procedures.
- False negative or invalid results may occur due to interference. The Internal Control is included in **cobas® SARS-CoV-2 Qualitative** to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- The addition of AmpErase enzyme into the **cobas® SARS-CoV-2 Qualitative** master mix reagent enables selective amplification of target RNA; however, good laboratory practices and careful adherence to the procedures specified in this Instructions For Use document are necessary to avoid contamination of reagents.
- Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the common variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS- CoV- 2 and their prevalence, which change over time.
- Performance of the **cobas SARS-CoV-2 Qualitative** has not been established for monitoring treatment of infection.

Non-clinical performance evaluation

Key performance characteristics performed on the cobas® 6800/8800 Systems

Analytical sensitivity (Limit of Detection)

The Limit of Detection (LoD) for cobas® SARS-CoV-2 Qualitative was determined using an inactivated quantified SARS-CoV-2 virus (WHO International Standard for SARS-CoV-2, NIBSC code: 20/146). LoD is defined as the lowest concentration of SARS-CoV-2 RNA that can be detected at a rate of at least 95%. A total of 5 concentration levels (500, 250, 125, 62.5, and 31.25 IU/ml) were prepared by diluting the SARS-CoV-2 target in negative simulated clinical matrix stabilized in UTM. Three independent dilution series with three lots of reagents were tested with a total of 24 replicates per concentration.

The concentration level with observed hit rates greater than or equal to 95% was determined to be the LoD for each of the two targets (SARS-CoV-2 and pan-Sarbecovirus) as described in Table 16 and Table 17.

Table 16 Summary of LoD for SARS-CoV-2 using WHO International Standard (NIBSC code: 20/146)

Viral Strain	Kit lot	Hit rate ≥ 95% [IU/mL]	Mean Ct at ≥ 95% Hit rate
WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)	Lot 1	250 (24/24)	33.2
	Lot 2	125 (23/24)	34.1
	Lot 3	250 (23/24)	33.2

The LoD was confirmed at 250 IU/mL for SARS-CoV-2 (Target 1). For all three reagent lots, at least 23/24 replicates detected the target at 250 IU/ml.

Table 17 Summary of LoD for pan-Sarbecovirus using WHO International Standard (NIBSC code: 20/146)

Viral Strain	Kit lot	Hit rate ≥ 95% [IU/mL]	Mean Ct at ≥ 95% Hit rate
WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)	Lot 1	125 (24/24)	35.2
	Lot 2	125 (24/24)	36.0
	Lot 3	125 (23/24)	34.8

The LoD was confirmed at 125 IU/mL for pan-Sarbecovirus (Target 2). For all three reagent lots, at least 23/24 replicates detected the target at 125 IU/ml.

Inclusivity

The inclusivity of cobas® SARS-CoV-2 Qualitative for the detection of SARS-CoV-2 was confirmed by testing nine SARS-CoV-2 strains, including six variant strains. The lowest target analyte at which all four tested replicates were positive are reported in Table 18. In silico analysis of additional SARS-CoV-2 sequences indicates that >99.9% of sequences for SARS-CoV-2 have no changes in primer/probe binding sites at both target regions simultaneously. All known sequences are predicted to be detected by at least one of the two target regions.

Table 18 Summary of inclusivity

Strain	Catalog Number	Lot Number	Test Concentration with 100% Positivity
Hong Kong/VM20001061/2020	0810590CFHI	325659	1.06E+02 cp/mL
Italy-INMI1	0810589CFHI	325658	1.00E+02 cp/mL
USA-WA1/2020	0810587CFHI	325656	5.03E+01 cp/mL
UK (B.1.1.7)	0810614CFHI	326230	2.4E+01 cp/mL
Japan / Brazil (P.1)	NR-54982	70042875	1.9E+02 cp/mL
South Africa (B.1.351)	0810613CFHI	326229	2.4E+01 cp/mL
US NY (B.1.526)	NR-55359	70043342	1.9E+02 cp/mL
India (B.1.617.1)	NR-55486	70044706	2.5E+02 cp/mL
India (B.1.617.2)	NR-55611	70045238	7.0E+01 cp/mL

Precision

Within-laboratory precision was examined using a panel of SARS-CoV-2 (USA-WA1/2020, heat-inactivated) cultures diluted in simulated clinical matrix in universal transport media. Sources of variability were examined with a panel consisting of three concentration levels, using three lots of cobas® SARS-CoV-2 Qualitative reagents and three instruments over a course of 15 instrument days (2 runs/day x 3 instruments x 5 days/instrument x 3 replicates) for a total of 30 runs containing a total of 90 replicates per concentration. A description of the precision panel and the observed positivity rates are shown in Table 19. All negative panel members tested negative throughout the study. Analysis of standard deviation and percent coefficient of variation (CV) of the Ct values from tests performed on positive panel members (see Table 20) yielded overall CV percentage ranging from 1.1% to 2.2% for cobas® SARS-CoV-2 Qualitative.

