Rx Only

cobas® Paraflu 1-4 UC

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

For in vitro diagnostic use

cobas® Paraflu 1-4 UC	P/N: 09555617190
cobas® Paraflu 1-4 UC Control Kit	P/N: 09555587190
cobas omni Utility Channel Reagent Kit	P/N: 09052011190
cobas® Buffer Negative Control Kit	P/N: 09051953190

Table of contents

Intended use

The **cobas**® Paraflu 1-4 UC Qualitative Nucleic Acid test for use with the **cobas omni** Utility Channel on **cobas**® 6800/8800 Systems is an automated, multiplex, real-time reverse transcriptase polymerase chain reaction (PCR) for the timely in vitro qualitative detection and discrimination of human Parainfluenza virus serotypes 1, 2, 3, and 4 (HPIV1-4). This test is intended for use as an aid in the diagnosis of HPIV1-4 in nasopharyngeal swab specimens from patients with signs and symptoms of a respiratory infection in conjunction with clinical and epidemiological risk factors.

The results from **cobas**® Paraflu 1-4 UC must be interpreted within the context of all relevant clinical and laboratory findings. Negative results do not preclude viral infection and should not be used as the sole basis for treatment or other patient management decisions. Conversely, 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.

The **cobas**® Paraflu 1-4 UC Qualitative Nucleic Acid test for use with the **cobas omni** Utility Channel on the **cobas**® 6800/8800 Systems is intended for professional use in a clinical laboratory setting.

Summary and explanation of the test

Background

Human parainfluenza viruses (HPIVs) are enveloped negative-sense single-stranded RNA viruses of medium size (150-250 nm), belonging to the *Paramyxoviridae* family.[1,2] The HPIVs are represented by four serotypes (HPIV1-4) which are grouped into two different genera: *Respirovirus* (HPIV1 and HPIV3) and *Rubulavirus* (HPIV2 and HPIV4). HPIV4 includes two subtypes: HPIV4a and HPIV4b, based on antigenic differences.[3] All four subtypes are highly contagious, seasonal respiratory tract pathogens which can infect both the Upper Respiratory Tract (URT) and Lower Respiratory Tract (LRT) in children and adults. Transmission occurs primarily through respiratory droplets and contact with contaminated surfaces. Following infection, HPIVs bind and replicate in the ciliated epithelial cells of the URT and LRT.[2] Re-infection is common and protective immunity acquired during childhood is incomplete, resulting in recurrent re-infections throughout adult life with generally mild and self-limited symptoms observed, except in elder or immunocompromised adults where there is a higher risk of severe and life-threatening pneumonia.[2]

Infections of the URT and LRT can be caused by a variety of viral, fungal and bacterial agents in adults and children.[4-6] The HPIVs are one of the common etiologic agents of respiratory tract infections and responsible for presentation in approximiately 17% of children under 5 years of age in outpatient studies.[2] The different HPIV serotypes have different prevalence, seasonal patterns, epidemiologic implications, and clinical profiles. The National Respiratory and Enteric Viruses Surveillance System found that, in the USA between 1990 and 2004, HPIV3 was the most prevalent serotype (52%), followed by HPIV1 (26%), HPIV2 (12%) and HPIV4 (2%).[7] HPIV1 and HPIV2 are the principal causative agents of croup (acute laryngotracheobronchitis) causing 60-75% of cases and HPIV3 has been closely associated with bronchiolitis and viral pneumonia.[2] Importantly, timely identification of the etiology of respiratory tract infections can reduce the use of antibiotics.[8]

Rationale for PCR testing

Real-time Polymerase Chain Reaction (PCR) is a nucleic acid amplification method used to detect specific DNA sequences obtained after extraction and by reverse transcription of RNA. Real-time PCR technology allows a rapid and specific measurement of the presence of genes from microorganisms associated with infectious diseases. One of the primary benefits of this technology is a combination of speed and sensitivity unrivaled by antigen detection or viral culture.[9,10]

Explanation of the test

cobas® Paraflu 1-4 UC for use with the **cobas** omni Utility Channel on the **cobas**® 6800/8800 Systems is an automated, multiplex, real-time reverse transcription polymerase chain reaction (RT-PCR) assay for the rapid in vitro qualitative detection and discrimination of human Parainfluenza virus serotypes 1, 2, 3 and 4 (HPIV1-4) in nasopharyngeal swab (NPS) specimens collected in Copan Universal Transport Medium System (UTM-RT), BD™ Universal Viral Transport System (UVT), or equivalent. 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® Paraflu 1-4 UC for use with the **cobas omni** Utility Channel, 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 Systems 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 RNA Internal Control (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 reagent 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**® Paraflu 1-4 UC run.

cobas® Paraflu 1-4 UC contains the HPIV1-4 primers and probes which are used in combination with the **cobas omni** Utility Channel Master Mix Reagent 2 (UC MMX-R2) and the 192-test cassette included in the **cobas omni** Utility Channel Reagent Kit. The 192-test cassette contains an Internal Control recognized by specific primers and probes included in the **cobas omni** Utility Channel Master Mix Reagent 2 (UC MMX-R2).

