cobas®

cobas® eplex
respiratory pathogen panel 2

For in vitro Diagnostic Use

For Professional Laboratory Use Only

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INTENDED USE

The **cobas® eplex** respiratory pathogen panel 2 (RP2 panel) is a multiplexed nucleic acid in vitro diagnostic test intended for use on the **cobas® eplex** system for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids, including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), in nasopharyngeal swabs (NPS) in transport media obtained from individuals suspected of coronavirus disease 2019 (COVID-19) or respiratory infection by their healthcare provider.

The following virus types, subtypes, and bacteria are identified using the **cobas® eplex** RP2 panel: adenovirus, coronavirus 229E, coronavirus HKU1, coronavirus NL63, coronavirus OC43, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), human bocavirus, human metapneumovirus, human rhinovirus/enterovirus, influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, parainfluenza virus 4, respiratory syncytial virus (RSV) A, respiratory syncytial virus (RSV) B, *Bordetella pertussis*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*.

The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection aids in the diagnosis of respiratory infection when used in conjunction with other clinical and epidemiological information.

Results are for the detection of nucleic acid from SARS-CoV-2 and other respiratory pathogens that are detectable in NPS specimens during infection. Positive results are indicative of active infection with the identified respiratory pathogen; 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 respiratory infection due to other non-panel organisms and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Positive results do not rule out co-infection with other organisms; the organism(s) detected by the **cobas® eplex** RP2 panel may not be the definite cause of disease. The use of additional laboratory testing (e.g., bacterial and viral culture, immunofluorescence and radiography) and clinical presentation must be taken into consideration in the final diagnosis of respiratory tract infection.

Positive results do not rule out co-infection with other organisms; the organism(s) detected by the **cobas® eplex** RP2 panel may not be the definite cause of disease. Additional laboratory testing (*e.g.*, bacterial and viral culture, immunofluorescence and radiography) may be necessary when evaluating a patient with possible COVID-19.

SUMMARY AND EXPLANATION OF TEST

The **cobas® eplex** RP2 panel is an automated qualitative nucleic acid multiplex in vitro diagnostic test for simultaneous detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS). The test is able to detect 21 respiratory viral targets and three bacterial targets as summarized in **Table 1**. This test is performed on **cobas® eplex** system.

Respiratory viruses and bacteria are responsible for a wide range of respiratory tract infections including the common cold, influenza, and croup, and represent the most common cause of acute illness. Disease severity can be especially high in the young, the immunocompromised, and elderly patients. Respiratory infections cause more doctor visits and absences from school and work than any other illness.[1] It is estimated that 10-30% of Europeans are infected with influenza in any given year.[2] Globally, seasonal influenza results in about 3-5 million severe cases and 250,000–500,000 deaths annually.[3] In late 2019, a novel coronavirus was identified in Wuhan, China. The disease caused by this novel coronavirus was initially called “2019 novel coronavirus” or “2019-nCoV” and was later renamed Coronavirus Disease 2019, or COVID-19.[4] As of July 2020, cases have been identified in 188 countries around the world with over 25 million cases and 851,000 deaths.[5,6]

Influenza-like illness is a nonspecific respiratory illness characterized by fever, fatigue, cough, and other symptoms. The majority of influenza-like illnesses are not caused by influenza but by other viruses (*e.g.*, rhinovirus, respiratory syncytial virus, adenovirus, and parainfluenza virus).[7] Less common causes of influenza-like illness include bacteria such as *Legionella pneumophila* and *Mycoplasma pneumoniae*.[7]

Table 1: Targets detected by the **cobas® eplex** RP2 panel

Target	Classification (Genome Type)	Seasonal Prevalence*	Most Commonly Infected Demographic
Adenovirus	Adenovirus (DNA)	Late winter to early summer[8]	All ages, immunocompromised[9]
Coronavirus 229E	Coronavirus (RNA)	Winter, spring[10]	All ages[10]
Coronavirus HKU1			
Coronavirus NL63			
Coronavirus OC43			
Middle East Respiratory Syndrome Coronavirus		April through June[11]	All ages[11]
SARS-CoV-2	Coronavirus (RNA)	Unknown[12]	Not established[12]
Human Bocavirus	Parvovirus (DNA)	No peak season identified[13]	Infants, children[13]
Human Metapneumovirus	Paramyxovirus (RNA)	Winter[14]	Children, elderly, immunocompromised[15]
Human Rhinovirus/ Enterovirus	Picornavirus (RNA)	Fall, Spring[16]/ Summer[17]	All ages, immunocompromised[16-18]
Influenza A	Orthomyxovirus (RNA)	Winter[3]	All ages[3]
Influenza A H1			
Influenza A H1-2009			
Influenza A H3			
Influenza B			
Parainfluenza Virus 1	Paramyxovirus (RNA)	Fall[19]	All ages[20]
Parainfluenza Virus 2		Fall, early winter[19]	
Parainfluenza Virus 3		Spring, summer[19]	
Parainfluenza Virus 4		Fall, early winter[19]	
Respiratory Syncytial Virus A	Paramyxovirus (RNA)	Winter[21,22]	Infants, children, older adults[21,22]
Respiratory Syncytial Virus B			
Bordetella pertussis	Bacterium (DNA)	No peak season[23]	All ages[23]
Legionella pneumophila	Bacterium (DNA)	No peak season [24,25]	Older adults, smokers, immunocompromised[24,25]
Mycoplasma pneumoniae	Bacterium (DNA)	Late summer, fall[26]	Children, young adults[26]

* Based on northern hemisphere seasons

SUMMARY OF DETECTED ORGANISMS

Adenovirus: Adenoviruses are non-enveloped DNA viruses that include seven human species (A - G) and more than 60 serotypes.[27] Adenovirus species B, C, and E are frequently associated with upper respiratory infections; infections are common in children, and outbreaks often occur in crowded environments, such as military barracks.[9,28] There is no vaccine available to the general public, but the introduction of a live, oral vaccine to the US military in 2011 has reduced the incidence of adenovirus outbreaks in this population.[9,29] Adenovirus infections generally cause mild illness but can result in severe disease in infants or in immunocompromised people, particularly in hematopoietic stem cell transplant recipients.[9,27] In addition to respiratory infections, adenovirus can also cause gastroenteritis, conjunctivitis, and cystitis.[9,27]

Coronavirus: There are 6 coronaviruses that can infect humans; 229E and NL63 (alpha coronaviruses), OC43, HKU1, SARS (the coronavirus that causes severe acute respiratory syndrome), and MERS-CoV (beta coronaviruses).[30] Human coronaviruses usually cause mild to moderate upper respiratory infections, but can cause significant disease in the elderly, young children, and immunocompromised individuals.[30-32] Infection with coronavirus 229E, HKU1, NL63, and OC43 is common worldwide, but infections due to SARS and MERS-CoV are rare. There have been no cases of SARS (not on the **cobas® eplex** RP panel) reported since 2004.[33] MERS-CoV was first reported in Saudi Arabia in 2012 and causes severe disease in people with underlying medical conditions, with a fatality rate of 40%.[34]

SARS-CoV-2: In late 2019, a novel coronavirus was identified in Wuhan, China. The disease caused by this novel coronavirus was initially called “2019 novel coronavirus” or “2019-nCoV” and was later renamed Coronavirus Disease 2019, or COVID-19.[4] This novel coronavirus was named Severe Acute Respiratory Syndrome Coronavirus, or SARS-CoV-2 due to genetic similarity to the coronavirus responsible for an outbreak in 2003.[4] As of July 2020, cases have been identified in 188 countries around the world with over 16 million cases and 655,000 deaths.[5,6]

Human Bocavirus: The role of human bocavirus as a causative pathogen in respiratory infections is controversial. Human bocavirus was first described in 2005 in respiratory samples in Sweden and is believed to play a role in respiratory infections, but because the virus is often found in both symptomatic and asymptomatic individuals, questions remain about its role as the causative agent.[35,36] Studies have shown high prevalence rates in respiratory samples from children; however, bocavirus is often co-detected with other viruses and it has demonstrated prolonged or persistent detection even in asymptomatic individuals, making it difficult to determine the true etiology.[13,35] While most cases are mild, severe respiratory disease has been reported.[13]

Human Metapneumovirus: Human metapneumovirus is a member of the *Paramyxoviridae* virus family and is closely related to RSV.[15] Metapneumovirus has been identified as an important respiratory pathogen in young children and is the second most common virus identified in pediatric respiratory tract infections.[15] Illness is more severe in children who are immunocompromised or have underlying conditions, such as human immunodeficiency virus (HIV) or cardiac disease; it can also cause more severe disease in immunocompromised adults, especially those with chronic obstructive pulmonary disease (COPD), asthma, cancer, or in transplant patients.[37]

Human Rhinovirus and Enterovirus: Rhinovirus and enterovirus are closely related RNA viruses in the *Picornaviridae* family.[18] There are more than 100 different serotypes that all share high sequence homology.[38] Rhinovirus causes up to 80% of all cases of the common cold worldwide and is more common in children than adults. It is the cause of a significant number of mild upper respiratory tract infections throughout the year, especially during the spring and fall seasons.[16,39] Most infections are mild, but rhinovirus has been associated with severe infections in at-risk populations including young children, the elderly, immunocompromised patients, and those with asthma.[16,17]

There are 62 non-polio enteroviruses that can cause disease in humans.[18] Enterovirus primarily infects the gastrointestinal tract but can also cause respiratory illness, which is generally mild, like the common cold, but can result in serious complications, especially in infants.[18] A 2014 outbreak of enterovirus D68 (EV-D68) resulted in severe respiratory infections, some of which were fatal.[40]

Influenza virus: There are three types of influenza viruses: A, B, and C.[3] In the northern hemisphere, influenza A and B circulate during the winter months causing seasonal epidemics most years; influenza C infections are less common and not believed to cause epidemics.[3,41] Both influenza A and B mutate, and the impact of influenza varies from year to year depending on the severity of the changes and effectiveness of influenza vaccines.[42] The two most common Influenza A subtypes infecting humans are H1N1 (including the 2009 Pandemic H1N1 variant) and H3N2, and prevalence varies annually.[41] Other rare Influenza A subtypes also known to infect humans, such as H5N1 (avian influenza) and H3N2v, can cause severe illness and, in some cases, death.[43] Influenza is easily spread from person to person and those most at risk for complications from infection include infants and children, the elderly, and anyone who is immunocompromised or who has co-morbidities such as heart or lung disease.[44]

