Rx Only

cobas® SARS-CoV-2 & Influenza A/B v2

Qualitative nucleic acid test for use on the cobas® 5800/6800/8800 Systems

For in vitro diagnostic use

cobas® SARS-CoV-2 & Influenza A/B v2	P/N: 10033401190
cobas® SARS-CoV-2 & Influenza A/B Control Kit	P/N: 09446133190
cobas® Buffer Negative Control Kit	P/N: 09051953190

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Summary and explanation of the test

Intended use

cobas® SARS-CoV-2 & Influenza A/B v2 assay for use on the **cobas**® 5800/6800/8800 Systems (**cobas**® SARS-CoV-2 & Influenza A/B v2) is an automated multiplex real-time RT-PCR assay intended for simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus RNA in healthcare provider-collected nasal and nasopharyngeal swab specimens, and self-collected nasal swab specimens (collected in a healthcare setting with instruction by a healthcare provider) from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. **cobas**® SARS-CoV-2 & Influenza A/B v2 is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B in humans and is not intended to detect influenza C.

RNA from SARS-CoV-2, influenza A, and influenza B is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, influenza A, and/or influenza B 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. The agent detected may not be the definite cause of disease.

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

cobas® SARS-CoV-2 & Influenza A/B v2 is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and on the use of the **cobas**® 5800/6800/8800 Systems.

Explanation of the test

cobas® SARS-CoV-2 & Influenza A/B v2 is a qualitative nucleic acid test for the use on the **cobas**® 5800 System, **cobas**® 6800 System or **cobas**® 8800 System for the detection of the 2019 novel coronavirus (SARS-CoV-2), influenza A, and influenza B RNA in both nasal and nasopharyngeal swab samples collected in Copan Universal Transport Medium System (UTM-RT®) or BD™ Universal Viral Transport System (UVT) and additionally for nasal swab samples collected in **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 (a low titer positive control and a negative control).

Principles of the procedure

cobas® SARS-CoV-2 & Influenza A/B v2 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, which assigns 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 SARS-CoV-2 target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for ORF1a/b non-structural region that is unique to SARS-CoV-2. Additionally, a conserved region in the structural protein envelope E-gene was chosen for pan-Sarbecovirus detection. The pan-Sarbecovirus detection set will also detect SARS-CoV-2 virus. For influenza A, selective amplification of target nucleic acid from the sample is achieved by the use of two target-specific sets of forward and reverse primers: one for the genomic region ecoding matrix proteins 1 and 2 (M1/M2) and one for the gene encoding polymerase basic protein 2 (PB2). For influenza B, selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for the nuclear export protein (NEP) / nonstructural protein 1(NS1) genomic region. 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 or influenza genomes. Amplified target is detected by cleavage of fluorescently labeled oligonucleotide probe. A thermostable DNA polymerase enzyme is used for amplification.

The **cobas**® SARS-CoV-2 & Influenza A/B v2 master mix contains detection probes which are specific for the coronavirus type SARS-CoV-2, members of the Sarbecovirus subgenus, influenza A virus, influenza B virus and the RNA Internal Control nucleic acid. The coronavirus, influenza A, influenza B 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 targets, influenza targets and the RNA Internal Control. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythimidine 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 & Influenza A/B v2 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, Table 10 and Table 11.

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

cobas® SARS-CoV-2 & Influenza A/B v2 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 & Influenza A/B v2

(SCoV2-FluA/B v2)

Store at 2-8°C

192 test cassette (P/N 10033401190)

Kit components	Reagent ingredients	Quantity per kit 192 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 *Bacillus subtilis*. May produce an allergic reaction.	22.3 mL
RNA Internal Control (RNA IC)	Tris buffer, < 0.05% EDTA, < 0.001% non-target related armored RNA construct containing primer and probe specific sequence regions (non-infectious RNA in MS2 bacteriophage), < 0.1% sodium azide	21.2 mL
Elution Buffer (EB)	Tris buffer, 0.2% methyl-4 hydroxybenzoate	21.2 mL
Master Mix Reagent 1 (MMX-R1)	Manganese acetate, potassium hydroxide, < 0.1% sodium azide	7.5 mL
SCoV2-FluA/B v2 Master Mix Reagent 2 (SCoV2-FluA/B v2 MMX-R2)	Tricine buffer, potassium acetate, < 18% dimethyl sulfoxide, glycerol, < 0.1% Tween 20, EDTA, < 0.15% dATP, dCTP, dGTP, dUTPs, < 0.01% upstream and downstream SARS-CoV-2, Sarbecovirus, influenza A and influenza B primers, < 0.01% Internal Control forward and reverse primers, < 0.01% fluorescent-labeled oligonucleotide probes specific for SARS-CoV-2, Sarbecovirus, influenza A, influenza B 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 & Influenza A/B Control Kit

(SCoV2-FluA/B CTL)

Store at 2–8°C

(P/N 09446133190)

Kit components	Reagent ingredients	Quantity per kit
SCoV2-FluA/B Positive Control (SCoV2-FluA/B (+) 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, < 0.01% Non-infectious plasmid DNA (microbial) containing influenza A sequence, < 0.01% Non-infectious plasmid DNA (microbial) containing influenza B sequence	16 mL (16 x 1 mL)

Table 3 cobas® Buffer Negative Control Kit

(BUF (-) C)

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	 **DANGER** H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H411: Toxic to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. EUH071: Corrosive to the respiratory tract. P273: Avoid release to the environment. P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. P391: Collect spillage. 593-84-0 Guanidinium thiocyanate 9002-92-0 Polidocanol 3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol
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 & Influenza A/B v2 test kit. See listing of additional materials required (Table 8, Table 9, Table 10 and Table 11).

** 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.

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 & Influenza A/B v2	2–8°C
cobas® SARS-CoV-2 & Influenza A/B 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 & Influenza A/B v2	Date not passed	90 days from first usage	Max 40 runs	Max 36 days[b]
cobas® SARS-CoV-2 & Influenza A/B Control Kit	Date not passed	Not applicable[a]	Not applicable	Max 36 days[b]
cobas® Buffer Negative Control Kit	Date not passed	Not applicable[a]	Not applicable	Max 36 days[b]
cobas® omni Lysis Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® omni MGP Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® omni Specimen Diluent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® omni Wash Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable

[a]Single use reagents

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

Reagent handling requirements for cobas® 6800/8800 Systems

Reagents loaded onto the **cobas**® 6800/8800 Systems are stored at appropriate temperatures and their expiration is monitored by the system. The **cobas**® 6800/8800 Systems allow reagents to be used only if all of the conditions shown in 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 & Influenza A/B v2	Date not passed	90 days from first usage	Max 40 runs	Max 40 hours
cobas® SARS-CoV-2 & Influenza A/B Control Kit	Date not passed	Not applicable[a]	Not applicable	Max 8 hours
cobas® Buffer Negative Control Kit	Date not passed	Not applicable[a]	Not applicable	Max 10 hours
cobas® **omni** Lysis Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® **omni** MGP Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® **omni** Specimen Diluent	Date not passed	30 days from loading[b]	Not applicable	Not applicable
cobas® **omni** Wash Reagent	Date not passed	30 days from loading[b]	Not applicable	Not applicable

[a]Single use reagents

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

Additional materials required for cobas® 5800 System

Table 8 Material 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, 1 mL	04639642001
Tip CORE TIPS with Filter, 300 µL	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 13 or 16 MM[a]	N/A
RD5 RACK – RD Standard rack[a]	N/A
16-position tube carrier[a]	09224319001
5-position rack carrier[a,b]	09224475001

[a]Please contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack carriers accepted on the instruments and compatible with the assay.

[b]RD5 or MPA racks are required in combination with the 5-position Rack Carrier on the **cobas**® 5800 System.

Additional materials required for cobas® 6800/8800 Systems

Table 9 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 13 or 16 MM[a]	N/A
RD5 RACK – RD Standard rack[a]	N/A

[a] Please contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack carriers accepted on the instruments and compatible with the assay.

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 & Influenza A/B v2

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 & Influenza A/B v2 analysis package (SW **cobas**® SCoV2-FluA/B ASAP) for the **cobas**® 5800 System must be installed on the **cobas**® 5800 instrument. The Data Manager software and computer unit for the **cobas**® 5800 System will be provided with the system.