Table 19 Summary of within laboratory precision

Target	Panel Member	Level (x LoD)	Positive Results	Total Results	Positivity %	Two-sided 95% CI Lower Bound	Two-sided 95% CI Upper Bound
Target 1 (SARS-CoV-2)	Weak positive	~0.3x	9	90	10%	5%	18%
	Low positive	~1.0x	82	90	91%	83%	96%
	Moderate positive	~3.0x	90	90	100%	96%	100%
Target 2 (pan-Sarbecovirus)	Weak positive	~0.3x	31	90	34%	25%	45%
	Low positive	~1.0x	84	90	93%	86%	97%
	Moderate positive	~3.0x	90	90	100%	96%	100%
N/A	Negative	Blank	0	90	0%	0%	4%

Table 20 Overall mean, standard deviation, and percent coefficient of variation for Ct values by positive panel member

Target	Level (x LoD)	Hit rate	Mean Ct	Instrument-to-Instrument		Lot-to-Lot		Day-to-Day		Run-to-Run		Within Run		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Target 1 (SARS-CoV-2)	~0.3x	10.0%	32.51	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	1.4	0.5	1.4
	~1.0x	91.1%	32.1	0.0	0.0	0.2	0.6	0.1	0.3	0.0	0.0	0.6	1.8	0.6	1.9
	~3.0x	100.0%	31.18	0.0	0.0	0.2	0.7	0.0	0.0	0.0	0.0	0.3	0.9	0.4	1.1
Target 2 (pan-Sarbecovirus)	~0.3x	34.4%	35.36	0.0	0.0	0.5	1.3	0.3	0.8	0.1	0.2	0.5	1.5	0.8	2.2
	~1.0x	93.3%	34.21	0.0	0.0	0.1	0.3	0.2	0.6	0.0	0.0	0.7	2	0.7	2.2
	~3.0x	100.0%	32.9	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.4	1.1	0.4	1.1

Reproducibility

The reproducibility of cobas® SARS-CoV-2 Qualitative was evaluated across multiple variables that theoretically could affect reported results, including: reagent lot, testing site/instrument, day, and run. The evaluation was conducted at 3 testing sites, using 3 reagent lots, with a 4-member panel of positive and negative samples resulting in a total number 216 tests per concentration (not including controls). The positive panel members contained SARS-CoV-2 viral culture material [WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)] at 3 different concentrations in universal transport medium (UTM) based simulated clinical matrix. Each site tested two reagent lots for 6 days. Two runs were performed each day and 3 replicates of each panel member were performed for each run. An overall SARS-CoV-2 positive result was determined by a positive detection in either or both of the SARS-CoV-2 or/and pan-Sarbecovirus channels. The evaluation results are summarized in Table 21.

The system showed a 99.1% negative percent agreement with a 95% CI of 96.7%-99.9%. The test results showed good lot-to-lot, instrument-to-instrument (site), day-to-day, and between run variation for the ~0.3x LoD, ~1x LoD, and ~3x LoD panel members (Table 21).

Table 21 Overall percentage agreement, mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values by viral target and expected viral concentration

