

# **cobas<sup>®</sup> SARS-CoV-2**

---

## **Qualitative assay for use on the cobas<sup>®</sup> 6800/8800 Systems**

*For use under the Emergency Use Authorization (EUA) only*

*For in vitro diagnostic use*

**cobas<sup>®</sup> SARS-CoV-2**

P/N: 09175431190

**cobas<sup>®</sup> SARS-CoV-2 Control Kit**

P/N: 09175440190

**cobas<sup>®</sup> 6800/8800 Buffer Negative Control Kit**

P/N: 07002238190

# Table of Contents

|   |           |
|---|-----------|
| <b>Intended use .....</b>   | <b>4</b>  |
| <b>Summary and explanation of the test.....</b>   | <b>4</b>  |
| <b>Reagents and materials.....</b>  | <b>6</b>  |
| cobas® SARS-CoV-2 reagents and controls.....  | 6         |
| cobas omni reagents for sample preparation.....   | 8         |
| Reagent storage and handling requirements.....  | 9         |
| Additional materials required.....  | 10        |
| Instrumentation and software required.....  | 11        |
| <b>Precautions and handling requirements .....</b>  | <b>12</b> |
| Warnings and precautions .....  | 12        |
| Reagent handling.....   | 12        |
| Good laboratory practice.....   | 13        |
| <b>Sample collection, transport, and storage.....</b>                                       | <b>13</b> |
| Sample collection.....  | 13        |
| Nasal (anterior nares) swab specimen collection - clinician or self-collected on site ..... | 13        |
| Transport and storage .....   | 14        |
| <b>Instructions for use.....</b>  | <b>15</b> |
| Procedural notes .....  | 15        |
| Running cobas® SARS-CoV-2.....  | 15        |
| Specimens collected in cobas® PCR Media, 0.9% physiological saline, UTM-RT or UVT ....      | 15        |
| Specimens collected using cobas® PCR Media Uni or Dual Swab Sample Kit.....                 | 15        |
| <b>Results.....</b>   | <b>17</b> |
| Quality control and validity of results .....   | 17        |
| Interpretation of results .....   | 18        |
| cobas® SARS-CoV-2 for System Software v1.2.....   | 18        |
| cobas® SARS-CoV-2 for System Software v1.3 or higher .....                                  | 18        |
| Interpretation of results .....   | 19        |

---

|   |           |
|---|-----------|
| Procedural limitations.....                                   | 21        |
| Conditions of Authorization for the Laboratory.....           | 21        |
| <b>Non-clinical performance evaluation.....</b>               | <b>23</b> |
| Key performance characteristics .....                         | 23        |
| Analytical sensitivity.....                                   | 23        |
| Reactivity/inclusivity .....                                  | 24        |
| Cross-reactivity .....  | 24        |
| Sample type equivalency .....                                 | 26        |
| Matrix equivalency – UTM-RT and cobas® PCR Media .....        | 27        |
| Matrix equivalency –UTM-RT and 0.9% physiological saline..... | 28        |
| <b>Clinical evaluation .....</b>                              | <b>29</b> |
| <b>Additional information .....</b>                           | <b>30</b> |
| Key test features .....                                       | 30        |
| Symbols.....  | 31        |
| Manufacturer and distributors .....                           | 32        |
| Trademarks and patents .....                                  | 32        |
| Copyright.....  | 32        |
| References.....   | 33        |
| Document revision.....  | 34        |

## 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 clinician-instructed self-collected nasal swab specimens (collected on site), and clinician-collected nasal, nasopharyngeal, and oropharyngeal swab specimens from individuals who meet COVID-19 clinical and/or epidemiological criteria. **cobas® SARS-CoV-2** is for use only under Emergency Use Authorization (EUA) in U.S. laboratories certified under CLIA to perform high or moderate complexity tests.

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; 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. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

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 qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and on the use of the **cobas® 6800/8800 Systems**. **cobas® SARS-CoV-2** is only for use under the Food and Drug Administration's Emergency Use Authorization.

## 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 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.

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

| cobas® SARS-CoV-2<br>Store at 2-8°C<br>192 test cassette (P/N 09175431190) |  |                               |
|--|--|-------------------------------|
| Kit components   | Reagent ingredients  | Quantity per kit<br>192 tests |
| <b>Proteinase Solution (PASE)</b>  | Tris buffer, <0.05% EDTA, calcium chloride, calcium acetate, 8% proteinase<br><br>EUH210: Safety data sheet available on request.<br>EUH208: Contains Subtilisin. May produce an allergic reaction.  | 22.3 mL                       |
| <b>RNA Internal Control (RNA IC)</b>                                       | 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                       |
| <b>Elution Buffer (EB)</b>   | Tris buffer, 0.2% methyl-4 hydroxybenzoate   | 21.2 mL                       |
| <b>Master Mix Reagent 1 (MMX-R1)</b>                                       | Manganese acetate, potassium hydroxide, <0.1% sodium azide   | 7.5 mL                        |
| <b>SARS-CoV-2 Master Mix Reagent 2 (SARS-CoV-2 MMX-R2)</b>                 | 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                        |