Influenza A 2009 H1N1: During the 2009 - 2010 influenza season, a new strain of influenza A, now known as 2009 H1N1 became the dominant circulating virus, accounting for approximately 95% of reported influenza infections.[45] This strain replaced the H1N1 virus that was previously circulating in humans and is common in both Europe and the U.S.[3,41]

Parainfluenza Virus: The parainfluenza viruses are members of the paramyxovirus family that commonly cause respiratory infections in children.[46] Prevalence of parainfluenza viruses is seasonal and varies by type; most infections are mild and self-limited, but parainfluenza virus can cause life threatening pneumonia in immunocompromised people, such as those with cystic fibrosis or transplant recipients.[47]

Respiratory Syncytial Virus: RSV is the most common cause of pediatric viral respiratory infections.[15] Infection with RSV can occur at any age, and those most at risk for complications and more severe disease are the very young, especially premature infants, the elderly, and anyone with a weakened immune system.[48] There are two types of respiratory syncytial virus, RSV A and B. Infections with RSV A are thought to be more severe than infections with RSV B.[22,49]

***Bordetella pertussis*:** Pertussis, or whooping cough, is a highly contagious, acute respiratory illness that is caused by the gram-negative bacteria *Bordetella pertussis*.[23] Pertussis is known for severe, uncontrollable coughing that makes it hard to breathe, resulting in a “whooping” sound when the person tries to breathe.[50] Infants have the highest mortality from pertussis; in adults, it is usually a mild infection, and it is suspected to be under-recognized as adults often do not develop the characteristic cough.[51] Recently, cases of pertussis have increased, particularly in young children and adolescents; the increase is thought to be due to several factors including improved diagnostics and waning immunity.[50] Despite high global vaccination coverage (82%) among infants, it is estimated that in 2008 about 16 million cases of pertussis occurred worldwide, and 195,000 children died from the disease.[52] *B. pertussis* is a notifiable infection in the US and in all EU and EEA member states.[53,54]

Legionella pneumophila**:** *Legionella pneumophila* is a bacterium that is found naturally in fresh water, such as lakes, rivers and hot springs, around the world.[24,55] It also grows easily in warm, man-made water sources like hot tubs, cooling towers, and plumbing systems.[24,55] Infection occurs via inhalation of aerosolized water that contains *L. pneumophila;* person-to-person transmission is rare but possible. Legionellosis, or infection with *Legionella*, can result in Legionnaires' disease, a severe form of pneumonia, or Pontiac Fever, which is mild.[24] Legionnaires' disease is fatal in about 10% of cases, but can be treated with antibiotics; there is no benefit to antibiotic treatment for Pontiac fever.[24,25] Risk factors for Legionnaires' disease include chronic lung disease, smoking, diabetes, alcohol or drug dependence, and the effect of medicines which affect the immune system.[56] *L. pneumophila* is a notifiable infection in the US and in all EU and EEA member states.[57,58]

Mycoplasma pneumoniae**:** *Mycoplasma pneumonia*e is a bacterium lacking a cell wall and is a major cause of respiratory disease.[26] *M. pneumonia*e is transmitted person-to-person by respiratory droplets and is a common cause of atypical, or walking pneumonia.[59] *M. pneumoniae* is frequently undiagnosed, but is estimated to be involved in up to 30% of respiratory infections.[26] Infection often results in mild illness such as tracheobronchitis, or a chest cold, and is most prevalent in young adults and school-aged children.[26,59] Outbreaks of *M. pneumoniae* occur mostly in crowded environments, like schools, college dormitories, military barracks, and nursing homes.[59]

PRINCIPLES OF TECHNOLOGY

The **cobas® eplex** system automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and eSensor technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA hybridization and electrochemical detection, which is highly specific and is not based on fluorescent or optical detection.

Electrowetting, or digital microfluidics, uses electrical fields to directly manipulate discrete droplets on the surface of a hydrophobically coated printed circuit board (PCB). Sample and reagents are moved in a programmable fashion in the eplex cartridge to complete all portions of the sample processing from nucleic acid extraction to detection.

A sample is loaded onto the **cobas® eplex** cartridge, and nucleic acids are extracted and purified from the specimen via magnetic solid phase extraction. For RNA targets, a reverse transcription step is performed to generate complementary DNA from the RNA, followed by PCR to amplify the targets. Exonuclease digestion creates single-stranded DNA in preparation for eSensor detection.

The target DNA is mixed with ferrocene-labeled signal probes that are complementary to the specific targets on the panel. Target DNA hybridizes to its complementary signal probe and capture probes, which are bound to gold-plated electrodes, as shown below in **Figure 1**. The presence of each target is determined by voltammetry, which generates specific electrical signals from the ferrocene-labeled signal probe.

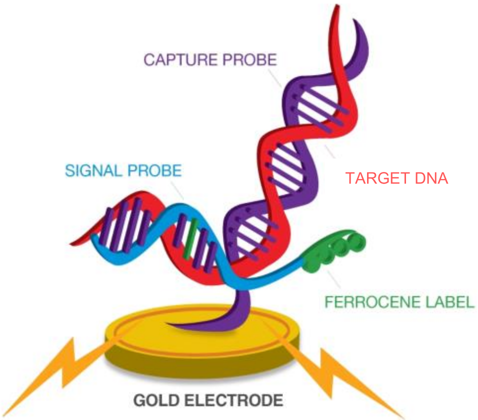

Figure 1: Hybridization complex. Target-specific capture probes are bound to the gold electrodes in the eSensor microarray on the **cobas®** **eplex** cartridge. The amplified target DNA hybridizes to the capture probe and to a complementary ferrocene-labeled signal probe. Electrochemical analysis determines the presence or absence of targets using voltammetry.

MATERIALS PROVIDED

Table 2: cobas® **eplex** respiratory pathogen panel 2 kit contents

Product	Material number	Components (quantity)	Storage
cobas® **eplex** respiratory pathogen panel 2	9556486001	**cobas®** **eplex** respiratory pathogen panel 2 cartridge (12)	2 – 8 ºC (through printed expiration date) or 30 days at up to 25 °C (cartridges must be used within 30 days of up to 25 ºC storage start date)

Safety Data Sheets (SDS) for all reagents provided in this kit may be obtained at: https://navifyportal.roche.com/. For paper copies, please reach out to your local affiliate: https://www.roche.com/about/business/roche_worldwide.htm.

COMPOSITION OF REAGENTS

Table 3: Composition of reagents on the **cobas®** **eplex** RP2 panel cartridges

Composition of Reagents on the cobas® eplex RP2 panel Cartridges	
2-(N-morpholino)ethanesulfonic acid (MES)	NaH_2PO_4 /$NaHPO_4$
6-mercapto-1-hexanol	NaN_3
Acetonitrile	PEG 8000
Calcium Chloride	Phenol Red
Cysteamine HCl	Polydimethylsiloxane trimethyl terminated, 5cSt
Dynol-604	Ribonuclease inhibitor
EDTA	SDS, pH adjusted with HCl
EGTA	Sodium perchlorate

Composition of Reagents on the cobas® eplex RP2 panel Cartridges	
Ethanol	Sorbitane trioleate
Glycerol	Super Q water
Guanidinium Hydrochloride	Trehalose
Lithium Dodecyl Sulfate	Tris-HCl
Magnesium Chloride ($MgCl_2$)	Tween-20
MTG, pH adjusted with sodium hydroxide + Tween-20	Urea
NaCl	

REAGENT STORAGE, STABILITY, AND HANDLING

- Store the **cobas® eplex** RP2 panel kit components at 2-8 ºC. Alternatively, cartridges can be stored at up to 25 ºC for up to 30 days. Cartridges must be used within 30 days from start of storage up to 25 ºC and should be considered expired once stored for 30 days at up to 25 ºC. Users should not return the kit to cold storage after storage at up to 25 ºC.
- Do not use **cobas® eplex** RP2 panel kit components beyond the expiration date.
- Do not open a cartridge pouch until you are ready to perform testing.

MATERIALS NOT PROVIDED

Equipment

- **cobas® eplex** system and software
- Pipettes calibrated to deliver 200 µL
- Vortex mixer
- Printer (optional) - See **cobas® eplex** User Assistance Manual for compatibility guidelines

Consumables

- Pipette tips, aerosol resistant, RNase/DNase-free
- Disposable, powder free gloves
- 10% bleach for appropriate surfaces
- 70% ethanol or isopropyl alcohol

WARNINGS AND PRECAUTIONS

General

- For in vitro diagnostic use, by laboratory professionals.
- A trained healthcare professional should carefully interpret the results from the **cobas® eplex** RP2 panel in conjunction with a patient’s signs and symptoms and results from other diagnostic tests.
- Positive results do not rule out co-infection with other viruses or bacteria. The agent detected may not be the definite cause of disease. The use of additional laboratory testing (*e.g.*, bacterial and viral culture, immunofluorescence and radiography) and clinical presentation must be taken into consideration in the final diagnosis of respiratory infection.
- Do not reuse **cobas® eplex** RP2 panel kit components.
- Do not use reagents beyond the expiration date printed on the labeling.

- Do not use a reagent that is damaged.
- Follow the procedure as described in this package insert. Read all instructions before starting the test. Any deviation from the procedures and guidelines may affect optimal test performance.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions.
- The use of sterile, disposable, nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Inform your local competent authority and the manufacturer about any serious incidents which may occur when using this assay.

Safety

- Handle all specimens and waste materials as if they were capable of transmitting infectious agents in accordance with Universal Precautions. Observe safety guidelines such as those outlined in CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories,* CLSI Document M29 *Protection of Laboratory Workers from Occupationally Acquired Infections*, or other appropriate guidelines.
- Do not eat, smoke, drink, apply cosmetics, or handle contact lenses in areas where reagents or human specimens are handled.
- Follow routine laboratory safety procedures for handling of reagents (*e.g.*, do not pipette by mouth, wear appropriate protective clothing and eye protection).
- Follow your institution's safety procedures for handling biological samples.
- If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
- Dispose of materials used in this test, including reagents, specimens, and used vials, in accordance with all federal, state, and local regulations.
- Do not stick fingers or other objects inside the **cobas® eplex** system bays.
- Wash hands thoroughly with soap and water after handling reagents. Launder contaminated clothing prior to re-use.
- Do not puncture or pierce reagent blisters on the **cobas® eplex** cartridge. Reagents may cause irritation to skin, eyes, and respiratory tract. Harmful if swallowed or inhaled. Contains oxidizing liquids.
- The **cobas® eplex** RP2 panel cartridge contains chemicals that are classified as hazardous. Review the Safety Data Sheet (SDS) before use, and in cases of exposure, refer to the SDS for more information. Safety Data Sheets (SDS) are available on request from your local Roche representative or can be accessed via https://navifyportal.roche.com/.
- Observe safety guidelines such as wearing proper protective equipment including laboratory coats, gowns, gloves, eye protection, and a biological safety cabinet as outlined in Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition https://www.cdc.gov/labs/BMBL.html.
- If infection with SARS-CoV-2 is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent) prior to processing a specimen.
- Immediately clean up any spill containing potentially infectious material with a 0.5-1% (w/v) sodium hypochlorite (20% v/v bleach).
- Performance characteristics have been determined with nasopharyngeal swab samples from human patients suspected of coronavirus disease 2019 (COVID-19) or respiratory infection by their healthcare provider.
- Specimens should be processed in a Class II (or higher) biological safety cabinet.