Viral Target	Panel Member Concentration	n ^a /N	Percent Agreement* (%) ^b	Mean Ct	Site SD	Site CV(%)	Lot SD	Lot CV(%)	Day SD	Day CV(%)	Run SD	Run CV(%)	Within Run SD	Within Run CV(%)	Total SD	Total CV(%)
Negative	0	214/216 ^c	99.1	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc
SARS-CoV-2	~0.3x LoD	45/216	20.8	33.6	0.00	0.0	0.00	0.0	0.11	0.3	0.00	0.0	0.35	1.1	0.37	1.1
SARS-CoV-2	~1x LoD	196/216	90.7	33.2	0.00	0.0	0.09	0.3	0.00	0.0	0.17	0.5	0.37	1.1	0.42	1.3
SARS-CoV-2	~3x LoD	216/216	100.0	32.2	0.05	0.2	0.02	0.1	0.00	0.0	0.03	0.1	0.24	0.8	0.25	0.8
pan-Sarbecovirus	~0.3x LoD	158/216	73.1	36.5	0.18	0.5	0.00	0.0	0.00	0.0	0.00	0.0	0.71	2.0	0.74	2.0
pan-Sarbecovirus	~1x LoD	214/216	99.1	35.4	0.00	0.0	0.00	0.0	0.00	0.0	0.00	0.0	0.67	1.9	0.67	1.9
pan-Sarbecovirus	~3x LoD	216/216	100.0	34.1	0.11	0.3	0.05	0.2	0.00	0.0	0.00	0.0	0.32	0.9	0.34	1.0

Ct = cycle threshold, LoD = limit of detection, SD = standard deviation, CV(%) = percent coefficient of variation, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, nc = not calculable

Note: SARS-CoV-2 is a dual target assay. Inactivated viral culture material was diluted to ~0.3/1/3x LoD based on the target 2 (SARS-CoV-2) LoD.

^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.

^b Percent agreement with expected results.

^c 2 negative panel members were tested positive. Sequencing showed that one of these samples was positive and the other was negative. The Ct values and the curve analysis of these samples may suggest a low level of contamination during specimen handling.

Analytical specificity / cross-reactivity

A panel of 47 viruses, bacteria, and fungi (including those commonly found in respiratory tract) and pooled human nasal wash were tested with cobas® SARS-CoV-2 Qualitative to assess analytical specificity. The organisms listed in Table 22 were spiked at concentrations of 1×10^5 units/mL for viruses and 1×10^6 units/mL for other organisms, unless otherwise noted.

Testing was performed with each potential interfering organism in the absence and presence of SARS-CoV-2 target (spiked at $\sim 3x$ LoD). None of the organisms interfered with the test performance by generating false-negative or false-positive results. Testing of SARS-CoV-1 generated an expected pan-Sarbecovirus positive result.

Additional *in silico* analysis conducted with other coronaviruses and respiratory flora indicated no concerns with the test performance by predicting any false-negative or false-positive results.

Table 22 Cross-reactivity test results

Microorganism	Concentration
Human coronavirus 229E	1.0E+05 TCID ₅₀ /mL
Human coronavirus OC43	1.0E+05 TCID ₅₀ /mL
Human coronavirus HKU1	1.0E+05 TCID ₅₀ /mL
Human coronavirus NL63	1.0E+05 TCID ₅₀ /mL
MERS coronavirus	1.0E+05 genomic equivalent/mL
SARS coronavirus	1.0E+05 PFU/mL
Adenovirus B (Type 34)	1.0E+05 TCID ₅₀ /mL
Bocavirus	1.0E+05 cp/mL
Cytomegalovirus	1.0E+05 TCID ₅₀ /mL
Epstein Barr virus	1.0E+05 cp/mL
Human Metapneumovirus (hMPV)	1.0E+05 TCID ₅₀ /mL
Measles virus	1.0E+05 TCID ₅₀ /mL
Mumps virus	1.0E+05 TCID ₅₀ /mL
Parainfluenza virus Type 1	1.0E+05 TCID ₅₀ /mL
Parainfluenza virus Type 2	1.0E+05 TCID ₅₀ /mL
Parainfluenza virus Type 3	1.0E+05 TCID ₅₀ /mL
Parainfluenza virus Type 4	1.0E+05 TCID ₅₀ /mL
Influenza A (H1N1)	1.0E+05 TCID ₅₀ /mL
Influenza A virus (H1N1-2009, H1N3, H3N2)	1.0E+05 TCID ₅₀ /mL
Influenza B	1.0E+05 TCID ₅₀ /mL
Enterovirus E (Type 1)	1.0E+05 TCID ₅₀ /mL
Parechovirus	1.0E+05 TCID ₅₀ /mL
Respiratory syncytial virus	1.0E+05 PFU/mL