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



| <b>cobas® SARS-CoV-2 Control Kit</b><br>Store at 2–8°C<br>(P/N 09175440190) |  |                      |
|---|--|----------------------|
| Kit components  | Reagent ingredients  | Quantity per kit     |
| <b>SARS-CoV-2 Positive Control (SARS-CoV-2 (+)C)</b>                        | 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<br>(16 x 1 mL) |

**Table 3** cobas® Buffer Negative Control Kit

| <b>cobas® Buffer Negative Control Kit</b><br>Store at 2–8°C<br>(P/N 07002238190) |  |                      |
|--|--|----------------------|
| Kit components   | Reagent ingredients  | Quantity per kit     |
| <b>cobas® Buffer Negative Control (BUF (-) C)</b>                                | Tris buffer, < 0.1% sodium azide, EDTA, < 0.002% Poly rA RNA (synthetic) | 16 mL<br>(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**   |
|--|---|------------------|---|
| <b>cobas omni MGP Reagent (MGP)</b><br>Store at 2–8°C<br>(P/N 06997546190)           | Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide                       | 480 tests        | Not applicable  |
| <b>cobas omni Specimen Diluent (SPEC DIL)</b><br>Store at 2–8°C<br>(P/N 06997511190) | Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide   | 4 x 875 mL       | Not applicable  |
| <b>cobas omni Lysis Reagent (LYS)</b><br>Store at 2–8°C<br>(P/N 06997538190)         | 43% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate | 4 x 875 mL       |  <br><b>DANGER</b><br>H302 + H332: Harmful if swallowed or if inhaled.<br>H314: Causes severe burns and eye damage.<br>H412: Harmful to aquatic life with long lasting effects.<br>EUH032: Contact with acids liberates very toxic gas.<br>P261: Avoid breathing dust/fume/gas/mist/vapours/spray.<br>P273: Avoid release to the environment.<br>P280: Wear protective gloves/ protective clothing/ eye protection/ face protection.<br>P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.<br>P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor.<br>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.<br>593-84-0 Guanidinium thiocyanate<br>9002-92-0 Polidocanol<br>3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol |
| <b>cobas omni Wash Reagent (WASH)</b><br>Store at 15–30°C<br>(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 kit. See listing of additional materials required (Table 7).

\*\* Product safety labeling primarily follows EU GHS guidance

\*\*\*Hazardous substance



## 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 |
|--|---------------------|
| <b>cobas</b> ® SARS-CoV-2 - 192            | 2–8°C               |
| <b>cobas</b> ® SARS-CoV-2 Control Kit      | 2–8°C               |
| <b>cobas</b> ® Buffer Negative Control Kit | 2–8°C               |
| <b>cobas</b> <b>omni</b> Lysis Reagent     | 2–8°C               |
| <b>cobas</b> <b>omni</b> MGP Reagent       | 2–8°C               |
| <b>cobas</b> <b>omni</b> Specimen Diluent  | 2–8°C               |
| <b>cobas</b> <b>omni</b> 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) |
|--|---------------------|-----------------------------|---|--|
| <b>cobas</b> ® SARS-CoV-2 - 192            | Date not passed†    | 90 days from first usage*†  | Max 40 runs†                                  | Max 40 hours†  |
| <b>cobas</b> ® SARS-CoV-2 Control Kit      | Date not passed†    | Not applicable <sup>a</sup> | Not applicable                                | Max 8 hours†   |
| <b>cobas</b> ® Buffer Negative Control Kit | Date not passed     | Not applicable <sup>a</sup> | Not applicable                                | Max 10 hours   |
| <b>cobas</b> <b>omni</b> Lysis Reagent     | Date not passed     | 30 days from loading*       | Not applicable                                | Not applicable   |
| <b>cobas</b> <b>omni</b> MGP Reagent       | Date not passed     | 30 days from loading*       | Not applicable                                | Not applicable   |
| <b>cobas</b> <b>omni</b> Specimen Diluent  | Date not passed     | 30 days from loading*       | Not applicable                                | Not applicable   |
| <b>cobas</b> <b>omni</b> Wash Reagent      | Date not passed     | 30 days from loading*       | Not applicable                                | Not applicable   |

