

**WHO Emergency Use Assessment Coronavirus disease (COVID-19) IVDs
PUBLIC REPORT**

**Product: cobas SARS-CoV-2 Qualitative assay for use on the
cobas 5800/6800/8800 Systems**

Manufacturer: Roche Molecular Systems, Inc.

EUL Number: EUL 0504-046-00

Outcome: Accepted.

The EUL process is intended to expedite the availability of in vitro diagnostics needed in public health emergency situations and to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products in the context of a Public Health Emergency of International Concern (PHEIC), based on an essential set of available quality, safety and performance data. The EUL procedure includes the following:

- Quality Management Systems Review and Plan for Post-Market Surveillance: desk-top review of the manufacturer's Quality Management System documentation and specific manufacturing documents;
- Product Dossier Review: assessment of the documentary evidence of safety and performance.

The cobas SARS-CoV-2 Qualitative assay for use on the cobas 5800/6800/8800 Systems with product codes 09175431190, 09343733190, 09446109190, 09448870190, 09175440190 (cobas SARS-CoV-2 Control Kit), 09446117190 (cobas SARS-CoV-2 Qualitative Control Kit), 09051953190 (Negative Control kit), and 07002238190 (Negative Control Kit for use cobas 6800/8800 Systems), CE-mark regulatory version, manufactured by Roche Molecular Systems, Inc., 1080 US Highway 202 South Branchburg, NJ 08876, United States of America, was listed as eligible for WHO procurement on 3 April 2020 until further notice.

Report amendments and product changes

This public report has since been amended. Amendments may have arisen because of changes to the product under EUL, for which WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
2.0	1. Addition of sample types: Added nasal swab (flocked or polyester-tipped) collection using the cobas PCR Media Uni Swab Sample Kit, cobas PCR Media Dual Swab Sample Kit, 0.9% physiological saline, Copan Universal Transport Medium (UTM-RT), and BD Universal Viral Transport (UVT). Additional intended use: Clinician-instructed self-collected (collected on site) and clinician-collected nasal swab specimens. Amendments	20 April 2021

	<p>to the instructions for use (IFU): Add instructions for the collection of nasal swab specimens using the cobas PCR swab kits and additional performance characteristics for matrix equivalency. Replaced “container” with “collection tube” to improve clarity. Corrected typographical errors, organism names, and table references.”</p>	
	<p>2. Update to the Assay Specific Analysis Package (ASAP) software associated with the cobas 6800/8800 Systems performing the SARS-CoV-2 test to:</p> <ul style="list-style-type: none"> - Allow use of the cobas Media PCR tube as the primary tube for processing without removing the swab; - Adjust liquid handling parameters to reduce dispense clot rates; - Adjust the PCR fluorescence curve analysis algorithm <p>Amendments to IFU:</p> <ul style="list-style-type: none"> - Add instructions for the cobas PCR media primary tube processing; - Add limit of detection study in copies/ml; - Revise the results interpretation table by removing the need for retesting for presumptive positives based on real-world data; - Updated the nasal swab pictogram to show a gloved hand; - Correction of confidence intervals in Table 17, “Result comparison of UTM-RT to cobas PCR media.” - Other minor edits were made for clarification. 	
	<p>3. Update to CE IFU: Addition of specimen collection kit and clarification of which collection kits are to be used with which sample types Product code (09175431190).</p>	
3.0	<p>Addition of a 480 test kit format, sample pooling claims for CE-marked IFU, and minor edits to improve clarity for the user. Correction of regulatory version from USFDA Emergency Use Authorization to CE-mark in the public report.</p>	25 November 2021
4.0	<p>1. Amendment of the intended use to include asymptomatic screening in the “Intended Use” statement.</p> <p>2. Add clinical data to the “Clinical Performance Evaluation” section.</p> <p>3. IFU updates for document numbers NAT9179909001EN and NAT9343784001EN</p>	10 November 2022
5.0	<p>The following changes were made to the listed product:</p> <ul style="list-style-type: none"> -Added the cobas SARS-CoV-2 Qualitative test to the listed product EUL 0504-046-00. The product codes for the additional product are the following: 	26 April 2023

	<ul style="list-style-type: none"> • 192T/kit: 09446109190 • 480T/kit: 09448870190 • Positive Control kit: 09446117190 • Negative Control kit: 09051953190 <p>-Addition of cobas 5800 System.</p> <p>-Addition of Saliva Specimen Type.</p> <p>-Algorithm Update.</p>	
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Intended use:

According to the claim of intended use from Roche Molecular Systems, Inc., “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 healthcare provider-instructed self-collected anterior nasal (nasal) swab and saliva specimens (collected on site), and healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens collected from any individuals, including those suspected of COVID-19 by their healthcare provider, and those without symptoms or other reasons to suspect COVID-19.

This test is also intended for the qualitative detection of nucleic acids from SARS-CoV-2 in pooled samples containing up to and including six individual samples from healthcare provider-instructed self-collected nasal swab specimens (collected on site), or healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens. Negative results from pooled samples should be treated as presumptive and, if inconsistent with clinical signs and symptoms or necessary for patient management, pooled samples should be tested individually. Specimens included in pools with a positive or presumptive positive result must be tested individually prior to reporting a result. Specimens with low SARS-CoV-2 RNA concentrations may not be detected in sample pools due to the decreased sensitivity of pooled testing.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA but may not represent 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 viruses.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

cobas SARS-CoV-2 Qualitative is intended for use by trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures.”¹

Specimen types that were validated:

Clinician-collected nasal, nasopharyngeal and oropharyngeal swabs and saliva specimens.

Test kit contents:

Amplification reagent in cassette format	192 tests (product code 09175431190)	480 tests (product code 09343733190)
Proteinase Solution (PASE)	22.3 mL	38 mL
RNA Internal Control (RNA IC)	21.2 mL	38 mL
Elution Buffer (EB)	21.2 mL	38 mL
Master Mix Reagent 1 (MMX-R1)	7.5 mL	14.5 mL
SARS-CoV-2 Master Mix Reagent 2 (SARS-CoV-2 MMX-R2)	9.7 mL	17.5 mL
cobas SARS-CoV-2 Control Kit		
SARS-CoV-2 Positive Control (SARS-CoV-2 (+) C) (P/N 09175440190 and P/N 09446117190)	16 x 1 mL	
Cobas Buffer Negative Control Kit (P/N 09051953190 and P/N 07002238190)	16 x 1 mL	

¹ The WHO EUL assessment was abridged based on reliance on the product authorization under the USFDA Emergency Use Authorization. WHO does not recommend the use of health care provider instructed/observed self-collected nasal, nasopharyngeal or oropharyngeal swab specimens. Please refer to the WHO guidance on Diagnostic testing for SARS-CoV-2 on the following link,

<https://apps.who.int/iris/discover?query=Diagnostic+testing+for+SARS-CoV-2%3A+Interim+guidance>

Items required but not provided:

Item:	Description
cobas omni reagents for sample preparation	
cobas omni MGP Reagent (MGP)	480 tests (P/N 06997546190)
cobas omni Specimen Diluent (SPEC DIL)	4 x 875 mL (P/N 06997511190)
cobas omni Lysis Reagent (LYS)	4 x 875 mL (P/N 06997538190)
cobas omni Wash Reagent (WASH)	4.2 L (P/N 06997503190)
cobas omni Processing Plate	P/N 05534917001
cobas omni Amplification Plate	P/N 05534941001
cobas omni Pipette Tips	P/N 05534925001
cobas omni Liquid Waste Container	P/N 07094388001
cobas omni Lysis Reagent	P/N 06997538190
cobas omni MGP Reagent	P/N 06997546190
cobas omni Specimen Diluent	P/N 06997511190
cobas omni Wash Reagent	P/N 06997503190
Solid Waste Bag	P/N 07435967001
Solid Waste Bag and Solid Waste Container or Solid Waste Bag with Insert and Kit Drawer	P/N 07435967001 and P/N 07094361001 or P/N 08030073001 and P/N 08387281001
Solid Waste Container	P/N 07094361001
cobas omni Secondary Tubes 13x75 (optional)	P/N 06438776001

Additional materials required for cobas 5800 System:

Materials and consumables for use on the cobas 5800 System	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, 300uL	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	07435967001

or Solid Waste Bag With Insert	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*,**	03143449001
RD5 RACK – RD Standard rack 0001-0050 LR*,**	11902997001
16-position tube carrier*	09224319001
5-position rack carrier*	09224475001

* Please refer to the instructions for use for more details.

Additional materials required for 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

* Please refer to the instructions for use for more details.

Instrumentation and software

The cobas 5800 software and cobas SARS-CoV-2 Qualitative analysis package for the cobas 5800 System must be installed on the cobas 5800 instruments. 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.

Instrument	Product number
cobas 5800 System	08707464001
cobas 6800 System (Moveable Platform)	05524245001 and 06379672001
cobas 6800 System (Fixed Platform)	05524245001 and 06379664001
cobas 8800 System	05412722001
Sample Supply Module	06301037001

Storage:

The test kit must be stored at 2-8 °C.

Shelf-life upon manufacture:

Initial shelf life of 12 months has been assigned; a real-time stability study is ongoing.

Warnings/limitations:

Please refer to the instructions for use.

Product dossier assessment

Roche Molecular Systems, Inc. submitted a product dossier for cobas SARS-CoV-2 Qualitative assay for use on the cobas 5800/6800/8800 Systems as per the “*Instructions for Submission Requirements: In vitro diagnostics (IVDs) Detecting SARS-CoV-2 Nucleic Acid (PQDx_0347)*”. The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and an external assessor appointed by WHO.

Post listing Commitments for EUL:

1. As a requirement to listing, the manufacturer is required to participate in the WHO collaborative study for the assessment of the suitability of an interim standard for SARS-CoV-2 virus nucleic acid amplification tests. This commitment was fulfilled and issued closed.
2. The manufacturer is requested to share the primer/probe sequences with WHO. The commitment was fulfilled, and the issue was closed.
3. The manufacturer will submit a precision study report to WHO by 30 April 2021. The commitment was fulfilled, and the issue was closed.

4. The manufacturer is currently undertaking real-time stability studies and will submit the final report to WHO within one month of completion. WHO will be notified of any interim results which will result in a change to the claimed shelf life.
5. The manufacturer will submit an in-use stability study report to WHO by 31 May 2021. The commitment was fulfilled, and the issue was closed.

The risk-benefit assessment is acceptable.

Quality Management Systems Review

To establish eligibility for WHO procurement, Roche Molecular Systems, Inc was asked to provide up-to-date information about the status of their quality management system.

Based on the review of the submitted quality management system documentation by WHO staff and external technical experts (assessors), it was established that sufficient information was provided by Roche Molecular Systems, Inc to fulfil the requirements described in the *“Instructions for Submission Requirements: In vitro diagnostics (IVDs) Detecting SARS-CoV-2 Nucleic Acid, PQDx_347 version 3”*.

The quality management system assessment is acceptable.

Plan for Post-Market Surveillance

Post-market surveillance, including monitoring all customer feedback, detecting and acting on adverse events, product problems, non-conforming goods and processes is a critical component of minimizing potential harm of an IVD listed for emergency use.

The following post-EUL activities are required to maintain the EUL listing status:

1. Notification to WHO of any planned changes to a EUL-listed product, in accordance with *“WHO procedure for changes to a WHO prequalified in vitro diagnostic”* (document number PQDx_121); and
2. Post-market surveillance activities, in accordance with *“Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics”* (ISBN 978-92-4-001531-9).²

Roche Molecular Systems, Inc must also submit all categories of complaints in a summarized form. Certain categories of complaints and changes to the product must be notified immediately to WHO, as per the above-mentioned documents.

Scope and duration of procurement eligibility

² Available on the web page

<https://www.who.int/publications/i/item/guidance-for-post-market-surveillanceand-market-surveillance-of-medical-devices-including-in-vitro-diagnostics>

The cobas SARS-CoV-2 Qualitative assay for use on the cobas 5800/6800/8800 Systems with product codes 09175431190, 09343733190, 09446109190, 09448870190, 09175440190 (cobas SARS-CoV-2 Control Kit), 09446117190 (cobas SARS-CoV-2 Qualitative Control Kit), 09051953190 (Negative Control kit), and 07002238190 (Negative Control Kit for use cobas 6800/8800 Systems), manufactured by Roche Molecular Systems, Inc., is considered to be eligible for WHO procurement until further notice.

As part of the ongoing requirements for listing as eligible for WHO procurement, Roche Molecular Systems, Inc. must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality and performance requirements. Roche Molecular Systems, Inc., is required to notify WHO of any complaints, including adverse events related to the use of the product, within seven days.

WHO reserves the right to rescind eligibility for WHO procurement if additional information on the safety, quality, and performance during post-market surveillance activities and if new data becomes available to WHO that changes the risk-benefit balance of the product.

Labelling

1. Labels

1.1 cobas SARS-CoV-2 Qualitative (192 test cassette (P/N 09446109190))

cobas



Rx Only



IVD



REF 09446109190

cobas[®] SARS-CoV-2 Qualitative

CONTENT

SARS-CoV-2 QL Cassette	x 1
MMX-R1	7.5 mL
SARS-CoV-2 QL MMX-R2	9.7 mL
PASE	22.3 mL
EB	21.2 mL
RNA IC	21.2 mL

EUH210 Safety data sheet available on request./ Sicherheitsdatenblatt auf Anfrage erhältlich./ Fiche de données de sécurité disponible sur demande./ Scheda dati di sicurezza disponibile su richiesta./ Puede solicitarse la ficha de datos de seguridad./ Ficha de segurança fornecida a pedido./ Sikkerhedsdatablad kan på anmodning rekvireres./ Säkerhetsdatablad finns att rekvirera.

EUH208 Contains Subtilisin. May produce an allergic reaction./ Enthält Subtilisin. Kann allergische Reaktionen hervorrufen./ Contient de la subtilisine. Peut produire une réaction allergique./ Contiene Subtilisina. Può provocare una reazione allergica./ Contiene subtilisina. Puede provocar una reacción alérgica./ Contém subtilisina. Pode provocar uma reação alérgica./ Innehåller subtilisin. Kan orsaka en allergisk reaktion.

For USA:
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.
Refer to the product specific Instructions For Use for detailed information regarding hazards.

SARS-CoV-2 QL



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



Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany

EC Importer¹

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)²

¹ Symbol text required by USA only.
² For USA only.