- To mitigate the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.
- Contamination of the sample may occur if the sample is loaded in an area where PCR amplicons for respiratory pathogens are generated. Avoid loading sample in areas that are potentially contaminated with PCR amplicon.

Laboratory

- Contamination of the sample may occur if laboratory personnel processing the sample are infected with common respiratory pathogens. To avoid this, specimens should be processed in biosafety cabinets. If a biosafety cabinet is not used, a splash shield or face mask should be used when processing samples.
- A biosafety cabinet that is used for viral or bacterial culture should not be used for sample preparation.
- Change gloves frequently during testing to reduce the risk of contamination.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
- Contamination of the sample may occur if the sample is loaded in an area where PCR amplicons for respiratory pathogens are generated. Avoid loading sample in areas that are potentially contaminated with PCR amplicon.

SPECIMEN COLLECTION, HANDLING, AND STORAGE

Refer to hospital procedures and collection swab/kit manufacturer instructions for use for proper collection of nasopharyngeal swab samples.

Per the World Health Organization, the following steps should be performed for collection of a nasopharyngeal swab sample[60]:

- The swab should be slid straight into the nostril with the patient’s head held slightly back.
- The swab is inserted following the base of the nostril towards the auditory pit and will need to be inserted at least 5–6 cm in adults to ensure that it reaches the posterior pharynx. (Do NOT use rigid shafted swabs for this sampling method —a flexible shafted swab is essential).
- Leave the swab in place for a few seconds.
- Withdraw slowly with a rotating motion.
- Put the swab into viral transport media (VTM) or transport media designed for use with viral identification by molecular diagnostic methods. Refer to **Table 37**, Interfering Substances and **Table 38**, Collection and Transport Media Tested for Interference, for collection swabs and media that are compatible with the **cobas® eplex** RP2 panel.
- **Note:** Nasopharyngeal sampling is an invasive process that can cause considerable distress to the patient.

Additional guidance on proper collection of a nasopharyngeal swab sample (including graphics and videos) can be found on the manufacturer’s website for commonly used swab and collection kits, such as BD, Remel, and Copan.

Nasopharyngeal Swab Collection – Nasopharyngeal swab specimen collection should be performed according to standard technique and placed in viral transport media.

Minimum Sample Volume – 200 µL nasopharyngeal swab specimen in viral transport media is required for testing.

Transport and Storage – Clinical specimens can be stored at room temperature (15-30 ºC) for up to 12 hours or refrigerated at 2-8 ˚C for up to 10 days after collection in viral transport media. Specimens can also be stored at -20 °C or -80 °C for 30 months with up to 2 freeze/thaw cycles.

PROCEDURE

Procedural Notes

- All frozen samples should be thawed completely before testing.
- Samples should be nasopharyngeal swab in transport media.
- Reagents and cartridge can be used immediately upon removal from 2-8 °C storage. There is no need to equilibrate to room temperature before use.
- Alternatively, cartridges can be stored at up to 25 °C for up to 30 days. Cartridges must be used within 30 days from start of storage up to 25°C and should be considered expired once stored for 30 days at up to 25°C. Users should not return the kit to cold storage after storage at up to 25°C.
- Once cartridge is removed from foil pouch, it should be used within 2 hours. Do not open the cartridge pouch until the sample is ready to be tested.
- Once the sample is loaded into the **cobas® eplex** RP2 panel cartridge, the sample should be tested as soon as possible or within 2 hours.
- Do not re-use cartridges.
- Use a new, sterile pipette tip for loading each sample.
- Do not insert a wet cartridge into the **cobas® eplex** system. If liquid is present on outside of test cartridge, use a Kimwipe™ to remove liquid prior to inserting into **cobas® eplex** bay.
- Samples should be transferred to **cobas® eplex** RP2 panel cartridge in an amplicon-free, clean environment.
- Samples, consumables, and lab areas should be protected from aerosol or direct contamination with amplicon. Decontaminate laboratory areas and affected equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
- Change gloves frequently during testing to reduce the risk of contamination.
- Specimens should be processed in biosafety cabinets. If a biosafety cabinet is not used, a splash shield or face mask should be used when processing samples.
- Dispose of materials used in this test, including reagents, specimens, and used vials, in accordance with all regulations.

Detailed Procedure

1. Decontaminate the clean area used for setting up the **cobas® eplex** RP2 panel with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove one **cobas® eplex** RP2 panel cartridge pouch from kit packaging.
3. Open the RP2 panel cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the RP2 panel cartridge.
5. Vortex the sample for 3-5 seconds.
6. Use a calibrated pipette to aspirate 200 µL of sample and dispense into the sample inlet of the **cobas® eplex** RP2 panel cartridge.
7. Close the sample inlet by sliding the cap over the inlet and firmly pushing down on the cap to securely seal the sample inlet.
   NOTE: Bubbles can be present when closing the cap.
8. Scan the RP2 panel cartridge using the barcode reader provided with the **cobas® eplex** system.
   NOTE: If an accession ID barcode label is not used, manually enter accession ID with the on-screen keyboard and scan the cartridge barcode when prompted by the **cobas® eplex** system.
   NOTE: The barcode scanner will read both the accession ID barcode (if placed on the cartridge by the operator) and the 2D barcode printed on the cartridge label; however, the barcode scanner will only beep once to indicate that both barcodes have been read.
9. Insert the RP2 panel cartridge into any available bay, indicated by a flashing, white LED light.
   The test will begin automatically when the cartridge has been inserted into the bay and the pre-run check (cartridge initialization) is completed, indicated by a blue LED light.

QUALITY CONTROL

Internal Controls

Each cartridge includes internal controls that monitor performance of each step of the testing process. A DNA control verifies extraction, amplification and detection of DNA targets, and RNA controls verify amplification and detection of RNA targets.

Each amplification reaction on the cartridge has at least one internal control and in each reaction either the internal control or a target must generate signal above the defined threshold for a valid test result. Internal control results are interpreted by the **cobas**® **eplex** software and displayed on the RP2 panel reports as Internal Control with a result of PASS, FAIL, N/A or INVALID. **Table 4** includes details on the interpretation of Internal Control results.

Table 4: Internal control results

Internal Control Result	Explanation	Action
PASS	The internal control or a target from each amplification reaction has generated signal above the threshold. The test was completed and internal controls were successful, indicating valid results were generated.	All results are displayed on the RP2 panel Detection Report. Test is valid, report results.
FAIL	Neither the internal control nor any target in at least one amplification reaction generated signal above the threshold. The test was completed but at least one internal control was not detected, indicating that results are not valid.	No results are displayed on the RP2 panel Detection Report. Test is not valid, repeat the test using a new cartridge.
N/A	The internal control in every amplification reaction did not generate signal above the threshold, but a target in every amplification reaction generated signal above the threshold. The test was completed and internal controls were not successful, however detection of signal above the threshold for a target in every amplification reaction indicates valid results were generated.	All results are displayed on the RP2 panel Detection Report. Test is valid, report results.
INVALID	An error has occurred during processing that prevented analysis of signal data. The test has not successfully completed and results for this test are not valid. This is likely due to an instrument or software error.	No results are displayed on the RP2 panel Detection Report. Test is not valid, repeat the test using a new cartridge.

External Controls

Positive and negative external controls should be tested with each new lot of reagents or monthly, whichever occurs first. Viral transport medium can be used as the negative control. Previously characterized positive samples or viral transport medium spiked with well characterized organisms can be used as the external positive control. External controls should be run in accordance with laboratory protocols and accrediting organizations, as applicable.

RESULTS

Table 5: Interpretation of results on the **cobas® eplex** RP2 detection report

Target Result	Explanation	Action
Detected	The test was completed successfully, and the target has generated signal above its defined threshold, and the Internal Control was reported as PASS.	All results are displayed on the RP2 panel Detection Report. Test is valid, report results.
Multiple Targets Detected	The test was completed successfully, and multiple targets have generated signal above their defined threshold, and the Internal Control was reported as PASS.	All results are displayed on the RP2 panel Detection Report. Test is valid, report results. Detection of more than 3 pathogens may indicate contamination. Re-test of the sample is recommended to confirm results.
Not Detected	The test was completed successfully, and the target did not generate signal above its defined threshold, and the Internal Control was reported as PASS.	All results are displayed on the RP2 panel Detection Report. Test is valid, report results.
Invalid	The test has not successfully completed, and results for this test are not valid. This is often due to an instrument or software error or failure of an internal control.	No results are displayed on the RP2 panel Detection Report. Test is not valid, repeat test.

Influenza A Results

The **cobas® eplex** RP2 panel detects Influenza A and the H1, H1-2009, and H3 subtypes using unique assays for each. Interpretation of results for Influenza A are described in **Table 6**.

Table 6: Results for influenza A

Results for Influenza A and Subtypes	Explanation	Results on Report	Recommended Action
Influenza A Detected, at least one subtype (H1, H1-2009, or H3) reported as detected.	This is an expected result.	Result reported as influenza A and influenza A subtype detected.	None
Influenza A Detected, all subtypes (H1, H1-2009 , and H3) reported as not detected	Low virus titers can result in detection of influenza A without a subtype. Detection of influenza A without a subtype can indicate the presence of a novel strain.	Result reported as influenza A detected. No Influenza A subtype detected. Re-testing of this sample to confirm Influenza A (subtype) is recommended. Refer to package insert for additional information	If subtyping is required, repeat test.
Influenza A Detected and more than one subtype	Sample is co-infected with multiple influenza subtypes. Infection with multiple	Result reported as influenza A and multiple subtypes detected.	Retest recommended to confirm result.