<sup>a</sup>Single use reagents

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

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

## Additional materials required

**Table 7** Materials and consumables for use on **cobas®** 6800/8800 Systems

| Material  | P/N  |
|---|--|
| <b>cobas omni</b> Processing Plate  | 05534917001  |
| <b>cobas omni</b> Amplification Plate   | 05534941001  |
| <b>cobas omni</b> Pipette Tips  | 05534925001  |
| <b>cobas omni</b> Liquid Waste Container  | 07094388001  |
| <b>cobas omni</b> Lysis Reagent   | 06997538190  |
| <b>cobas omni</b> MGP Reagent   | 06997546190  |
| <b>cobas omni</b> Specimen Diluent  | 06997511190  |
| <b>cobas omni</b> Wash Reagent  | 06997503190  |
| Solid Waste Bag   | 07435967001  |
| Solid Waste Bag and Solid Waste Container<br>or<br>Solid Waste Bag With Insert and Kit Drawer | 07435967001 and 07094361001<br>or<br>08030073001 and 08387281001 |
| Solid Waste Container   | 07094361001  |
| <b>cobas omni</b> Secondary Tubes 13x75 (optional)  | 06438776001  |
| <b>cobas®</b> PCR Media Tube Replacement Cap Kit  | 07958056190  |
| <b>cobas®</b> 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** Specimen collection kits used with **cobas®** SARS-CoV-2

| Collection Kit                               | P/N         |
|--|-------------|
| <b>cobas®</b> PCR Media Uni Swab Sample Kit  | 07958030190 |
| <b>cobas®</b> PCR Media Dual Swab Sample Kit | 07958021190 |
| <b>cobas®</b> PCR Media 100 tube kit         | 06466281190 |

## 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         |
|--|-------------|
| <b>cobas</b> ® 6800 System (Moveable Platform) | 05524245001 |
| <b>cobas</b> ® 6800 System (Fixed Platform)    | 06379664001 |
| <b>cobas</b> ® 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 under Emergency Use Authorization only.
- Positive results are indicative of the presence of SARS-CoV-2 RNA.
- Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
- 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.<sup>1,2</sup> 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.

## 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.

## 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

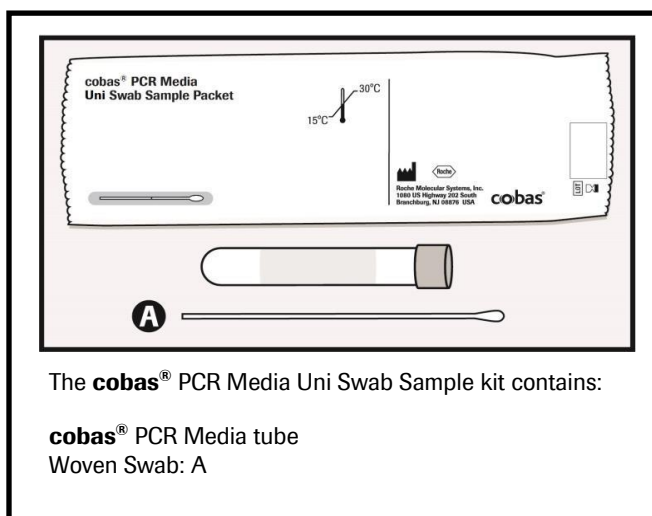
**Note:** Handle all samples and controls as if they are capable of transmitting infectious agents.

### Sample collection

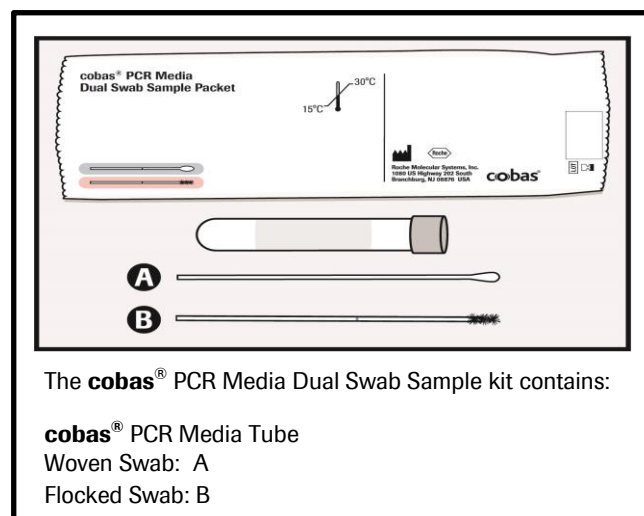
- Collect nasal, nasopharyngeal and oropharyngeal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT) or BD™ Universal Viral Transport (UVT).
- Collect nasal specimens according to standard 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.