Selective amplification of target nucleic acid from the sample, and the positive control is achieved by the use of target virus-specific forward and reverse primers which are selected from conserved regions of the HPIV1 (L polymerase protein), HPIV2 (Large protein), HPIV3 (Nucleocapsid protein) and HPIV4 (Large protein) genes. Selective amplification of the RNA Internal Control is achieved by the use of non-competitive sequence specific forward and reverse primers, which have no homology with the HPIV1-4 genomes. Amplified target is detected by cleavage of fluorescently labeled oligonucleotide probe. A thermostable DNA polymerase enzyme is used for amplification.

The prepared **cobas**® Paraflu 1-4 UC master mix contains detection probes which are specific for human parainfluenza viruses 1-4 and the RNA Internal Control nucleic acid. HPIV1-4 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 target

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**® Paraflu 1-4 UC can be found in Table 1. Materials required, but not provided can be found in Table 2, Table 3, Table 4, Table 5, and Table 9.

cobas® Paraflu 1-4 UC reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 5.

Table 1 cobas® Paraflu 1-4 UC (primers and probes)

Store at 2-8°C
(P/N 09555617190)

Kit components	Reagent ingredients	Quantity per kit 192 tests
Paraflu 1-4 UC PP	Tris buffer, 0.015% EDTA, upstream and downstream primers for HPIV1-4, fluorescent-labeled oligonucleotide probes specific for HPIV1-4, 0.05% sodium azide	1 x 0.65 mL

Table 2 cobas® Paraflu 1-4 UC Control Kit

Store at 2–8°C
(P/N 09555587190)

Kit components	Reagent ingredients	Quantity per kit
Paraflu 1-4 UC (+) C	Linear synthetic HPIV1-4 DNA, Tris buffer, 0.05% Sodium Azide, 0.01% EDTA, <0.003% Poly rA	16 mL (10 x 1.60 mL)

Table 3 cobas omni Utility Channel Reagent Kit (UC)

Store at 2–8°C
(P/N 09052011190)

Reagents	Reagent ingredients	Quantity per kit 192 tests
192 test cassette		
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-QS)	Tris buffer, <0.05% EDTA, <0.001% 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
R2 Empty Vessel (R2 EV)	not applicable	1
Master Mix Reagent 2 bottle		
cobas omni Utility Channel Master Mix Reagent 2 (UC MMX-R2)	Tricine buffer, potassium acetate, < 18% dimethyl sulfoxide, glycerol, < 0.1% Tween 20, EDTA, < 0.12% dATP, dCTP, dGTP, dUTPs, < 0.01% internal control forward and reverse primers, < 0.01% fluorescent-labeled oligonucleotide probes specific for RNA-IC, < 0.01% oligonucleotide aptamer, < 0.01% Z05D DNA polymerase, < 0.1% AmpErase (uracil-N-glycosylase) enzyme (microbial), < 0.1% sodium azide	19.6 mL (2 x 9.8 mL)

Table 4 cobas® Buffer Negative Control Kit

Store at 2-8°C
(P/N 09051953190)

Kit components	Reagent ingredients	Quantity per kit
cobas® Buffer Negative Control (BUF (-) C)	Tris buffer, < 0.1% sodium azide, EDTA, < 0.002% Poly rA RNA (synthetic)	16 mL (16 x 1mL)

cobas omni reagents for sample preparation

Table 5 **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 × 875 mL	Not applicable
cobas omni Lysis Reagent (LYS) Store at 2–8°C (P/N 06997538190)	42.56% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate EUH032: Contact with acids liberates very toxic gas.	4 × 875 mL	 **DANGER** H302 + H332: Harmful if swallowed or if inhaled. H314: Causes severe skin burns and eye damage. H411: Toxic to aquatic life with long lasting effects. 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**® Paraflu 1-4 UC kit. See listing of additional materials required (Table 8).

** 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 6 and Table 7.

When reagents are not loaded on the **cobas**® 6800/8800 Systems, store them at the corresponding temperature specified in Table 6.

Table 6 Reagent storage (when reagent is not on the system)

Reagent	Storage temperature
cobas® Paraflu 1-4 UC[a]	2–8°C
cobas® Paraflu 1-4 UC Control Kit	2–8°C
cobas omni Utility Channel Reagent 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

[a] The prepared reagent cassette can be stored for up to 7 days at 2-8 °C before first usage. After first usage, please refer to expiry conditions of the **cobas omni** Utility Channel Reagent Kit in Table 7.