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Made in USA



cobas[®] SARS-CoV-2 Qualitative

cobas

SARS-CoV-2 QL

EC REP

Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
Germany



UDI label here

09465685001-03

cobas[®]

SW cobas[®] SARS-CoV-2 ASAP

Version: 10.1.0

REF 09255478001

GTIN 07613336179055

This software is for use on **cobas**[®]
6800/8800 System

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**Emergency Use
Authorization**

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SW cobas® SCoV2-QL ASAP

Software version: 12.2.0

This software is for use on the cobas® 6800/8800 System

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cobas®



SW cobas[®] SARS-CoV-2 ASAP

Software version: 11.1.0

This software is for use on the
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cobas[®]



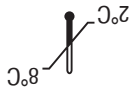
1.2 cobas SARS-CoV-2 Qualitative (480 test cassette (P/N 09343733190))

cobas

IVD



Rx Only



For USA: Emergency Use Authorization only

Qualitative nucleic acid test for use on the
cobas® 6800/8800 Systems

REF P/N: 09343733190

cobas® SARS-CoV-2

Qualitative nucleic acid test for use on the
cobas® 6800/8800 Systems
Qualitativer Nukleinsäuretest zur Verwendung auf
den **cobas® 6800/8800 Systems**
Test qualitatif d'acide nucléique destiné à une
utilisation sur les **cobas® 6800/8800 Systems**
Test qualitativo dell'acido nucleico per l'uso sui
cobas® 6800/8800 Systems
Prueba cualitativa de ácidos nucleicos para el uso
en los **cobas® 6800/8800 Systems**
Teste de ácido nucleico qualitativo para utilização
com os **cobas® 6800/8800 Systems**
Kvalitativ nukleinsyretest til bruk på
cobas® 6800/8800 Systems
Kvalitativt nukleinsyretest for anvandning med
cobas® 6800/8800 Systems

CONTENT

SARS-CoV-2 Cassette	x 1
MMX-R1	14.5 mL
SARS-CoV-2 MMX-R2	17.5 mL
PASE	38 mL
EB	38 mL
RNA IC	38 mL

EUH210 Safety data sheet available on request./ Sicherheitsdatenblatt auf Anfrage erhältlich./ Fiche de données de sécurité disponible sur demande./ Scheda dati di sicurezza disponibile su richiesta./ Puede solicitarse la ficha de datos de seguridad./ Ficha de segurança fornecida a pedido./ Sikkerhedsdatablad kan på anmodning rekvireres./ Säkerhetsdatablad finns att rekvirera.

EUH208 Contains Subtilisin. May produce an allergic reaction./ Enthält Subtilisin. Kann allergische Reaktionen hervorrufen./ Contient de la subtilisine. Peut produire une réaction allergique./ Contiene Subtilisina. Può provocare una reazione allergica./ Contiene subtilisina. Puede provocar una reacción alérgica./ Contém subtilisina. Pode provocar uma reação alérgica./ Innehåller subtilisin. Kan utlösa allergisk reaktion./ Innehåller subtilisin. Kan orsaka en allergisk reaktion.

SARS-CoV-2



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cobas® SARS-CoV-2

Qualitative nucleic acid test for use on the
cobas® 6800/8800 Systems



cobas

SARS-CoV-2

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Germany



UDI label here

09343741001-02

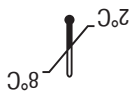
1.3 cobas SARS-CoV-2 Control Kit labels (P/N 09175440190 and P/N 09446117190)

cobas

IVD



Rx Only



For USA: Emergency Use Authorization only



Positive control kit for use on the **cobas**® 6800/8800 Systems

REF P/N: 09175440190

cobas® SARS-CoV-2 Control Kit

Cont.

MiniRack x 4
SARS-CoV-2 (+)C 16 mL (16 x 1.0 mL)

09168591001-02

SARS-CoV-2 CTL



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



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cobas® SARS-CoV-2 Control Kit

Positive control kit for use on the **cobas**® 6800/8800 Systems



cobas

SARS-CoV-2 CTL

EC REP

Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
Germany



UDI label here

NOTICE: The instructions for use for this product are contained in the target specific **cobas**® 6800/8800 test package insert.
HINWEIS: Die Gebrauchsanleitung für dieses Produkt finden Sie in der testspezifischen Packungsbeilage des jeweiligen **cobas**® 6800/8800-Tests.
INDICATION: Les instructions d'utilisation de ce produit sont contenues dans la notice relative au test **cobas**® 6800/8800 spécifique aux cibles.
AVISO: Le istruzioni per l'uso di questo prodotto sono contenute nel foglio illustrativo del test **cobas**® 6800/8800 specifico per il target.
AVISO: Las instrucciones de uso de este producto figuran en el boletín técnico específico de la prueba **cobas**® 6800/8800.
AVISO: As instruções de utilização deste produto encontram-se no folheto informativo do teste **cobas**® 6800/8800 específico do alvo.
BEMERKUNG: Bitte lesen Sie die detaillierte Produktfindes på det testspecifika pakningsbladet til **cobas**® 6800/8800-Testen.
MEDELÄNDE: Beskrivningarna för den här produkten finns på den testspecifika bipackningen för **cobas**® 6800/8800-Testet.

Positive control kit for use on the **cobas**® 6800/8800 Systems
Positivkontrollkit zur Verwendung auf den **cobas**® 6800/8800 Systemen
Kit de controles positivos à utiliser avec les systèmes **cobas**® 6800/8800
Kit di controllo positivo per l'utilizzo su sistemi **cobas**® 6800/8800
Kit de control positivo para uso en sistemas **cobas**® 6800/8800
Kit de control positivo para utilização nos sistemas **cobas**® 6800/8800
Kit med positiv kontrol til brug på **cobas**® 6800/8800-systemer
Kit for positiva kontroll för användning på **cobas**® 6800/8800-systemen

cobas



Rx Only



IVD

8°C
2°C

Positive Control Kit

cobas[®] SARS-CoV-2 Qualitative Control Kit

REF

09446117190

NOTICE: The instructions for use for this product are contained in the test-specific package insert.

HINWEIS: Die Gebrauchsanleitung für dieses Produkt finden Sie in den test-spezifischen Packungsbeilagen.

INDICATION: Les instructions d'utilisation de ce produit sont contenues dans la notice relative au test.

AVVISO: Le istruzioni per l'uso di questo prodotto sono contenute nel foglio illustrativo specifico per il test.

AVISO: Las instrucciones de uso de este producto figuran en el boletín técnico específico de la prueba.

AVISO: As instruções de utilização deste produto encontram-se no folheto informativo específico do teste.

REMARK: Brogsveledningen til dette produkt findes på det test-specifikke pakningsindlæg.

MEMORANDI: Instrukcijen za uporabo tega produkta so na voljo v posameznih pakcijskih priložnostih.

UWAGA: Instrukcje dotyczące stosowania tego produktu umieszczone są w osobnej w omieszczone do testu ulotce.

ОЗНАЧЕНИЕ: Наведен на použitie тоhto produktu sa nachádza v osobitnom špecifickom príbalovom letáku.

SARS-CoV-2 QL (+)C

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

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany
EC Importer¹

¹Symbol text required by USA only.
²For USA only.

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Made in USA

cobas[®] SARS-CoV-2 Qualitative Control Kit

Positive Control Kit



cobas

SARS-CoV-2 QL (+)C

EC REP

Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
Germany



UDI label here

Positive Control Kit
Positivkontrollkit
Kit de contrôle positif
Kit di controllo positivo
Kit de control positivo
Kit de control positivo
Kit med positiv kontroll
Kit für positive kontroll
Zestaw kontrolni dodatki
Súprava pozitívnej kontroly
Positiverekontrollkit

CONTENT

MiniRack x 4
SARS-CoV-2 QL (+)C 16 mL (16 x 1.0 mL)

For USA:
Positive control kit for use on the **cobas[®] 5800/6800/8800** Systems.
Refer to the product specific Instructions For Use for detailed information regarding hazards.

09465693001-03

2. Instructions for use³

³ English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.



Rx Only

cobas[®] SARS-CoV-2

Qualitative assay for use on the cobas[®] 6800/8800 Systems

For in vitro diagnostic use

cobas[®] SARS-CoV-2 - 192T

P/N: 09175431190

cobas[®] SARS-CoV-2 - 480T

P/N: 09343733190

cobas[®] SARS-CoV-2 Control Kit

P/N: 09175440190

cobas[®] 6800/8800 Buffer Negative Control Kit

P/N: 07002238190

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Intended use

cobas® SARS-CoV-2 for use on the **cobas**® 6800/8800 Systems is a real-time RT-PCR test intended for the qualitative detection of nucleic acids from SARS-CoV-2 in healthcare provider-instructed self-collected anterior nasal (nasal) swab specimens (collected on site), and healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens collected from any individuals, including those suspected of COVID-19 by their healthcare provider, and those without symptoms or other reasons to suspect COVID-19.

This test is also intended for the qualitative detection of nucleic acids from SARS-CoV-2 in pooled samples containing up to and including six individual samples from healthcare provider-instructed self-collected nasal swab specimens (collected on site), or healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens. Negative results from pooled samples should be treated as presumptive and, if inconsistent with clinical signs and symptoms or necessary for patient management, pooled samples should be tested individually. Specimens included in pools with a positive or presumptive positive result must be tested individually prior to reporting a result. Specimens with low SARS-CoV-2 RNA concentrations may not be detected in sample pools due to the decreased sensitivity of pooled testing.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory samples during the acute phase of infection. Positive results are indicative of SARS-CoV-2 RNA detection, but may not represent 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 viruses.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

cobas® SARS-CoV-2 is intended for use by trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures.

Summary and explanation of the test

Explanation of the test

cobas® SARS-CoV-2 is a qualitative test for use on the **cobas**® 6800 System and **cobas**® 8800 System for the detection of the 2019 novel coronavirus (SARS-CoV-2) RNA in individual or pooled nasal, nasopharyngeal and oropharyngeal swab samples collected in Copan Universal Transport Medium System (UTM-RT), BD™ Universal Viral Transport System (UVT), **cobas**® PCR Media, or 0.9% physiological saline. 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 is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. 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**® 6800/8800 software, which assigns test results for all tests. Results can be reviewed directly on the system screen, and printed as a report.

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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 with each cobas® SARS-CoV-2 run.

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 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 can be found in Table 1. Materials required, but not provided can be found in Table 2, Table 3, Table 4, Table 7, Table 8, and Table 9.

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

cobas® SARS-CoV-2 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

Kit components	Reagent ingredients	Quantity per kit	
		192 tests	480 tests
cobas® SARS-CoV-2 Store at 2-8°C 192 test cassette (P/N 09175431190) 480 test cassette (P/N 09343733190)			
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. 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 Master Mix Reagent 2 (SARS-CoV-2 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 Control Kit

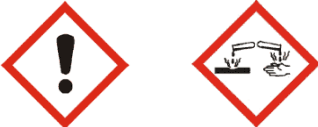
cobas® SARS-CoV-2 Control Kit		
Store at 2–8°C (P/N 09175440190)		
Kit components	Reagent ingredients	Quantity per kit
SARS-CoV-2 Positive Control (SARS-CoV-2 (+)C)	Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, < 0.003% Poly rA, < 0.01% Non-infectious plasmid DNA (microbial) containing SARS-CoV-2 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 07002238190)		
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</p> <p>H302 + H332: Harmful if swallowed or if inhaled. H314: Causes severe burns and eye damage. H412: Harmful to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. P261: Avoid breathing dust/fume/gas/mist/vapours/spray. P273: Avoid release to the environment. P280: Wear protective gloves/ protective clothing/ eye protection/ face 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. 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 test kits. See listing of additional materials required (Table 7).

** Product safety labeling primarily follows EU GHS guidance

***Hazardous substance

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Reagent storage and handling requirements

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

When reagents are not loaded on the 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 -192T	2–8°C
cobas® SARS-CoV-2 -480T	2–8°C
cobas® SARS-CoV-2 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

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 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® 6800/8800 Systems.

Table 6 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 – 192T	Date not passed ¹	90 days from first usage ¹	Max 40 runs ¹	Max 40 hours ¹
cobas® SARS-CoV-2 – 480T	Date not passed ¹	90 days from first usage ¹	Max 20 runs ¹	Max 20 hours ¹
cobas® SARS-CoV-2 Control Kit	Date not passed ¹	Not applicable ²	Not applicable	Max 8 hours ¹
cobas® Buffer Negative Control Kit	Date not passed	Not applicable ²	Not applicable	Max 10 hours
cobas omni Lysis Reagent	Date not passed	30 days from loading ³	Not applicable	Not applicable
cobas omni MGP Reagent	Date not passed	30 days from loading ³	Not applicable	Not applicable
cobas omni Specimen Diluent	Date not passed	30 days from loading ³	Not applicable	Not applicable
cobas omni Wash Reagent	Date not passed	30 days from loading ³	Not applicable	Not applicable

¹ The performance has not been established for suggested use cycles and time, but is based on similar reagents used on the same system.

² Single use reagents

³ Time is measured from the first time that reagent is loaded onto the cobas® 6800/8800 Systems.

Additional materials required

Table 7 Materials and consumables for use on **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 16mm and RD5 racks are required to use **cobas®** SARS-COV-2. 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 16mm rack is the preferred rack for use with samples collected in **cobas® PCR Media tubes. If RD5 racks are used, make sure to fill in the sample tubes with not less than the recommended minimum sample input. The tubes sit higher in an RD5 rack because of the rubber gasket at the bottom of each tube position. Therefore, it is possible that when using RD5 racks, the system could accept tubes that are below the minimum sample input volume and cause pipetting errors later in the run.

Table 8 Alternative specimen collection kits used with **cobas®** SARS-CoV-2

Collection Kit	P/N
cobas® PCR Media Uni Swab Sample Kit	07958030190
cobas® PCR Media Dual Swab Sample Kit	07958021190
cobas® PCR Media 100 tube kit	06466281190
cobas® Uni Swab 100 Kit	09205098190

Instrumentation and software required

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

Table 9 Instrumentation

Equipment	P/N
cobas ® 6800 System (Option Moveable)	05524245001 and 06379672001
cobas ® 6800 System (Fix)	05524245001 and 06379664001
cobas ® 8800 System	05412722001
Sample Supply Module	06301037001
Instrument Gateway	06349595001

For additional information, please refer to the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide.

Note: Contact your local Roche representative for a detailed order list for 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 and cobas® 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.
- **Some positive samples may not be detected when diluted and tested in pools.** SARS-CoV-2 RNA concentration is reduced when a positive sample is pooled with other samples, and the reduction corresponds inversely to the pool size. For example, if there is only one positive sample in a pool of 6, the concentration in the original sample would need to be 6 times the assay limit of detection in order for the concentration in the pool to be at the limit of detection.

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 test kit, **cobas®** SARS-CoV-2 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.

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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 kits, **cobas**® SARS-CoV-2 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**® 6800/8800 instrument, follow the instructions in the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide to properly clean and decontaminate the surface of instrument(s).