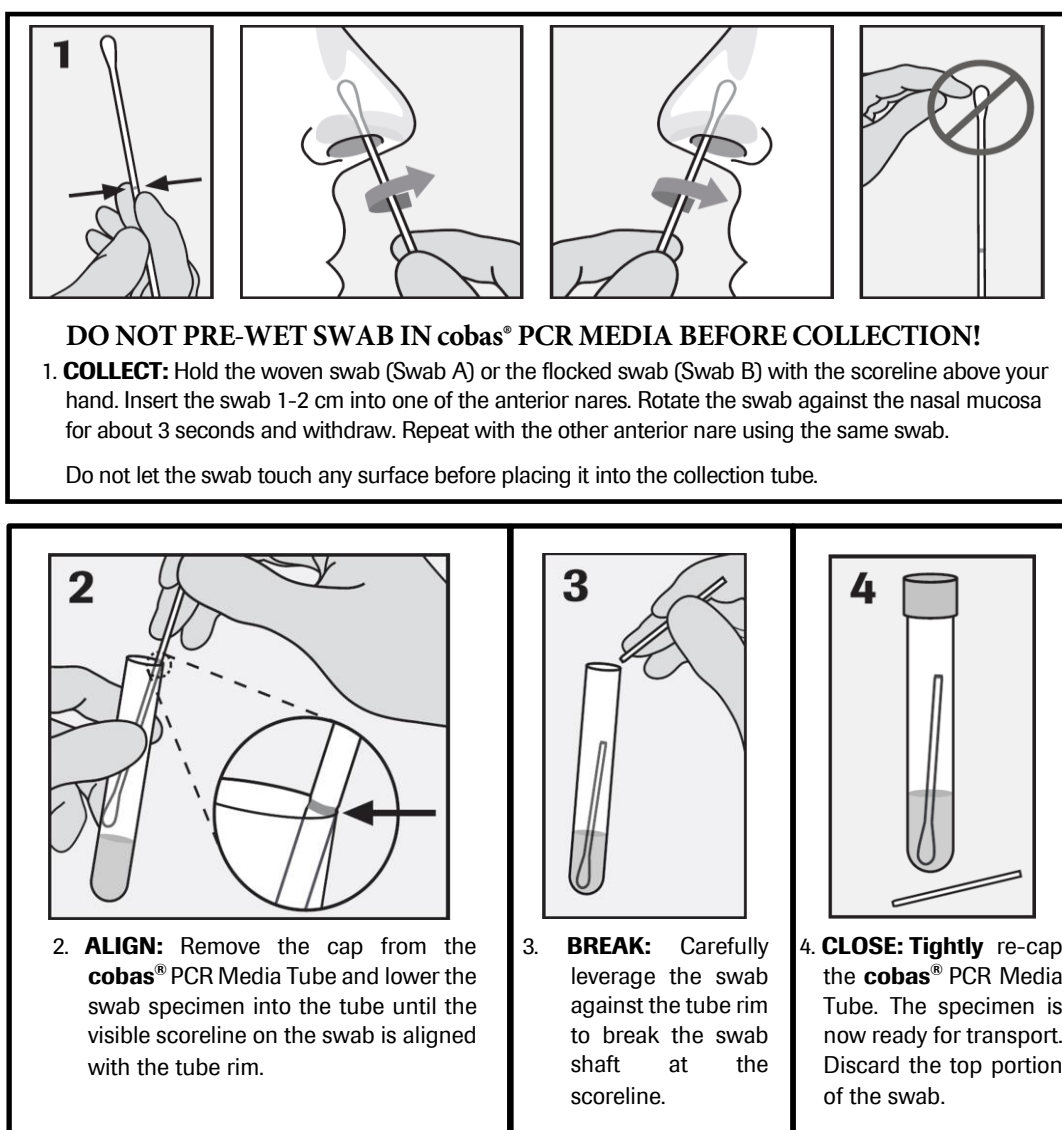
### Nasal (anterior nares) swab specimen collection - clinician or self-collected on site

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



OR





- 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.

## 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 10.

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

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

*Always use a new pipette tip for each specimen.*

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

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

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

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

Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit must be uncapped and can be loaded directly onto racks for processing on the cobas® 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 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 10.

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.