The **cobas**® 6800/8800 software and **cobas**® SARS-CoV-2 & Influenza A/B v2 analysis package (SW **cobas**® SCoV2-FluA/B ASAP) 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 and 06379672001
cobas® 6800 System (Fixed Platform)	05524245001 and 06379664001
cobas® 8800 System	05412722001
Sample Supply Module (**cobas**® 6800/8800 Systems only)	06301037001
Instrument Gateway	06349595001

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

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.
- 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 & Influenza A/B v2 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 0.6% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10) or follow appropriate site procedures.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.
- Inform your local competent authority and manufacturer about any serious incidents which may occur when using this assay.

Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- **cobas**® **omni** Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- **cobas**® SARS-CoV-2 & Influenza A/B v2 test kit, **cobas**® SARS-CoV-2 & Influenza A/B 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 & Influenza A/B v2 kits, **cobas**® SARS-CoV-2 & Influenza A/B 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 0.6% 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 instrument, follow the instructions in the **cobas**® 5800 Systems User Assistance and/or User Guide to properly clean and decontaminate the surface of the instrument.
- If spills occur on the **cobas**® 6800/8800 instruments, follow the instructions in the **cobas**® 6800/8800 Systems – User Assistance and/or User Guides 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.
Store all samples at specified temperatures.
Sample stability is affected by elevated temperatures.
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 secondary tube

Sample collection

Table 12 summarizes what collection devices can be used with specific sample types.

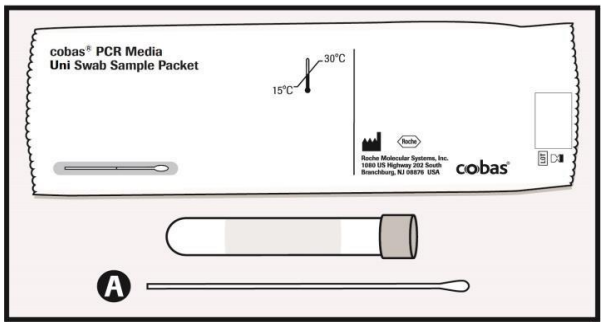
Table 12 Overview of collection devices and sample types

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

- Collect nasal and nasopharyngeal 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) or equivalent.
- 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 – healthcare worker or self-collected on site

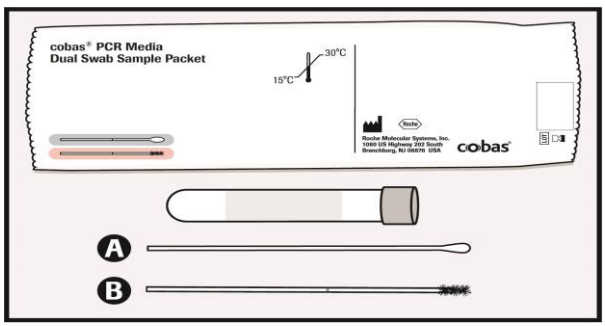
WARNING: DO NOT PRE-WET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!



The **cobas®** PCR Media Uni Swab Sample kit contains:

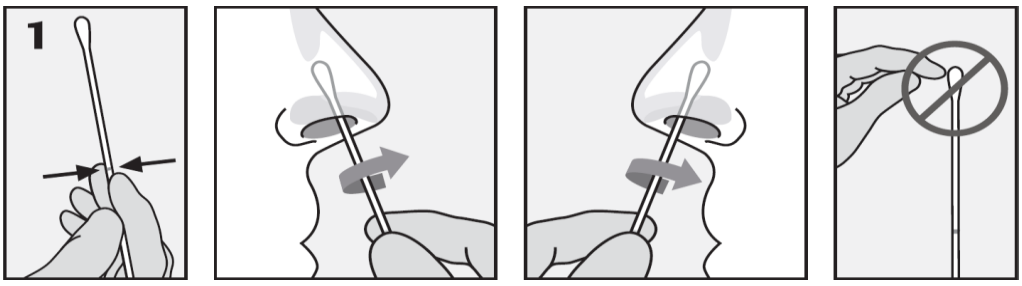
cobas® PCR Media Tube
Woven Swab: A

OR



The **cobas®** PCR Media Dual Swab Sample kit contains:

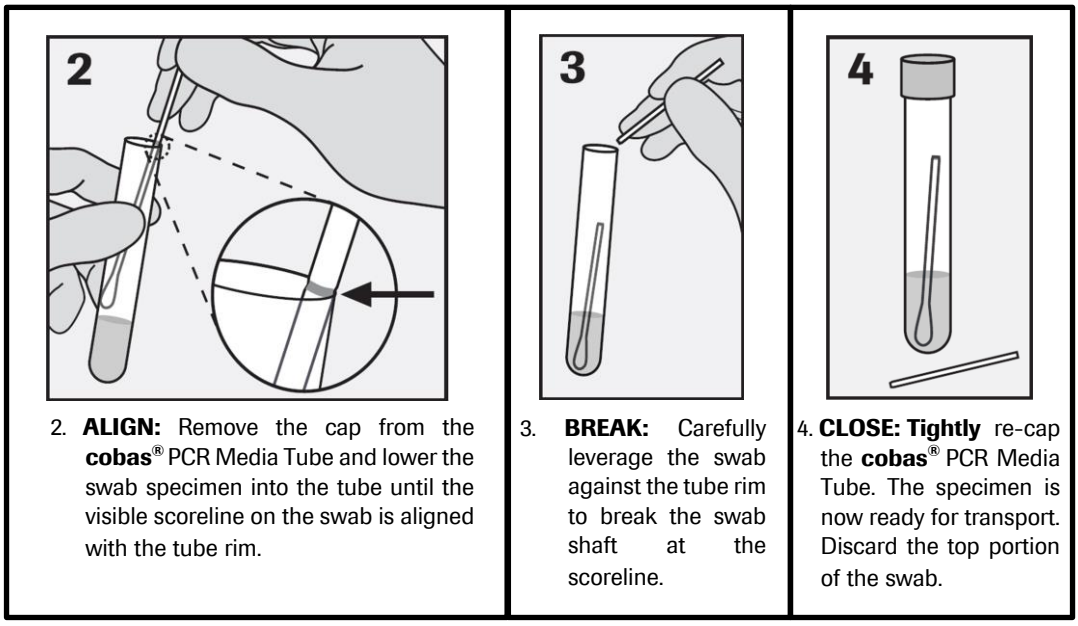
cobas® PCR Media Tube
Woven Swab: A
Flocked Swab: B



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

Transport and storage

- 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 ≤-18°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 ≤ -18°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 ≤-18°C for up to 30 days.
- Specimens are stable for up to two freeze/thaw cycles when frozen at ≤ -18°C.

Instructions for use

Procedural notes

- Do not use **cobas**® SARS-CoV-2 & Influenza A/B v2 reagents, **cobas**® SARS-CoV-2 & Influenza A/B 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 & Influenza A/B v2

cobas® SARS-CoV-2 & Influenza A/B v2 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. The swab must be removed from the sample tube prior to direct loading onto the system. Specimens collected in 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. If using frozen samples in secondary tubes, place the samples at room temperature (15-30°C) until completely thawed and then briefly mix (e.g., vortex for 3-5 seconds) and centrifuge to collect all sample volume at the bottom of the tube. 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 & Influenza A/B v2 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.

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 at least 0.6 mL into the prepared barcoded secondary tube.
- Transfer secondary tube to a rack. Close the primary sample tube cap.

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

Samples collected using **cobas**® PCR Media Uni Swab Sample Kit or **cobas**® PCR Media Dual Swab Sample Kit must be uncapped and can be loaded directly onto racks for processing on the **cobas**® 5800/6800/8800 Systems. Transfer into a secondary tube is not necessary. **cobas**® PCR Media tubes fit on to the MPA RACK 16 or the 16-position tube carrier on (P/N 09224319001) on the **cobas**® 5800 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 & Influenza A/B v2 as described in Table 13.

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

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

Occasionally, incoming swab specimens contain excessive mucus which may induce a pipetting error (e.g., clot or other obstruction) on the **cobas**® 5800/6800/8800 Systems. Prior to retesting of specimens that exhibited clots during initial processing, remove and discard the swab, then re-cap and vortex these specimens for 30 seconds to disperse the excess mucus. Swab specimens can be processed twice on the **cobas**® 5800/6800/8800 Systems while the swab is in the collection tube. If additional testing is required, or if the first test fails due to specimen pipetting error (e.g., clot or other obstruction), the swab must be removed and the remaining fluid must have a minimum volume of 1.0 mL.