Sample collection, transport, and storage

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

Sample collection

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

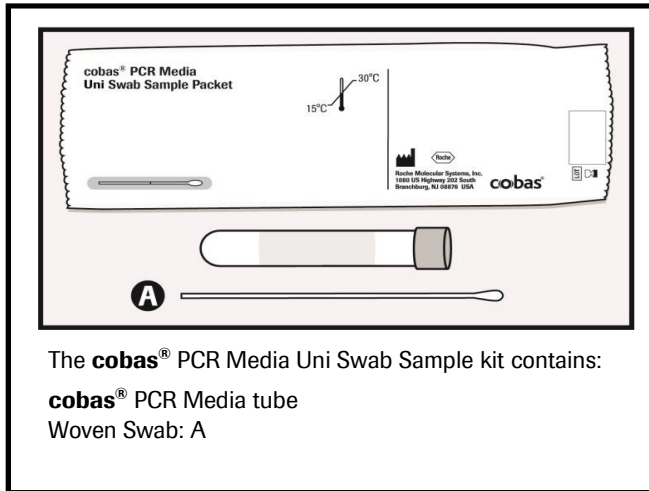
Table 10 Overview of collection devices and sample types

Collection Device	Sample Type		
	Nasopharyngeal	Oropharyngeal	Nasal
Copan Universal Transport Media (UTM-RT)	√	√	√
BD™ Universal Viral Transport (UVT)	√	√	√
cobas ® PCR Media Uni Swab Sample Kit			√
cobas ® Uni Swab 100 Kit			√
cobas ® PCR Media Dual Swab Sample Kit			√
cobas ® PCR Media Kit (and 100 tube PCR Media Kit)			√
0.9% Physiological Saline			√

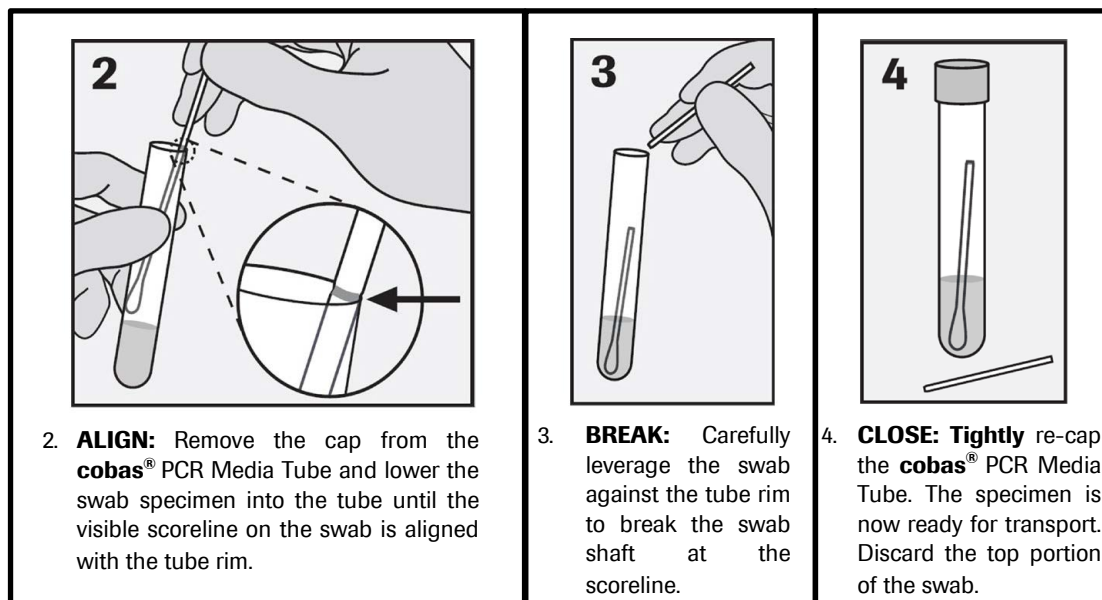
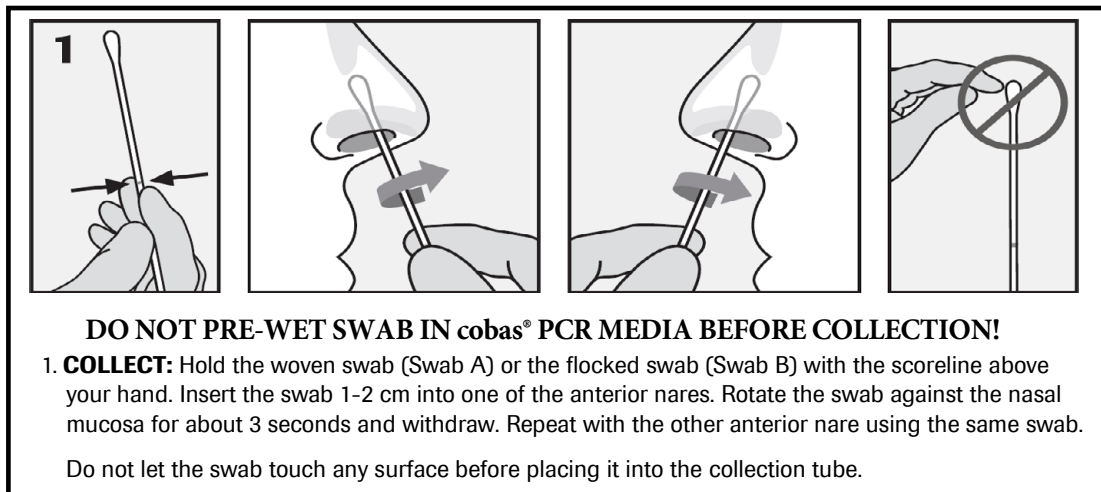
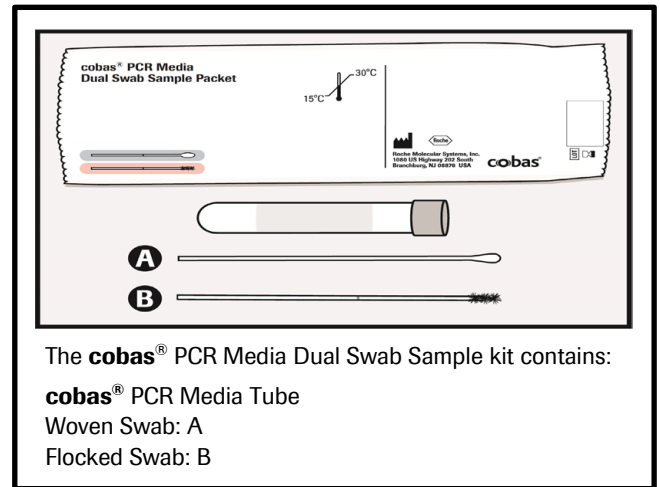
- Collect nasal, nasopharyngeal and oropharyngeal specimens according to standard collection technique using flocced or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT) or BD™ Universal Viral Transport (UVT).
- Collect nasal specimens according to standard collection technique using flocced or polyester-tipped swabs and immediately place into **cobas**® PCR Media tube from **cobas**® PCR Media Kit (P/N 06466281190).
- Collect nasal specimens using the **cobas**® PCR Media Uni Swab Sample Kit (P/N 07958030190) or **cobas**® PCR Media Dual Swab Sample Kit (P/N 07958021190) according to instructions below.
- Refer to the Instructions for Use of the Collection Devices for hazard information.

Nasal (anterior nares) swab specimen collection - clinician or self-collected on site

WARNING: DO NOT PRE-WET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!



OR



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- Collect nasal specimens according to standard collection technique using flocced or polyester-tipped swabs and immediately place in 3 mL of 0.9% physiological saline.

Transport and storage

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- Transport and store samples collected in **cobas**® PCR Media or 0.9% physiological saline as follows:
 - After collection, specimens in **cobas**® PCR Media or 0.9% physiological saline should be stored at 2-8°C and processed within 48 hours.
- Sample stability when using **cobas**® SARS-CoV-2 has not been established for suggested temperatures and time, but is based on viability data from testing similar viruses in the UTM-RT or UVT Systems as stated in Copan UTM-RT System Instructions For Use and shown below:
 - After collection, the specimen should be stored at 2-25°C and processed within 48 hours.
 - If delivery and processing exceed 48 hours, specimens should be transported in dry ice and once in laboratory frozen at -70°C or colder.

Instructions for use

Procedural notes

- Do not use cobas® SARS-CoV-2 reagents, cobas® SARS-CoV-2 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.
- Refer to the cobas® 6800/8800 Systems – User Assistance and/or User Guide for proper maintenance of instruments.

Running cobas® SARS-CoV-2

cobas® SARS-CoV-2 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 Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT), cobas® PCR Media or 0.9% physiological saline must be transferred into a cobas omni Secondary tube prior to processing on the cobas® 6800/8800 Systems. Samples transferred to cobas omni Secondary tubes should be processed using the 'Swab' sample type selection in the user interface (UI) of the cobas® SARS-CoV-2 as described in Table 11.

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 or cobas® PCR Media together with cobas® Uni Swab 100 Kit

Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit or cobas® PCR Media together with the cobas® Uni Swab 100 Kit must be uncapped and can be loaded directly onto racks for processing on the cobas® 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) and 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 or cobas® PCR Media together with the cobas® Uni Swab 100 Kit should be processed using the 'cobas® PCR Media swab' sample type selection in the user interface (UI) of the cobas® SARS-CoV-2 as described in Table 11.

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® 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 IFU 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® 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® 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 11 Sample type selection in the user interface of the cobas® SARS-CoV-2

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 cobas® PCR Media Kit	0.6 mL cobas omni Secondary tube	Swab
cobas® PCR Media Uni or Dual Swab Sample Kit cobas® PCR Media Kit together with the cobas® Uni Swab 100 Kit	1.0 mL Primary tube	cobas® PCR Media swab

Sample pooling for SARS-CoV-2 testing

Pools of up to and including 6 samples may be tested using cobas® SARS-CoV-2. The pool size implemented by the laboratory should be based on the required efficiency gains, the positivity rate of SARS-CoV-2 in the testing population, and the potential risks of testing in pools. Combination of multiple sample types in a pool has not been validated.

When resource availability is sufficient to meet testing demand, it is recommended that laboratories consider whether the risks of reduced test sensitivity with pooling outweigh the benefits of resource conservation.

- Use a process that ensures traceability between individual sample IDs and pool IDs.
- To reduce potential contamination of the cobas® 6800/8800 Systems, do not transfer samples into the secondary tubes while the samples are in the Roche 5 position racks (RD5 and/or MPA).
- Ensure appropriate sample handling techniques to reduce the risk of cross-contamination of pools and original patient samples.

Pooling methods

1. Identify a uniquely labeled secondary tube for pooling.
2. Associate the samples to be pooled with the pool tube identification using either a pooling worksheet or validated sample tracking system.
3. Roche suggests using Biological Safety Cabinet or other approved safety measures during sample handling (i.e., sample transfer to secondary tube).
4. For manual pooling, it is recommended to work with only the samples for one pool at a time.
5. Ensure each sample has sufficient volume for pool construction and any possible resolution testing (pool deconvolution) that may be required. Example: for pools of 6, a minimum volume of 100 µL (for pool) plus 600 µL (for resolution) are required for a minimum sample volume of 700 µL available prior to pooling (Table 12).

Table 12 Minimum sample volumes for pooling

Pool Size	Volume required for pool (mL)	Volume required for resolution testing (mL)	Minimum volume required prior to pooling (mL)
6	0.100	0.600	0.700
5	0.120	0.600	0.720
4	0.150	0.600	0.750
3	0.200	0.600	0.800
2	0.300	0.600	0.900

6. Using a calibrated micropipettor with a fresh pipette tip for each sample, carefully pipette each individual sample associated with that pool into the appropriate secondary tube to prepare the pool.
7. Ensure complete mixing after addition of all samples to the secondary tube (i.e., through pipetting up and down). Use caution to avoid creating bubbles, foam or aerosols while mixing.
8. For manual pooling, it is recommended to visually compare the pooled sample volume in the secondary tube to a secondary tube containing the target pool volume. If the pooling tube level is less or more than the standard pool volume, then the manually prepared pool should be discarded and prepared again.
9. Process pooled samples as described in Figure 1.

Pool result reporting and follow-up testing

Interpretation of pool results is the same as for individual results as described in the **Interpretation of results** section.

- If the result of the pool is negative, then each constituent sample is reported as negative. The result report should include a comment that pooling was used during testing. Refer to the **Warnings and precautions** section for additional information regarding decreased sensitivity of pool testing.
- If the result of the pool is positive or presumptive positive, then each of the constituent samples must be re-tested as a separate individual sample. Use the laboratory defined tracking system to ensure the correct individual samples are tested. Individual test results supersede the pool result.

cobas® SARS-CoV-2 procedure

The test procedure is described in detail in the **cobas® 6800/8800 Systems – User Assistance and/or User Guide**. Figure 1 below summarizes the procedure.

Figure 1 cobas® SARS-CoV-2 procedure

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**® 6800/8800 Systems automatically detect the SARS-CoV-2 , for each individually processed or pooled 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

- One **cobas**® Buffer Negative Control [(-) Ctrl] and one [SARS-CoV-2 (+)C] are processed with each batch.
- In the **cobas**® 6800/8800 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 software based on negative and positive control performance.

Interpretation of results

cobas® SARS-CoV-2 for System Software v1.2

Display examples for cobas® SARS-CoV-2 for System Software v1.2 are shown in Figure 2.

Figure 2 Example of cobas® SARS-CoV-2 results display for System Software v1.2

Test	Sample ID	Valid*	Flags	Sample type	Overall result*	Target 1	Target 2
SARS-CoV-2 400 µL	Swab_01	Yes		Swab	Negative	Negative	Negative
SARS-CoV-2 400 µL	Swab_C1	No	Y40T	Swab	Invalid	Invalid	Invalid
SARS-CoV-2 400 µL	Swab_B1	Yes		Swab	Reactive	Negative	Positive
SARS-CoV-2 400 µL	Swab_B2	Yes		Swab	Positive	Positive	Positive
SARS-CoV-2 400 µL	Swab_D1	Yes		Swab	Negative	Negative	Negative
SARS-CoV-2 400 µL	Swab_A6	Yes		Swab	Reactive	Positive	Negative
SARS-CoV-2 400 µL	Swab_E1	No	C01H2	Swab	Invalid	Positive	Invalid
SARS-CoV-2 400 µL	Swab_A2	No	C01H1	Swab	Invalid	Invalid	Positive
SARS-CoV-2	C161420284090428828404	Yes		(-) Ctrl	Valid	Valid	Valid
SARS-CoV-2	C161420284093009580264	Yes		SARS-CoV-2 (+) C	Valid	Valid	Valid

* The “Valid” and “Overall Result” columns are not applicable to sample results for the cobas® SARS-CoV-2. 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 13, cobas® SARS-CoV-2 results interpretation, for specific instructions on test results interpretation.

cobas® SARS-CoV-2 for System Software v1.3 or higher

Display examples for cobas® SARS-CoV-2 for System Software v1.3 or higher are shown in Figure 3.

Figure 3 Example of cobas® SARS-CoV-2 results display for System Software v1.3 or higher

Test	Sample ID	Valid*	Flags	Sample type	Overall result*	Target 1	Target 2
SARS-CoV-2 400 µL	Swab_01	NA		Swab	NA	Negative	Negative
SARS-CoV-2 400 µL	Swab_C1	NA	Y40T	Swab	NA	Invalid	Invalid
SARS-CoV-2 400 µL	Swab_B1	NA		Swab	NA	Negative	Positive
SARS-CoV-2 400 µL	Swab_B2	NA		Swab	NA	Positive	Positive
SARS-CoV-2 400 µL	Swab_D1	NA		Swab	NA	Negative	Negative
SARS-CoV-2 400 µL	Swab_A6	NA		Swab	NA	Positive	Negative
SARS-CoV-2 400 µL	Swab_E1	NA	C01H2	Swab	NA	Positive	Invalid
SARS-CoV-2 400 µL	Swab_A2	NA	C01H1	Swab	NA	Invalid	Positive
SARS-CoV-2	C161420284090428828404	Yes		(-) Ctrl	Valid	Valid	Valid
SARS-CoV-2	C161420284093009580264	Yes		SARS-CoV-2 (+) C	Valid	Valid	Valid

* The “Valid” and “Overall Result” columns are not applicable to sample results for the cobas® SARS-CoV-2. 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 13, cobas® SARS-CoV-2 results interpretation, for specific instructions on test results interpretation.