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 the kit can be used	On-board stability (cumulative time on board outside refrigerator)
cobas omni Utility Channel Reagent Kit	Date not passed	90 days from first usage	Max 40 runs	Max 40 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

Table 8 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 Sample Diluent	06997511190
cobas omni Wash Reagent	06997503190
Solid Waste Bag and Solid Waste Container or Solid Waste Bag With Insert and Kit Drawer Solid Waste Update	07435967001 and 07094361001 or 08030073001 and 08387281001
cobas omni Secondary Tubes 13x75 (optional)	06438776001

Instrumentation and software required

The **cobas**® 6800/8800 software and **cobas**® Paraflu 1-4 UC analysis package shall be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

Table 9 Instrumentation

Equipment	P/N
cobas® 6800 System (Option Moveable)	05524245001 and 06379672001
cobas® 6800 System (Fix)	05524245001 and 06379664001
cobas® 8800 System	05412722001
Sample Supply Module	06301037001
Instrument Gateway	06349595001
TWN3 Legic NFC USB (RFID Reader/Writer)	07450460001
External PC with remote connection provided by the customer	N/A
Barcode Printer	N/A

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 only.
- **cobas**® Paraflu 1-4 UC is not evaluated for use as a screening test for the presence of HPIV1-4 in other samples than NPS specimens.
- 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.[11,12] Only personnel proficient in handling infectious materials and the use of **cobas**® Paraflu 1-4 UC 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.
- Inform your local competent authority about any serious incidents which may occur when using this assay.

Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect reagent cassette and vials, 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**® Paraflu 1-4 UC**, cobas omni** Utility Channel Reagent 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**® Paraflu 1-4 UC kits, **cobas**® Paraflu 1-4 UC Control Kits, **cobas omni** Utility Channel Reagent kits, **cobas**® Buffer Negative Control kits 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 were capable of transmitting infectious agents.
Store all samples at specified temperatures.
Sample stability is affected by elevated temperatures.
Ensure samples are equilibrated to room temperature prior to transfer into a **cobas omni** Secondary Tube.

Samples collection

- Nasopharyngeal specimens should be collected according to standard collection technique using flocked swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT), or equivalent.
- Refer to the Instructions for Use of the Collection Devices for hazard information.

Transport and storage

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- After collection, specimens can be stored in primary tubes for up to 4 hours at 15-25°C, up to 3 days at 2-8°C or up to 30 days at -20°C to -80°C with maximum 3 freeze and thaw cycles.

Instructions for use

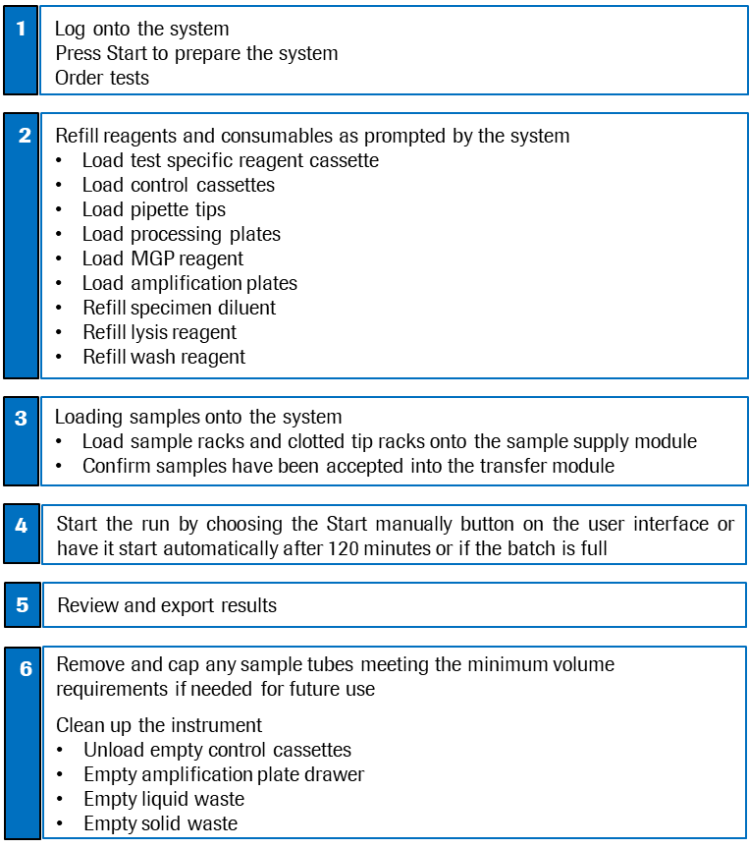
Procedural notes

- The assay is only intended for use with **cobas**® Paraflu 1-4 UC USAP from Roche.
- Do not use **cobas omni** Utility Channel Reagent kit, **cobas**® Buffer Negative Control Kit, **cobas**® Paraflu 1-4 UC, **cobas**® Paraflu 1-4 UC Control Kit or **cobas omni** reagents after their expiry dates.
- Only use the UC MMX-R2 bottles provided with the reagent cassette.
- 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**® 6800/8800 Systems User Guide for proper barcode specifications and additional information on loading sample tubes.
- Refer to the **cobas**® 6800/8800 Systems – User Assistance and/or User Guide for proper maintenance of instruments.