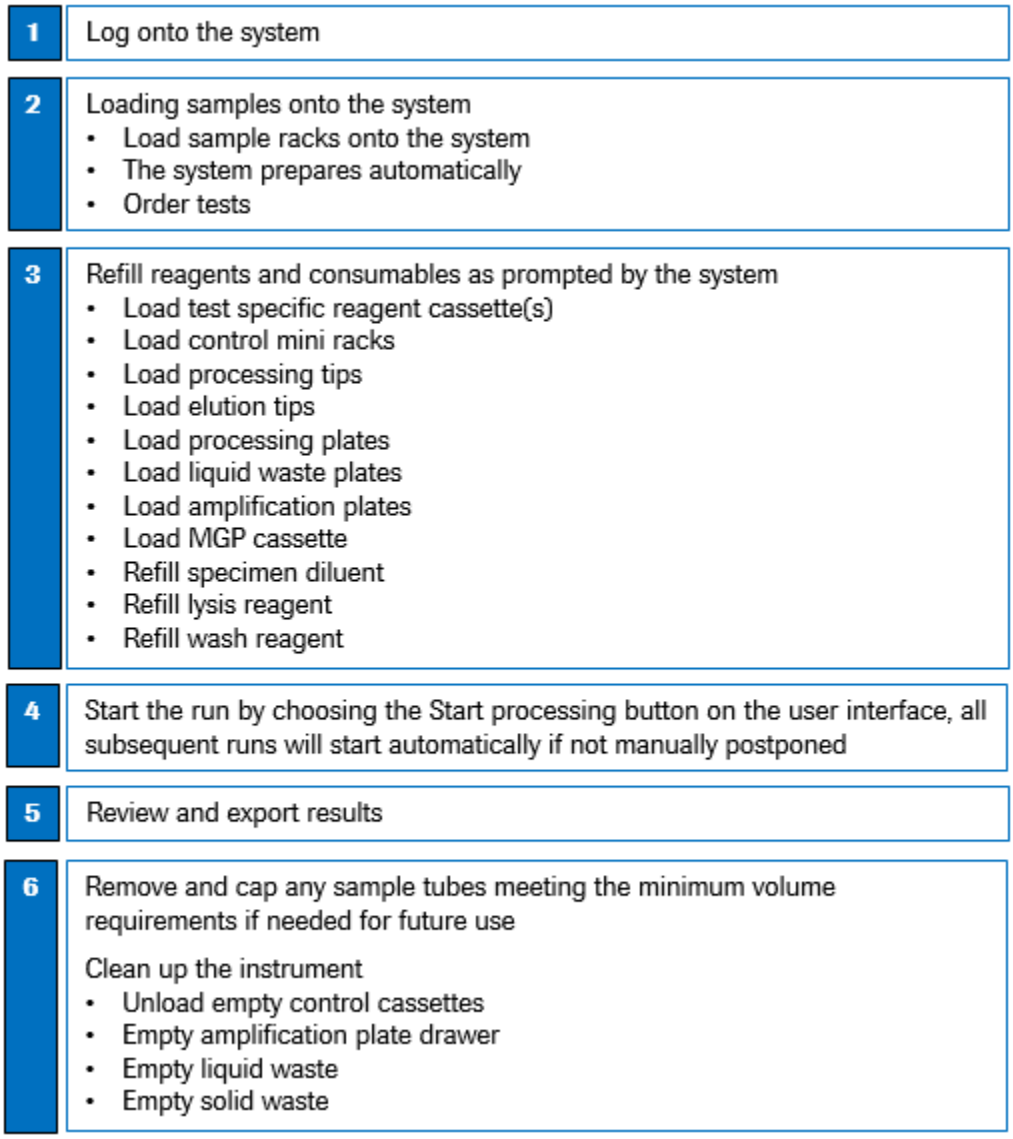
Table 13 Sample type selection in the user interface of the **cobas**® SARS-CoV-2 & Influenza A/B v2

Collection kit/Matrix type	**Minimum volume (mL)** **Processing tube**	**Process as Sample Type**
Copan Universal Transport Medium (UTM-RT®) BD™ Universal Viral Transport 0.9% Physiological saline **cobas**® PCR Media Kit	0.6 mL **cobas**® **omni** Secondary Tube	**VTM**
Copan Universal Transport Medium (UTM-RT®) BD™ Universal Viral Transport 0.9% Physiological saline **cobas**® PCR Media Kit	Compatible tubes without swab inside the tube; for dead volume contact your local Roche representative	**VTM**
cobas® PCR Media Uni or Dual Swab Sample Kit	1.0 mL Primary tube	**cobas**® **PCR Media swab**

Running cobas® SARS-CoV-2 & Influenza A/B v2 on cobas® 5800 System

Figure 1 below summarizes the system workflow.

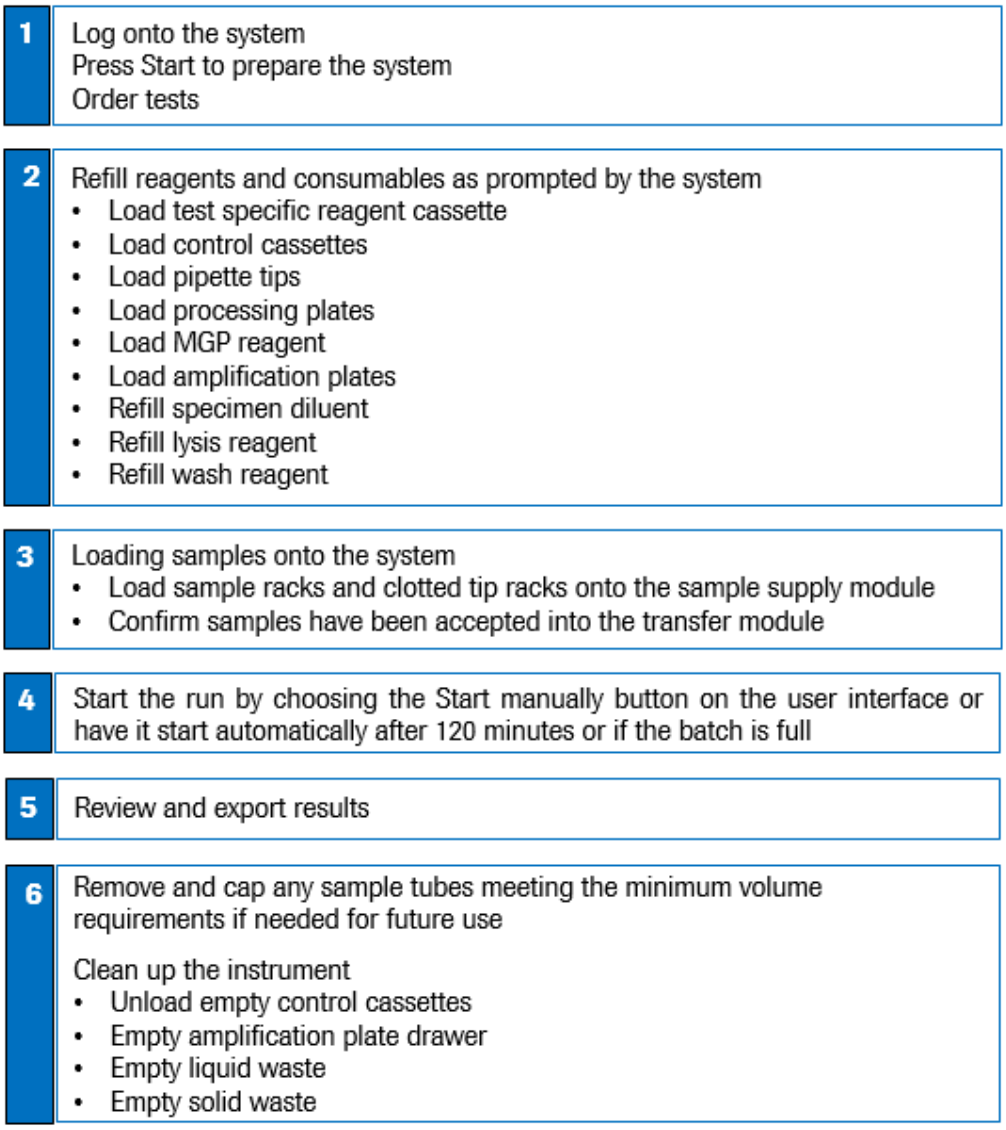
Figure 1 **cobas**® SARS-CoV-2 & Influenza A/B v2 test procedure on **cobas**® 5800 System



Running cobas® SARS-CoV-2 & Influenza A/B v2 on cobas® 6800/8800 Systems

Figure 2 below summarizes the system workflow.