Interpretation of results

The following result interpretation applies to both **cobas**® 6800/8800 software version 1.2 and **cobas**® 6800/8800 software version 1.3 and higher.

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

- A valid batch may include both valid and invalid sample results.
- **The “Valid” and “Overall Result” columns are not applicable to sample results for the cobas® SARS-CoV-2. Values reported in these columns are not applicable and do not impact the validity of results reported within individual Target Result columns.**
- Invalid results for one or more target combinations are possible and are reported out specifically for each channel.
- Results of this test should only be interpreted in conjunction with information available from clinical evaluation of the patient and patient history.

Results and their corresponding interpretation for detecting SARS-CoV-2 are shown below (Table 13).

Table 13 cobas® SARS-CoV-2 results interpretation

Target 1	Target 2	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

- **cobas**® SARS-CoV-2 has been evaluated only for use in combination with the **cobas**® SARS-CoV-2 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**® 6800/8800 Systems.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test is intended to be used for the detection of SARS-CoV-2 RNA in nasal, nasopharyngeal and oropharyngeal swab samples collected in a Copan UTM-RT System (UTM-RT) or BD™ Universal Viral Transport System (UVT) and nasal swab samples collected in **cobas**® PCR Media and 0.9% physiological saline. Testing of other sample types with **cobas**® SARS-CoV-2 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 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 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 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.

Use of pooling based on prevalence

Pooling may increase throughput in laboratories testing samples from populations with low prevalence of SARS-CoV-2. In populations with higher prevalence, smaller pool sizes or individual sample testing may be indicated.

When considering pooling strategies, laboratories should consider the appropriateness of the pooling strategy based on the positivity rate in the testing population and efficiency of the pooling workflow. Laboratories may also consider the sensitivity of pooled testing based on the assay's limit of detection.

Table 14 provides estimated maximal efficiency gained based on N-sample pooling and on the percent of SARS-CoV-2 positive samples in a population.

Table 14 Efficiency of pooling based on prevalence

P, percent of positive subjects in the tested population	$n_{\text{maxefficiency}}$ (n corresponding to the maximal efficiency)	Efficiency (F) of n-sample pooling (a maximum increase in the number of tested patients when Dorfman n-pooling strategy used)
1% - 4%	6	4.44 - 2.60
5% - 6%	6	2.32 - 2.10
7% - 12%	6	1.92 - 1.42
13% - 25%	6	1.36 - 1.01
1% - 4%	5	4.02 - 2.60
5% - 6%	5	2.35 - 2.15
7% - 12%	5	1.98 - 1.49
13% - 25%	5	1.43 - 1.04
1% - 4%	4	3.46 - 2.50
5% - 6%	4	2.30 - 2.13
7% - 12%	4	1.99 - 1.54
13% - 25%	4	1.48 - 1.07
1% - 4%	3	2.75 - 2.23
5% - 6%	3	2.10 - 1.99
7% - 12%	3	1.89 - 1.53
13% - 25%	3	1.48 - 1.10
1% - 4%	2	1.92 - 1.73
5% - 6%	2	1.67 - 1.62
7% - 12%	2	1.57 - 1.38
13% - 25%	2	1.35 - 1.07

Because a positive pool requires individual retesting of each sample in the pool, the efficiency of any pooling strategy depends on the positivity rate. The efficiency (F) of n-sample pooling for positivity rate (P) can be calculated using the following formula $F=1/(1+1/n-(1-P)n)$. The efficiency (F) indicates how many more samples can be tested with n-sample pools compared to individual testing. For example, a 6-sample pooling strategy increases the number of tested samples by 2.10 times for positivity rate P of 6% ($F = 2.10$). At $F = 2.10$, 1,000 tests can cover testing of 2100 samples on average.

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Non-clinical performance evaluation

Key performance characteristics

Analytical sensitivity

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.

To determine the LoD, a cultured virus of an isolate from a US patient (USA-WA1/2020, catalog number NR-52281, lot number 70033175, 2.8E+05 TCID₅₀/mL[§]) was serially diluted in simulated clinical matrix. A total of 7 concentration levels, with 3-fold serial dilutions between the levels, were tested with a total of 21 replicates per concentration, with an additional 10 replicates of a blank sample (i.e., simulated clinical matrix).

As shown in Table 15, the concentration level with observed hit rates greater than or equal to 95% were 0.009 and 0.003 TCID₅₀/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively. As shown in Table 16, the Probit predicted 95% hit rates were 0.007 and 0.004 TCID₅₀/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively.

Table 15 LoD determination using USA-WA1/2020 strain

Strain	Concentration [TCID ₅₀ /mL]	Total valid results	Hit rate [%] [^]		Mean Ct*	
			Target 1	Target 2	Target 1	Target 2
USA-WA1/2020 [§] (stock concentration 2.8E+05 TCID ₅₀ /mL)	0.084	21	100	100	31.0	33.0
	0.028	21	100	100	31.8	34.1
	0.009	21	100	100	32.7	35.2
	0.003	21	38.1	100	33.5	36.4
	0.001	21	0	52.4	n/a	37.9
	0.0003	21	0	14.3	n/a	37.2
	0.0001	21	0	9.5	n/a	38.5
	0 (blank)	10	0	0	n/a	n/a

[§] The following reagent was deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, NIAID, NIH: SARS-Related Coronavirus 2, Isolate USA-WA1/2020, NR-52281

[^]All replicates where Target 1 was positive were also positive for Target 2.

* Calculations only include positive results.

Table 16 Probit predicted 95% hit rates using USA-WA1/2020 strain

Strain	Probit Predicted 95% Hit Rate [TCID ₅₀ /mL]	
	Target 1	Target 2
USA-WA1/2020 (stock concentration 2.8E+05 TCID ₅₀ /mL)	0.007 (95% CI: 0.005 – 0.036)	0.004 (95% CI: 0.002 – 0.009)

The analytical sensitivity of the assay was tested with AccuPlex SARS-CoV-2 (Lot #105324), a quantitated reference material – recombinant Sindbis virus particle containing target sequences from the SARS-CoV-2 genome. The concentration level in a dilution series with observed hit rates greater than or equal to 95% was 46 copies/mL for both Target 1 and Target 2. Probit model 95% LoD estimates based on these data were 25 copies/mL (95% CI: 17 – 58 copies/mL) for Target 1 and 32 copies/ml (95% CI: 21 – 73 copies/mL) for Target 2.

Cross-reactivity

In silico analysis

The in silico analysis for possible cross-reactions with all the organisms listed in Table 17 was conducted by mapping primers in cobas® SARS-CoV-2 individually to the sequences downloaded from NCBI and GISAID databases. If any two of the primers were mapped to a sequence on opposite strands with short distance apart, potential amplifications were flagged. No potential unintended cross reactivity is expected based on this in silico analysis.

Table 17 In silico analysis for SARS-CoV-2

Strain	In Silico Analysis for % Identity to Target 1 (nCoV)	In Silico Analysis for % Identity to Target 2 (Pan-Sarbecovirus 1)
CoV 229E	74.47	No alignment was found*
CoV OC43	72.26	No alignment was found*
CoV HKU1	76.52	No alignment was found*
CoV NL63	71.32	No alignment was found*
SARS-CoV	95.04	100
MERS	No alignment was found*	No alignment was found*
AdV	No alignment was found*	No alignment was found*
HMPV	No alignment was found*	No alignment was found*
HPIV1	No alignment was found*	No alignment was found*
HPIV2	No alignment was found*	No alignment was found*
HPIV3	No alignment was found*	No alignment was found*
HPIV4	No alignment was found*	No alignment was found*
Flu A	No alignment was found*	No alignment was found*
Flu B	No alignment was found*	No alignment was found*
EV	No alignment was found*	No alignment was found*
RSV	No alignment was found*	No alignment was found*
RV	No alignment was found*	No alignment was found*
<i>Chlamydia pneumoniae</i>	No alignment was found*	No alignment was found*
<i>Haemophilus influenzae</i>	No alignment was found*	No alignment was found*
<i>Legionella pneumophila</i>	No alignment was found*	No alignment was found*
<i>MTB Mycobacterium bovis subsp. Bovis</i>	No alignment was found*	No alignment was found*
<i>Streptococcus pneumoniae</i>	No alignment was found*	No alignment was found*
<i>Streptococcus pyrogenes</i>	No alignment was found*	No alignment was found*
<i>Bordetella pertussis</i>	No alignment was found*	No alignment was found*
<i>Mycoplasma pneumoniae</i>	No alignment was found*	No alignment was found*

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Strain	In Silico Analysis for % Identity to Target 1 (nCoV)	In Silico Analysis for % Identity to Target 2 (Pan-Sarbecovirus 1)
<i>Pneumocystis jirovecii</i>	No alignment was found*	No alignment was found*
Influenza C	No alignment was found*	No alignment was found*
Parechovirus	No alignment was found*	No alignment was found*
<i>Candida albicans</i>	No alignment was found*	No alignment was found*
<i>Corynebacterium diphtheriae</i>	No alignment was found*	No alignment was found*
<i>Legionella non-pneumophila</i>	No alignment was found*	No alignment was found*
<i>Bacillus anthracis (Anthrax)</i>	No alignment was found*	No alignment was found*
<i>Moraxella catarrhalis</i>	No alignment was found*	No alignment was found*
<i>Neisseria elongate and meningitides</i>	No alignment was found*	No alignment was found*
<i>Pseudomonas aeruginosa</i>	No alignment was found*	No alignment was found*
<i>Staphylococcus epidermidis</i>	No alignment was found*	No alignment was found*
<i>Staphylococcus salivarius</i>	No alignment was found*	No alignment was found*
<i>Leptospira</i>	No alignment was found*	No alignment was found*
<i>Chlamydia psittaci</i>	No alignment was found*	No alignment was found*
<i>Coxiella burnetii (Q-Fever)</i>	No alignment was found*	No alignment was found*
<i>Staphylococcus aureus</i>	No alignment was found*	No alignment was found*

Note: * The amplicon sequences were blasted against all the exclusive sequences with very low stringency cutoff (50% and 100bp). No alignment were found passing the cutoff and no concerns for cross-reactivity were observed.

Cross reactivity testing

Cross-reactivity of cobas® SARS-CoV-2 was evaluated by testing whole organisms. As listed in Table 18, a panel of multiple unique sub-species of microorganisms were tested. High titer stocks of the potentially cross-reacting microorganisms were spiked into negative simulated clinical matrix to a concentration level of 1.0E+05 units/mL for viruses and 1.0E+06 units/mL for other microorganisms, unless otherwise noted.

None of the organisms tested interfered with cobas® SARS-CoV-2 performance by generating false positive results.

Table 18 Cross-reactivity test results

Microorganism	Concentration	Target 1 Result	Target 2 Result
Human coronavirus 229E	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Human coronavirus OC43	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Human coronavirus HKU1	1.0E+05 cp/mL	Negative	Negative
Human coronavirus NL63	1.0E+05 TCID ₅₀ /mL	Negative	Negative
MERS coronavirus	1.0E+05 genomic equivalent/mL	Negative	Negative
SARS coronavirus	1.0E+05 PFU/mL	Negative	Positive
Adenovirus B (Type 34)	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Human Metapneumovirus (hMPV)	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Parainfluenza virus Type 1	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Parainfluenza virus Type 2	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Parainfluenza virus Type 3	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Parainfluenza virus Type 4	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Influenza A (H1N1)	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Influenza B	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Enterovirus E (Type 1)	1.0E+05 TCID ₅₀ /mL	Negative	Negative
Respiratory syncytial virus	1.0E+05 PFU/mL	Negative	Negative
Rhinovirus	1.0E+05 TCID ₅₀ /mL	Negative	Negative
<i>Chlamydia pneumonia</i>	1.0E+06 TCID ₅₀ /mL	Negative	Negative
<i>Haemophilus influenzae</i>	1.0E+06 CFU/mL	Negative	Negative
<i>Legionella pneumophila</i>	1.0E+06 CFU/mL	Negative	Negative
<i>Mycobacterium tuberculosis</i>	1.0E+06 cells/mL	Negative	Negative
<i>Streptococcus pneumonia</i>	1.0E+06 CFU/mL	Negative	Negative
<i>Streptococcus pyrogenes</i>	1.0E+06 CFU/mL	Negative	Negative
<i>Bordetella pertussis</i>	1.0E+06 CFU/mL	Negative	Negative
<i>Mycoplasma pneumoniae</i>	1.0E+06 CFU/mL	Negative	Negative
Pooled human nasal wash	5 - 50%	Negative	Negative

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Sample type equivalency

Equivalence between nasopharyngeal swab (NPS) and oropharyngeal swab (OPS) sample types was evaluated using cultured virus (USA-WA1/2020 strain) spiked into paired negative samples (individual samples, not pooled) to prepare contrived low positive (approximately 1.5x Target 1 LoD) and moderate positive (approximately 4x Target 1 LoD) samples for each sample type. A total of 21 low positive paired samples, 11 moderate positive paired samples, and 11 negative paired samples were tested.

As shown in Table 19, all low positive and moderate positive paired samples were positive in both sample matrices. All negative paired samples were negative in both sample types. The observed Ct values for contrived positive samples were comparable in both sample types.

Table 19 Result comparison of nasopharyngeal to oropharyngeal sample types

Sample Type	Sample Concentration	N	Target 1		Target 2	
			% Positive	Mean Ct (95% CI)	% Positive	Mean Ct (95% CI)
NPS	~1.5x LoD (Target 1)	21	100	31.9 (31.7 – 32.0)	100	33.6 (33.5 – 33.7)
OPS			100	32.2 (31.8 – 32.6)	100	33.7 (33.4 – 34.1)
NPS	~4x LoD (Target 1)	11	100	30.9 (30.3 – 31.5)	100	32.2 (31.6 – 32.9)
OPS			100	31.5 (31.2 – 31.9)	100	32.7 (32.4 – 33.0)
NPS	Negative	11	0	n/a	0	n/a
OPS			0	n/a	0	n/a

Matrix equivalency – UTM-RT and cobas® PCR Media

Equivalence between samples collected in UTM-RT and cobas® PCR Media (CPM) was evaluated using cultured virus (USA-WA1/2020 strain) spiked into paired negative nasopharyngeal samples from patients with signs and symptoms of an upper respiratory infection (individual samples, not pooled) to prepare contrived low positive (approximately 1.5x LoD) and moderate positive (approximately 4x LoD) samples for each collection media. A total of 21 low positive paired samples, 11 moderate positive paired samples, and 11 negative paired samples were tested.

As shown in Table 20, all low positive and moderate positive paired samples were positive in both sample matrices. All negative paired samples were negative in both sample matrices. The observed Ct values for contrived positive samples were comparable in both sample matrices.