Results for Influenza A and Subtypes	Explanation	Results on Report	Recommended Action
(H1, H1-2009, or H3) reported as detected.	subtypes of influenza are possible but rare. A live intranasal multivalent influenza virus vaccine may cause false positive results for influenza A, A/H1, A/H3, A/H1-2009, and/or influenza B. Contamination has occurred.		
Influenza A not detected, at least one subtype (H1, H1-2009, or H3) reported as detected.	Low virus titers can result in detection of influenza A subtype without the influenza A matrix. Detection of influenza A subtype without the influenza A matrix can also indicate the presence of a novel strain.	Influenza A (subtype) detected. Re-testing of this sample to confirm Influenza A (subtype) is recommended. Refer to package insert for additional information.	Re-test to confirm result. If the re-test result confirms the original result, the influenza A subtype is considered positive.

TEST REPORTS

There are several different reports that are available on the **cobas® eplex** system. Results are provided in a printable format, may be viewed electronically, or may be exported for additional analysis. Reports can be customized with account specific information such as the address, logo, and institution specific footers on each report. For more information on **cobas® eplex** reports, refer to the **cobas® eplex** User Assistance Manual.

Detection Report

The RP2 panel detection report includes the results for each individual sample run on the **cobas® eplex** system.

The summary section indicates the overall test result and lists all detected targets in that sample. The results section includes a list of all targets on the panel with an individual result for each. Results for each target are reported as Detected, Not Detected, or Invalid (displayed as a red **x**); results for the Internal Control are reported as PASS, FAIL, INVALID, or N/A.

External Control Report

The **cobas® eplex** RP2 panel external control report is generated for an external control that has been pre-defined in the **cobas® eplex** RP2 panel software. For more information on defining external controls on the **cobas® eplex** system, refer to the **cobas® eplex** User Assistance Manual.

The summary section indicates the overall result (pass or fail status) and lists all detected targets for that external control. The results section includes a list of all panel targets with the result, expected result, and pass/fail status for each. Results are reported as detected, not detected, or invalid (displayed as a red **x**).

A target is reported as pass if the actual result matches the expected result (as defined for that control); a target is reported as fail if the actual result does not match the expected result. If the actual results for each target match the expected result for each target (all targets reported as pass), the overall result for the external control is reported as pass in the summary section. If the actual result for any target does not match the expected result, the overall result for the external control is reported as fail in the summary section.

Summary Report

The summary report allows the operator to use searchable criteria to create customized reports, using specified targets, dates, range of dates, sample, external control, test bay, or operator. For more information on creating summary reports, refer to the **cobas® eplex** User Assistance Manual.

LIMITATIONS OF THE PROCEDURE

- This product can be used only with the **cobas® eplex** system.
- Due to the genetic similarity between human rhinovirus/enterovirus and poliovirus, the **cobas® eplex** RP2 panel cannot reliably differentiate them. If a poliovirus infection is suspected, a **cobas® eplex** RP2 panel human rhinovirus/enterovirus result of detected should be confirmed using an alternate method (*e.g.*, cell culture).
- Due to the genetic similarity between human rhinovirus and enterovirus, the **cobas® eplex** RP2 panel cannot reliably differentiate them. If differentiation is required, a positive human rhinovirus/enterovirus result may be followed-up using an alternative method.
- At high titers, cross-reactivity with SARS-CoV-1 was observed with the **cobas® eplex** RP2 panel.
- This test is a qualitative test and does not provide a quantitative value of detected organism present.
- The performance of the test has been evaluated for use with human sample material only.
- This test has not been validated for testing samples other than nasopharyngeal swab specimens.
- The performance of this test has not been established for immunocompromised individuals.
- The performance of this test has not been established for patients not suspected of coronavirus disease 2019 (COVID-19) or respiratory infection by their healthcare provider.
- Results from this test must be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- The effect of antibiotic treatment on test performance has not been evaluated.
- Targets (viral and bacterial nucleic acids) may persist *in vivo*, independent of viral or bacterial viability. Detection of target(s) does not imply that the corresponding virus(es) or bacteria are infectious or are the causative agents for clinical symptoms.
- The detection of viral or bacterial nucleic acid is dependent upon proper sample collection, handling, transportation, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results. There is a risk of false negative values resulting from improperly collected, transported, or handled samples.
- There is a risk of false negative values due to the presence of sequence variants in the viral or bacterial targets of the test, the presence of inhibitors, technical error, sample mix-up, or an infection caused by an organism not detected by the panel. Test results may be affected by concurrent antibacterial or antiviral therapy or levels of bacteria or virus in the sample that are below the limit of detection for the test. A result of no targets detected on the **cobas® eplex** RP2 panel should not be used as the sole basis for diagnosis, treatment or other patient management decisions.
- A result of no targets detected on the **cobas® eplex** RP2 panel in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or lower respiratory tract infection that is not detected by a nasopharyngeal swab sample.
- If four or more organisms are detected in a sample, retesting is recommended to confirm polymicrobial result.

- The **cobas® eplex** RP2 panel influenza A subtyping reagents target the influenza A hemagglutinin gene only. The **cobas® eplex** RP2 panel does not detect or differentiate the influenza A neuraminidase gene.
- The performance of this test has not been established for monitoring treatment of infection with any of the panel organisms.
- Positive and negative predictive values are highly dependent on prevalence. False negative test results are more likely during peak activity when prevalence of disease is high. False positive test results are more likely during periods when prevalence is moderate to low.
- Clinical performance was established when influenza A H3 and influenza A H1-2009 were the predominant influenza A viruses in circulation. When other influenza A viruses emerge, performance may vary.
- Performance characteristics for Influenza A H1 were established using contrived clinical specimens only.
- The effect of interfering substances has only been evaluated for those listed in this package insert. Interference due to substances other than those described in the “Interfering Substances” section can lead to erroneous results.
- At concentrations greater than 1.0% weight/volume in the specimen, tobramycin was found to inhibit assay performance.
- At concentrations greater than 1.0% volume/volume in the sample, Phenylephrine HCl was found to inhibit assay performance.
- The performance of this test has not been specifically evaluated for specimens collected from individuals who recently received influenza vaccine. Recent administration of a live intranasal influenza virus vaccine may cause false positive results for influenza A, H1, H3, H1-2009, and/or influenza B.
- The **cobas® eplex** RP2 panel cannot differentiate variant viruses, such as H3N2v, from seasonal influenza A viruses. If variant virus infection is suspected, clinicians should contact their state or local health department to arrange specimen transport and request a timely diagnosis at a state public health laboratory.

PERFORMANCE CHARACTERISTICS

Clinical performance of the SARS-CoV-2

Performance characteristics of the **cobas® eplex** RP2 panel for SARS-CoV-2 detection were established using previously frozen clinical specimens (nasopharyngeal swab (NPS) samples) collected from U.S. patients.

In the first arm of the study, a total of 189 samples, 174 NPS samples (60 known SARS-CoV-2 positive, 114 from the initial RP panel clinical study), and 15 contrived samples, were tested with the **cobas® eplex** RP2 panel in the clinical evaluation study. Samples with final, valid results and a comparator result were considered evaluable. Four samples (1 known SARS-CoV-2 positive, 3 from the initial RP panel clinical study) were not evaluable because they did not have final, valid **cobas® eplex** RP2 panel results and were excluded from analysis.

The comparator methods for the SARS-CoV-2 target were COVID-19 molecular diagnostic tests authorized by the FDA for Emergency Use Authorization (EUA) in the U.S. Only the 60 SARS-CoV-2 known positive NPS samples were tested with these methods. There was no comparator method for the SARS-CoV-2 target in the remaining 114 NPS samples from the initial clinical study. These samples were presumed SARS-CoV-2 negative based on their collection prior to 2017. The comparator method for the other RP2 panel targets was the **cobas® eplex** RP panel. Only the 114 NPS samples from the initial RP panel clinical study were tested with this method.

Positive percent agreement (PPA) was calculated by dividing the number of true positive (TP) results by the sum of TP and false negative (FN) results, while negative percent agreement (NPA) was calculated by dividing the number of true negative (TN) results by the sum of TN and false positive (FP) results. A TP result was one where the detected **cobas® eplex** RP2 panel result matched the detected comparator method result, while a TN result was one where a negative **cobas® eplex** RP2 panel result matched a negative comparator method result. The two-sided 95% confidence interval was also calculated. Results are shown in **Table 7** below.

Table 7: Positive percent agreement (PPA) and negative percent agreement (NPA) for SARS-CoV-2 in the **cobas® eplex** RP2 panel clinical study

Organism	Positive % agreement		Negative % agreement	
	TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
SARS-CoV-2	59/59	100 (93.9-100)	111/111	100 (96.7-100)

CI=Confidence interval, FN=False Negative, FP=False Positive, TN=True Negative, TP=True Positive

ANALYTICAL PERFORMANCE CHARACTERISTICS

cobas® eplex RP and RP2 panels

The **cobas® eplex** RP2 panel was developed by incorporating the reagents required to detect the SARS-CoV-2 targets from the SARS-CoV-2 Test into the existing **cobas® eplex** respiratory pathogen panel (RP panel). The assays for detection of SARS-CoV-2 were added into PCR pools that contain additional targets. The targets that are now co-amplified with SARS-CoV-2 are influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, and adenovirus; assays for all other targets were unchanged. Studies were conducted to demonstrate that the performance characteristics of the RP panel were not affected by the addition of the SARS-CoV-2 assays. Additional studies to support the addition of SARS-CoV-2 are included in the sections below. The original studies from the RP panel are still relevant for the RP2 panel.

Limit of detection for SARS-CoV-2

The limit of detection (LoD), or analytical sensitivity was identified and verified for SARS-CoV-2 using quantified reference material. Serial dilutions were prepared in a natural clinical matrix (pooled, negative nasopharyngeal swab in VTM) and at least 20 replicates per concentration were tested in the study. The limit of detection was defined as the lowest concentration at which SARS-CoV-2 is detected at least 95% of the time. The confirmed LoD for detection of SARS-CoV-2 is shown in **Table 8.**

Table 8: SARS-CoV-2 LoD results summary

Target	Strain	LoD concentration
SARS-CoV-2	USA-WA1/2020	1 x 10^{-2} $TCID_{50}$/mL[a]

[a] The LoD concentration for detection of SARS-CoV-2 was determined to be 0.01 $TCID_{50}$/mL, which corresponds to 250 genomic copies per milliliter, as determined by digital droplet PCR.