Figure 2 **cobas**® SARS-CoV-2 & Influenza A/B v2 procedure on the **cobas**® 6800/8800 Systems



Results

The **cobas**® 5800 System and **cobas**® 6800/8800 Systems automatically detects the SARS-CoV-2, influenza A and influenza B, 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 [SCoV2-FluA/B CTL] are processed at least every 72 hours or 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 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 14 Example of **cobas**® SARS-CoV-2 & Influenza A/B v2 results display on **cobas**® 5800 System

Sample ID*	Test	Control Result	Flags **	Status	Result				Creation date/time
Sample_01	SCoV2-FluA/B	Valid		Released	FluA Negative	SCoV2 Negative	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_C1	SCoV2-FluA/B	Invalid	⚑	Released	Invalid	Invalid	Invalid	Invalid	7/7/2021 8:27:39 AM
Sample_B1	SCoV2-FluA/B	Valid		Released	FluA Negative	SCoV2 Negative	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_B2	SCoV2-FluA/B	Valid		Released	**FluA Positive (Ct 36.41)**	SCoV2 Negative	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_D1	SCoV2-FluA/B	Valid		Released	FluA Negative	SCoV2 Negative	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_A6	SCoV2-FluA/B	Valid		Released	FluA Negative	**SCoV2 Positive (Ct 35.25)**	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_E1	SCoV2-FluA/B	Valid	⚑	Released	**FluA Positive (Ct 37.69)**	Invalid	PanSarb Negative	FluB Negative	7/7/2021 8:27:39 AM
Sample_A2	SCoV2-FluA/B	Valid	⚑	Released	Invalid	SCoV2 Negative	**PanSarb Positive (Ct 36.68)**	FluB Negative	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 "Results" column for individual sample target result should be interpreted as show in Table 16 below.

If one or more sample targets are marked with "Invalid" the **cobas**® 5800 software shows a flag in the "Flags" column. More information on why the sample target(s) is reported invalid including flag information is shown in the detail view.

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

- One **cobas**® Buffer Negative Control [BUF (-) C] and one positive control [SCoV2-FluA/B CTL] 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.
- The batch is valid if no flags appear for any controls. If the batch is invalid, repeat testing of the entire batch.
- All flags are described in the **cobas**® 6800/8800 Systems User Guide.

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.
- The "Valid" and "Overall Result" columns are not applicable to sample results for the **cobas**® SARS-CoV-2 & Influenza A/B v2.
- 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 the table. Results and their corresponding interpretation for detecting SARS-CoV-2 & Influenza A/B are shown in Table 16.

Results display examples for **cobas**® SARS-CoV-2 & Influenza A/B v2 are shown in Table 15.

Table 15 Example of **cobas**® SARS-CoV-2 & Influenza A/B v2 results display on **cobas**® 6800/8800 System

Test	Sample ID	Valid*	Flags	Sample type	Overall result*	Target 1	Target 2	Target 3	Target 4
SCoV2-FluA/B 400 µL	Sample_01	NA		VTM	**NA**	FluA Negative	SCoV2 Negative	PanSarb Negative	FluB Negative
SCoV2-FluA/B 400 µL	Sample _02	NA	Y40T	VTM	**NA**	Invalid	Invalid	Invalid	Invalid
SCoV2-FluA/B 400 µL	Sample _03	NA		VTM	**NA**	FluA Positive	SCoV2 Negative	PanSarb Negative	FluB Negative
SCoV2-FluA/B 400 µL	Sample _04	NA		VTM	**NA**	FluA Negative	SCoV2 Positive	PanSarb Positive	FluB Negative
SCoV2-FluA/B 400 µL	Sample _05	NA		VTM	**NA**	FluA Negative	SCoV2 Negative	PanSarb Negative	FluB Positive
SCoV2-FluA/B 400 µL	Sample _06	NA		VTM	**NA**	FluA Negative	SCoV2 Negative	PanSarb Positive	FluB Negative
SCoV2-FluA/B 400 µL	Sample _07	NA	C01H2	VTM	**NA**	FluA Positive	Invalid	Invalid	Invalid
SCoV2-FluA/B 400 µL	Sample _08	NA	C01H1	VTM	**NA**	Invalid	SCoV2 Positive	Invalid	FluB Positive
SCoV2-FluA/B	C161420284090428828404	Yes		(-) Ctrl	**Valid**	Valid	Valid	Valid	Valid
SCoV2-FluA/B	C161420284093009580264	Yes		SCoV2-FluA/B (+) C	**Valid**	Valid	Valid	Valid	Valid

*The "Valid" and "Overall Result" columns are not applicable to sample results for **cobas**® SARS-CoV-2 & Influenza A/B v2. Refer to Table 16, **cobas**® SARS-CoV-2 & Influenza A/B v2 results interpretation, for specific instructions on test results interpretation.

Interpretation of results

For a valid batch, check each individual sample for flags in the **cobas**® 5800 System and **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.
- 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 & Influenza A/B are shown below (Table 16).

Table 16 Target results for individual target result interpretation

Target 1 Influenza A	Target 2 SARS-CoV-2	Target 3 Pan-Sarbecovirus	Target 4 Influenza B	Interpretation
Negative	Negative	Negative	Negative	No target RNA Detected
Negative	Negative	Negative	**Positive**	Influenza B RNA Detected
Positive	Negative	Negative	Negative	Influenza A RNA Detected
Positive	Negative	Negative	**Positive**	Influenza A and Influenza B RNA Detected
Negative	Negative	**Positive**	Negative	Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 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	**Positive**	**Positive**	Presumptive Positive for SARS-CoV-2 RNA and influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 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.
Positive	Negative	**Positive**	Negative	Influenza A RNA Detected and Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 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.

Target 1 Influenza A	Target 2 SARS-CoV-2	Target 3 Pan-Sarbecovirus	Target 4 Influenza B	Interpretation
Positive	Negative	**Positive**	**Positive**	Influenza A RNA Detected, Presumptive Positive for SARS-CoV-2 RNA, and influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 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	**Positive**	Negative	Negative	SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Negative	**Positive**	Negative	**Positive**	SARS-CoV-2 RNA and influenza B RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Positive	**Positive**	Negative	Negative	Influenza A RNA and SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Positive	**Positive**	Negative	**Positive**	Influenza A RNA, SARS-CoV-2 RNA, and influenza B RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Negative	**Positive**	**Positive**	Negative	SARS-CoV-2 RNA Detected
Negative	**Positive**	**Positive**	**Positive**	SARS-CoV-2 RNA and influenza B RNA Detected
Positive	**Positive**	**Positive**	Negative	Influenza A RNA and SARS-CoV-2 RNA Detected
Positive	**Positive**	**Positive**	**Positive**	Influenza A RNA, SARS-CoV-2 RNA, and influenza B RNA Detected

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 16.

Procedural limitations

- **cobas**® SARS-CoV-2 & Influenza A/B v2 has been evaluated only for use in combination with the **cobas**® SARS-CoV-2 & Influenza A/B Control Kit, **cobas**® Buffer Negative Control Kit, **cobas**® **omni** MGP Reagent, **cobas**® **omni** Lysis Reagent, **cobas**® **omni** Specimen Diluent, and **cobas**® **omni** Wash Reagent for use on the **cobas**® 5800/6800/8800 Systems.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test is intended to be used for the detection of SARS-CoV-2, influenza A, and influenza B RNA in nasopharyngeal and nasal swab samples collected in a Copan Universal Transport Medium (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 & Influenza A/B v2 may result in inaccurate results.
- Detection of SARS-CoV-2 and influenza A/B 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 & Influenza A/B v2 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 & Influenza A/B v2 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 & Influenza A/B v2 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.

Non-clinical performance evaluation

cobas® SARS-CoV-2 & Influenza A/B v2 is an updated version of **cobas**® SARS-CoV-2 & Influenza A/B comprised of an influenza A dual target assay design which improves inclusivity and resilience of the test to future mutations that may arise. The influenza B- and SARS-CoV-2-targeting assays of **cobas**® SARS-CoV-2 & Influenza A/B remained unchanged in **cobas**® SARS-CoV-2 & Influenza A/B v2.

Performance studies were conducted to demonstrate that the general performance of each target of the assay is unchanged and to prove the effectiveness of the updated design of the influenza A target. The following key performance characteristics data was generated with either **cobas**® SARS-CoV-2 & Influenza A/B or **cobas**® SARS-CoV-2 & Influenza A/B v2.

Key performance characteristics

Analytical sensitivity (Limit of Detection)

The LoD study determines the lowest detectable concentration of SARS-CoV-2, influenza A, and influenza B at which greater or equal to 95% of all (true positive) replicates test positive.