Running cobas® Paraflu 1-4 UC

cobas® Paraflu 1-4 UC 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) or equivalent.

Figure 1 **cobas**® Paraflu 1-4 UC test procedure

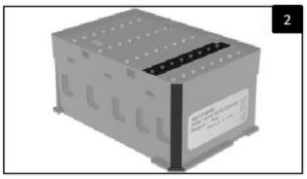


Preparing the reagent cassette

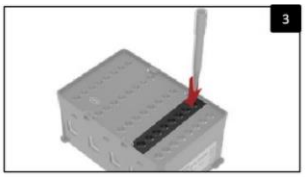
The PCR MMX R2 is prepared from the mix of Master Mix Reagent 2 (UC-MMX-R2) and **cobas**® Paraflu 1-4 UC primers and probes loaded in the **cobas omni** Utility Channel Reagent kit 192-test cassette.

- Remove the Master Mix Reagent 2 (UC-MMX-R2, see picture 1) from **cobas omni** Utility Channel Reagent Kit and **cobas**® Paraflu 1-4 UC primers and probes from their 2-8°C storage location.
- Mix UC-MMx-R2 on the roller mixer for 5 minutes at room temperature.
  Note: If no roller mixer is available, invert the bottle 20 times.
- Transfer 10 mL of UC MMX-R2 reagent to a light-protected polypropylene tube.
  Note: Refer to the **cobas omni** Utility Channel User Assistance for details on transfer option steps.
- Mix and spin the **cobas**® Paraflu 1-4 UC primers and probes.
- Add 0.600 mL of the **cobas**® Paraflu 1-4 UC primers and probes (refer Table 1) to the light-protected polypropylene tube.
- Mix the polypropylene tube for 5 minutes on the roller mixer.
  Note: If no roller mixer is available, invert the bottle 20 times.

The reagent cassette is prepared by loading the PCR Mix into the reagent cassette from the **cobas omni** Utility Channel Reagent Kit.

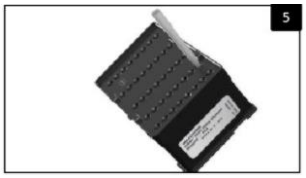


- Position the reagent cassette by placing the slanted edge to the lower right corner (see picture 2).
  Note: The second row from the right side contains the empty MMX container.



- Place a 1 mL plastic pipette tip into the top septum hole row 2 (see picture 3).
  Note: The pipette tip allows air pressure in the vessel to adjust while the prepared PCR Mix is added.
- Take a repeater pipette with a 10 mL pipette tip. Load the pipette tip with 9.7 mL of the prepared PCR Mix.
- Insert the loaded pipette into the bottom septum hole of the reagent cassette. Puncture the septum deeply enough to avoid spillage in the row 2 (see picture 4).

- Tilt the reagent cassette to a 45° angle lengthwise from the bottom. Make sure the cassette is tipped along the edge where the pipette with the 10 mL tip is inserted (see picture 5).
- Slowly and carefully pipette 9.7 mL of the prepared PCR Mix through the bottom septum into the empty container in row 2 (see picture 5). If possible, dispense the prepared PCR Mix in a single movement. Ensure that the correct volume of prepared PCR Mix is pipetted.



- Ensure that there is no fluid in the 1 mL pipette tip and then remove it from the septum.
  Note: if there is fluid in the tip, carefully rotate the tip to release the fluid from the tip back into the cassette. If fluid still remains in the 1 mL tip, perform the following: Using the repeater pipette with a 10 mL tip, remove some of the pipetted PCR Mix from the cassette vessel until no fluid remains in the 1 mL tip. Slowly and carefully pipette any fluid in the 10 mL pipette tip back into the vessel. Once both tips are empty, the tips can be removed from the cassette.

- Slowly tilt the reagent cassette 20 times to remove any air bubbles from the newly filled container (see picture 6).
- On the label of the 192-test cassette from **cobas omni** Utility Channel Reagent Kit, document the assay name

(**cobas**® Paraflu 1-4 UC), the date the cassette was prepared, the lot number of the assay kits primers and probes used (P&P Mix Lot) and check the box 'P&P Added' to confirm that primers and probes mix have been added.