Limit of detection for all other RP2 panel targets

The limit of detection (LoD), or analytical sensitivity was identified and verified for each viral and bacterial target on the **cobas® eplex** RP2 panel using quantified reference strains or synthetic transcripts. Serial dilutions were prepared in a natural clinical matrix (pooled, negative nasopharyngeal swab in VTM samples) with one or more organisms per series and at least 20 replicates per target were tested. The limit of detection was defined as the lowest concentration of each target that is detected ≥95% of the time. The confirmed LoD for each **cobas® eplex** RP2 panel organism is shown in **Table 9**.

Table 9: LoD results summary

Target	**Strain**	**LoD concentration**
Adenovirus	Type 1 (C)	1 x 10^{3} TCID$_{50}$/mL
	Type 4 (E)	2 x 10^{0} TCID$_{50}$/mL
	Type 7 (B)	2 x 10^{0} TCID$_{50}$/mL
Coronavirus 229E	229E	1 x 10^{0} TCID$_{50}$/mL
Coronavirus HKU1	HKU1[a]	5 x 10^{4} copies/mL
Coronavirus NL63	NL63	7.5 x 10^{0} TCID$_{50}$/mL
Coronavirus OC43	OC43	5 x 10^{2} TCID$_{50}$/mL
Middle East Respiratory Syndrome Coronavirus	MERS-CoV[b]	1 x 10^{4} copies/mL
Human Bocavirus	Bocavirus plasmid[c]	1 x 10^{4} copies/mL
Human Metapneumovirus	A1 IA3-2002	2 x 10^{-1} TCID$_{50}$/mL
	A2 IA14-2003[d]	2 x 10^{3} TCID$_{50}$/mL
	B1 Peru2-2002	2 x 10^{2} TCID$_{50}$/mL
	B2 Peru1-2002	2.25 x 10^{2} TCID$_{50}$/mL
Human Rhinovirus/Enterovirus	Enterovirus Type 68 (2007)	1 x 10^{0} TCID$_{50}$/mL
	Rhinovirus 1A	1.5 x 10^{0} TCID$_{50}$/mL
	Rhinovirus B14	1 x 10^{0} TCID$_{50}$/mL
	Rhinovirus C[a]	1 x 10^{5} copies/mL
Influenza A	H1N1 Brisbane/59/07	3 x 10^{-1} TCID$_{50}$/mL
Influenza A H1	H1N1 Brisbane/59/07	3 x 10^{-1} TCID$_{50}$/mL
Influenza A H1-2009	NY/01/2009	1 x 10^{-1} TCID$_{50}$/mL
Influenza A H3	A/Perth/16/2009	1 x 10^{1} TCID$_{50}$/mL
	A/Texas/50/2012	1 x 10^{0} TCID$_{50}$/mL
	A/Victoria/361/2011	5 x 10^{-1} TCID$_{50}$/mL
	H3N2 Brisbane/10/07	5 x 10^{1} TCID$_{50}$/mL
Influenza B (Victoria Lineage)	B/Brisbane/60/2008	1 x 10^{0} TCID$_{50}$/mL
	B/Montana/5/2012	1 x 10^{0} TCID$_{50}$/mL
	B/Nevada/03/2011	1 x 10^{0} TCID$_{50}$/mL
Influenza B (Yamagata Lineage)	B/Florida/02/06	1 x 10^{-1} TCID$_{50}$/mL
	B/Massachusetts/02/2012	1 x 10^{2} TCID$_{50}$/mL
	B/Texas/06/2011	1 x 10^{-1} TCID$_{50}$/mL
	B/Wisconsin/01/2010	1 x 10^{0} TCID$_{50}$/mL
Parainfluenza virus 1	Clinical Isolate	4 x 10^{-1} TCID$_{50}$/mL
Parainfluenza virus 2	Clinical Isolate	5 x 10^{1} TCID$_{50}$/mL
Parainfluenza virus 3	Clinical Isolate	5 x 10^{0} TCID$_{50}$/mL
Parainfluenza virus 4	Type 4a	3 x 10^{1} TCID$_{50}$/mL
Respiratory Syncytial Virus A	2006 Isolate	1.5 x 10^{0} TCID50/mL

Target	Strain	LoD concentration
Respiratory Syncytial Virus B	CH93(18)-18	2 x 10^{-1} $TCID_{50}$/mL
Bordetella pertussis	18323 [NCTC 10739]	5 x 10^{4} CFU/mL
Legionella pneumophila	Philadelphia-1	3 x 10^{1} CFU/mL
Mycoplasma pneumoniae	FH strain of Eaton Agent [NCTC 10119]	3 x 10^{2} CCU/mL

[a] Clinical samples confirmed positive for coronavirus HKU1 and human rhinovirus C by bi-directional sequencing and quantified by real-time RT-PCR were used for determination of LoD.
[b] Synthetic RNA transcript used for determination of LoD.
[c] Plasmid DNA used for determination of LoD.
[d] Customer communication from manufacturer dated July 9, 2020 indicated that the human metapneumovirus strain sold as IA14-2003 was actually type B.

Analytical reactivity (inclusivity)

Reactivity of SARS-CoV-2 assays

Inclusivity was evaluated using RNA for SARS-CoV-2 (Hong Kong/VM20001061/2020) at 7.5 x 10^{2} copies/mL. All replicates were detected as expected as shown in **Table 10.**

Table 10: Analytical reactivity (inclusivity) results for SARS-CoV-2

Target	Test Material	Concentration
SARS-CoV-2	Hong Kong/VM20001061/2020 (BEI Resource – Isolated RNA)	7.5 x 10^{2} copies/mL

Predicted (in silico) reactivity (inclusivity) results for SARS-CoV-2

In silico analysis of sequences from GISAID are conducted routinely to assess the ability of the **cobas® eplex** RP2 panel to detect the most recent COVID-19 strains. The results of these analyses show that the sequences the RP2 panel will detect all variants in circulation. For the most up to date information on detection of SARS-CoV-2 strains currently in circulation, please contact your local affiliate: https://www.roche.com/about/business/roche_worldwide.htm.

Inclusivity of all other RP2 targets

A panel of 115 strains/isolates representing the genetic, temporal, and geographic diversity of each target on the **cobas® eplex** RP2 panel was evaluated to demonstrate analytical reactivity. Each strain was tested in triplicate at 3x LoD in natural clinical matrix (pooled, negative nasopharyngeal swab samples); if the organism was not detected at this concentration, testing of higher concentrations was performed. Additional in silico analysis was performed on a subset of **cobas® eplex** RP2 panel organisms.

All of the 115 strains/isolates tested for inclusivity were detected by the **cobas® eplex** RP2 panel. Results of analytical reactivity are shown in **Table 11-Table 24**.

Table 11: Analytical reactivity (inclusivity) results for adenovirus

Note: Adenovirus species B, C, and E are associated with respiratory infections; species A, D, and F are not typically associated with respiratory infections.

Adenovirus species	Serotype	Concentration	Multiple of LoD detected
A	Type 31	3 x 10^3 $TCID_{50}$/mL	3x
B	Type 3	6 x 10^0 $TCID_{50}$/mL	3x
	Type 11	6 x 10^0 $TCID_{50}$/mL	3x
	De Wit Type 14	6 x 10^0 $TCID_{50}$/mL	3x
	Ch.79 Type 16	2 x 10^2 $TCID_{50}$/mL	100x[a]
	Type 21	6 x 10^0 $TCID_{50}$/mL	3x
	Compton Type 34	6 x 10^0 $TCID_{50}$/mL	3x
	Holden Type 35	6 x 10^0 $TCID_{50}$/mL	3x
	Wan Type 50	2 x 10^1 $TCID_{50}$/mL	10x[b]
C	Type 2	3 x 10^3 $TCID_{50}$/mL	3x
	Type 5	3 x 10^3 $TCID_{50}$/mL	3x
	Type 6	3 x 10^3 $TCID_{50}$/mL	3x
D	Type 26	3 x 10^3 $TCID_{50}$/mL	3x
	Type 37	3 x 10^3 $TCID_{50}$/mL	3x
F	Type 40 Dugan	3 x 10^3 $TCID_{50}$/mL	3x
	Type 41/ Strain Tak	3 x 10^3 $TCID_{50}$/mL	3x

[a] In silico analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles).

[b] In silico analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.

Table 12: Analytical reactivity (inclusivity) results for coronavirus

Coronavirus subtype	Strain	Concentration	Multiple of LoD detected
229E	229E	1 x 10^0 $TCID_{50}$/mL	1x
HKU1	Clinical sample[a]	5 x 10^4 copies/mL	1x
NL63	NL63	7.5 x 10^0 $TCID_{50}$/mL	1x
OC43	OC43	5 x 10^2 $TCID_{50}$/mL	1x
MERS	MERS (IVT)	1 x 10^4 copies/mL	1x

[a] A clinical sample confirmed positive for coronavirus HKU1 by bi-directional sequencing and quantified by real-time RT-PCR was used for determination of LoD.

Table 13: Analytical reactivity (Inclusivity) results for human bocavirus

Bocavirus subtype	Strain	Concentration	Multiple of LoD detected
A1	Plasmid	1 x 10^4 copies/mL	1x

Table 14: Analytical reactivity (inclusivity) results for human metapneumovirus

Metapneumovirus subtype	Strain	Concentration	Multiple of LoD detected
B2	Peru6-2003 G, B2	6.75 x 10^2 $TCID_{50}$/mL	3x

Table 15: Analytical reactivity (inclusivity) results for human rhinovirus/enterovirus

Rhinovirus/Enterovirus	**Strain**	**Concentration**	**Multiple of LoD detected**
Human Rhinovirus	Type A2	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type A7	1.5 x 10^1 $TCID_{50}$/mL	10x[a]
	Type A16	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type A18	1.5 x 10^2 $TCID_{50}$/mL	100x[a]
	Type A34	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type A57	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type A77	4.5 x 10^0 $TCID_{50}$/mL	3x
	277G	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type B3	1.5 x 10^1 $TCID_{50}$/mL	10x[a]
	Type B17	1.5 x 10^1 $TCID_{50}$/mL	10x[a]
	Type B42	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type B83	4.5 x 10^0 $TCID_{50}$/mL	3x
	Type B84	4.5 x 10^0 $TCID_{50}$/mL	3x
	FO2-2547	4.5 x 10^0 $TCID_{50}$/mL	3x
Enterovirus	Type 71	3 x 10^0 $TCID_{50}$/mL	3x
Coxsackievirus	A9	3 x 10^0 $TCID_{50}$/mL	3x
	A10	3 x 10^0 $TCID_{50}$/mL	3x
	A21	3 x 10^0 $TCID_{50}$/mL	3x
	A24	3 x 10^0 $TCID_{50}$/mL	3x
	B2	1 x 10^2 $TCID_{50}$/mL	100x[a]
	B3	3 x 10^0 $TCID_{50}$/mL	3x
	B4	3 x 10^0 $TCID_{50}$/mL	3x
	B5	1 x 10^1 $TCID_{50}$/mL	10x[a]
Echovirus	9	3 x 10^0 $TCID_{50}$/mL	3x
	E6	1 x 10^1 $TCID_{50}$/mL	10x[b]
	25	1 x 10^1 $TCID_{50}$/mL	10x[a]
	30	3 x 10^0 $TCID_{50}$/mL	3x
Poliovirus	1	1 x 10^2 $TCID_{50}$/mL	100x[a]

[a] In silico analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.