To determine the LoD, six cultured viruses – two each of influenza A and influenza B strains as well as the live and the heat-inactivated form of SARS-CoV-2 isolate from a US patient – were serially diluted in simulated clinical matrix to build two co-formulated target panels and three target single-formulated panels with one strain per virus. Seven to eight concentration levels, with two-fold serial dilutions between the levels, were prepared on three days and tested with a total of 63 replicates per concentration across three reagent lots for co-formulated panels and with a total of 21 replicates per concentration using one reagent lot for single-formulated panels. Table 17 to Table 20 summarize the established LoD values.

Table 17 Summary of LoD for influenza A determined with **cobas**® SARS-CoV-2 & Influenza A/B*

Viral Strain	Kit lot	Panel	95% Probit [$TCID_{50}$/mL]	95% CI of Probit [$TCID_{50}$/mL]	Hit rate ≥ 95% [$TCID_{50}$/mL]	Mean Ct at ≥95% Hit rate
A/Kansas/14/2017 (H3N2)** Cat No 0810586CF Lot 323540	Lot 1	single-formulated	**0.050**	0.034 – 0.098	**0.036**	38.2
	Lot 1	co-formulated	**0.12**	0.073 – 0.28	**0.071**	36.6
	Lot 2	co-formulated	**0.083**	0.054 – 0.17	**0.14**	36.7
	Lot 3	co-formulated	**0.062**	0.040 – 0.14	**0.071**	37.0
	Lot 1-3	co-formulated	**0.086**	0.065 – 0.12	**0.071**	37.5
A/Brisbane/02/2018 (H1N1)*** Cat No 0810585CF Lot 323771	Lot 1	co-formulated	**0.020****	0.013 – 0.048	**0.026**	37.4
	Lot 2	co-formulated	**0.020**	0.013 – 0.064	**0.026**	38.4
	Lot 3	co-formulated	**0.025**	0.016 – 0.059	**0.026**	38.1
	Lot 1-3	co-formulated	**0.022**	0.017 – 0.034	**0.026**	38.0

* LoD equivalency was demonstrated via performance studies with **cobas**® SARS-CoV-2 & Influenza A/B v2.

** Lot specific factor to convert $TCID_{50}$ into copy number was determined using NATrol™ Influenza A H3 Stock (Catalog# NATFLUAH3-STQ, Lot: 331079) material. 1 $TCID_{50}$/mL corresponds to 631 cp/mL.

*** Lot specific factor to convert $TCID_{50}$ into copy number was determined using NATrol™ Influenza A H1 Stock (Catalog# NATFLUAH1-STQ, Lot: 331080) material. 1 $TCID_{50}$/mL corresponds to 5811 cp/mL.

**** Claimed LoD was verified testing influenza A H1N1pdm09 strains containing the C124A (GISAID: EPI_ISL_14387941), and the C124A plus G141A mutations in the M gene (GISAID: EPI_ISL_15803829) with **cobas**® SARS-CoV-2 & Influenza A/B v2.

Table 18 Summary of LoD for influenza B determined with **cobas**® SARS-CoV-2 & Influenza A/B*

Viral Strain	Kit lot	Panel	95% Probit [$TCID_{50}$/mL]	95% CI of Probit [$TCID_{50}$/mL]	Hit rate ≥95% [$TCID_{50}$/mL]	Mean Ct at ≥95% Hit rate
B/Phuket/3073/2013 (Yamagata lineage) Cat No 0810515CF Lot 320436	Lot 1	single-formulated	**0.011**	0.0076 – 0.023	**0.017**	35.4
	Lot 1	co-formulated	**0.019**	0.012 – 0.044	**0.034**	35.1
	Lot 2	co-formulated	**0.016**	0.0095 – 0.050	**0.017**	35.4
	Lot 3	co-formulated	**0.019**	0.010 – 0.084	**0.017**	35.3
	Lot 1-3	co-formulated	**0.017**	0.012 – 0.026	**0.017**	35.3
B/Colorado/06/2017 (Victoria lineage) Cat No 0810573CF Lot 323459	Lot 1	co-formulated	**0.027**	0.017 – 0.065	**0.026**	34.9
	Lot 2	co-formulated	**0.032**	0.019 – 0.084	**0.053**	34.5
	Lot 3	co-formulated	**0.019**	0.012 – 0.050	**0.026**	35.0
	Lot 1-3	co-formulated	**0.026**	0.019 – 0.040	**0.026**	34.9

*LoD equivalency was demonstrated via performance studies with **cobas**® SARS-CoV-2 & Influenza A/B v2.

Table 19 Summary of LoD for SARS-CoV-2 determined with **cobas**® SARS-CoV-2 & Influenza A/B*

Viral Strain	Kit lot	Panel	95% Probit [$TCID_{50}$/mL]	95% CI of Probit [$TCID_{50}$/mL]	Hit rate ≥95% [$TCID_{50}$/mL]	Mean Ct at ≥95% Hit rate
USA-WA1/2020 heat-inactivated Cat No 0810587CFHI Lot 324045	Lot 1	single-formulated	**0.068**	0.044 – 0.15	**0.058**	36.9
	Lot 1	co-formulated	**0.14**	0.086 – 0.35	**0.12**	36.3
	Lot 2	co-formulated	**0.13**	0.083 – 0.26	**0.12**	36.4
	Lot 3	co-formulated	**0.10**	0.065 – 0.25	**0.12**	35.9
	Lot 1-3	co-formulated	**0.13**	0.094 – 0.19	**0.12**	36.2
USA-WA1/2020 infectious culture Cat No NR-52281 Lot 70033175**	Lot 1	co-formulated	**0.0081**	0.0041 – 0.049	**0.0079**	36.2
	Lot 2	co-formulated	**0.0071**	0.0044 – 0.018	**0.0079**	36.2
	Lot 3	co-formulated	**0.0052**	0.0032 – 0.013	**0.0079**	35.9
	Lot 1-3	co-formulated	**0.0063**	0.0046 – 0.010	**0.0079**	36.1

* LoD equivalency was demonstrated via performance studies with **cobas**® SARS-CoV-2 & Influenza A/B v2.

** Based on the information provided in the Certificate of Analysis from the vendor, 1 $TCID_{50}$/mL is equal to 7,393 genome equivalents by ddPCR.

Table 20 Summary of LoD for pan-Sarbecovirus determined with **cobas**® SARS-CoV-2 & Influenza A/B*

Viral Strain	Kit lot	Panel	95% Probit [$TCID_{50}$/mL]	95% CI of Probit [$TCID_{50}$/mL]	Hit rate ≥95% [$TCID_{50}$/mL]	Mean Ct at ≥95% Hit rate
USA-WA1/2020 heat-inactivated Cat No 0810587CFHI Lot 324045	Lot 1	single-formulated	**0.14**	0.082 – 0.37	**0.12**	35.6
	Lot 1	co-formulated	**0.28**	0.17 – 0.67	**0.55**	34.5
	Lot 2	co-formulated	**0.23**	0.14 – 0.49	**0.23**	35.1
	Lot 3	co-formulated	**0.18**	0.11 – 0.37	**0.23**	34.8
	Lot 1-3	co-formulated	**0.23**	0.17 – 0.34	**0.55**	34.2
USA-WA1/2020 infectious culture Cat No NR-52281 Lot 70033175**	Lot 1	co-formulated	**0.0090**	0.0057 – 0.020	**0.016**	34.6
	Lot 2	co-formulated	**0.0076**	0.0049 – 0.016	**0.016**	34.7
	Lot 3	co-formulated	**0.0080**	0.0053 – 0.017	**0.0079**	35.3
	Lot 1-3	co-formulated	**0.0082**	0.0062 – 0.012	**0.016**	34.7

* LoD equivalency was demonstrated via performance studies with **cobas**® SARS-CoV-2 & Influenza A/B v2.

** Based on the information provided in the Certificate of Analysis from the vendor, 1 $TCID_{50}$/mL is equal to 7,393 genome equivalents by ddPCR.

Analytical sensitivity using WHO International Standard

The SARS-CoV-2 and pan-Sarbecovirus specific limit of detection, tested **cobas**® SARS-CoV-2 & Influenza A/B, was evaluated additionally by using the following standard.

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

The WHO International Standard was diluted in simulated clinical matrix stabilized in UTM™ to prepare a low positive panel.

Five concentration levels plus blank, with two-fold serial dilutions between the levels, were prepared on three days and tested with a total of 62 replicates per concentration and lots. Table 21 and Table 22 summarize the established LoD values.