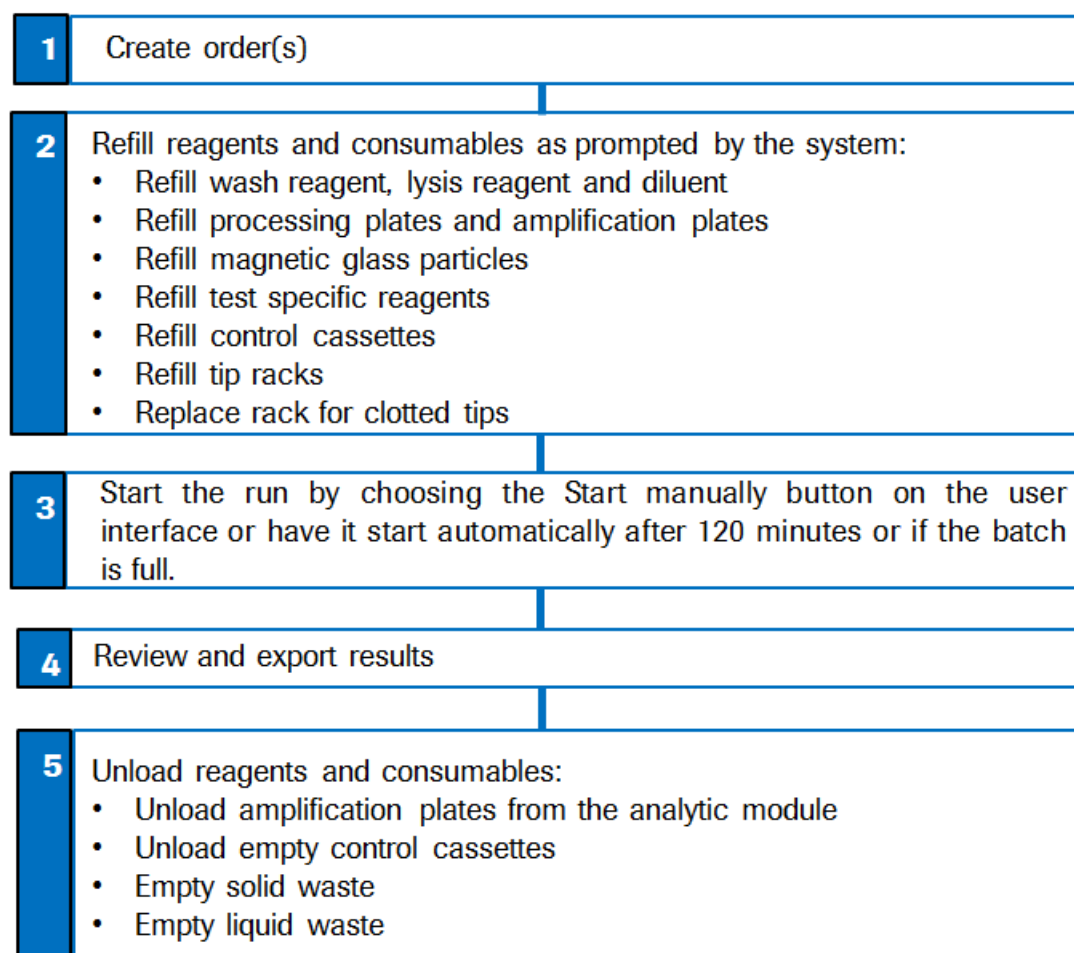
Occasionally, incoming swab specimens contain excessive mucus which may induce a pipetting error (e.g., clot or other obstruction) on the cobas® 6800/8800 Systems. Prior to retesting of specimens that exhibited clots during initial processing, remove and discard the swab, then re-cap and vortex these 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 10** Sample type selection in the user interface of the cobas® SARS-CoV-2

| Collection kit/Matrix type   | Minimum volume (mL)<br>Processing tube | Process as Sample Type |
|--|--|------------------------|
| Copan Universal Transport Medium<br>BD™ Universal Viral Transport<br>0.9% physiological saline<br>cobas® PCR Media Kit | 0.6 mL<br>cobas omni Secondary tube    | Swab                   |
| cobas® PCR Media Uni or Dual Swab Sample Kit   | 1.0 mL<br>Primary tube                 | cobas® PCR media swab  |