[b] In silico analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles).

Table 16: Analytical reactivity (inclusivity) results for influenza A

Note: Due to different assays for influenza A matrix and influenza A subtypes on the **cobas® eplex** RP panel, if different LoDs are observed for inclusivity for Influenza A matrix vs. a subtype, the differences are noted in the Multiple of LoD Detected column.

Influenza A subtype	**Strain**	**Concentration**	**Multiple of LoD detected**
Influenza A H1	A/New Caledonia/20/1999	3 x 10^1 $TCID_{50}$/mL	100x[b]
	A/PR/8/34	9 x 10^{-1} $TCID_{50}$/mL	3x (Influenza A matrix) H1 subtype not detected[a]

Influenza A subtype	Strain	Concentration	Multiple of LoD detected
	A/Solomon Islands/3/2006	3×10^0 $TCID_{50}$/mL	10x[b]
	A/Taiwan/42/06	3×10^1 $TCID_{50}$/mL	100x[b]
Influenza A H3	A/Port Chalmers/1/73	1.5×10^2 $TCID_{50}$/mL	3x
	A/Nanchang/933/95		
	A/Victoria/3/75		
	A/Wisconsin/67/05		
Influenza A 2009 H1N1	A/California/7/2009	3×10^{-1} $TCID_{50}$/mL	3x
	A/Mexico/4108/09	3×10^{-1} $TCID_{50}$/mL	3x
	A/NY/02/2009	3×10^{-1} $TCID_{50}$/mL	3x
	A/Swine NY/03/2009	3×10^{-1} $TCID_{50}$/mL	3x

[a] In silico analysis revealed little homology between this non-contemporary influenza strain sequence and the H1 primer sequences.

[b] For Influenza A matrix, in silico analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles). For H1 subtype, in silico analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.

Table 17: Analytical reactivity (inclusivity) results for influenza A strains titered with methods different from the reference strain

Influenza A subtype	Strain	Concentration
Influenza A H1	A/FM/1/47	2.81×10^4 $CEID_{50}$/mL
	A/NWS/33	7.40×10^2 $CEID_{50}$/mL (Influenza A matrix) H1 subtype not detected[c]
Influenza A H3	A/Hong Kong/8/68	1.58×10^2 $CEID_{50}$/mL
Influenza A H1N1	A/Virginia/ATCC1/2009	2.90×10^0 PFU/mL
	A/Virginia/ATCC2/2009	6.10×10^2 PFU/mL
	A/Virginia/ATCC3/2009	1.80×10^3 PFU/mL
Influenza A H5N8	A/Gyrfalcon/Washington/41088-6/2014 BPL	1.58×10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[a]
Influenza A H5N2	A/Northern Pintail/Washington/40964/2014 BPL	2.51×10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[a]
Influenza A H7N9	A/ANHUI/1/2013	7.94×10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[b]
Influenza A H3N2v	A/Indiana/21/2012	2.51×10^4 EID_{50}/mL (Influenza A matrix and H3 subtype)

[a] Detection of the H5 Subtype not expected

[b] Detection of the H7 Subtype not expected

[c] In silico analysis revealed little homology between this non-contemporary strain sequence and the H1 signal probe/capture probe sequences.

NOTE: $CEID_{50}$/mL= Chicken Embryo Infectious Dose; EID_{50}/mL= Egg Infectious Dose; PFU/mL = Plaque Forming Units Quantitation

Supplemental analytical reactivity (inclusivity) of influenza

For human, avian, and swine influenza strains not available for testing on the **cobas® eplex** RP panel, in silico analysis was performed. Bioinformatics analysis was used to generate a simulated result based on number and location of mismatches based on alignment of GenBank sequences to the primers, capture probes, and signal probes found in the **cobas® eplex** RP panel.

Table 18: Simulated (in silico) reactivity (inclusivity) results for influenza A

Influenza A subtype	Host	Strain	GenBank ID	Simulated cobas® eplex result
H2N2	Human	A/Albany/20/1957(H2N2)	CY022014	Influenza A
		Kilbourne F38: A/Korea/426/68 (HA, NA) x A/Puerto Rico/8/34	CY037296	Influenza A
	Avian	A/chicken/New York/13828-3/1995(H2N2)	CY014822	Influenza A
		A/Japan/305/1957(H2N2)	CY014977	Influenza A
		A/Korea/426/1968(H2N2)	CY031596	Influenza A
H4N6	Avian	A/Blue-winged teal/Minnesota/Sg-00043/2007(H4N6)	CY063978	Influenza A
H5N1		A/Peregrine falcon/Aomori/7/2011	AB629716	Influenza A
		A/Chicken/West Bengal/239022/2010	CY061305	Influenza A
		A/Chicken/West Bengal/193936/2009	GU272009	Influenza A
		A/Chicken/Hunan/1/2009	HM172150	Influenza A
		A/Chicken/Hunan/8/2008	GU182162	Influenza A
		A/Chicken/West Bengal/106181/2008	GU083632	Influenza A
		A/Chicken/Primorsky/85/2008	FJ654298	Influenza A
		A/Chicken/West Bengal/82613/2008	GU083648	Influenza A
		A/Duck/France/080036/2008	CY046185	Influenza A
		A/Duck/Vietnam/G12/2008	AB593450	Influenza A
		A/Chicken/Thailand/PC-340/2008	EU620664	Influenza A
		A/Great egret/Hong Kong/807/2008	CY036240	Influenza A
		A/Rook/Rostov-on-Don/26/2007(H5N1)	EU814504	Influenza A
		A/Turkey/VA/505477-18/2007(H5N1)	GU186510	Influenza A
		A/Chicken/Bangladesh/1151-10/2010(H5N1)	HQ156766	Influenza A
	Human	A/Bangladesh/3233/2011	CY088772	Influenza A
		A/Cambodia/R0405050/2007(H5N1)	HQ200572	Influenza A
		A/Cambodia/S1211394/2008	HQ200597	Influenza A
		A/Hong Kong/486/97(H5N1)	AF255368	Influenza A
	Swine	A/Swine/East Java/UT6010/2007(H5N1)	HM440124	Influenza A
H5N2	Avian	A/Duck/Pennsylvania/10218/1984(H5N2)	AB286120	Influenza A
		A/American black duck/Illinois/08OS2688/2008	CY079453	Influenza A
		A/American green-winged teal/California/HKWF609/2007	CY033447	Influenza A
		A/Canada goose/New York/475813-2/2007	GQ923358	Influenza A
		A/Blue-winged teal/Saskatchewan/22542/2007	CY047705	Influenza A
		A/Chicken/Taiwan/A703-1/2008	AB507267	Influenza A
		A/Duck/France/080032/2008	CY046177	Influenza A
		A/Duck/New York/481172/2007	GQ117202	Influenza A
		A/Gadwall/Altai/1202/2007	CY049759	Influenza A
		A/Mallard/Louisiana/476670-4/2007	GQ923390	Influenza A
		A/Waterfowl/Colorado/476466-2/2007	GQ923374	Influenza A
H5N3	Avian	A/Duck/Singapore/F119/3/1997(H5N3)	GU052803	Influenza A

Influenza A subtype	Host	Strain	GenBank ID	Simulated cobas® eplex result
H6N1		A/Duck/PA/486/1969(H6N1)	EU743287	Influenza A
H6N2		A/Mallard/Czech Republic/15902-17K/2009(H6N2)	HQ244433	Influenza A
H7N2	Avian	A/Chicken/Hebei/1/2002	AY724263	Influenza A
		A/Chicken/PA/149092-1/02	AY241609	Influenza A
		A/Chicken/NJ/294508-12/2004	EU743254	Influenza A
		A/Chicken/New York/23165-6/2005	CY031077	Influenza A
		A/Muscovy duck/New York/23165-13/2005	CY033226	Influenza A
		A/Muscovy duck/New York/87493-3/2005	CY034791	Influenza A
		A/Mallard/Netherlands/29/2006	CY043833	Influenza A
		A/Northern shoveler/California/JN1447/2007	CY076873	Influenza A
	Human	A/New York/107/2003(H7N2)	EU587373	Influenza A
H7N3		A/Canada/rv504/2004(H7N3)	CY015007	Influenza A
H7N7	Avian	A/American green-winged teal/Mississippi/09OS046/2009	CY079309	Influenza A
		A/Chicken/Germany/R28/03	AJ619676	Influenza A
		A/Chicken/Netherlands/1/03	AY340091	Influenza A
		A/Mallard/California/HKWF1971/2007	CY033383	Influenza A
		A/Mallard/Korea/GH171/2007	FJ959087	Influenza A
		A/Mute swan/Hungary/5973/2007	GQ240816	Influenza A
		A/Northern shoveler/Mississippi/ 09OS643/2009	CY079413	Influenza A
	Human	A/Netherlands/219/03(H7N7)	AY340089	Influenza A
H7N9	Human	A/Shanghai/1/2013(H7N9)	EPI439493	Influenza A
	Avian	A/Northern shoveler/Mississippi/11OS145/2011(H7N9)	CY133650	Influenza A
		A/Ruddy turnstone/Delaware Bay/220/1995(H7N9)	CY127254	Influenza A
		A/Turkey/Minnesota/1/1988(H7N9)	CY014787	Influenza A
		A/Blue-winged teal/Ohio/566/2006(H7N9)	CY024819	Influenza A
H9N2	Human	A/Hong Kong/1073/99(H9N2)	AJ278647	Influenza A
	Avian	A/Turkey/Wisconsin/1/1966(H9N2)	CY014664	Influenza A
H10N7		A/chicken/Germany/N/1949(H10N7)	GQ176135	Influenza A
H11N9		A/Duck/Memphis/546/1974(H11N9)	GQ257441	Influenza A
H1N1	Swine	A/Swine/Wisconsin/1/1971(H1N1)	CY022414	Influenza A
	Human	A/California/UR06-0393/2007(H1N1)	CY026540	Influenza A H1
			CY026539	
H1N2		A/New York/297/2003(H1N2)	CY002664	Influenza A H1
			CY002665	
H1N1 (2009)		A/Aalborg/INS133/2009(H1N1)	CY063606	Influenza A H1-2009
			CY063607	
		A/South Carolina/02/2010(H1N1)	KC781370	Influenza A H1-2009
			KC781372	