Microorganism	Concentration
Rhinovirus	1.0E+05 TCID ₅₀ /mL
<i>Candida albicans</i>	1.0E+06 CFU/mL
<i>Chlamydia pneumoniae</i>	1.0E+06 TCID ₅₀ /mL
<i>Corynebacterium diphtheriae</i>	1.0E+06 CFU/mL
<i>Escherichia coli</i>	1.0E+06 CFU/mL
<i>Haemophilus influenzae</i>	1.0E+06 CFU/mL
<i>Lactobacillus gasseri</i>	1.0E+06 CFU/mL
<i>Legionella pneumophila</i>	1.0E+06 CFU/mL
<i>Legionella jordanis (non-pneumophila)</i>	1.0E+06 CFU/mL
<i>Moraxella catarrhalis</i>	1.0E+06 CFU/mL
<i>Mycobacterium tuberculosis</i>	1.0E+06 cells/mL
<i>Neisseria elongata</i>	1.0E+06 CFU/mL
<i>Neisseria meningitidis</i>	1.0E+06 CFU/mL
<i>Pseudomonas aeruginosa</i>	1.0E+06 CFU/mL
<i>Pneumocystis jirovecii</i>	1:20 of Patient Sample
<i>Staphylococcus aureus</i>	1.0E+06 CFU/mL
<i>Staphylococcus epidermidis</i>	1.0E+06 CFU/mL
<i>Streptococcus pneumoniae</i>	1.0E+06 CFU/mL
<i>Streptococcus pyrogenes</i>	1.0E+06 CFU/mL
<i>Streptococcus salivarius</i>	1.0E+06 CFU/mL
<i>Bordetella pertussis</i>	1.0E+06 CFU/mL
<i>Mycoplasma pneumoniae</i>	1.0E+06 CFU/mL

Interference

The effect of exogenous substances potentially secreted into respiratory specimens was evaluated (Table 23). Each potentially interfering substance was tested at or above clinically relevant levels in negative simulated clinical matrix stabilized in universal transport media in absence and presence of SARS-CoV-2 target (spiked at ~3x LoD).

None of the substances interfered with the test performance by generating false-negative, false-positive or invalid results at the concentrations shown below.

Table 23 List of exogenous substances tested for interference

Substance*	Product Name	Concentration
Oxymetazoline	Afrin Nasal Spray	0.011 mg/mL
Galphimia glauca, Luffa operculata, Sabadilla	Zicam nasal spray	0.023 mg/mL
Lidocaine and Phenylephrine	Liposomal NUMB520 Spray	2.68 mg/mL
Budesonide	Budesonide Nasal spray	0.039 mg/mL
Phenol	Chloraseptic	0.47 mg/mL
Fluticasone propionate	Flovent Diskus	166.67 µg/mL
Mupirocin	Mupirocin ointment UPS (each gram contain 20 mgs)	0.20 mg/mL
Zanamivir	Relenza (Inhalation powder)	0.0015 mg/mL
Oseltamivir	Antiviral drug – Tamiflu	0.0073 mg/mL
Benzocaine and Menthol	Cepacol (Sore throat Lozenges)	5.00 mg/mL
Tobramycin	Tobramycin ophthalmic solution	0.018 mg/mL
Petroleum Jelly	Vaseline	1% (w/v)
Nicotine	Snuff Tobacco	1% (w/v)
Camphor-synthetic eucalyptus oil and menthol ointment	Analgesic ointment (Vicks@VapoRubR)	1% (w/v)
0.65% NaCl, Phenylcarbino, Benzalkonium chloride	Saline Nasal Spray with Preservatives	1% (w/v)

* FluMist was not evaluated to assess potential interference.

Endogenous substances that may be present in respiratory specimens were tested for interference (Table 24). Each potentially interfering substance was tested at or above clinically relevant levels in negative simulated clinical matrix stabilized in universal transport media in absence and presence SARS-CoV-2 target (spiked at ~3x LoD).

None of the substances interfered with the test performance by generating false-negative, false-positive or invalid results at the concentrations shown below.