Table 20 Result comparison of UTM-RT to cobas® PCR Media

Collection Media	Sample Concentration	N	Target 1		Target 2	
			% Positive	Mean Ct (95% CI)	% Positive	Mean Ct (95% CI)
UTM	~1.5x LoD	21	100	31.8 (31.6 - 32.0)	100	34.0 (33.8 - 34.2)
CPM			100	32.2 (31.9 - 32.4)	100	34.7 (34.4 - 35.0)
UTM	~4x LoD	11	100	30.7 (30.1 - 31.2)	100	32.4 (31.7 - 33.1)
CPM			100	31.6 (31.0 - 32.1)	100	33.7 (32.9 - 34.5)
UTM	Negative	11	0	n/a	0	n/a
CPM			0	n/a	0	n/a

Matrix equivalency – UTM-RT and 0.9% physiological saline

Equivalence between samples collected in UTM-RT and 0.9% physiological saline was evaluated using cultured virus (USA-WA1/2020 strain) spiked into paired negative samples (individual samples, not pooled) to prepare contrived low positive (approximately 1.5x LoD) and moderate positive (approximately 4x LoD) samples for each collection media. Three samples were collected from each of 45 healthy donors using swabs from cobas® PCR Media Dual Swab Sample Kit; two nasal samples (NS) collected using dual flocked/woven polyester swabs stored in UTM and one nasal sample (other nostril) collected using a woven polyester swab stored in 0.9% physiological saline. A total of 17 low positive paired samples, 11 moderate positive paired samples, and 45 negative paired samples were tested.

As shown in Table 21, all low positive and moderate positive paired samples were positive in both sample matrices. All negative paired samples were negative in both sample matrices. The observed Ct values for contrived positive samples were comparable in both sample matrices.

Table 21 Result comparison of UTM-RT to 0.9% physiological saline

Collection Device	Sample Concentration	N	Target 1		Target 2	
			% Positive	Mean Ct (95% CI)	% Positive	Mean Ct (95% CI)
Flocked Swab in UTM-RT	~1.5x LoD	17	100	32.2 (32.0 - 32.4)	100	33.6 (33.6 - 33.7)
Woven Swab in UTM-RT		16	100	31.6 (31.1 - 32.1)	100	33.2 (32.7 - 33.8)
Woven Swab in Saline		17	100	31.7 (31.4 - 32.0)	100	33.5 (33.2 - 33.8)
Flocked Swab in UTM-RT	~4x LoD	11	100	31.2 (31.1 - 31.4)	100	32.6 (32.4 - 32.7)
Woven Swab in UTM-RT			100	30.9 (30.4 - 31.4)	100	32.4 (31.9 - 33.0)
Woven Swab in Saline			100	31.0 (30.8 - 31.3)	100	32.6 (32.5 - 32.7)
Flocked Swab in UTM-RT	Negative	45	0	n/a	0	n/a
Woven Swab in UTM-RT			0	n/a	0	n/a
Woven Swab in Saline			0	n/a	0	n/a

Performance in sample pools

The performance of cobas® SARS-CoV-2 when testing nasopharyngeal samples collected in UTM or UVT was evaluated using one cobas® 6800 System and one cobas® 8800 System. Thirty positive samples were tested individually and in pools of 6 containing 1 positive and 5 negative samples, and in pools of 3 containing 1 positive and 2 negative samples. Additionally, negative samples were tested individually, in 20 negative pools of 6, and in 20 negative pools of 2.

The 30 individual positive specimens had pan-Sarbecovirus Target 2 Ct values between 15.1 – 35.3, including a subset of 8 Low Positive samples (~27% of the samples) with Target 2 Ct values between 33.4 and 35.3. The Low Positive subset of samples targeted within 2-3 Ct (actual 1.1 – 3) of the mean Ct for Target 2 at the Limit of Detection.

The performance of testing sample pools of 6 and pools of 3 containing one positive sample each, compared to testing individual samples, is shown in Table 22 and Table 23, respectively. Positive and presumptive positive results (as defined in Table 13) were used for the Positive Percent Agreement (pools vs. individual) calculations, as all the constituent samples would require re-testing as a separate individual samples. Results are summarized for all samples, and separately summarized for the subset of Low Positive samples, for each tested pool size.

Table 22 Reactivity in positive sample pools of 6

Samples in Pools of 6	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Positive Percent Agreement (pools vs, individual)
Positive (Including Low Positive)	0	0	30*	30	100% (30/30) (95% CI: 88.6 – 100%)
Low Positive	0	0	8*	8	100% (8/8) (95% CI: 67.6 – 100%)

*Note: One low positive sample was presumptive positive when tested in a pool of 6.

Table 23 Reactivity in positive sample pools of 3

Samples in Pools of 3	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Positive Percent Agreement (pools vs, individual)
Positive (Including Low Positive)	0	0	30	30	100% (30/30) (95% CI: 88.6 – 100%)
Low Positive	0	0	8	8	100% (8/8) (95% CI: 67.6 – 100%)

The performance of testing sample pools of 6 and pools of 2 containing only negative samples compared to testing individual samples, is shown in Table 24.

Table 24 Specificity in negative sample pools of 6 and pools of 2

Pool Size	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Observed Negative Rate
Pools of 6	20	0	0	20	100% (20/20) (95% CI: 83.9 – 100%)
Pools of 2	20	0	0	20	100% (20/20) (95% CI: 83.9 – 100%)

Note: Some positive samples may not be detected when diluted and tested in pools. Performance estimations above may underestimate the loss of detection from testing in pools. Laboratories should also consider the assay's limit of detection when evaluating testing in pools (see **Warnings and precautions**).

Clinical performance evaluation

The performance of cobas® SARS-CoV-2 with prospectively collected nasopharyngeal swab clinical samples was evaluated using 100 individual negative clinical samples and 50 contrived positive clinical samples collected from patients with signs and symptoms of an upper respiratory infection.

Clinical samples were collected by qualified personnel according to the package insert of the collection device. Samples were handled as described in the package insert of the collection device and stored frozen until use. Samples were tested to be negative by a commercially available nucleic acid test for the qualitative detection of microorganisms associated with common upper respiratory tract infections.

Low positive and moderate positive contrived positive clinical samples were prepared by spiking cultured virus (USA-WA1/2020 strain) into individual negative clinical samples to approximately ~1.5x LoD (Target 1) (25 samples) and ~4x LoD (Target 1) (25 samples), respectively.

As shown in Table 25 all low positive and moderate positive samples were positive and all negative samples were negative in the background of individual clinical sample matrix.

Table 25 Clinical evaluation with nasopharyngeal swab samples

Sample Concentration	N	Target 1		Target 2	
		% positive (two-sided 95% CI)	Mean Ct	% positive (two-sided 95% CI)	Mean Ct
~1.5x LoD	25	100 (86.7 - 100)	31.6	100 (86.7 - 100)	33.2
~4x LoD	25	100 (86.7 - 100)	31.1	100 (86.7 - 100)	32.4
Negative	100	0 (n/a)	n/a	0 (n/a)	n/a

Performance against the expected results are:

Positive Percent Agreement 50/50 = 100% (95% CI: 92.9% - 100%)

Negative Percent Agreement 100/100 = 100% (95% CI: 96.3% - 100%)

Clinical performance with samples from individuals suspected of COVID-19

The performance of cobas® SARS-CoV-2 was compared to a highly sensitive RT-PCR EUA SARS-CoV-2 test (comparator) using nasopharyngeal samples collected in UTM from individuals suspected of COVID-19.

A total of 162 archived, de-identified, and prospectively collected fresh individual nasopharyngeal samples from individuals suspected of COVID-19 were included in the study. Thirty of these nasopharyngeal swab samples stored in Viral Transport Media (Copan UTM, BD™ UVT) were positive and 132 were negative for SARS-CoV-2 by the comparator. The study included 33.3% low positive samples (LP) with comparator Ct values that are within 3 Cts of the

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mean Ct value at the established comparator LoDs according to the respective instruction for use. The Cts of other positive samples were distributed over a broad range. Results are shown in Table 26.

Table 26 Clinical evaluation with nasopharyngeal swab samples from individuals suspected of COVID-19

		Highly Sensitive Comparator RT-PCR EUA Test			Percent Agreement	Result (%)	95% Score Confidence Interval (%)
		Positive	Negative	Total			
cobas® SARS-CoV-2	Positive	30	6*	36	PPA	100.0 (30/30)	88.6 – 100.0
	Negative	0	126	126			
	Total	30	132	162			

*confirmed as true positives by post-amplification analysis of the amplicon

Performance against the comparator results are:

Positive Percent Agreement $30/30 = 100\%$ (95% CI: 88.6% - 100%)

Negative Percent Agreement $126/132 = 95.5\%$ (95% CI: 90.4%-97.9%)

Discordant results between the cobas® SARS-CoV-2 assay and the comparator method were observed for 6 samples. These samples showed late Ct values, which are indicative of samples from individuals with viral loads close to or below the limit of detection of both the cobas® SARS-CoV-2 assay and the comparator test. Post-PCR analysis of the amplicon from all discordant samples confirmed the presence of SARS-CoV-2.

Clinical performance with samples from individuals without symptoms or other reasons to suspect COVID-19.

The performance of cobas® SARS-CoV-2 was compared to a highly sensitive RT-PCR EUA SARS-CoV-2 test (comparator) using nasopharyngeal samples collected in UTM from individuals without symptoms or other reasons to suspect COVID-19.

A total of 143 consecutively collected, archived, de-identified, individual nasopharyngeal samples from individuals without symptoms or other reasons to suspect COVID-19 were included in the study. Twenty-two of these nasopharyngeal swab samples were positive and 121 were negative for SARS-CoV-2 by the comparator. Results are shown in Table 27.

Table 27 Clinical evaluation with nasopharyngeal swab samples from individuals without symptoms or other reasons to suspect COVID-19

		Highly Sensitive Comparator RT-PCR EUA Test			Percent Agreement	Result (%)	95% Score Confidence Interval (%)
		Positive	Negative	Total			
cobas® SARS-CoV-2	Positive	21	0	21	PPA	95.5 (21/22)	78.2 -99.2
	Negative	1	121	122			
	Total	22	121	143			

Performance against the comparator results are:

Positive Percent Agreement $21/22 = 95.5\%$ (95% CI: 78.2% - 99.2%)

Negative Percent Agreement $121/121 = 100\%$ (95% CI: 96.9%-100%)

Discordant results between the **cobas®** SARS-CoV-2 assay and the comparator method were observed for 1 sample. This sample showed late Ct values, which are indicative of samples from individuals with viral loads close to or below the limit of detection of both the **cobas®** SARS-CoV-2 assay and the comparator test.

Additional information

Key test features

Sample type	Nasopharyngeal and oropharyngeal swab samples collected in the Copan UTM-RT System or the BD™ UVT System 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	0.6 or 1.0 mL **
Sample processing volume	0.4 mL
Test duration	Results are available within less than 3.5 hours after loading the sample on the system.





























* 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**® 6800/8800 Systems (consult User Assistance Guide) may have different dead volume and require more or less minimum volume.

**Additional volume is required if pooling.

Symbols

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

Table 28 Symbols used in labeling for Roche PCR diagnostics products

 Age/DOB	Age or Date of Birth		Date of manufacture
	Ancillary Software		Distributed by
	Assigned Range (copies/mL)		Do not re-use
	Assigned Range (IU/mL)		Female
	Authorized representative in the European Community		For IVD performance evaluation only
	Barcode Data Sheet		Global Trade Item Number
	Batch code		<i>In vitro</i> diagnostic medical device
	Biological risks		Lower Limit of Assigned Range
	Catalogue number		Male
	Collect date		Manufacturer
	Consult instructions for use		Negative control
	Contains sufficient for <n> tests		Non sterile
	Contents of kit		Patient number
	Control		Patient Name



Peel here



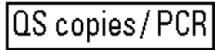
This way up



Positive control



Unique Device Identification



QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.



Ultrasensitive Procedure



Upper Limit of Assigned Range



QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results.



Urine Fill Line



Serial number

Rx Only

US Only: Federal law restricts this device to sale by or on the order of a physician.



Site



Use-by date



Standard Procedure



Device for near-patient testing



Sterilized using ethylene oxide



Device Not for Near Patient Testing



Store in the dark



Device for self-testing



Temperature limit



Device not for self-testing



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

Technical support

For technical support (assistance) please reach out to your local affiliate:

https://www.roche.com/about/business/roche_worldwide.htm

Manufacturer and distributors

Table 29 Manufacturer and distributors



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

Made in USA

Distributed by

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany

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

This product is covered by one or more of US Patent Nos. 8962293, 9102924, 8609340, 9234250, 8097717, 8192958, 10059993, 10358675, 8129118, and 6727067, and foreign equivalent patents of each.

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All other product names and trademarks are the property of their respective owners.

Carryover prevention technology in the AmpErase® enzyme is covered by U.S. Patent 7,687,247 owned by Life Technologies and licensed to Roche Molecular Systems, Inc.

See <http://www.roche-diagnostics.us/patents>

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68305 Mannheim
Germany



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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 10/2020	First Publishing.
Doc Rev. 2.0 02/2021	Remove check mark from Table 10 corresponding to the collection of nasopharyngeal sample types using cobas® PCR Media Uni Swab Sample Kit. Added Made in statement. Please contact your local Roche Representative if you have any questions.
Doc Rev. 3.0 05/2021	Added text pointing to the sample collection kits' IFU for hazard information. "Refer to the Instructions for Use of the Collection Devices for hazard information." Updated Trademarks and patents section. Please contact your local Roche Representative if you have any questions.
Doc Rev. 4.0 05/2021	Changed Intended Use statement to include Asymptomatic Screening Added clinical data to the Clinical performance evaluation section. Please contact your local Roche Representative if you have any questions.



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

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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 healthcare provider-instructed self-collected anterior nasal (nasal) swab and saliva specimens (collected on site), and healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens collected from any individuals, including those suspected of COVID-19 by their healthcare provider, and those without symptoms or other reasons to suspect COVID-19.

This test is also intended for the qualitative detection of nucleic acids from SARS-CoV-2 in pooled samples containing up to and including six individual samples from healthcare provider-instructed self-collected nasal swab specimens (collected on site), or healthcare provider-collected nasal, nasopharyngeal, and oropharyngeal swab specimens. Negative results from pooled samples should be treated as presumptive and, if inconsistent with clinical signs and symptoms or necessary for patient management, pooled samples should be tested individually. Specimens included in pools with a positive or presumptive positive result must be tested individually prior to reporting a result. Specimens with low SARS-CoV-2 RNA concentrations may not be detected in sample pools due to the decreased sensitivity of pooled testing.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA but may not represent 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 viruses.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

cobas® SARS-CoV-2 Qualitative is intended for use by trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures.

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 System, **cobas**® 6800 System or **cobas**® 8800 System for the detection of the 2019 novel coronavirus (SARS-CoV-2) RNA in individual saliva specimens collected in a sterile empty collection container and individual or pooled nasal, nasopharyngeal and oropharyngeal swab samples collected in Copan Universal Transport Medium System (UTM-RT), BD™ Universal Viral Transport System (UVT), **cobas**® PCR Media, or 0.9% physiological saline. 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 System 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 10.

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 + H332: Harmful if swallowed or if inhaled. 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. 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 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**
cobas® SARS-CoV-2 Qualitative 480T	Date not passed	90 days from first usage	Max 40 runs	Max 36 days**
cobas® SARS-CoV-2 Qualitative Control Kit	Date not passed	Not applicable*	Not applicable	Max 36 days**
cobas® Buffer Negative Control Kit	Date not passed	Not applicable*	Not applicable	Max 36 days**
cobas omni Lysis Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni MGP Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni Specimen Diluent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni Wash Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable

*Single use reagents.