Influenza A subtype	Host	Strain	GenBank ID	Simulated cobas® eplex result
H1N2	Swine	A/Swine/Hong Kong/NS857/2001(H1N2)	GQ229350	Influenza A
		A/Swine/Sweden/1021/2009(H1N2)	GQ495135	Influenza A
H3N1	Avian	A/Blue-winged teal/ALB/452/1983(H3N1)	CY004635	Influenza A
H3N2v	Human	A/Iowa/07/2011(H3N2)	JQ070760	Influenza A H3
			JQ290177	
		A/Iowa/08/2011(H3N2)	JQ070768	Influenza A H3
			JQ290167	
		A/Iowa/09/2011(H3N2)	JQ070776	Influenza A H3
			JQ290183	
		A/Indiana/08/2011(H3N2)	JQ070800	Influenza A H3
			JQ070795	
		A/Maine/06/2011(H3N2)	JN866181	Influenza A H3
			JN866186	
		A/Maine/07/2011(H3N2)	JN992746	Influenza A
		A/Pennsylvania/09/2011(H3N2)	JN655534	Influenza A
		A/Pennsylvania/11/2011(H3N2)	JN655540	Influenza A
		A/Pennsylvania/10/2011(H3N2)	JN655550	Influenza A
		A/West Virginia/06/2011(H3N2)	JQ290159	Influenza A H3
			JQ290164	
		A/West Virginia/07/2011(H3N2)	JQ348839	Influenza A
		A/Indiana/10/2011(H3N2)	KJ942592	Influenza A H3
			JQ070787	
		A/Boston/38/2008(H3N2)	CY044580	Influenza A H3
			CY044581	
	Swine	A/swine/NY/A01104005/2011(H3N2v)	JN940422	Influenza A H3
		A/Maine/06/2011(H3N2)	JN866181	Influenza A H3
			JN866186	Influenza A H3
		A/Indiana/08/2011(H3N2)	JN655558	Influenza A H3
			JN638733	
	Avian	A/American black duck/North Carolina/675-075/2004(H3N2)	GU051135	Influenza A
			GU051136	Influenza A
H3N5		A/Mallard/Netherlands/2/1999(H3N5)	CY060261	Influenza A
			CY060264	Influenza A
H3N6		A/American black duck/New Brunswick/25182/2007(H3N6)	CY047696	Influenza A
			CY047697	Influenza A
H3N7		A/Northern shoveler/California/HKWF1367/2007(H3N7)	CY033372	Influenza A
			CY033375	Influenza A
H3N8		A/American black duck/Washington/699/1978(H3N8)	GU052300	Influenza A H3
			GU052299	

Table 19: Analytical reactivity (inclusivity) results for influenza B

Influenza B subtype	Strain	Concentration	Multiple of LoD detected
Influenza B (Yamagata Lineage)	B/Lee/40	3 x 10^{-1} $TCID_{50}$/mL	3x
	B/Allen/45	1 x 10^{0} $TCID_{50}$/mL	10x[a]
	B/Maryland/1/59	3.38 x 10^{1} $CEID_{50}$/mL	N/A (Strain titered differently from reference strain)
	B/Taiwan/2/62	1 x 10^{2} $TCID_{50}$/mL	1000x[a]
Influenza B (Victoria Lineage)	B/Hong Kong/5/72	1 x 10^{1} $TCID_{50}$/mL	100x[b]
	B/Malaysia/2506/04	3 x 10^{-1} $TCID_{50}$/mL	3x
Influenza B (Lineage unknown)	B/GL/1739/54	3 x 10^{-1} $TCID_{50}$/mL	3x

[a] No sequence data available. Lower sensitivity may be a result of mismatches in the assay primers and/or probes. In addition, the reduced sensitivity may be the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$/mL value is based only on infectious virus particles).

[b] In silico analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.

Table 20: Analytical reactivity (inclusivity) results for parainfluenza virus

Parainfluenza subtype	Strain	Concentration	Multiple of LoD detected
Parainfluenza Virus 1	C35	1.2 x 10^{0} $TCID_{50}$/mL	3x
Parainfluenza Virus 2	Greer	1.5 x 10^{2} $TCID_{50}$/mL	3x
Parainfluenza Virus 3	C-243	5 x 10^{1} $TCID_{50}$/mL	10x[a]
Parainfluenza Virus 4	4b	9 x 10^{1} $TCID_{50}$/mL	3x

[a] In silico analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.

Table 21: Analytical reactivity (inclusivity) results for respiratory syncytial virus

RSV subtype	Strain	Concentration	Multiple of LoD detected
Respiratory Syncytial Virus A	A2	4.5 x 10^{0} $TCID_{50}$/mL	3x
	Long	4.5 x 10^{0} $TCID_{50}$/mL	3x
Respiratory Syncytial Virus B	9320	6 x 10^{-1} $TCID_{50}$/mL	3x
	Wash/18537/62	6 x 10^{-1} $TCID_{50}$/mL	3x
	WV/14617/85	6 x 10^{-1} $TCID_{50}$/mL	3x

Table 22: Analytical reactivity (inclusivity) results for *Bordetella pertussis*

Bordetella pertussis	Strain	Concentration	Multiple of LoD detected
Bordetella pertussis	5 [17921]	1.5 x 10^{5} CFU/mL	3x
	5374 [3747]		3x
	589		3x
	F		3x
	PT9/28G [W28]		3x
	Tohama I		3x

Table 23: Analytical reactivity (inclusivity) results for *Legionella pneumophila*

Legionella pneumophila	**Strain**	**Concentration**	**Multiple of LoD Detected**
Legionella pneumophila	11EJ	3 x 10^3 CFU/mL	10x
	Chicago 8 [NCTC 11984]	3 x 10^5 CFU/mL	1000x
	FAUC 19	3 x 10^4 CFU/mL	100x
	Reims 97 II no. 1	3 x 10^4 CFU/mL	100x
	RIO	3 x 10^4 CFU/mL	100x

Table 24: Analytical reactivity (inclusivity) results for *Mycoplasma pneumoniae*

Mycoplasma pneumoniae	**Strain**	**Concentration**	**Multiple of LoD detected**
Mycoplasma pneumoniae	[Bru]	9 x 10^2 CCU/mL	3x
	M129-B170	9 x 10^2 CCU/mL	3x
	M129-B7	9 x 10^2 CCU/mL	3x
	[M52]	9 x 10^2 CCU/mL	3x
	[Mac]	9 x 10^2 CCU/mL	3x
	Mutant 22	3 x 10^4 CCU/mL	100x[a]
	PI 1428	3 x 10^4 CCU/mL	100x[b]

[a] No sequence data available. Lower sensitivity may be a result of mismatches in the assay primers and/or probes. In addition, the reduced sensitivity may be the result of incorrect estimation of genetic material present in the culture of this or the reference strain (CCU/ml value is based only on live bacteria).

[b] In silico analysis revealed good homology to primers and probes. The reduced sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain (CCU/ml value is based only on live bacteria).

Analytical specificity (Cross-reactivity and exclusivity)

Cross-reactivity of the SARS-CoV-2 assays

Cross-reactivity of the SARS-CoV-2 assays was evaluated using both in silico analysis and by testing quantified analytes for organisms likely to be found in circulation and other pathogens in the same genetic family. Synthetic constructs were used for analytes where high-titer cultures were not available (SARS-CoV-1, MERS-CoV, Human Bocavirus, and Coronavirus HKU1). A pool of two to four analytes were tested in triplicate. Viral analytes were diluted to testing concentrations ranging from $1x10^4$ - $1x10^6$ $TCID_{50}$/mL. Bacterial and fungal analytes were diluted to a testing concentration of $1x10^7$ - $1x10^8$ CFU/mL. Synthetic constructs were tested at a concentration of $1x10^5$ - $1x10^6$ copies/mL. Parainfluenza virus 3 was a clinical sample that was used as a diluent to generate a viral pool and therefore a viral concentration is not provided. A summary of the results of cross-reactivity testing are shown in **Table 25** below. At high titers, cross-reactivity with SARS-CoV-1 was observed with the **cobas® eplex** RP2 panel.

Table 25: Cross-reactivity of SARS-CoV-2 assays with on and off-panel organisms

Virus/bacteria	**Strain**	**Concentration**	**Cross-reactivity**
Adenovirus C	1	1 x 10^3 $TCID_{50}$/mL	Not observed
Coronavirus	229E	1 x 10^4 $TCID_{50}$/mL	Not observed
Coronavirus	HKU1[a]	1 x 10^5 copies/mL	Not observed
Coronavirus	NL63	1 x 10^5 $TCID_{50}$/mL	Not observed
Coronavirus	OC43	1 x 10^6 $TCID_{50}$/mL	Not observed
Coronavirus	MERS-CoV[b]	1 x 10^5 copies/mL	Not observed