Table 21 Summary of WHO Standard LoD for Target 1 (SARS-CoV-2)

Kit Lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	Hit rate ≥95% [IU/mL]	Mean Ct at ≥95% Hit rate
Lot 1	**45**	29-114	**63**	36.9
Lot 2	**28**	20-71	**63**	36.5
Lot 3	**24**	18-47	**31**	36.6
Combined	**32**	26-46	**63**	36.7

Table 22 Summary of WHO Standard LoD for Target 2 (Pan-Sarbecovirus)

Kit Lot	95% Probit [IU/mL]	95% CI of Probit [IU/mL]	Hit rate ≥95% [IU/mL]	Mean Ct at ≥95% Hit rate
Lot 1	**82**	53-192	**63**	35.0
Lot 2	**54**	35-141	**63**	34.8
Lot 3	**33**	24-64	**63**	35.0
Combined	**56**	43-82	**63**	35.1

Inclusivity

The inclusivity for the detection of influenza A was confirmed by testing thirteen influenza A strains (Table 23) with **cobas**® SARS-CoV-2 & Influenza A/B v2. All strains tested showed 100 % hitrate at approximately 3 x LoD.

Table 23 Summary of inclusivity for influenza A tested with cobas® SARS-CoV-2 & Influenza A/B v2

Viral Target	Strain	Catalog Number
Influenza A	A/Canada/6294/09 (H1N1)	0810109CFJ
	A/California/07/09 (H1N1)	0810165CF
	A/Mexico/4108/09 (H1N1)	0810166CF
	A/Singapore/63/04 (H1N1)	0810246CF
	A/Michigan/45/15 (H1N1)	0810538CF
	A/California/04/09 (pdm09) (H1N1)	VR-1805
	A/England/224020815/2022 (H1N1)*	n/a
	A/England/221740513/2022 (H1N1)**	n/a
	A/Perth/16/09 (H3N2)	0810251CF
	A/Wisconsin/67/05 (H3N2)	0810252CF
	A/Switzerland/9715293/13 (H3N2)	0810511CF
	A/HongKong/4801/14 (H3N2)	0810526CF
	A/Texas/50/12 (H3N2)	0810238CF

* GISAID ID EPI_ISL_15803829, containing the C124A and G141A mutations in the M gene (Strain is not commercially available)
** GISAID ID EPI_ISL_14387941, containing the C124A mutation in the M gene (Strain is not commercially available)

The inclusivity for the detection of influenza B and SARS-CoV-2 was confirmed by testing five influenza B and six SARS-CoV-2 strains with **cobas**® SARS-CoV-2 & Influenza A/B. The lowest target analyte at which all four tested replicates were positive are reported (Table 24 and Table 25).

Table 24 Summary of inclusivity influenza B tested with **cobas**® SARS-CoV-2 & Influenza A/B

Viral Target	Strain	Catalog Number	Lot Number	Lowest Concentration Detected
Influenza B	B/Brisbane/60/2008 (Victoria lineage)	0810254CF	313257 (sublot: 513438)	0.002 $TCID_{50}$/mL
	B/Utah/9/14 (Yamagata lineage)	0810516CF	317295 (sublot: 527062)	0.017 $TCID_{50}$/mL
	B/Alabama/2/17 (Victoria lineage)	0810572CF	322548	0.0064 $TCID_{50}$/mL
	B/Florida/78/2015 (Victoria Lineage)	VR-1931	70020870	0.076 $TCID_{50}$/mL
	B/Wisconsin/1/2010 (Yamagata Lineage)	VR-1883	70012127	0.070 $CEID_{50}$/mL

Table 25 Summary of inclusivity for SARS-CoV-2 tested with **cobas®** SARS-CoV-2 & Influenza A/B

Viral Target	Strain	Catalog Number	Lot Number	Lowest Concentration Detected
SARS-CoV-2	UK (B.1.1.7)	0810614CFHI	326230	7.1E+00 cp/mL
	Japan/Brazil (P.1)	NR-54982	70042875	1.4E+02 cp/mL
	South Africa (B.1.351)	0810613CFHI	326229	7.0E+00 cp/mL
	US NY (B.1.526)	NR-55359	70043342	2.8E+02 cp/mL
	India (B.1.617.1)	NR-55486	70044706	2.5E+02 cp/mL
	India (B.1.617.2)	NR-55611	70045238	4.7E+01 cp/mL

Analytical specificity (cross-reactivity and microbial interference)

A panel of 40 viruses, bacteria, and fungi (including those commonly found in respiratory tract) plus pooled human nasal wash was tested with **cobas®** SARS-CoV-2 & Influenza A/B v2 to assess analytical specificity. The organisms listed in Table 26 were spiked at concentrations of 1 x 10^5 units/mL for viruses and 1 x 10^6 units/mL for other organisms, unless otherwise noted. Testing was performed with each potential interfering organism in the absence and presence of influenza A, influenza B, and SARS-CoV-2 target (spiked at ~3x LoD – 0.42, 0.10 and 0.36 $TCID_{50}$/mL, respectively). None of the organisms interfered with the test performance by generating false positive results. Testing of SARS-CoV-1 generated an expected pan-Sarbecovirus positive result. Detection of influenza A, influenza B, and SARS-CoV-2 targets was not affected in the presence of the organisms tested. Potential cross-reactivity of influenza C, *Leptospira interrogans*, *Pneumocystis jirovecii, Chlamydia psittaci*, *Bacillus anthracis* and *Coxiella burnetii* was evaluated in silico. Based on the in silico analyses, selected organisms are highly unlikely to interfere with the performance of **cobas®** SARS-CoV-2 & Influenza A/B v2.

Table 26 Microorganisms tested for analytical specificity/cross reactivity

Microorganism	**Concentration**
Adenovirus (AdV-1)	1.0E+05 $TCID_{50}$/mL
Bordetella pertussis	1.0E+06 CFU/mL
Candida albicans	1.0E+06 CFU/mL
Chlamydia pneumoniae	7.9E+04 $TCID_{50}$/mL
Corynebacterium diphtheriae	1.0E+06 CFU/mL
Cytomegalovirus	1.0E+05 IU/mL
Enterovirus (EV68)	1.0E+05 $TCID_{50}$/mL
Epstein Barr virus	1.0E+05 cp/mL
Escherichia coli	1.0E+06 CFU/mL
Haemophilus influenzae	1.0E+06 CFU/mL
Human coronavirus 229E	1.0E+05 $TCID_{50}$/mL
Human coronavirus HKU1	6.9E+04 genome cp/mL
Human coronavirus NL63	7.0E+03 $TCID_{50}$/mL
Human coronavirus OC43	1.0E+05 $TCID_{50}$/mL
Human Metapneumovirus	1.0E+05 $TCID_{50}$/mL
Lactobacillus acidophilus	5.0E+05 CFU/mL
Legionella pneumophila	1.0E+06 CFU/mL
Legionella longbeachae	1.0E+06 CFU/mL
Measles virus	1.0E+05 $TCID_{50}$/mL
MERS-coronavirus	1.0E+05 cp/mL
Moraxella catarrhalis	1.0E+06 CFU/mL
Mumps virus	1.0E+05 U/mL
Mycobacterium bovis	1.0E+05 CFU/mL
Mycoplasma pneumoniae	1.0E+06 CCU/mL
Neisseria elongata	1.0E+06 CFU/mL
Neisseria meningitidis	1.0E+06 CFU/mL
Parainfluenza virus 1	1.0E+05 $TCID_{50}$/mL
Parainfluenza virus 2	1.0E+05 $TCID_{50}$/mL
Parainfluenza virus 3	1.0E+05 $TCID_{50}$/mL
Parainfluenza virus 4	1.0E+05 $TCID_{50}$/mL
Parechovirus	1.0E+05 U/mL
Pseudomonas aeruginosa	1.0E+06 CFU/mL
Respiratory syncytial virus	1.0E+05 PFU/mL
Human Rhinovirus	1.0E+05 PFU/mL
SARS-coronavirus (SARS-CoV-1)	1.0E+07 PFU/mL
Staphylococcus aureus	1.0E+06 CFU/mL
Staphylococcus epidermidis	1.0E+06 CFU/mL
Streptococcus salivarius	1.0E+06 CFU/mL
Streptococcus pneumoniae	1.0E+06 CFU/mL
Streptococcus pyogenes	1.0E+06 CFU/mL

Interference

The effect of exogenous substances potentially secreted into respiratory specimens was evaluated (Table 27). Each potentially interfering substance was tested at or above clinically relevant levels in negative simulated clinical matrix stabilized in UTM™ in absence and presence of influenza A, influenza B, and SARS-CoV-2 target (spiked at ~3x LoD – 0.42, 0.10 and 0.36 $TCID_{50}$/mL, respectively) using **cobas**® SARS-CoV-2 & Influenza A/B.