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

## Results

The **cobas**® 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

- 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 or higher 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             | <b>Negative</b> | Negative | Negative |
| SARS-CoV-2 400 µL | Swab_C1                | No     | Y40T  | Swab             | <b>Invalid</b>  | Invalid  | Invalid  |
| SARS-CoV-2 400 µL | Swab_B1                | Yes    |       | Swab             | <b>Reactive</b> | Negative | Positive |
| SARS-CoV-2 400 µL | Swab_B2                | Yes    |       | Swab             | <b>Positive</b> | Positive | Positive |
| SARS-CoV-2 400 µL | Swab_D1                | Yes    |       | Swab             | <b>Negative</b> | Negative | Negative |
| SARS-CoV-2 400 µL | Swab_A6                | Yes    |       | Swab             | <b>Reactive</b> | Positive | Negative |
| SARS-CoV-2 400 µL | Swab_E1                | No     | C01H2 | Swab             | <b>Invalid</b>  | Positive | Invalid  |
| SARS-CoV-2 400 µL | Swab_A2                | No     | C01H1 | Swab             | <b>Invalid</b>  | Invalid  | Positive |
| SARS-CoV-2        | C161420284090428828404 | Yes    |       | (-) Ctrl         | <b>Valid</b>    | Valid    | Valid    |
| SARS-CoV-2        | C161420284093009580264 | Yes    |       | SARS-CoV-2 (+) C | <b>Valid</b>    | 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 11, 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             | <b>NA</b>       | Negative | Negative |
| SARS-CoV-2 400 µL | Swab_C1                | NA     | Y40T  | Swab             | <b>NA</b>       | Invalid  | Invalid  |
| SARS-CoV-2 400 µL | Swab_B1                | NA     |       | Swab             | <b>NA</b>       | Negative | Positive |
| SARS-CoV-2 400 µL | Swab_B2                | NA     |       | Swab             | <b>NA</b>       | Positive | Positive |
| SARS-CoV-2 400 µL | Swab_D1                | NA     |       | Swab             | <b>NA</b>       | Negative | Negative |
| SARS-CoV-2 400 µL | Swab_A6                | NA     |       | Swab             | <b>NA</b>       | Positive | Negative |
| SARS-CoV-2 400 µL | Swab_E1                | NA     | C01H2 | Swab             | <b>NA</b>       | Positive | Invalid  |
| SARS-CoV-2 400 µL | Swab_A2                | NA     | C01H1 | Swab             | <b>NA</b>       | Invalid  | Positive |
| SARS-CoV-2        | C161420284090428828404 | Yes    |       | (-) Ctrl         | <b>Valid</b>    | Valid    | Valid    |
| SARS-CoV-2        | C161420284093009580264 | Yes    |       | SARS-CoV-2 (+) C | <b>Valid</b>    | 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 11, 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 11).

**Table 11** cobas® SARS-CoV-2 results interpretation

| Target 1        | Target 2        | Interpretation  |
|-----------------|-----------------|---|
| <b>Positive</b> | <b>Positive</b> | All Target Results were valid. Result for SARS-CoV-2 RNA is Detected.   |
| <b>Positive</b> | <b>Negative</b> | All Target Results were valid.<br>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.  |
| <b>Negative</b> | <b>Positive</b> | All Target Results were valid.<br>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. |
| <b>Negative</b> | <b>Negative</b> | All Target Results were valid.<br>Result for SARS-CoV-2 RNA is Not Detected.  |
| <b>Positive</b> | <b>Invalid</b>  | Not all Target Results were valid.<br>Result for SARS-CoV-2 RNA is Detected.  |
| <b>Invalid</b>  | <b>Positive</b> | Not all Target Results were valid.<br>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.   |
| <b>Negative</b> | <b>Invalid</b>  | Not all Target Results were valid.<br>Sample should be retested. If the result is still invalid, a new specimen should be obtained.   |
| <b>Invalid</b>  | <b>Negative</b> | Not all Target Results were valid.<br>Sample should be retested. If the result is still invalid, a new specimen should be obtained.   |
| <b>Invalid</b>  | <b>Invalid</b>  | All Target Results were invalid.<br>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.

## Conditions of Authorization for the Laboratory

The **cobas**® SARS-CoV-2 test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients and authorized labeling are available on the FDA website: <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd>

To assist clinical laboratories running the **cobas**® SARS-CoV-2 test, the relevant Conditions of Authorization are listed verbatim below, and are required to be met by laboratories performing the EUA test.

- A. Authorized laboratories<sup>1</sup> using the **cobas**® SARS-CoV-2 test will include with result reports of the **cobas**® SARS CoV-2 test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- B. Authorized laboratories using the **cobas**® SARS-CoV-2 test will perform the **cobas**® SARS-CoV-2 test as outlined in the **cobas**® SARS-CoV-2 Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to perform the **cobas**® SARS-CoV-2 test are not permitted.
- C. Authorized laboratories that receive the **cobas**® SARS-CoV-2 test must notify the relevant public health authorities of their intent to run the test prior to initiating testing.

- D. Authorized laboratories using the **cobas**® SARS-CoV-2 test will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- E. Authorized laboratories will collect information on the performance of the test and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: [CDRH-EUA-Reporting@fda.hhs.gov](mailto:CDRH-EUA-Reporting@fda.hhs.gov)) and Roche Diagnostics US Customer Technical Support 1-800-526-1247 any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which they become aware.
- F. All laboratory personnel using the test must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.
- G. RMS, its authorized distributor(s) and authorized laboratories using the **cobas**® SARS-CoV-2 test will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

<sup>1</sup>For ease of reference, this letter will refer to, “United States (U. S.) laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity tests, and in U.S. laboratories certified under CLIA to perform high complexity tests” as “authorized laboratories.”