**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 Table 7 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*	Not applicable	Max 8 hours**
cobas® Buffer Negative Control Kit	Date not passed	Not applicable*	Not applicable	Max 10 hours**
cobas omni Lysis Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni MGP Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni Specimen Diluent	Date not passed	30 days from loading**	Not applicable	Not applicable
cobas omni Wash Reagent	Date not passed	30 days from loading**	Not applicable	Not applicable

* Single use reagents.

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

Additional materials required for 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, 300uL	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***	03143449001
RD5 RACK – RD Standard rack 0001-0050 LR***	11902997001
16-position tube carrier*	09224319001
5-position rack carrier*	09224475001

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

*** MPA 16mm rack or 16-position tube carrier are the preferred racks for use with samples collected in **cobas**® PCR Media tubes. If RD5 racks are used, make sure to fill in the sample tubes with not less than the recommended minimum sample input. The tubes sit higher in an RD5 rack because of the rubber gasket at the bottom of each tube position. Therefore, it is possible that when using RD5 racks, the system could accept tubes that are below the minimum sample input volume and cause pipetting errors later in the run.

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. If RD5 racks are used, make sure to fill in the sample tubes with not less than the recommended minimum sample input. The tubes sit higher in an RD5 rack because of the rubber gasket at the bottom of each tube position. Therefore, it is possible that when using RD5 racks, the system could accept tubes that are below the minimum sample input volume and cause pipetting errors later in the run.

Alternative collection kits for swab specimens for use on the cobas® 5800/6800/8800 Systems

Table 10 Alternative specimen collection kits used with cobas® SARS-CoV-2 Qualitative for swab specimens

Collection Kit	P/N
cobas® PCR Media Uni Swab Sample Kit	07958030190
cobas® PCR Media Dual Swab Sample Kit	07958021190
cobas® PCR Media 100 tube kit	06466281190
cobas® Uni Swab 100 Kit	09205098190

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 11 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 (cobas® 6800/8800 Systems only)	06301037001

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

Note: Contact your local Roche representative for a detailed order list for 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.
- **Some positive samples may not be detected when diluted and tested in pools.** SARS-CoV-2 RNA concentration is reduced when a positive sample is pooled with other samples, and the reduction corresponds inversely to the pool size. For example, if there is only one positive sample in a pool of 6, the concentration in the original sample would need to be 6 times the assay limit of detection in order for the concentration in the pool to be at the limit of detection.
- Inform your local competent authority about any serious incidents which may occur when using this assay.
- Reliable saliva results are dependent on proper specimen collection, handling, and storage. In case of visible particles or discoloration in the saliva sample, samples should not be further processed, but patient shall be asked to provide a new sample. Food particles and increased levels of mucin might cause failures in processing of the saliva specimen.

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.

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**® Systems – User Assistance and/or User Guide to properly clean and decontaminate the surface of the instrument(s).

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:

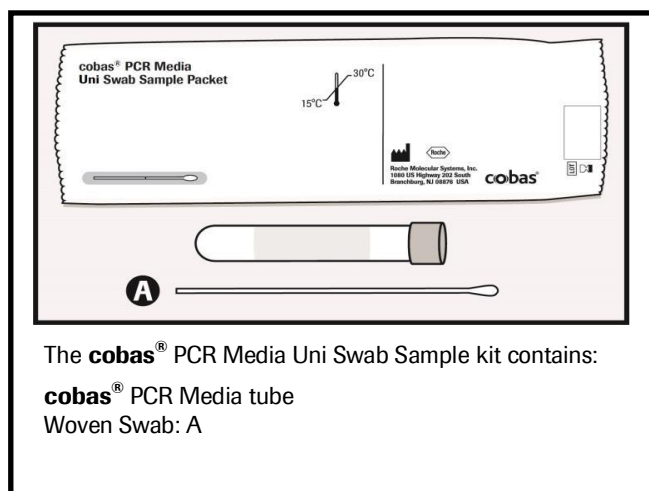
Table 12 Overview of collection devices and sample types

Collection Device	Sample Type		
	Nasopharyngeal	Oropharyngeal	Nasal
Copan Universal Transport Media (UTM-RT®)	✓	✓	✓
BD™ Universal Viral Transport (UVT)	✓	✓	✓
cobas® PCR Media Uni Swab Sample Kit			✓
cobas® PCR Media Dual Swab Sample Kit			✓
cobas® PCR Media Kit (and 100 tube PCR Media Kit)			✓
0.9% Physiological saline			✓

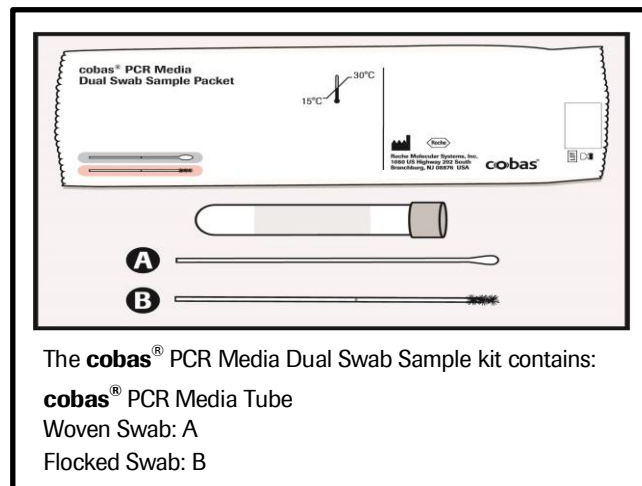
- Collect nasal, nasopharyngeal and oropharyngeal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT) or BD™ Universal Viral Transport (UVT).
- Collect nasal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place into cobas® PCR Media tube from cobas® PCR Media Kit (P/N 06466281190).
- Collect nasal specimens using the cobas® PCR Media Uni Swab Sample Kit (P/N 07958030190) or cobas® PCR Media Dual Swab Sample Kit (P/N 07958021190) according to instructions below.
- Refer to the Instructions for Use of the Collection Devices for hazard information.

Nasal (anterior nares) swab specimen collection - clinician or self-collected on site

WARNING: DO NOT PRE-WET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!



OR



1

DO NOT PRE-WET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!

1. **COLLECT:** Hold the woven swab (Swab A) or the flocked swab (Swab B) with the scoreline above your hand. Insert the swab 1-2 cm into one of the anterior nares. Rotate the swab against the nasal mucosa for about 3 seconds and withdraw. Repeat with the other anterior nare using the same swab.

Do not let the swab touch any surface before placing it into the collection tube.

2

2. **ALIGN:** Remove the cap from the cobas® PCR Media Tube and lower the swab specimen into the tube until the visible scoreline on the swab is aligned with the tube rim.

3

3. **BREAK:** Carefully leverage the swab against the tube rim to break the swab shaft at the scoreline.

4

4. **CLOSE:** Tightly re-cap the cobas® PCR Media Tube. The specimen is now ready for transport. Discard the top portion of the swab.

- Collect nasal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of 0.9% physiological saline.

Sample collection – saliva

- Do NOT eat or brush teeth 60 minutes before collecting the saliva sample.
- Collect saliva on the floor of your mouth and allow to pool without swallowing. Do not cough.
- Spit passively collected saliva into a sterile collection container.
- Repeat the procedure above until at least 1 mL, but no more than 5 mL of saliva are collected in the container.
- Replace cap on the saliva collection container.
- Return the saliva collection container.

Raw saliva needs to be liquified within 9 days of collection (48 hours at 2-25°C followed by 7 days below -18°C) by estimating the volume of saliva and adding double the amount of 0.9% physiological saline solution to the saliva collection container. After addition of saline, the sample needs to be mixed (e.g., vortex 10 – 20 seconds) prior to further storage or processing.

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®,
 - 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.
- 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.
- 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.
- Specimen are stable for up to two freeze/thaw cycles when frozen at ≤ -70°C.

Transport and storage – saliva

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- Raw saliva samples collected in a sterile polypropylene collection device,
 - After collection, specimens can be stored for up to 48 hours at 2-25°C followed by up to 7 days ≤ -18°C.
- Liquified saliva,
 - After addition of 2 parts of 0.9% physiological saline solution and intensive mixing, the liquified saliva specimens can be stored for up to 48 hours at 2-25°C followed by up to 7 days at 2-8°C.

Instructions for use

Procedural notes

- Do not use cobas® SARS-CoV-2 Qualitative, 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 and cobas® 6800/8800 Systems may be loaded directly onto the cobas® 5800 and cobas® 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 and cobas® 6800/8800 Systems must be transferred into a secondary tube prior to processing on the cobas® 5800 and cobas® 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 or cobas® PCR Media together with cobas® Uni Swab 100 Kit

Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit or cobas® PCR Media together with the cobas® Uni Swab 100 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) or the 16-position tube carrier (P/N 09224319001) and 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 or cobas® PCR Media together with the cobas® Uni Swab 100 Kit should be processed using the 'cobas® PCR media swab' sample type selection in the user interface (UI) of the 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.

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

Raw saliva specimens collected in a sterile polypropylene container need to be liquified prior to processing. For liquifaction, the volume of raw saliva is estimated and the double amount of 0.9% physiological saline is added. The collection device must be recapped and the solution mixed (e.g., vortex 10 – 20 seconds) prior to the required transfer into a secondary tube and processing on the cobas® 5800/6800/8800 Systems. The cobas® **omni** Secondary Tube is the preferred option. Liquified saliva samples transferred to secondary tubes should be processed using the 'Saliva' sample type selection in the user interface (UI) of the cobas® SARS-CoV-2 Qualitative.

Always use caution when transferring specimens from a primary collection container to the 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 liquifaction and transfer into a secondary tube.

Follow the steps below to transfer saliva samples from a primary collection container into a secondary tube:

- Unscrew the primary sample container cap and lift the cap.
- Estimate the volume of raw saliva and add the double amount of 0.9% physiological saline.
- Recap the container and mix (e.g., vortex 10-20 seconds) until a homogenous solution results.
- Unscrew the primary sample container cap and lift the cap.
- Transfer 1.2 mL into the prepared barcoded secondary tube.
- Close the primary sample container cap.
- Transfer secondary tube to the rack.

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

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 cobas® PCR Media Kit	0.6 mL cobas omni Secondary Tube	VTM
cobas® PCR Media Uni or Dual Swab Sample Kit cobas® PCR Media Kit together with the cobas® Uni Swab 100 Kit	1.0 mL Primary tube	cobas® PCR media swab
Liquified Saliva in a sterile polypropylene container	1.2 mL cobas omni Secondary Tube	Saliva

Sample pooling for SARS-CoV-2 testing

Pools of up to and including 6 samples may be tested using cobas® SARS-CoV-2 Qualitative. The pool size implemented by the laboratory should be based on the required efficiency gains, the positivity rate of SARS-CoV-2 in the testing population, and the potential risks of testing in pools. Combination of multiple sample types in a pool has not been validated.

When resource availability is sufficient to meet testing demand, it is recommended that laboratories consider whether the risks of reduced test sensitivity with pooling outweigh the benefits of resource conservation.

- Use a process that ensures traceability between individual sample IDs and pool IDs.
- To reduce potential contamination of the cobas® 5800/6800/8800 Systems, do not transfer samples into the secondary tubes while the samples are in the Roche 5 position racks (RD5 and/or MPA and /or 16 position tube carrier).
- Ensure appropriate sample handling techniques to reduce the risk of cross-contamination of pools and original patient samples.

Note: Sample pooling does not apply to saliva specimen.

Pooling methods

1. Identify a uniquely labeled secondary tube for pooling.
2. Associate the samples to be pooled with the pool tube identification using either a pooling worksheet or validated sample tracking system.
3. Roche suggests using Biological Safety Cabinet or other approved safety measures during sample handling (i.e., sample transfer to secondary tube).
4. For manual pooling, it is recommended to work with only the samples for one pool at a time.
5. Ensure each sample has sufficient volume for pool construction and any possible resolution testing (pool deconvolution) that may be required. Example: for pools of 6, a minimum volume of 100 µL (for pool) plus 600 µL (for resolution) are required for a minimum sample volume of 700 µL available prior to pooling (Table 14).

Table 14 Minimum sample volumes for pooling

Pool Size	Volume required for pool (mL)	Volume required for resolution testing (mL)	Minimum volume required prior to pooling (mL)
6	0.100	0.600	0.700
5	0.120	0.600	0.720
4	0.150	0.600	0.750
3	0.200	0.600	0.800
2	0.300	0.600	0.900

6. Using a calibrated micropipettor with a fresh pipette tip for each sample, carefully pipette each individual sample associated with that pool into the appropriate secondary tube to prepare the pool.
7. Ensure complete mixing after addition of all samples to the secondary tube (i.e., through pipetting up and down). Use caution to avoid creating bubbles, foam or aerosols while mixing.
8. For manual pooling, it is recommended to visually compare the pooled sample volume in the secondary tube to a secondary tube containing the target pool volume. If the pooling tube level is less or more than the standard pool volume, then the manually prepared pool should be discarded and prepared again.
9. Process pooled samples as described in Figure 1 and Figure 2.

Pool result reporting and follow-up testing

Interpretation of pool results is the same as for individual results as described in the **Interpretation of results** section.

- If the result of the pool is negative, then each constituent sample can be reported as negative. The result report should include a comment that pooling was used during testing. Refer to the **Warnings and precautions** section for additional information regarding decreased sensitivity of pool testing.
- If the result of the pool is positive or presumptive positive, then each of the constituent samples must be re-tested as a separate individual sample. Use the laboratory defined tracking system to ensure the correct individual samples are tested. Individual test results supersede the pool result.

Running cobas® SARS-CoV-2 Qualitative on 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 test 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 [BUF (-) C] 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 System 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 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 System software in the “Results” app.

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

Table 15 Example of cobas® SARS-CoV-2 Qualitative results display cobas® 5800 System

Sample ID*	Test	Control Result	Flags**	Status	Result		Creation date/time
Sample_01	SCoV2-QL	Valid		Released	SCoV2 Negative	PanSarb Negative	7/7/2021 8:27:39 AM
Sample_C1	SCoV2-QL	Invalid		Released	Invalid	Invalid	7/7/2021 8:27:39 AM
Sample_B1	SCoV2-QL	Valid		Released	SCoV2 Negative	PanSarb Positive	7/7/2021 8:27:39 AM
Sample_B2	SCoV2-QL	Valid		Released	SCoV2 Positive	PanSarb Positive	7/7/2021 8:27:39 AM

Sample _D1	SCoV2-QL	Valid		Released	SCoV2 Negative	PanSarb Negative	7/7/2021 8:27:39 AM
Sample _A6	SCoV2-QL	Valid		Released	SCoV2 Positive	PanSarb Negative	7/7/2021 8:27:39 AM
Sample _E1	SCoV2-QL	Valid		Released	SCoV2 Positive	Invalid	7/7/2021 8:27:39 AM
Sample _A2	SCoV2-QL	Valid		Released	Invalid	PanSarb Positive	7/7/2021 8:27:39 AM

*Table applies for all sample types used.

** The result overview shows a flag symbol in case of invalid results. Detailed flag descriptions are available in the result details.