The RFID label of the prepared **cobas omni** Utility Channel Reagent Kit reagent cassette is labelled as follows:

- Open the **cobas omni** Utility Channel Tool using the Roche Utility Channel Tool start icon on the desktop.
- Click the "Open UC analysis package" button and select the USAP.zip file from the Recently used UC specific analysis packages section or load the UC_PARA USAP via "Open published UC analysis package to write on reagent cassette RFID tag". The UC analysis package screen in UCAP tab opens up.
- On the UC analysis package panel, Click the "Reagent cassette" button.
- Enter the **cobas omni** Utility Channel Reagent Kit lot number in the field corresponding to Reagent cassette lot ID.
- Place the RFID reader/writer next to the RFID tag of the Utility Channel reagent cassette to be written on.
- Click the "Write data on the RFID tag" button to write the RFID label.
- Load the prepared reagent cassette onto the **cobas**® 6800/8800 Systems.
- The prepared reagent cassette can be stored for up to 7 days at 2-8 °C before first usage. After first usage, please refer to expiry conditions of the **cobas omni** Utility Channel Reagent Kit in Table 7.

Prepare samples and controls

One positive control has to be performed as sample in each run and for each new reagent cassette. To guarantee that each control batch contains a positive control, it is recommended to use the entire **cobas omni** Utility Channel reagent cassette before loading a new **cobas omni** Utility Channel reagent cassette.

Specimens collected in Copan Universal Transport Medium (UTM-RT), BD™ Universal Viral Transport (UVT) or equivalent and positive control must be vortexed and transferred into separate **cobas omni** Secondary Tubes (0.6 mL) prior to processing on the **cobas**® 6800/8800 Systems. Samples transferred to **cobas omni** Secondary Tubes should be processed using the 'VTM' sample type selection.

Note: If using frozen NPS specimens, place the samples at room temperature until completely thawed and vortex for 3 to 5 seconds before use.

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.

Define test ordering

Create a test order as described in **cobas**® 6800/8800 Systems User Guide.

- In the Sample type field, select "VTM" from the drop down menu.
- In the Test region, select "UC_PARA" from the drop down menu.
- In the Volume region, ensure that the volume equals "400 µL".
- Save and perform the test as described in the **cobas**® 6800/8800 Systems User Guide.

Refer to the **cobas**® 6800/8800 Systems User Guide for more details.

Results

The **cobas**® 6800/8800 Systems automatically detect HPIV1-4, for each individually processed sample and control, displaying individual target results for samples and the positive control, as well as test validity and overall results for the negative control.

Quality control and validity of results

- One **cobas**® Buffer Negative Control [BUF (-) C] and one **cobas**® Paraflu 1-4 UC Control [Paraflu 1-4 UC (+) C] need to be 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 the negative control and if the positive control is positive for all targets. 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 control performance. The positive control validation has to be performed by the operator based on the positive control performance.

To determine this validity, interpret the results from the controls and IC as described in Table 12 below.

Table 10 Run and result validity interpretation

Validity	Control	Valid	Invalid	Validation
Run	(-) Ctrl	Indicated as "Valid" in Test Result column	Indicated as "Invalid" in Overall Result column (All samples of the run must be retested)	**cobas**® 6800/8800 Systems
	(+) Ctrl	Ct value indicated in each Target column	Indicated as “Invalid” or "Negative" in one of the Target columns (1, 2, 3 OR 4) (All samples of the run must be retested)	Operator
Sample	IC	Indicated as "Yes" in Valid column	Indicated as "No" in Valid column AND Targets 1, 2, 3 AND 4: Invalid (Invalidated sample must be retested)	**cobas**® 6800/8800 Systems

Interpretation of results

If the run and sample are valid, the result interpretation for each target is based on the results provided by the **cobas**® 6800/8800 Systems and described in Table 11. Invalid results for one or more target combinations are possible and are reported out specifically for each channel on the **cobas**® 6800/8800 Systems. In these cases, original sample should be re-tested to obtain a valid target result. If the target result is still invalid, a new sample should be obtained.

Table 11 cobas® Parflu 1-4 UC result interpretation

Target 1 (HPIV2)	Target 2 (HPIV4)	Target 3 (HPIV1)	Target 4 (HPIV3)	Interpretation
HPIV2 Negative	Any	Any	Any	Target Result for HPIV2 is valid. Result for HPIV2 RNA is Not Detected.
HPIV2 Ct value	Any	Any	Any	Target Result for HPIV2 is valid. Result for HPIV2 RNA is Detected.
Invalid	Any	Any	Any	Target Result for HPIV2 is invalid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Any	**HPIV4 Negative**	Any	Any	Target Result for HPIV4 is valid. Result for HPIV4 RNA is Not Detected.
Any	**HPIV4 Ct value**	Any	Any	Target Results for HPIV4 is valid. Result for HPIV4 RNA is Detected.
Any	**Invalid**	Any	Any	Target Result for HPIV4 is invalid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Any	Any	**HPIV1 Negative**	Any	Target Result for HPIV1 is valid. Result for HPIV1 RNA is Not Detected.
Any	Any	**HPIV1 Ct value**	Any	Target Results for HPIV1 is valid. Result for HPIV1 RNA is Detected.
Any	Any	**Invalid**	Any	Target Result for HPIV1 is invalid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Any	**Any**	**Any**	**HPIV3 Negative**	Target Result for HPIV3 is valid. Result for HPIV3 RNA is Not Detected.
Any	**Any**	**Any**	**HPIV3 Ct value**	Target Results for HPIV3 is valid. Result for HPIV3 RNA is Detected.
Any	**Any**	**Any**	**Invalid**	Target Result for HPIV3 is invalid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	**Invalid**	**Invalid**	**Invalid**	None of the Targets Results are valid. Sample should be retested. If the result is still invalid, a new specimen should be obtained.