Table 24 List of endogenous substances tested for interference

Substance	Concentration
Human Genomic DNA	20 ng/µL
Mucus	One sputum swab/mL
Human Peripheral Blood Mononuclear Cells (PBMC)	1.0E+03 cells/µL
Human Whole Blood	1% (v/v)
Human Whole Blood	2% (v/v)
Human Whole Blood	5% (v/v)

Matrix equivalency

Equivalence between simulated and real clinical matrix was evaluated using nasopharyngeal and nasal swabs. The WHO International Standard was used to formulate panels to a target concentration of approximately 3x LoD (above LoD), 1x LoD (at LoD) and 0.3x LoD (below LoD) into pooled negative clinical samples of each sample type (NPS, NS and simulated), stabilized in universal transport media. Twenty-five replicates per concentration were tested for each sample type. All replicates tested at the 1x LoD and 3x LoD concentrations were positive for SARS-CoV-2 for all three sample types. Simulated clinical matrix, nasopharyngeal swabs and nasal swab sample types are acceptable for use with cobas® SARS-CoV-2 Qualitative.

Collection media equivalency – UTM-RT, cobas® PCR Media and 0.9% physiological saline

Equivalence between different collection media (UTM-RT, cobas® PCR Media, and saline) was evaluated using the WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146). The WHO International Standard was used to formulate to a target concentration of approximately 2x LoD (low positive) and 4x LoD (moderate positive) into paired individual negative clinical samples, stabilized either in Universal Transport Media (UTM-RT), cobas® PCR Media (CPM), or 0.9% physiological saline (NaCl). At least 20 replicates per low positive sample and 10 replicates per moderate positive sample were tested for each collection media type. All replicates tested were positive for SARS-CoV-2 in all the three collection media types. UTM-RT, cobas® PCR Media, and 0.9% physiological saline are acceptable for use with cobas® SARS-CoV-2 Qualitative. The performance of cobas® SARS-CoV-2 Qualitative for use on the cobas® 6800/8800 Systems in cobas® PCR Media and 0.9% physiological saline has been established in analytical studies. Clinical performance of the assay in these media types was not established.

Clinical performance evaluation performed on the cobas® 6800/8800 Systems

Performance with clinical specimens

The performance of cobas SARS-CoV-2 Qualitative was evaluated in a multi-center study with three external testing sites evaluating prospectively collected clinical specimens in UTM-RT® or UVT from individuals with signs and symptoms of respiratory infection. Participants from 12 geographically distributed enrollment centers each provided nasopharyngeal swab (NPS) and nasal swab (NS, anterior nares) specimens as part of a dual collection where (a) the collection order (first specimen collected) was alternated between the NPS and NS specimen, and (b) the collection method for NS specimens was also alternated with 50% of the NS specimens were self-collected on-site with healthcare provider (HCP) instructions while the other 50% were collected by the healthcare provider. The study used a composite comparator method wherein laboratory sites used up to three highly sensitive EUA SARS-CoV-2 molecular assays, testing NPS specimen from each subject. The composite comparator result was defined as the concordant results from two comparator assays (test A and test B). In case of discordance between the initial two comparator assays, the sample was tested by a third assay (test C) and the result of the third test determined the composite comparator result. The composite comparator result was indetermined when valid results could not be obtained from two assays (i.e., insufficient volume for repeat testing of invalid/failed results).

From March to June 2021, a total of 1,154 participants were enrolled, of which samples from 968 participants were included in the evaluation. Samples from 186 participants were not included: 184 specimens were excluded due to issues associated with specimen shipments and/or being unable to complete testing within the times identified by manufacturer's instructions, and two subjects were excluded for being previously enrolled in the study (exclusion criteria). When self-reporting COVID-19 vaccination status, 207 (21.4%) of the 968 participants were fully vaccinated.

Of the 968 participants, 961 contributed a NPS specimen which resulted in 942 participants with a confirmed infected status. For NPS, 4 specimens had failed/invalid cobas® SARS-CoV-2 Qualitative results, resulting in 938 evaluable NPS results. For NS, 8 specimens were invalid/missing cobas® SARS-CoV-2 Qualitative NS results, resulting in 934 evaluable results.

When compared with the NPS composite comparator result, cobas® SARS-CoV-2 Qualitative yielded a positive percent agreement (PPA) of 98.7% for NPS and 97.4% for NS specimens. The negative percent agreement (NPA) was 99.7% and 99.9% for NPS and NS specimens, respectively (Table 25).