- 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 Control Results are 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 “Result” column for individual sample target result should be interpreted as show in Table 15 above.
- 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 [BUF (-) 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 16.
- The “Valid” and “Overall Result” columns are not applicable to sample results for the 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 17.

Table 16 Example of cobas® SARS-CoV-2 Qualitative results display on cobas® 6800/8800 Systems

Test	Sample ID	Valid*	Flags	Sample type	Overall result*	Target 1	Target 2
SCoV2- QL	Sample _01	NA		VTM	NA	SCoV2 Negative	PanSarb Negative
SCoV2- QL	Sample _C1	NA	Y40T	VTM	NA	Invalid	Invalid
SCoV2- QL	Sample _B1	NA		VTM	NA	SCoV2 Negative	PanSarb Positive
SCoV2- QL	Sample _B2	NA		VTM	NA	SCoV2 Positive	PanSarb Positive
SCoV2- QL L	Sample _D1	NA		VTM	NA	SCoV2 Negative	PanSarb Negative
SCoV2- QL	Sample _A6	NA		VTM	NA	SCoV2 Positive	PanSarb Negative
SCoV2- QL	Sample _E1	NA	C01H2	VTM	NA	SCoV2 Positive	Invalid
SCoV2- QL	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

**The “Valid” and “Overall Result” columns are not applicable to sample results for the cobas® SARS-CoV-2 Qualitative. Refer to Table 17, cobas® SARS-CoV-2 Qualitative results interpretation, for specific instructions on test results interpretation.

Table 17 cobas® SARS-CoV-2 Qualitative results interpretation

Target 1	Target 2	Interpretation
SCoV2 Positive	PanSarb Positive	All Target Results were valid. Result for SARS-CoV-2 RNA is Detected.
SCoV2 Positive	PanSarb 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.
SCoV2 Negative	PanSarb 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.
SCoV2 Negative	PanSarb Negative	All Target Results were valid. Result for SARS-CoV-2 RNA is Not Detected.
SCoV2	Invalid	Not all Target Results were valid. Result for SARS-CoV-2 RNA is Detected.
Invalid	PanSarb 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.
SCoV2 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	PanSarb 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.

*For further details also refer to section **Procedural limitations**

Procedural limitations

- 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.
- 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.
- Reliable results depend on proper sample collection, storage and handling procedures.
- Due to the nature of the saliva sample type and the individual patient sample variability, an increased invalid and clot rate may occur. Additionally, food particles and increased levels of mucin indicated by potentially discolored samples might cause failures in processing of the saliva specimen. Refer to the **Sample collection – saliva** section for the appropriate precautions to be taken during collection to assure optimal performance.
- Occasionally, incoming saliva specimens may induce a pipetting error (e.g. clot or other obstruction) on the cobas® 5800/6800/8800 Systems. A potential additional processing step prior to retesting the specimens that exhibited clots during initial processing is to centrifuge the samples at 2000g for 1 minute and reload the samples on the instrument. Aerosols might occur during centrifugation. To avoid any contamination or transmission of the virus, please handle centrifuged samples carefully .
- This test is intended to be used for the detection of SARS-CoV-2 RNA in nasal, nasopharyngeal and oropharyngeal swab samples collected in a Copan UTM-RT System (UTM-RT) or BD™ Universal Viral Transport System (UVT) and nasal swab samples collected in cobas® PCR Media and 0.9% physiological saline. Additionally the test is intended to be used for the detection of SARS-CoV-2 RNA in saliva specimens liquified with 0.9% physiological saline. Testing of other sample types with cobas® SARS-CoV-2 Qualitative may result in inaccurate results.
- 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.

Use of pooling based on prevalence

Pooling may increase throughput in laboratories testing samples from populations with low prevalence of SARS-CoV-2. In populations with higher prevalence, smaller pool sizes or individual sample testing may be indicated.

When considering pooling strategies, laboratories should consider the appropriateness of the pooling strategy based on the positivity rate in the testing population and efficiency of the pooling workflow. Laboratories may also consider the sensitivity of pooled testing based on the assay's limit of detection.

Table 18 provides estimated maximal efficiency gained based on N-sample pooling and on the percent of SARS-CoV-2 positive samples in a population.

Table 18 Efficiency of pooling based on prevalence

P, percent of positive subjects in the tested population	$n_{\text{maxefficiency}}$ (n corresponding to the maximal efficiency)	Efficiency (F) of n-sample pooling (a maximum increase in the number of tested patients when Dorfman n-pooling strategy used)
1% - 4%	6	4.44 - 2.60
5% - 6%	6	2.32 - 2.10
7% - 12%	6	1.92 - 1.42
13% - 25%	6	1.36 - 1.01
1% - 4%	5	4.02 - 2.60
5% - 6%	5	2.35 - 2.15
7% - 12%	5	1.98 - 1.49
13% - 25%	5	1.43 - 1.04
1% - 4%	4	3.46 - 2.50
5% - 6%	4	2.30 - 2.13
7% - 12%	4	1.99 - 1.54
13% - 25%	4	1.48 - 1.07
1% - 4%	3	2.75 - 2.23
5% - 6%	3	2.10 - 1.99
7% - 12%	3	1.89 - 1.53
13% - 25%	3	1.48 - 1.10
1% - 4%	2	1.92 - 1.73
5% - 6%	2	1.67 - 1.62
7% - 12%	2	1.57 - 1.38
13% - 25%	2	1.35 - 1.07

Because a positive pool requires individual retesting of each sample in the pool, the efficiency of any pooling strategy depends on the positivity rate. The efficiency (F) of n-sample pooling for positivity rate (P) can be calculated using the following formula $F=1/(1+1/n-(1-P)n)$. The efficiency (F) indicates how many more samples can be tested with n-sample pools compared to individual testing. For example, a 6-sample pooling strategy increases the number of tested samples by 2.10 times for positivity rate P of 6% ($F = 2.10$). At $F = 2.10$, 1,000 tests can cover testing of 2,100 samples on average.

Non-clinical performance evaluation

Analytical sensitivity (Limit of Detection) – swab specimen types

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 tested positive.

To determine the LoD, the WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146) was serially diluted in simulated clinical matrix. A total of 5 concentration levels, and 3 independent dilution series, were tested with a total of 24 replicates per concentration and lot, with an additional 60 replicates of a blank sample (i.e., clinical sample pools).

As shown in Table 19 and Table 20, the concentration level with observed hit rates greater than or equal to 95% were 250 and 125 IU/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively and the Probit predicted 95% hit rates were 200 and 102 IU/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively.

Table 19 Summary of LoD for SARS-CoV-2 using WHO International Standard (NIBSC code: 20/146)

Viral Strain	Kit lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	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	202	157-319	250	33.2
	Lot 2	121	97-183	125	34.1
	Lot 3	259	196-413	250	33.2
	Lot 1-3	200	170-252	250	33.4

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

Viral Strain	Kit lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	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	83	64-127	125	35.2
	Lot 2	67	46-454	125	36.0
	Lot 3	132	99-233	125	34.8
	Lot 1-3	102	83-140	125	35.3

Further, the sensitivity of the assay was determined using a cultured virus of an isolate from a US patient (USA-WA1/2020, catalog number NR-52281, lot number 70033175, $2.8E+05$ TCID₅₀/mL[§]) was serially diluted in simulated clinical matrix. A total of 7 concentration levels, with 3-fold serial dilutions between the levels, were tested with a total of 21 replicates per concentration, with an additional 10 replicates of a blank sample (i.e., simulated clinical matrix).

As shown in Table 21 the concentration level with observed hit rates greater than or equal to 95% were 0.009 and 0.003 TCID₅₀/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively. As shown in Table 22, the Probit predicted 95% hit rates were 0.007 and 0.004 TCID₅₀/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively.

Table 21 LoD determination using USA-WA1/2020 strain

Strain	Concentration [TCID ₅₀ /mL]	Total valid results	Hit rate [%]**		Mean Ct*	
			Target 1	Target 2	Target 1	Target 2
USA-WA1/2020* (stock concentration $2.8E+05$ TCID ₅₀ /mL) Lot 70033175***	0.084	21	100	100	31.0	33.0
	0.028	21	100	100	31.8	34.1
	0.009	21	100	100	32.7	35.2
	0.003	21	38.1	100	33.5	36.4
	0.001	21	0	52.4	n/a	37.9
	0.0003	21	0	14.3	n/a	37.2
	0.0001	21	0	9.5	n/a	38.5
	0 (blank)	10	0	0	n/a	n/a

* The following reagent was deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, NIAID, NIH: SARS-Related Coronavirus 2, Isolate USA-WA1/2020, NR-52281

** All replicates where Target 1 was positive were also positive for Target 2.

*** Based on the information provided in the Certificate of Analysis from the vendor, 1 TCID₅₀/mL is equal to 7,393 genome equivalents by ddPCR

Table 22 Probit Predicted 95% Hit Rates Using USA-WA1/2020 Strain

Strain	Probit Predicted 95% Hit Rate [TCID ₅₀ /mL]	
	Target 1	Target 2
USA-WA1/2020 (stock concentration $2.8E+05$ TCID ₅₀ /mL)	0.007 (95% CI: 0.005 – 0.036)	0.004 (95% CI: 0.002 – 0.009)

Analytical sensitivity (Limit of Detection) – saliva specimen types

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 tested positive.

To determine the LoD, the WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146) was serially diluted in pools of negative Saliva clinical specimens. A total of 8 concentration levels and 3 independent dilution series/saliva pools, were tested with a total of 32 replicates per concentration and lot, with an additional 96 replicates of a blank sample (i.e., clinical sample pools).

As shown in Table 23 and Table 24, the concentration levels with observed hit rates greater than or equal to 95% were 150 IU/mL and 75 IU/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively and the Probit predicted 95% hit rates were 92 and 72 IU/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively.

Table 23 Summary of LoD for SARS-CoV-2 using WHO International Standard (NIBSC code: 20/146)

Viral Strain	Kit lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	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	102	76-156	150	34.0
	Lot 2	92	71-140	150	33.9
	Lot 3	82	64-121	150	33.8
	Lot 1-3	92	78-114	150	33.9

Table 24 Summary of LoD for pan-Sarbecovirus using WHO International Standard (NIBSC code: 20/146)

Viral Strain	Kit lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	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	62	48-94	75	36.6
	Lot 2	75	54-128	150	35.6
	Lot 3	79	58-130	75	36.5
	Lot 1-3	72	60-92	75	36.5

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 25.

Table 25 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) for a total of 30 runs. A description of the precision panel and the observed positivity rates are shown in Table 26. 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 27) yielded overall CV percentage ranging from 1.1% to 2.2% for cobas® SARS-CoV-2 Qualitative.

Table 26 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 27 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

Analytical specificity / cross-reactivity

A panel of 48 viruses, bacteria, and fungi (including those commonly found in respiratory tract) were tested with cobas® SARS-CoV-2 Qualitative to assess analytical specificity. The organisms listed in Table 28 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 ~3x LoD). None of the organisms interfered with the test performance. Testing of SARS-CoV-1 generated an expected pan-Sarbecovirus positive result.

Table 28 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

Microorganism	Concentration
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
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
Pooled Nasal Wash	1:20 of Patient Sample

Interference

The effect of exogenous substances potentially secreted into respiratory specimens was evaluated (Table 29). 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.

Table 29 List of exogenous substances tested for interference

Substance	Concentration
Oxymetazoline	0.011 mg/mL
Galphimia glauca, Luffa operculata, Sabadilla	0.023 mg/mL
Lidocaine and Phenylephrine	2.68 mg/mL
Budesonide	0.039 mg/mL
Phenol	0.47 mg/mL
Fluticasone propionate	166.67 µg/mL
Mupirocin	0.20 mg/mL
Zanamivir	0.0015 mg/mL
Oseltamivir	0.0073 mg/mL
Benzocaine and Menthol	5.00 mg/mL
Tobramycin	0.018 mg/mL
Petroleum Jelly	1% (w/v)
Nicotine	1% (w/v)
Camphor-synthetic eucalyptus oil and menthol ointment	1% (w/v)
0.65% NaCl, Phenylcarbinol, Benzalkonium chloride	1% (w/v)

Endogenous substances that may be present in respiratory specimens were tested for interference (Table 30). 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.

Table 30 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 – UTM-RT/UVT, cobas® PCR Media and 0.9% physiological saline

Equivalence between different collection media (UTM-RT/UVT, cobas® PCR Media, and saline) was evaluated.

Equivalence between UTM-RT/UVT and cobas® PCR Media was evaluated 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/UVT) or, cobas® PCR Media (CPM).

Equivalence between UTM-RT/UVT and 0.9% physiological saline was evaluated using cultured virus (USA-WA1/2020 strain). The cultured virus 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/UVT) 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/UVT, cobas® PCR Media, and 0.9% physiological saline are acceptable for use with cobas® SARS-CoV-2 Qualitative.

Whole system failure

The whole system failure rate was assessed by testing 100 specimens of simulated clinical matrix spiked with WHO International Standard for SARS-CoV-2 RNA (acid-heat inactivated England/02/2020 isolate, NIBSC code: 20/146) to a concentration of approximately 3x LoD. The results of this study determined that all replicates were valid and positive for SARS-CoV-2, resulting in a whole system failure rate of 0% with an upper one-sided 95% confidence interval of 2.95%.

Cross contamination

Studies were performed to evaluate potential cross contamination on the cobas® 6800/8800 Systems using cobas® SARS-CoV-2 Qualitative. Cross-contamination can cause false positive results. In this performance study, the sample-to-sample cross-contamination rate of cobas® SARS-CoV-2 Qualitative was 0.0% (0/239; with an upper one-sided 95% CI of 1.25%) in UTM samples and 0.6% (3/480; with a 95% CI from 0.1% to 1.8%) in Saliva samples when alternating high viral level positive and negative samples were tested over multiple runs. High viral level positive samples in the study were prepared to generate a Ct value that exceeds the 95th percentile of all positive samples observed via real world monitoring of cobas® SARS-CoV-2 Qualitative (>10 million results). The likelihood of encountering such specimens in the routine use of cobas® SARS-CoV-2 Qualitative is proportional to SARS-CoV-2 prevalence in the testing population. Therefore, the sample-to-sample cross-contamination rate for saliva samples in routine use of cobas® SARS-CoV-2 Qualitative will likely be less than 0.6% x 5% x SARS-CoV-2 prevalence (in percent) in the testing population. With an assumed prevalence of 10%, the estimated cross-contamination rate would be 0.6% x 5% x 10% = 0.003%.

Performance in sample pools

The performance of cobas® SARS-CoV-2 Qualitative when testing nasopharyngeal samples collected in UTM or UVT was evaluated using one cobas® 6800 System and one cobas® 8800 System. Thirty positive samples were tested individually and in pools of 6 containing 1 positive and 5 negative samples, and in pools of 3 containing 1 positive and 2 negative samples. Additionally, negative samples were tested individually, in 20 negative pools of 6, and in 20 negative pools of 2.

The 30 individual positive specimens had pan-Sarbecovirus Target 2 Ct values between 15.1 – 35.3, including a subset of 8 Low Positive samples (~27% of the samples) with Target 2 Ct values between 33.4 and 35.3. The Low Positive subset of samples targeted within 2-3 Ct (actual 1.1 – 3) of the mean Ct for Target 2 at the Limit of Detection.