None of the substances interfered with the test performance by generating false-negative or false-positive results. None of the substances interfered with the test performance by generating invalid results.

Table 27 List of exogenous substances tested for interference

Substance	Concentration
Oxymetazoline	0.011 mg/mL
Luffa operculata	2.99 mg/mL
Thryallis glauca	2.99 mg/mL
Histaminum	1.50 mg/mL
Sulfur	1.50 mg/mL
Lidocaine	2.68 mg/mL
Budesonide	0.039 mg/mL
Glycerin	10.31 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	5.00 mg/mL
Menthol	1.20 mg/mL
Tobramycin	0.018 mg/mL

Additionally, FluMist® Quadrivalent, a live quadrivalent vaccine for administration by intranasal spray, and containing two influenza A and two influenza B vaccine virus strains, was tested (Table 28) in negative simulated clinical matrix stabilized in UTM™ in absence and presence of influenza A, influenza B, and SARS-CoV-2 target (spiked at ~3x LoD – 0.42, 0.10 and 0.36 $TCID_{50}$/mL, respectively). As expected, **cobas**® SARS-CoV-2 & Influenza A/B generated positive results for the influenza A and influenza B targets and negative results for the SARS-CoV-2 targets when solely testing FluMist® Quadrivalent and all positive results for influenza A, influenza B and SARS-CoV-2 targets when additionally spiking with low levels of co-formulated influenza A, influenza B and SARS-CoV-2.

Table 28 FluMist® Quadrivalent tested for interference

Product	Substance	Concentration
FluMist® Quadrivalent (Influenza Vaccine Live, Intranasal)	influenza A virus A/Hawaii/6 6/20 19 (H1N1) live (attentuated) antigen influenza A virus A/Hong Kong/26 71/20 19 (H3N2) live (attentuated) antigen influenza B virus B/Phuket/30 73/20 13 live (attentuated) antigen influenza B virus B/Washington/0 2/20 19 live (attentuated) antigen	1336620.81 FFU/mL

Endogenous substances that may be present in respiratory specimens were tested for interference (Table 29). Each potentially interfering substance was tested at or above clinically relevant levels in negative simulated clinical matrix stabilized in UTM™ in absence and presence of influenza A, influenza B, and SARS-CoV-2 target (spiked at ~3x LoD – 0.42, 0.10 and 0.36 $TCID_{50}$/mL, respectively) using **cobas**® SARS-CoV-2 & Influenza A/B.

None of the substances interfered with the test performance by generating false-negative, false-positive or invalid/non-reportable results.

Table 29 List of endogenous substances tested for interference

Substance	Concentration
Mucin	0.5 % (w/v)
Human Whole Blood	1.5 % (v/v)

Co-infection (competitive interference)

To assess potential competitive interference between influenza A, influenza B, and SARS-CoV-2, samples were tested using **cobas**® SARS-CoV-2 & Influenza A/B v2 in replicates of 4 where low (approximately 3x LoD) concentrations of any two targets were mixed with very high (1.0E+05 units/mL) concentrations of the third target. None of the targets present at very high concentration interfered with the detection of low levels of the other two targets.

Collection media equivalence

Equivalence between different collection media (UTM-RT®, **cobas**® PCR Media, and saline) was evaluated using one strain each for influenza A (A/Kansas/14/2017 (H3N2)), influenza B (B/Phuket/3073/2013 (Yamagata lineage)) and SARS-CoV-2 (USA-WA1/2020, heat-inactivated culture). Testing was performed using **cobas**® SARS-CoV-2 & Influenza A/B. Virus cultures were co-formulated to a target concentration of approximately 2x LoD into simulated clinical matrix formulated either in Universal Transport Media (UTM-RT®), **cobas**® PCR Media (CPM), or in 0.9% physiological saline. A total of 21 replicates were tested for each collection media type. All replicates tested were positive in all simulated matrices for influenza A and influenza B. For SARS-CoV-2, positivity rates were 100% for both UTM-RT® and CPM and 95.2% for saline.

Whole system failure

The whole system failure rate was assessed using **cobas**® SARS-CoV-2 & Influenza A/B by testing 100 specimens of simulated clinical matrix co-spiked with one strain each for influenza A (A/Kansas/14/2017 (H3N2)), influenza B (B/Phuket/3073/2013 (Yamagata lineage)) and SARS-CoV-2 (USA-WA1/2020, heat-inactivated culture) to a concentration of approximately 3x LoD of the respective target. The results of this study determined that all replicates were valid and positive for influenza A, influenza B and SARS-CoV-2, resulting in a whole system failure rate of 0% with an upper one-sided 95% confidence interval of 3.0%.

Precision (repeatability)

Within-laboratory precision was examined using cobas® SARS-CoV-2 & Influenza A/B by testing a panel composed of co-spiked influenza A (A/Kansas/14/2017), influenza B (B/Phuket/3073/2013) and SARS-CoV-2 (USA-WA1/2020, heat-inactivated) cultures diluted in simulated clinical matrix in UTM-RT®. Sources of variability were examined with a panel consisting of three concentration levels, using three lots of cobas® SARS-CoV-2 & Influenza A/B reagents and two instruments over a time course of 15 days for a total of 30 runs. A description of the precision panel and the observed positivity rates are shown in Table 30. 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 31) yielded overall CV percentage ranging from 1.1% to 5.2% for influenza A, influenza B, and SARS-CoV-2.

Table 30 Summary of within laboratory precision

Target Concentration	N Tested	N Positive	Positivity Rate	95% Confidence Interval	
				Lower Limit	Upper Limit
Influenza A					
Negative	90	0	0%	0%	4.1%
Weak Positive ~ 0.3x LoD (0.043 $TCID_{50}$/mL)	90	87	96.7%	90.7%	98.9%
Low Positive ~ 1x LoD (0.14 $TCID_{50}$/mL)	90	90	100%	95.9%	100%
Moderate Positive ~ 3x LoD (0.43 $TCID_{50}$/mL)	90	90	100%	95.9%	100%
Influenza B					
Negative	90	0	0%	0%	4.1%
Weak Positive ~ 0.3x LoD (0.010 $TCID_{50}$/mL)	90	81	90.0%	82.1%	94.7%
Low Positive ~ 1x LoD (0.034 $TCID_{50}$/mL)	90	90	100%	95.9%	100%
Moderate Positive ~ 3x LoD (0.10 $TCID_{50}$/mL)	90	90	100%	95.9%	100%
SARS-CoV-2					
Negative	90	0	0%	0%	4.1%
Weak Positive ~ 0.3x LoD (0.035 $TCID_{50}$/mL)	90	83	92.2%	84.8%	96.2%
Low Positive ~ 1x LoD (0.12 $TCID_{50}$/mL)	90	87	96.7%	90.7%	98.9%
Moderate Positive ~ 3x LoD (0.35 $TCID_{50}$/mL)	90	90	100%	95.9%	100%
pan-Sarbecovirus					
Negative	90	0	0%	0%	4.1%
Weak Positive ~ 0.06x LoD (0.035 $TCID_{50}$/mL)	90	73	81.1%	71.8%	87.9%
Low Positive ~ 0.2x LoD (0.12 $TCID_{50}$/mL)	90	87	96.7%	90.7%	98.9%
Moderate Positive ~ 0.6x LoD (0.35 $TCID_{50}$/mL)	90	90	100%	95.9%	100%

Table 31 Overall mean, standard deviation, and percent coefficient of variation for Ct values by positive panel member