# 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 TCID<sub>50</sub>/mL<sup>1</sup>) 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 12, the concentration level with observed hit rates greater than or equal to 95% were 0.009 and 0.003 TCID<sub>50</sub>/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively. As shown in Table 13, the Probit predicted 95% hit rates were 0.007 and 0.004 TCID<sub>50</sub>/mL for SARS-CoV-2 (Target 1) and pan-Sarbecovirus (Target 2), respectively.

**Table 12** LoD determination using USA-WA1/2020 strain

| Strain  | Concentration [TCID <sub>50</sub> /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 <sub>50</sub> /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      |

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

\* Calculations only include positive results.

**Table 13** Probit predicted 95% hit rates using USA-WA1/2020 strain

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

<sup>1</sup> 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.

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.

## Reactivity/inclusivity

*In silico* analysis concluded that cobas® SARS-CoV-2 will detect all analyzed SARS-CoV-2 sequences in NCBI and in GISAID databases.

cobas® SARS-CoV-2 had 100% match to all but one sequence for Target 1 (NCBI (n = 79); GISAID (n = 366)). For the one sequence, a single nucleotide mismatch was found that maps to the 5'-end of the reverse primer, with no predicted impact on the assay performance.

cobas® SARS-CoV-2 had 100% match to all but three sequences for Target 2 (NCBI (n = 81); GISAID (n = 364)). For one sequence, a single nucleotide mismatch was found close to the 3'-end of the probe binding region. For a second sequence, a single mismatch was found at the 3'-end of the forward primer binding region. For a third sequence, a single mismatch was found at the 3'-end of the reverse primer binding region. None of these single base mismatches are predicted to impact the performance.

## Cross-reactivity

### In silico analysis

The *in silico* analysis for possible cross-reactions with all the organisms listed in Table 14 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 14** 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*  |

09179917001-03EN



| Strain                                      | <i>In Silico</i> Analysis for % Identity to Target 1 (nCoV) | <i>In Silico</i> Analysis for % Identity to Target 2 (Pan-Sarbecovirus 1) |
|---|---|---|
| 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 pyogenes</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*   |
| <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 15, 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 15** Cross-reactivity test results

| Microorganism                     | Concentration                  | Target 1 Result | Target 2 Result |
|-----------------------------------|--------------------------------|-----------------|-----------------|
| Human coronavirus 229E            | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Human coronavirus OC43            | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Human coronavirus HKU1            | 1.0E+05 cp/mL                  | Negative        | Negative        |
| Human coronavirus NL63            | 1.0E+05 TCID <sub>50</sub> /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 <sub>50</sub> /mL | Negative        | Negative        |
| Human Metapneumovirus (hMPV)      | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Parainfluenza virus Type 1        | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Parainfluenza virus Type 2        | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Parainfluenza virus Type 3        | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Parainfluenza virus Type 4        | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Influenza A (H1N1)                | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Influenza B                       | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Enterovirus E (Type 1)            | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| Respiratory syncytial virus       | 1.0E+05 PFU/mL                 | Negative        | Negative        |
| Rhinovirus                        | 1.0E+05 TCID <sub>50</sub> /mL | Negative        | Negative        |
| <i>Chlamydia pneumonia</i>        | 1.0E+06 TCID <sub>50</sub> /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 pyogenes</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        |

## 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 16, 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 16** 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<br>(31.7 – 32.0) | 100        | 33.6<br>(33.5 – 33.7) |
| OPS         |                      |    | 100        | 32.2<br>(31.8 – 32.6) | 100        | 33.7<br>(33.4 – 34.1) |
| NPS         | ~4x LoD (Target 1)   | 11 | 100        | 30.9<br>(30.3 – 31.5) | 100        | 32.2<br>(31.6 – 32.9) |
| OPS         |                      |    | 100        | 31.5<br>(31.2 – 31.9) | 100        | 32.7<br>(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 17, 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 17** 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<br>(31.6 – 32.0) | 100        | 34.0<br>(33.8 – 34.2) |
| CPM              |                      |    | 100        | 32.2<br>(31.9 – 32.4) | 100        | 34.7<br>(34.4 – 35.0) |
| UTM              | ~4x LoD              | 11 | 100        | 30.7<br>(30.1 – 31.2) | 100        | 32.4<br>(31.7 – 33.1) |
| CPM              |                      |    | 100        | 31.6<br>(31.0 – 32.1) | 100        | 33.7<br>(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 18, 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 18** 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<br>(32.0 - 32.4) | 100        | 33.6<br>(33.6 - 33.7) |
| Woven Swab in UTM-RT   |                      | 16 | 100        | 31.6<br>(31.1 - 32.1) | 100        | 33.2<br>(32.7 - 33.8) |
| Woven Swab in Saline   |                      | 17 | 100        | 31.7<br>(31.4 - 32.0) | 100        | 33.5<br>(33.2 - 33.8) |
| Flocked Swab in UTM-RT | ~4x LoD              | 11 | 100        | 31.2<br>(31.1 - 31.4) | 100        | 32.6<br>(32.4 - 32.7) |
| Woven Swab in UTM-RT   |                      |    | 100        | 30.9<br>(30.4 - 31.4) | 100        | 32.4<br>(31.9 - 33.0) |
| Woven Swab in Saline   |                      |    | 100        | 31.0<br>(30.8 - 31.3) | 100        | 32.6<br>(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                   |