The performance of testing sample pools of 6 and pools of 3 containing one positive sample each, compared to testing individual samples, is shown in Table 31 and Table 32, respectively. Positive and presumptive positive results (as defined in Table 17) were used for the Positive Percent Agreement (pools vs. individual) calculations, as all the constituent samples would require re-testing as separate individual samples. Results are summarized for all samples, and separately summarized for the subset of Low Positive samples, for each tested pool size.

Table 31 Reactivity in positive sample pools of 6

Samples in Pools of 6	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Positive Percent Agreement (pools vs, individual)
Positive (Including Low Positive)	0	0	30*	30	100% (30/30) (95% CI: 88.6 – 100%)
Low Positive	0	0	8*	8	100% (8/8) (95% CI: 67.6 – 100%)

*Note: One low positive sample was presumptive positive when tested in a pool of 6.

Table 32 Reactivity in positive sample pools of 3

Samples in Pools of 3	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Positive Percent Agreement (pools vs, individual)
Positive (Including Low Positive)	0	0	30	30	100% (30/30) (95% CI: 88.6 – 100%)
Low Positive	0	0	8	8	100% (8/8) (95% CI: 67.6 – 100%)

The performance of testing sample pools of 6 and pools of 2 containing only negative samples compared to testing individual samples, is shown in Table 33.

Table 33 Specificity in negative sample pools of 6 and pools of 2

Pool Size	Negative Pool Results	Invalid Pool Results	Positive or Presumptive Positive Pool Results	Total N valid Pool Results	Observed Negative Rate
Pools of 6	20	0	0	20	100% (20/20) (95% CI: 83.9 – 100%)
Pools of 2	20	0	0	20	100% (20/20) (95% CI: 83.9 – 100%)

Note: Some positive samples may not be detected when diluted and tested in pools. Performance estimations above may underestimate the loss of detection from testing in pools. Laboratories should also consider the assay's limit of detection when evaluating testing in pools (see **Warnings and precautions**).

Clinical performance evaluation

Performance with clinical specimens – swab specimen types

The performance of cobas® SARS-CoV-2 Qualitative was evaluated across three studies with archived or fresh, prospectively collected specimens. Combined, all three studies compared the performance of cobas® SARS-CoV-2 Qualitative across four external testing sites (one site in the EU, three in the US) using a common highly sensitive CE-IVD SARS-CoV-2 assay as the comparator method. The specimens in all studies were collected into VTM.

The first study consisted of archived nasopharyngeal swab (NPS) specimens from individuals with signs and symptoms of a respiratory infection evaluated at one external site. The second study consisted of one external site evaluating archived specimens from individuals without symptoms or other reasons to suspect COVID-19. The final study was a large multi-center study with three external testing sites evaluating prospectively collected fresh clinical specimens from individuals with signs and symptoms of a respiratory infection. Participants from 12 geographically distributed enrollment centers provided NPS and NS (nasal swab) specimens as part of a dual collection procedure where (a) the collection order was varied such that the first specimen collected will be ~50% NPS and ~50% NS, and (b) the collection method for NS specimens was also varied to yield ~50% self-collected and ~50% healthcare worker-collected.

Across the three studies, a total of 1,500 SARS-CoV-2 nasopharyngeal swab specimen results were evaluable and included in the data analysis. The accuracy (method correlation) of the cobas® SARS-CoV-2 Qualitative in comparison to a highly sensitive CE-IVD SARS-CoV-2 assay is shown in Table 34. Overall, the cobas® SARS-CoV-2 Qualitative Positive Percent Agreement (PPA) was 97.2% (140/144) and Negative Percent Agreement (NPA) was 99.9% (1,354/1,356).

Table 34 Summary of NPS clinical performance of cobas® SARS-CoV-2 Qualitative

Specimen Type	Target	Total (N)	PPA	PPA LCL 95% Score CI	PPA UCL 95% Score CI	NPA	NPA LCL 95% Score CI	NPA UCL 95% Score CI
Nasopharyngeal	SARS-CoV-2	1500	97.2% (140/144)	93.1%	98.9%	99.9% (1,354/1,356)	99.5%	100%

CI= confidence interval, LCL= lower confidence limit, NPA= negative percent agreement, PPA= positive percent agreement, UCL= upper confidence limit.

Additionally, the aforementioned prospective multi-center evaluation study was designed to evaluate the performance of the cobas® SARS-CoV-2 Qualitative test using NPS and NS specimens from subjects suspected of respiratory infection. This study used a composite comparator method wherein laboratory sites used up to 3 highly-sensitive CE-IVD SARS-CoV-2 assays to determine the infective status by majority rule. The composite comparator result was defined as the concordant results from 2 comparator assays (test A and test B). In case of discordance between the initial 2 comparator assays, the sample was tested by a third assay (test C) and the result of that test determined the composite comparator status.

When compared with the composite comparator result, cobas® SARS-CoV-2 Qualitative yielded a Positive Percent Agreement (PPA) of 98.7% for NPS and 96.2% for NS specimens. The Negative Percent Agreement (NPA) was 99.7% for NPS and 100% for NS specimens. cobas® SARS-CoV-2 Qualitative also demonstrated similar performance when using self-collected and healthcare worker collected nasal swab specimens as shown in Table 35.

Table 35 Summary of NPS/NS clinical performance of cobas® SARS-CoV-2 Qualitative - prospective evaluation

Specimen Type	Target	Total (N)	PPA	PPA LCL 95% Score CI	PPA UCL 95% Score CI	NPA	NPA LCL 95% Score CI	NPA UCL 95% Score CI
Nasopharyngeal*	SARS-CoV-2	938	98.7% (77/78)	93.1 %	99.8 %	99.7% (857/860)	99.0 %	99.9 %
Nasal Swab	SARS-CoV-2	941	96.2% (76/79)	89.4 %	98.7 %	100.0% (862/862)	99.6 %	100.0 %
Nasal Swab - Self Collected	SARS-CoV-2	481	100.0% (40/40)	91.2 %	100.0 %	100.0% (441/441)	99.1 %	100.0 %
Nasal Swab - HCW Collected	SARS-CoV-2	460	92.3% (36/39)	79.7 %	97.3 %	100.0% (421/421)	99.1 %	100.0 %

CI= confidence interval, LCL= lower confidence limit, NPA= negative percent agreement, PPA= positive percent agreement, UCL= upper confidence limit, HCW= healthcare worker.

* Nasopharyngeal specimen data from the prospective study are included in both Table 34 and Table 35. Test A of the SARS-CoV-2 composite comparator was the same method used as the single comparator in the summary analysis of all three studies.

Performance with clinical specimens – saliva specimen

The performance of cobas® SARS-CoV-2 Qualitative was evaluated with prospectively collected specimens. The study compared the performance of cobas® SARS-CoV-2 Qualitative at one external testing site within the EU against the paired nasopharyngeal swab result of cobas® SARS-CoV-2 Qualitative as the comparator. Nasopharyngeal specimens were collected into RT-UTM and saliva specimens were collected as raw saliva into a sterile device.

The study was evaluating prospectively collected clinical specimens from individuals with signs and symptoms of a respiratory infection, as well from individuals without signs and symptoms of a respiratory infection. Participants provided nasopharyngeal swab and saliva specimens as part of a dual collection procedure.

Paired specimens in a total of 652 subjects were evaluable and included in the data analysis, which included 298 (45.7%) who were symptomatic and 354 (54.3%) who were asymptomatic at the time of sample collection. The accuracy (method correlation) of the cobas® SARS-CoV-2 Qualitative using saliva in comparison to the cobas® SARS-CoV-2 Qualitative using nasopharyngeal swab specimen is shown in Table 36. Overall, the cobas® SARS-CoV-2 Qualitative Positive Percent Agreement (PPA) between the saliva and nasopharyngeal swab specimen types was 82.2% (120/146) and Negative Percent Agreement (NPA) was 97.2% (492/506).

Table 36 Summary of clinical performance of cobas® SARS-CoV-2 Qualitative using saliva in comparison to NPS

Specimen Type	Target	Total (N)	PPA	PPA LCL 95% Score CI	PPA UCL 95% Score CI	NPA	NPA LCL 95% Score CI	NPA UCL 95% Score CI
Saliva	SARS-CoV-2	652	82.2% (120/146)	75.2%	87.5%	97.2% (492/506)	95.4%	98.3%

CI= confidence interval, LCL= lower confidence limit, NPA= negative percent agreement, PPA= positive percent agreement, UCL= upper confidence limit.

The Positive Percent Agreement of the cobas® SARS-CoV-2 Qualitative using saliva in comparison to the cobas® SARS-CoV-2 Qualitative using nasopharyngeal swab specimen split into arbitrary viral level groups is shown in Table 37. The cobas® SARS-CoV-2 Qualitative Positive Percent Agreement (PPA) between the specimen types saliva and nasopharyngeal swab was 97.9.% (47/48) for NPS samples with a high viral level (Ct of target 1 (SARS-CoV-2) ≤ 23), 100.0% (50/50) for NPS samples with a moderate viral level (Ct of target 1 (SARS-CoV-2) > 23 to 30), and 47.9% (23/48) for NPS samples with a low viral level at and below the Limit of Detection of the NPS sample type (Ct of target 1 (SARS-CoV-2) > 30).

Table 37 Positive Percent Agreement cobas® SARS-CoV-2 Qualitative using saliva in comparison to the viral level detected in the paired NPS sample

Viral level based on Ct* of paired NPS specimen	Target	Total (N)	PPA	PPA LCL 95% Score CI	PPA UCL 95% Score CI
High (NPS Ct ≤ 23)	SARS-CoV-2	48	97.9% (47/48)	89.1%	99.6%
Moderate (NPS > Ct 23 to ≤ Ct 30)	SARS-CoV-2	50	100.0% (50/50)	92.9%	100.0%
Low (NPS Ct > 30, at and below LoD of NPS sample type)	SARS-CoV-2	48	47.9% (23/48)	34.5%	61.7%

CI= confidence interval, LCL= lower confidence limit, NPA= negative percent agreement, PPA= positive percent agreement, UCL= upper confidence limit.

* Ct of target 1 (SARS-CoV-2)

Testing of the 40 saliva specimens where results were discrepant between the paired nasopharyngeal swab and saliva specimen by an alternative highly sensitive CE-IVD NAT test resulted in a 100% agreement with the cobas® SARS-CoV-2 Qualitative saliva result. All 14 cobas® SARS-CoV-2 Qualitative NPS negative, but saliva positive results were confirmed as saliva positive by the alternative test, and all 26 cobas® SARS-CoV-2 Qualitative NPS positive, but saliva negative results were confirmed as saliva negative by the alternative test. This indicates that discrepant results when using saliva as a sample type are dependent on the differences between the two specimen types rather than on the assay performance.

Additionally, head-to-head comparison between saliva samples tested with the cobas® SARS-CoV-2 Qualitative and the Hologic Aptima™ SARS-CoV-2 tests was performed (Table 38). The two tests comparably detected SARS-CoV-2 RNA in saliva specimens with an overall Positive Percent Agreement (PPA) of 97.8% (131/134) and a Negative Percent Agreement (NPA) of 99.4% (514/517). The 95% confidence limits ranged from 93.6% to 99.2% for the PPA and from 98.3% to 99.8% for the NPA, respectively. All cobas-/Aptima+ saliva specimens generated negative results for the paired NPS specimens. For the cobas+/Aptima- saliva specimens, two of three results were positive for the paired NPS specimens. The third cobas+/Aptima- saliva specimen tested positive for target 2 only (pan-Sarbecovirus) with a late Ct value indicating a low SARS-CoV-2 RNA level near the limit of detection.

Table 38 Correlation between cobas® SARS-CoV-2 Qualitative and Aptima™ SARS-CoV-2 Test

Specimen Type	SARS-CoV-2				PPA [95% Score CI]	NPA [95% Score CI]
	Con +	Con -	cobas+ Aptima -	cobas - Aptima +		
Saliva	131	515	3	3	97.8% (131/134) [93.6–99.2%]	99.4% (515/518) [98.3–99.8%]

Con = Concordant; + = Positive; - = Negative, CI= confidence interval, NPA= negative percent agreement, PPA= positive percent agreement

Reproducibility

The reproducibility of cobas® SARS-CoV-2 Qualitative was evaluated across multiple factors 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 of 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 39.

The test results showed good lot-to-lot, instrument-to-instrument (site), day-to-day, and between batch variability for the ~0.3x LoD, ~1x LoD, and ~3x LoD panel members (Table 39). Regardless of viral targets and viral concentrations, most of the variability was within batches, ranging from 79.5% to 100%. Site-to-site variability ranged from 0.0% to 10.1%, and between-batch variability ranged from 0.0% to 16.0%.

Table 39 Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values by viral target and expected viral concentration (positive panel members)

Viral Target	Panel Member Concentration	N*/N	Mean Ct**	Site SD	Site CV(%)	Lot SD	Lot CV(%)	Day SD	Day CV(%)	Batch SD	Batch CV(%)	Within Batch SD	Within Batch CV(%)	Total SD**	Total CV(%)***
SARS-CoV-2	~0.3x LoD	45/216	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	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	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	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	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	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.

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.

* 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.

** The mean and total standard deviation (SD) estimates were calculated from the PROC MIXED procedure.

*** Total CV(%) = (SD/Mean)*100.

The system showed a 99.1% negative percent agreement with a 95% CI of 96.7 - 99.9%. Of the 216 valid tests, 2 tests were positive (1 each for SARS-CoV-2 and pan-Sarbecovirus). Post-amplification DNA sequencing confirmed the presence of an amplification product in 1 sample (pan-Sarbecovirus positive, Ct 36.7) and did not detect amplification product for either target in the other (SARS-CoV-2 positive, Ct 34.4). The Ct values and the curve analysis of the reactive negative panel member may suggest a low level of contamination during specimen handling.

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 and oropharyngeal swab samples collected in the Copan UTM-RT System or the BD™ UVT System Nasal swab samples collected in the Copan UTM-RT System, the BD™ UVT System, the cobas ® PCR Media, and 0.9% physiological saline Saliva samples
Minimum amount of sample required	Swab specimen types: 0.6 or 1.0 mL ^{***} Liquified Saliva: 1.2 mL
Sample processing volume	Swab specimen types: 0.4 mL Liquified Saliva: 0.85 mL














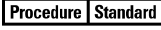

















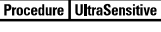




















*Dead volume of 0.2 mL is identified for the **cobas** **omni** Secondary Tubes. Dead volume of 0.6 mL is identified for the **cobas**® PCR Media primary tubes. Other tubes compatible with **cobas**® 5800/6800/8800 Systems (consult User Assistance Guides) may have different dead volume and require more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

**Additional volume is required if pooling.

Symbols

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

Table 40 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 importer

Table 41 Manufacturer and importer



Roche Molecular Systems, Inc.
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www.roche.com

Made in USA



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68305 Mannheim, Germany

Trademarks and patents

See <http://www.roche-diagnostics.us/patents>

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Sandhofer Str. 116
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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 11/2021	First Publishing.
Doc Rev. 2.0 01/2022	The claim was extended to run additionally on the cobas ® 5800 System, and with that all information required were added to the whole IFU. Please contact your local Roche Representative if you have any questions.