Target Concentration	Positivity Rate	Mean Ct	Between instrument		Between lot		Between day		Between run		Within run		Total	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Influenza A														
Weak Positive ~ 0.3x LoD (0.042 TCID50/mL)	96.7%	38.3	0.00	0.0	0.29	0.8	0.43	1.1	0.00	0.0	1.90	5.0	1.97	5.1
Low Positive ~ 1x LoD (0.14 TCID50/mL)	100%	35.7	0.00	0.0	0.00	0.0	0.19	0.5	0.15	0.4	0.90	2.5	0.93	2.6
Moderate Positive ~ 3x LoD (0.42 TCID50/mL)	100%	34.3	0.11	0.3	0.00	0.0	0.11	0.3	0.00	0.0	0.43	1.2	0.46	1.3
Influenza B														
Weak Positive ~ 0.3x LoD (0.010 $TCID_{50}$/mL)	90.0%	35.6	0.11	0.3	0.00	0.0	0.23	0.6	0.09	0.3	0.62	1.7	0.67	1.9
Low Positive ~ 1x LoD (0.034 $TCID_{50}$/mL)	100%	34.7	0.00	0.0	0.00	0.0	0.19	0.5	0.21	0.6	0.51	1.5	0.58	1.7
Moderate Positive ~ 3x LoD (0.10 $TCID_{50}$/mL)	100%	33.8	0.07	0.2	0.00	0.0	0.17	0.5	0.00	0.0	0.82	2.4	0.84	2.5
SARS-CoV-2														
Weak Positive ~ 0.3x LoD (0.035 $TCID_{50}$/mL)	92.2%	36.6	0.00	0.0	0.00	0.0	0.32	0.9	0.07	0.2	0.6	1.6	0.68	1.9
Low Positive ~ 1x LoD (0.12 $TCID_{50}$/mL)	96.7%	35.7	0.06	0.2	0.07	0.2	0.00	0.0	0.05	0.1	0.40	1.1	0.42	1.2
Moderate Positive ~ 3x LoD (0.35 $TCID_{50}$/mL)	100%	34.6	0.17	0.5	0.00	0.0	0.19	0.6	0.00	0.0	0.57	1.7	0.63	1.8
pan-Sarbecovirus														
Weak Positive ~ 0.06x LoD (0.035 $TCID_{50}$/mL)	81.1%	35.8	0.00	0.0	0.00	0.0	0.16	0.4	0.11	0.3	0.63	1.8	0.66	1.8
Low Positive ~ 0.2x LoD (0.12 $TCID_{50}$/mL)	96.7%	34.9	0.00	0.0	0.06	0.2	0.00	0.0	0.00	0.0	0.52	1.5	0.52	1.5
Moderate Positive ~ 0.6x LoD (0.35 $TCID_{50}$/mL)	100%	33.9	0.13	0.4	0.00	0.0	0.10	0.3	0.00	0.0	0.54	1.6	0.57	1.7

Clinical performance evaluation

Performance with clinical specimens

First, the clinical performance was evaluated at one external site using archived nasopharyngeal swab (NPS) samples from patients with signs and symptoms of a respiratory infection, collected in UTM-RT® or UVT between 2014 and 2020 for the SARS-CoV-2 and influenza B components with **cobas**® SARS-CoV-2 & Influenza A/B. Clinical samples were collected by qualified personnel according to the package insert of the collection device.

This clinical evaluation study included a total of 349 NPS samples, 57 of which were longitudinal samples from COVID-19 patients. **cobas**® SARS-CoV-2 Qualitative and **cobas**® Influenza A/B & RSV for use on the **cobas**® Liat® System were utilized as the comparator test for assessment of performance of the **cobas**® SARS-CoV-2 & Influenza A/B for SARS-CoV-2 and influenza B, respectively. One of the 349 NPS samples did not have a valid comparator SARS-CoV-2 result and five of the 349 NPS samples did not have valid comparator influenza A/B results, therefore, were excluded from the performance calculations for SARS-CoV-2 and influenza A and influenza B, respectively.

In a subsequent clinical evaluation, the performance of the **cobas**® SARS-CoV-2 & Influenza A/B v2 was assessed for the influenza A component at one internal site using archived NPS and NS samples from patients with signs and symptoms of a respiratory infection, collected in UTM-RT® or UVT in 2022-2023. Clinical samples were collected by qualified personnel according to the package insert of the collection device. This clinical evaluation study included a total of 75 NPS and 75 NS samples. **cobas**® Influenza A/B & RSV for use on the **cobas**® Liat® System was utilized as the comparator test for assessment of performance of the assay for the influenza A component.

As shown in Table 32, the **cobas**® SARS-CoV-2 & Influenza A/B and **cobas**® SARS-CoV-2 & Influenza A/B v2 demonstrated high percent agreement with the comparator tests for the detection of SARS-CoV-2, influenza A and influenza B.

Table 32 Comparison of **cobas**® SARS-CoV-2 & Influenza A/B and **cobas**® SARS-CoV-2 & Influenza A/B v2 with **cobas**® SARS-CoV-2 Qualitative and **cobas**® Influenza A/B & RSV for use on the **cobas**® Liat® System

Virus	Number of Samples	Test Results				Agreement Statistics		
		Concordant Positive (N)	Discordant Positive (N)	Concordant Negative (N)	Discordant Negative (N)	Agreement Parameter	Percent Agreement (%)	95% CI (LCL, UCL)*
SARS-CoV-2[#]	348	53	6	287	2	PPA	96.4%	(87.7%, 99.0%)
						NPA	98.0%	(95.6%, 99.1%)
Influenza A[†]	150	50	0	100	0	PPA	100.0%	(92.9%, 100.0%)
						NPA	100.0%	(96.3%, 100.0%)
Influenza B	344	37	1	306	0	PPA	100.0%	(90.6%, 100.0%)
						NPA	99.7%	(98.2%, 99.9%)

PPA = Positive Percent Agreement

NPA = Negative Percent Agreement

CI = Confidence Interval; LCL = Lower Confidence Limit; UCL = Upper Confidence Limit

*Confidence interval is calculated using Wilson's Score method

[#]A positive result is defined as detection of either of the two SARS-CoV-2 or pan-Sarbecovirus target of the assay

[†] Including six H1N1pdm09 positive samples containing the C124A and G141A mutations in the M gene

Discordant results between the **cobas**® SARS-CoV-2 & Influenza A/B assay and the comparator methods were observed for 9 samples. Of these, 8 were longitudinal samples with discordant results for SARS-CoV-2 that showed late Ct values (between 35-43), which are indicative of samples from recovery/convalescent patients with decreasing viral loads close to or below the limit of detection of both the **cobas**® SARS-CoV-2 & Influenza A/B and the **cobas**® SARS-CoV-2 Qualitative. **cobas**® SARS-CoV-2 & Influenza A/B detected an additional influenza B virus positive sample compared to **cobas**® Influenza A/B & RSV for use on the **cobas**® Liat® System. Post-PCR analysis of the amplicon from the discordant samples confirmed the presence of SARS-CoV-2 but not influenza B.

System equivalency/system comparison

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

Additional information

Key test features

Sample type	Nasopharyngeal swab samples collected in the Copan UTM-RT® System 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 mL 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**® 5800 and **cobas**® 6800/8800 Systems (consult User Assistance and/or User Guides) may have different dead volumes and require more or less minimum volume.

Symbols

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

Table 34 Symbols used in labeling for Roche PCR diagnostics products

Age/DOB Age or Date of Birth	Device not for near-patient testing	QS IU/PCR QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results.
SW Ancillary Software	Device not for self-testing	
Assigned Range [copies/mL] Assigned Range (copies/mL)	Distributor *(Note: The applicable country/region may be designated beneath the symbol)*	SN Serial number
Assigned Range [IU/mL] Assigned Range (IU/mL)	Do not re-use	Site Site
EC REP Authorized representative in the European Community	Female	Procedure Standard Standard Procedure
BARCODE Barcode Data Sheet	For IVD performance evaluation only	STERILE EO Sterilized using ethylene oxide
LOT Batch code	GTIN Global Trade Item Number	Store in dark
Biological risks	Importer	Temperature limit
REF Catalogue number	IVD In vitro diagnostic medical device	TDF Test Definition File
CE CE marking of conformity; this device is in conformity with the applicable requirements for CE marking of an in vitro diagnostic medical device	LLR Lower Limit of Assigned Range	This way up
	Male	Procedure UltraSensitive Ultrasensitive Procedure
Collect Date Collect date	Manufacturer	UDI Unique Device Identifier
Consult instructions for use	CONTROL − Negative control	ULR Upper Limit of Assigned Range
Σ Contains sufficient for <*n*> tests	NON STERILE Non-sterile	Urine Fill Line Urine Fill Line
CONTENT Content of kit	Patient Name	Rx Only US Only: Federal law restricts this device to sale by or on the order of a physician.
CONTROL Control	Patient number	Use-by date
Date of manufacture	Peel here	
Device for near-patient testing	CONTROL + Positive control	
Device for self-testing	QS copies / PCR 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 35 Manufacturer and importer

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

Made in USA

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany

Trademarks and patents

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

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EC REP

Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
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CE IVD

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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.

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