Procedural limitations

- **cobas**® Paraflu 1-4 UC has been evaluated only for use in combination with **cobas**® Paraflu 1-4 UC Control Kit, **cobas omni** Utility Channel Reagent 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.
- The assay is only intended for use with the UC_PARA USAP from Roche.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test is to be used for the detection of HPIV1-4 in nasopharyngeal swab samples collected in a Copan UTM-RT System (UTM-RT), BD™ Universal Viral Transport System (UVT) or equivalent. Testing of other sample types with **cobas**® Paraflu 1-4 UC may result in inaccurate results.
- Detection of HPIV1-4 nucleic acid 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**® Paraflu 1-4 UC could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- False negative or invalid results may occur due to interference. The Internal Control is included in **cobas**® Paraflu 1-4 UC (in the **cobas omni** Utility Channel Reagent kit) 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 omni** Utility Channel Master Mix reagent enables selective amplification of target nucleic acid; 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

Key performance characteristics

Limit of Detection (LoD)

The limits of detection of **cobas**® Paraflu 1-4 UC were determined by analyzing serial dilutions of HPIV1, HPIV2, HPIV3 and HPIV4 strains supplied and quantified in $TCID_{50}$/mL (ZeptoMetrix), in a pool of HPIV-negative NPS specimens. Panels of six concentration levels including a negative panel member were tested with **cobas**® Paraflu 1-4 UC. The study demonstrates that **cobas**® Paraflu 1-4 UC detects HPIV1, HPIV2, HPIV3 and HPIV4 at the respective concentrations of 8.56E-02, 1.12E-01, 4.35E-02 and 1.97E+01 $TCID_{50}$/mL (Table 12).

Table 12 LoD determination

Viral Strain	Matrix	LoD95% ($TCID_{50}$/mL)	95% CI of LoD ($TCID_{50}$/mL)	Hit Rate ≥95% ($TCID_{50}$/mL)	Mean Ct at ≥95% Hit Rate
HPIV1	NPS	8.56E-02	5.30E-02 – 2.00E-01	1.86E-01	34.35
HPIV2	NPS	1.12E-01	5.32E-02 – 1.71E-01	4.11E-01	38.56
HPIV3	NPS	4.35E-02	2.76E-02 – 9.78E-02	9.27E-02	35.26
HPIV4	NPS	1.97E+01	1.43E+01 – 3.43E+01	5.00E+01	37.31

Precision– within laboratory

The precision of **cobas**® Paraflu 1-4 UC was determined by analysing two concentrations (3 x and 10 x $LoD_{95\%}$) of the HPIV1, HPIV2, HPIV3 and HPIV4 isolates individually spiked into UTM supplemented with relevant concentrations of genomic DNA and mucin to mimic NPS specimen (UTM Matrix). The samples were tested over five days, using three **cobas**® Paraflu 1-4 UC reagent lots and three operators on one instrument. Each sample was carried through the entire **cobas**® Paraflu 1-4 UC procedure on fully automated **cobas**® 6800/8800 System. The results are shown in Table 13.

Table 13 Summary of precision

Target	Spiking Level	Variability Between Operators			Variability Between cobas® Paraflu 1-4 UC Reagents Lots			Variability Between Days / Runs		
		Mean Ct	SD	CV (%)	Mean Ct	SD	CV (%)	Mean Ct	SD	CV (%)
HPIV1	3 x $LoD_{95\%}$	34.37	0.50	1.46	34.03	0.51	1.49	34.46	0.48	1.41
	10 x $LoD_{95\%}$	33.08	0.33	1.00	33.04	0.84	2.55	33.39	0.35	1.05
HPIV2	3 x $LoD_{95\%}$	33.93	0.06	0.19	33.55	0.99	2.95	34.10	0.31	0.90
	10 x $LoD_{95\%}$	31.55	0.42	1.34	31.52	0.41	1.30	31.58	0.31	1.00
HPIV3	3 x $LoD_{95\%}$	33.53	0.51	1.52	33.19	0.89	2.67	33.98	0.45	1.32
	10 x $LoD_{95\%}$	31.70	0.27	0.84	31.48	0.72	2.27	31.81	0.40	1.27
HPIV4	3 x $LoD_{95\%}$	33.24	0.39	1.17	32.72	0.97	2.95	33.17	0.74	2.23
	10 x $LoD_{95\%}$	31.47	0.35	1.11	30.79	0.80	2.58	31.59	0.38	1.21