Table 25 Summary of clinical performance of cobas® SARS-CoV-2 Qualitative for nasopharyngeal (NPS) and nasal swabs (NS) versus the NPS composite comparator

Specimen Type	Total (N)	PPA	PPA 2-sided 95% Score CI	NPA	NPA 2-sided 95% Score CI
Nasopharyngeal (NPS)	938	98.7% (77/78)	(93.1 %, 99.8 %)	99.7% (857/860)	(99.0 %, 99.9 %)
Nasal Swab (NS)*	934	97.4% (76/78)	(91.1 %, 99.3 %)	99.9% (855/856)	(99.3 %, 100 %)

*Healthcare provider-collected nasal swab specimens and nasal swab specimens self-collected on-site with healthcare provider instructions

System equivalency / system comparison

System equivalency of the cobas® 5800, cobas® 6800 and cobas® 8800 Systems was demonstrated via performance studies. The results presented in the Instructions for Use support equivalent performance for all systems.

Additional information

Key test features



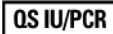










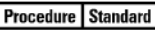

















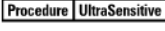




















Sample type	Nasopharyngeal swab samples collected in the Copan UTM-RT System, the BD™ UVT System and 0.9% physiological saline Nasal swab samples collected in the Copan UTM-RT System, the BD™ UVT System, the cobas® PCR Media, and 0.9% physiological saline
Minimum amount of sample required	Swab specimen types: 0.6 or 1.0 mL*
Sample processing volume	Swab specimen types: 0.4 mL

*Dead volume of 0.2 mL is identified for the cobas omni Secondary Tubes. Dead volume of 0.6 mL is identified for the cobas® PCR Media primary tubes. Other tubes compatible with cobas® 5800/6800/8800 Systems (consult User Assistance Guide) may have different dead volume and require more or less minimum volume.

Symbols

The following symbols are used in labeling for Roche PCR diagnostic products.

Table 26 Symbols used in labeling for Roche PCR diagnostics products

 Age or Date of Birth	 Device not for near-patient testing	 QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results.
 Ancillary Software	 Device not for self-testing	
 Assigned Range (copies/mL)	 Distributor <i>(Note: The applicable country/region may be designated beneath the symbol)</i>	 Serial number
 Assigned Range (IU/mL)	 Do not re-use	 Site
 Authorized representative in the European Community	 Female	 Standard Procedure
 Barcode Data Sheet	 For IVD performance evaluation only	 Sterilized using ethylene oxide
 Batch code	 Global Trade Item Number	 Store in dark
 Biological risks	 Importer	 Temperature limit
 Catalogue number	 In vitro diagnostic medical device	 Test Definition File
 CE marking of conformity; this device is in conformity with the applicable requirements for CE marking of an in vitro diagnostic medical device	 Lower Limit of Assigned Range	 This way up
 Collect date	 Male	 Ultrasensitive Procedure
 Consult instructions for use	 Manufacturer	 Unique Device Identifier
 Contains sufficient for <n> tests	 Negative control	 Upper Limit of Assigned Range
 Content of kit	 Non-sterile	 Urine Fill Line
 Control	 Patient Name	 US Only: Federal law restricts this device to sale by or on the order of a physician.
 Date of manufacture	 Patient number	 Use-by date
 Device for near-patient testing	 Peel here	
 Device for self-testing	 Positive control	
	 QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.	

Technical support

For technical support (assistance) please reach out to your local affiliate:
https://www.roche.com/about/business/roche_worldwide.htm

Manufacturer and distributor

Table 27 Manufacturer and distributor



Roche Molecular Systems, Inc.
1080 US Highway 202 South
Branchburg, NJ 08876 USA
www.roche.com

Made in USA

Distributed by Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46250-0457 USA
(For Technical Assistance call the
Roche Response Center
toll-free: 1-800-526-1247)

Trademarks and patents

See <https://diagnostics.roche.com/us/en/about-us/patents>

Copyright

©2022 Roche Molecular Systems, Inc.



References

1. Center for Disease Control and Prevention. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institutes of Health HHS Publication No. (CDC) 21-1112, revised December 2009.
2. Clinical and Laboratory Standards Institute (CLSI). Protection of laboratory workers from occupationally acquired infections. Approved Guideline-Fourth Edition. CLSI Document M29-A4:Wayne, PA;CLSI, 2014.

Document revision

Document Revision Information	
Doc Rev. 1.0 12/2022	First Publishing
Doc Rev. 2.0 12/2022	Updated with cobas ® 5800 information Please contact your local Roche Representative if you have any questions.