## Clinical 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 19, all low positive and moderate positive samples were positive and all negative samples were negative in the background of individual clinical sample matrix.

**Table 19** Clinical evaluation with nasopharyngeal swab samples

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

## Additional information

### Key test features

|  |  |
|--|--|
| <b>Sample type</b>                       | Nasopharyngeal and oropharyngeal swab samples collected in the Copan UTM-RT System or the BD™ UVT System<br>Nasal swab samples collected in the Copan UTM-RT System, the BD™ UVT System, the <b>cobas</b> ® PCR Media, and 0.9% physiological saline |
| <b>Minimum amount of sample required</b> | 0.6 or 1.0 mL*   |
| <b>Sample processing volume</b>          | 0.4 mL   |
| <b>Test duration</b>                     | 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.

## Symbols

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

**Table 20** Symbols used in labeling for Roche PCR diagnostics products

|                |   |  |                                   |  |   |
|----------------|---|--|-----------------------------------|--|---|
|                | Ancillary Software  |  | Lower Limit of Assigned Range     |  | Negative Control  |
|                | Authorized representative in the European community                                   |  | Upper Limit of Assigned Range     |  | Positive Control  |
|                | Barcode Data Sheet  |  | Store in the dark                 |  | Control   |
|                | Batch code  |  | Contains sufficient for <n> tests |  | Assigned Range (copies/mL)  |
|                | Biological risks  |  | Temperature limit                 |  | Assigned Range (IU/mL)  |
|                | Catalogue number  |  | Test Definition File              |  | Standard Procedure  |
|                | Consult instructions for use  |  | Manufacturer                      |  | Ultrasensitive Procedure  |
|                | Contents of kit   |  | Use-by date                       |  | QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.               |
|                | Distributed by  |  | Global Trade Item Number          |  | QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results. |
|                | For IVD performance evaluation only   |  | Serial number                     |  |   |
| <b>Rx Only</b> | US Only: Federal law restricts this device to sale by or on the order of a physician. |  | Date of manufacture               |  |   |
|                | <i>In Vitro</i> diagnostic medical device   |  | Do not reuse                      |  |   |

US Customer Technical Support 1-800-526-1247

## Manufacturer and distributors

**Table 21** Manufacturer and distributors



Roche Molecular Systems, Inc.  
1080 US Highway 202 South  
Branchburg, NJ 08876 USA  
[www.roche.com](http://www.roche.com)



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

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

## Copyright

©2020 Roche Molecular Systems, Inc.





## References

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

## Document revision

| Document Revision Information |   |
|-------------------------------|---|
| Doc Rev. 1.0<br>03/2020       | First Publishing.   |
| Doc Rev. 2.0<br>04/2020       | <p>Corrected typographical errors, organism names, and table references.</p> <p>Added nasal swabs (self-collected on site or by the physician), collected in UTM-RT, UVT, <b>cobas®</b> PCR Media and 0.9% physiological saline. Addition of the analytical performance data related to the added specimen and media types.</p> <p>Replaced “container” with “collection tube” to improve clarity.</p> <p>Please contact your local Roche Representative if you have any questions.</p>   |
| Doc Rev. 3.0<br>05/2020       | <p>Workflow descriptions of the new sample type “<b>cobas®</b> PCR Media swab”.</p> <p>Workflow to prepare the <b>cobas®</b> PCR Media tubes for processing.</p> <p>Data for analytical sensitivity for AccuPlex added.</p> <p>Removal of duplicate ingredients in formulation for positive control.</p> <p>Removal of repeat testing for samples with presumptive positive results.</p> <p>Update of figures in <b>Sample collection, transport, and storage</b> section with gloved hands.</p> <p>Removal of the limitation regarding nasal and mid-turbinate nasa collection in <b>Procedural limitations</b> section.</p> <p>Moved <b>Conditions of Authorization for the laboratory</b> section to the <b>Procedural limitations</b> section.</p> <p>Please contact your local Roche Representative if you have any questions.</p> |