Reproducibility

The reproducibility of **cobas**® Paraflu 1-4 UC was determined by testing positive panel members at two concentrations (3 x and 10 x $LoD_{95\%}$) of the HPIV1, HPIV2, HPIV3 and HPIV4 strains separately spiked into UTM Matrix. The samples were tested on two instruments/sites. Each sample was carried through the entire **cobas**® Paraflu 1-4 UC procedure on fully automated **cobas**® 6800/8800 System. The results are shown in Table 14.

Table 14 Summary of reproducibility

Reproducibility				
Target	**Spiking Level**	**Mean Ct**	**SD**	**CV (%)**
HPIV1	3 x $LoD_{95\%}$	35.11	0.32	0.92%
	10 x $LoD_{95\%}$	33.50	0.10	0.31%
HPIV2	3 x $LoD_{95\%}$	34.47	0.71	2.06%
	10 x $LoD_{95\%}$	31.70	0.41	1.31%
HPIV3	3 x $LoD_{95\%}$	33.51	0.78	2.34%
	10 x $LoD_{95\%}$	31.87	0.27	0.85%
HPIV4	3 x $LoD_{95\%}$	33.55	0.19	0.57%
	10 x $LoD_{95\%}$	31.35	0.69	2.21%

Inclusivity

One HPIV1, five HPIV2, two HPIV3, one HPIV4a and one HPIV4b isolates were tested at 3x $LoD_{95\%}$ in UTM Matrix. The results show that **cobas**® Paraflu 1-4 UC detects the isolates listed in Table 15.

Table 15 Summary of inclusivity

Target Pathogen	Isolate Information
HPIV1	0810014CF
HPIV2	0810015CF
	0810504CF
	0810355CF / 1/2015 Isolate #2
	0810356CF / 1/2015 Isolate #3
	0810357CF / 1/2015 Isolate #4
HPIV3	0810016CF
	0810368CF / 4/2015 Isolate #2
HPIV4a	0810060CF
HPIV4b	0810060BCF

Analytical specificity (cross-reactivity and microbial interference)

The analytical specificity of **cobas**® Paraflu 1-4 UC was evaluated by diluting viruses, bacteria, fungi or yeasts, with and without HPIV1, HPIV2, HPIV3 and HPIV4 strains co-formulated into UTM Matrix. Viruses were tested at either 1.00E+04 or 1.00E+05 $TCID_{50}$/mL or c/mL. Bacteria, yeasts and fungi were tested at 1.00E+06 CFU/mL, IFU/mL or CCU/mL. None of these non-HPIV pathogens interfered with the **cobas**® Paraflu 1-4 UC performance. In total, 100% of negative results were obtained with **cobas**® Paraflu 1-4 UC for all HPIV-negative samples and 100% of positive results were obtained for all HPIV1-4-positive samples.

Table 16 Microorganisms tested for analytical specificity/cross-reactivity

Microorganism Name	Tested Concentration
Adenovirus 5	1.00E+05 $TCID_{50}$/mL
Aspergillus fumigatus	1.00E+06 CFU/mL
Candida albicans	1.00E+06 CFU/mL
Chlamydia pneumoniae	1.00E+06 IFU/mL
Coronavirus-SARS-Cov-2	1.00E+05 $TCID_{50}$/mL
Corynebacterium diphtheriae	1.00E+06 CFU/mL
Cytomegalovirus (CMV)	1.00E+05 $TCID_{50}$/mL
Enterovirus 71	1.00E+05 $TCID_{50}$/mL
Epstein-Barr Virus (EBV)	1.00E+05 c/mL
Escherichia coli	1.00E+06 CFU/mL
Haemophilus influenza	1.00E+06 CFU/mL
Herpes Simplex Virus 1 (HSV-1)	1.00E+05 $TCID_{50}$/mL
Herpes Simplex Virus 2 (HSV-2)	1.00E+04 $TCID_{50}$/mL
Influenza A H1N1	1.00E+05 $TCID_{50}$/mL
Influenza B	1.00E+05 $TCID_{50}$/mL
Klebsiella pneumoniae	1.00E+06 CFU/mL
Lactobacillus acidophilus	1.00E+06 CFU/mL
Legionella pneumophila	1.00E+06 CFU/mL
Measles virus	1.00E+05 $TCID_{50}$/mL
Moraxella catarrhalis	1.00E+06 CFU/mL
Human Metapneumovirus 4 B2	1.00E+05 $TCID_{50}$/mL
Mumps virus	1.00E+05 $TCID_{50}$/mL
Mycobacterium avium	1.00E+06 CFU/mL
Mycobacterium tuberculosis	1.00E+06 CFU/mL
Mycoplasma pneumoniae	1.00E+06 CCU/mL
Neisseria elongata	1.00E+06 CFU/mL
Neisseria meningitidis	1.00E+06 CFU/mL
Pseudomonas aeruginosa	1.00E+06 CFU/mL
Rhinovirus B42	1.00E+05 $TCID_{50}$/mL
Respiratory Syncytial Virus A (RSV-A)	1.00E+05 $TCID_{50}$/mL
Respiratory Syncytial Virus B (RSV-B)	1.00E+05 $TCID_{50}$/mL
Staphylococcus aureus	1.00E+06 CFU/mL
Staphylococcus epidermidis	1.00E+06 CFU/mL

Microorganism Name	Tested Concentration
Streptococcus pneumoniae	1.00E+06 CFU/mL
Streptococcus pyogenes	1.00E+06 CFU/mL
Streptococcus salivarius	1.00E+06 CFU/mL
Varicella Zoster Virus (VZV)	1.00E+05 c/mL

Interfering substances

The impact of potentially interfering substances on the **cobas**® Paraflu 1-4 UC performance was evaluated by testing ten exogenous and two endogenous substances, with and without HPIV1, HPIV2, HPIV3 and HPIV4 strains co-formulated into UTM Matrix. Both exogenous and endogenous substances were tested at clinically relevant concentrations (Table 17). None of these substances interfered with the **cobas**® Paraflu 1-4 UC performance at the tested concentrations. In total, 100% of negative results were obtained with **cobas**® Paraflu 1-4 UC for all HPIV-negative samples and 100% of positive results were obtained for all HPIV1-4 positive samples.

Table 17 Exogenous and endogenous substances tested for interference

Substance	Final Concentration
Zanamivir	5 mg/mL
Fluticasone (Flixotide Nebules)	5% (v/v)
Budesonide	0.039 mg/mL
Mupirocin	5 mg/mL
Oxymetazoline (Nasivin)	5% (v/v)
Oseltamivir phosphate	8 mg/mL
Tobramycin	4 µg/mL
Lidocaine (Strepsils)	2.68 mg/mL
Benzocaine (Dolo-Dobendan)	5 mg/mL
Galphimia clauca, Histaminum hydrochloricum, Luffa operculata, Sulfur (Luffeel)	5% (v/v)
Mucin	0.5% (v/v)
Human Whole Blood EDTA	1.5% (v/v)

Clinical performance evaluation

The performance of **cobas**® Paraflu 1-4 UC was evaluated in comparison with a CE-IVD kit for the detection of HPIV1-4 (R-DiaHPIV™, Diagenode; product reference: DDGR-84-L100) internally using 222 archived nasopharyngeal swab (NPS) specimens, including both clinical and contrived samples.

As shown in Table 18, the **cobas**® Paraflu 1-4 UC demonstrated high percent agreement with the comparator test for the detection of HPIV1-4.

Table 18 Summary of clinical performance of **cobas**® Paraflu 1-4 UC

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)*
HPIV1	222	55	1	163	3	PPA	94.8%	(85.9%, 98.2%)
						NPA	99.4%	(96.6%, 99.9%)
HPIV2	222	58	2	162	0	PPA	100.0%	(93.8%, 100.0%)
						NPA	98.8%	(95.7%, 99.7%)
HPIV3	221*	30	0	190	1	PPA	96.8%	(83.8%, 99.4%)
						NPA	100.0%	(98.0%, 100.0%)
HPIV4	222	67	1	153	1	PPA	98.5%	(92.1%, 99.7%)
						NPA	99.4%	(96.4%, 99.9%)

* One sample was excluded from the HPIV3 analysis.

Discordant results between the **cobas**® Paraflu 1-4 UC and the comparator assay were observed for 9 samples. For HPIV1, three samples were resolved as in agreement with the retrospective clinical status and the sequencing results were not interepetable for the fourth. For HPIV2, 1 of the 2 discordant positives was resolved as in agreement with the retrospective clinical status of the sample source. For HPIV3, the single discordant negative was resolved as in agreement with the retrospective clinical status of the sample source. For HPIV, the discordant negative and discordant positive samples were both resolved as in agreement with the retrospective clinical status of the sample source.

Additional information

Key test features

Sample type	Nasopharyngeal swab samples collected in the Copan UTM-RT® System or the BD™ UVT System, or equivalent
Minimum amount of sample required	0.6 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. 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 19 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 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 20 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

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IVD EC REP Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
Germany CE

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