Virus/bacteria	Strain	Concentration	Cross-reactivity
Coronavirus	SARS-CoV-1[a]	1 x 10^6 copies/mL	Observed
Human bocavirus	HBoV1[b]	1 x 10^6 copies/mL	Not observed
Echovirus	30	1 x 10^5 $TCID_{50}$/mL	Not observed
Enterovirus	68	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza A	H1N1/NY01/2009	1 x 10^{-1} $TCID_{50}$/mL	Not observed
Influenza B	Yamagata B/Florida/02/06	1 x 10^{-1} $TCID_{50}$/mL	Not observed
Human metapneumovirus	B2 Peru1-2002	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	1	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	2	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	3	N/A	Not observed
Parainfluenza	4a	1 x 10^5 $TCID_{50}$/mL	Not observed
Respiratory Syncytial Virus A	2006	1 x 10^5 $TCID_{50}$/mL	Not observed
Human rhinovirus	B14	1 x 10^6 $TCID_{50}$/mL	Not observed
Bordetella pertussis	ATCC53894	1 x 10^8 CFU/mL	Not observed
Candida albicans	ATCC24433	1 x 10^7 CFU/mL	Not observed
Corynebacterium diphtheriae	ATCC53281	1 x 10^7 CFU/mL	Not observed
Haemophilus influenzae	ATCC43065	1 x 10^8 CFU/mL	Not observed
Legionella pneumophila	ATCC35096	1 x 10^8 CFU/mL	Not observed
Mycobacterium tuberculosis	ATCC25177	1 x 10^8 CFU/mL	Not observed
Moraxella catarrhalis	ATCC23246	1 x 10^7 CFU/mL	Not observed
Mycoplasma pneumoniae	ATCC29085	1 x 10^8 CFU/mL	Not observed
Neisseria meningitidis	NCTC10026	1 x 10^8 CFU/mL	Not observed
Pseudomonas aeruginosa	ATCC BAA-1744	1 x 10^8 CFU/mL	Not observed
Staphylococcus aureus	ATCC25923	1 x 10^8 CFU/mL	Not observed
Staphylococcus epidermidis	ATCC700567	1 x 10^8 CFU/mL	Not observed
Staphylococcus salivarius	ATCC25975	1 x 10^7 CFU/mL	Not observed
Streptococcus pneumoniae	ATCC49136	1 x 10^8 CFU/mL	Not observed
Streptococcus pyogenes	ATCC49399	1 x 10^8 CFU/mL	Not observed
Pooled Nasal Swab	Human Clinical Sample	N/A	Not observed

[a] in vitro transcript
[b] plasmid

In silico analysis of the cobas® eplex RP2 panel SARS-CoV-2 assays

In silico analysis was performed for the gene regions targeted by the **cobas® eplex** RP2 panel to evaluate cross-reactivity. Roche conducted a primer BLAST® search of the NCBI database against all bacteria, negative-stranded RNA viruses (Negarnaviricota), picornaviruses, adenoviruses, common human coronaviruses, MERS-CoV, *Candida albicans*, and *Pneumocysitis*. The BLAST searches did not identify any cross-reactivity with the exception of SARS coronavirus, which is in the same subgenus (Sarbecovirus) as SARS-CoV-2.

Analytical specificity (Cross-reactivity and exclusivity) of other RP2 panel targets

The design of the **cobas® eplex** RP2 panel incorporates assays for the detection of SARS-CoV-2 without affecting the original designs of the **cobas® eplex** RP panel assays. The original RP panel targets impacted by the addition of the SARS-CoV-2 assays (influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, and adenovirus) were tested and no cross-reactivity was observed. Therefore, the established cross-reactivity claims of the **cobas® eplex** RP panel are applicable to the RP2 panel.

Cross-reactivity of each viral and bacterial target on the **cobas® eplex** RP panel was evaluated at high concentrations (1 x 10^5 $TCID_{50}$/mL for viruses, 1 x 10^6 CFU/mL or CCU/mL for bacterial strains, or 1 x 10^6 copies/mL for in vitro transcripts) of quantified strains diluted in viral transport media. In vitro transcript for coronavirus HKU1 was diluted in PBS. Additional Influenza A strains were tested at the following concentrations: Influenza A H7N9 at 7.94 x 10^5 EID_{50}/mL, Influenza A H3N2v at 2.51 x 10^5 EID_{50}/mL, Influenza A H5N2 at 2.51 x 10^5 EID_{50}/mL, Influenza A H5N8 at 1.58 x 10^5 EID_{50}/mL. **Table 26** summarizes the results of the viral and bacterial strains tested. No cross-reactivity was observed between any of the on-panel viruses or bacteria.

Table 26: Cross-reactivity with **cobas® eplex** RP panel target organisms

Target	Strain	Concentration	Cross-reactivity results
Adenovirus A	Type 31	1 x 10^5 $TCID_{50}$/mL	Not observed
Adenovirus B	Type 7A	1 x 10^5 $TCID_{50}$/mL	Not observed
Adenovirus C	Type 1	1 x 10^5 $TCID_{50}$/mL	Not observed
Adenovirus D	Type 9	1 x 10^5 $TCID_{50}$/mL	Not observed
Adenovirus E	Type 4	1 x 10^5 $TCID_{50}$/mL	Not observed
Adenovirus F	Type 41	1 x 10^5 $TCID_{50}$/mL	Not observed
Coronavirus	229E	1 x 10^5 $TCID_{50}$/mL	Not observed
Coronavirus	HKU1 in vitro transcript	1 x 10^6 copies/mL	Not observed
Coronavirus	NL63	1 x 10^5 $TCID_{50}$/mL	Not observed
Coronavirus	MERS in vitro transcript	1 x 10^6 copies/mL	Not observed
Coronavirus	OC43	1 x 10^5 $TCID_{50}$/mL	Not observed
Enterovirus	Type 68 2007 isolate	1 x 10^5 $TCID_{50}$/mL	Not observed
Human bocavirus	Bocavirus plasmid	1 x 10^6 copies/mL	Not observed
Human metapneumovirus	B1	1 x 10^5 $TCID_{50}$/mL	Not observed
Human rhinovirus	1A	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza A	A/Brisbane/59/07	1 x 10^5 $TCID_{50}$/mL	Not observed
H1	A/Brisbane/59/07	1 x 10^5 $TCID_{50}$/mL	Not observed
H1-2009	A/NY/01/2009	1 x 10^5 $TCID_{50}$/mL	Not observed
H3	A/Brisbane/10/07	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza B	B/Florida/02/06	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza Virus 1	C35	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza Virus 2	Type 2	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza Virus 3	Type 3	1 x 10^5 $TCID_{50}$/mL	Not observed

Target	Strain	Concentration	Cross-reactivity results
Parainfluenza Virus 4	Type 4a	1 x 10^5 $TCID_{50}$/mL	Not observed
RSV A	2006 Isolate	1 x 10^5 $TCID_{50}$/mL	Not observed
RSV B	CH93(18)-18	1 x 10^5 $TCID_{50}$/mL	Not observed
Bordetella pertussis	18323 [NCTC 10739]	1 x 10^6 CFU/mL	Not observed
Legionella pneumophila	Philadelphia-1	1 x 10^6 CFU/mL	Not observed
Mycoplasma pneumoniae	FH strain of Eaton Agent [NCTC 10119]	1 x 10^6 CCU/mL	Not observed

Cross-reactivity of viruses, bacteria, and fungi that are not targets on the **cobas® eplex** RP panel was evaluated at high concentrations (1 x 10^5 $TCID_{50}$/mL for viruses, 1 x 10^6 CFU/mL for bacterial and yeast isolates) by diluting quantified strains in viral transport media. Varicella Zoster Virus was not diluted and was tested at the stock titer of 8.9 x 10^3 $TCID_{50}$/mL. **Table 27** summarizes the results of the strains tested. No cross-reactivity was observed between any of the off-panel viruses, bacteria or fungi with the **cobas® eplex** RP panel targets.

Table 27: Cross-reactivity with organisms not detected by the **cobas® eplex** RP panel (exclusivity)

Target	Strain	Concentration	Cross-reactivity results
Acinetobacter baumanii	ATCC® 19606	1 x 10^6 CFU/mL	Not observed
Bordetella parapertussis	ATCC 15311	1 x 10^6 CFU/mL	Not observed
Burkholderia cepacia	ATCC 25416	1 x 10^6 CFU/mL	Not observed
Candida albicans	ATCC 10231	1 x 10^6 CFU/mL	Not observed
Candida glabrata	ATCC 15126	1 x 10^6 CFU/mL	Not observed
Chlamydia pneumoniae	AR-39	1 x 10^6 CFU/mL	Not observed
Corynebacterium diphtheriae	ATCC 13812	1 x 10^6 CFU/mL	Not observed
Cytomegalovirus	AD 169	1 x 10^5 $TCID_{50}$/mL	Not observed
Epstein Barr Virus	Strain B95-8	1 x 10^5 $TCID_{50}$/mL	Not observed
Escherichia coli	ATCC 10279	1 x 10^6 CFU/mL	Not observed
Haemophilus influenzae	ATCC 43065	1 x 10^6 CFU/mL	Not observed
Herpes Simplex Virus	Isolate 2	1 x 10^5 $TCID_{50}$/mL	Not observed
Klebsiella pneumoniae	ATCC 51504	1 x 10^6 CFU/mL	Not observed
Lactobacillus acidophilus	ATCC 314	1 x 10^6 CFU/mL	Not observed
Lactobacillus plantarum	ATCC 8014	1 x 10^6 CFU/mL	Not observed
Measles	N/A	1 x 10^5 $TCID_{50}$/mL	Not observed
Moraxella catarrhalis	ATCC 23246	1 x 10^6 CFU/mL	Not observed
Mumps	Isolate 2	1 x 10^5 $TCID_{50}$/mL	Not observed
Mycobacterium tuberculosis	ATCC 25177	1 x 10^6 CFU/mL	Not observed
Neisseria meningiditis	ATCC 13077	1 x 10^6 CFU/mL	Not observed
Neisseria sicca	ATCC 29193	1 x 10^6 CFU/mL	Not observed
Porphyromonas gingivalis	ATCC 33277	1 x 10^6 CFU/mL	Not observed
Proteus vulgaris	ATCC 33420	1 x 10^6 CFU/mL	Not observed
Pseudomonas aeruginosa	ATCC 15442	1 x 10^6 CFU/mL	Not observed
Serratia marcescens	ATCC 13880	1 x 10^6 CFU/mL	Not observed

Target	Strain	Concentration	Cross-reactivity results
Staphylococcus aureus (MRSA)	NRS384	1 x 10^6 CFU/mL	Not observed
Staphylococcus aureus (MSSA)	ATCC 25923	1 x 10^6 CFU/mL	Not observed
Staphylococcus epidermidis (MRSE)	ATCC 35983	1 x 10^6 CFU/mL	Not observed
Staphylococcus epidermidis (MSSE)	ATCC 49134	1 x 10^6 CFU/mL	Not observed
Staphylococcus haemolyticus	ATCC 29970	1 x 10^6 CFU/mL	Not observed
Streptococcus agalactiae	ATCC 12401	1 x 10^6 CFU/mL	Not observed
Streptococcus dysgalactiae	ATCC 35666	1 x 10^6 CFU/mL	Not observed
Streptococcus mitis	ATCC 15914	1 x 10^6 CFU/mL	Not observed
Streptococcus pneumoniae	ATCC 49619	1 x 10^6 CFU/mL	Not observed
Streptococcus pyogenes	ATCC 12384	1 x 10^6 CFU/mL	Not observed
Streptococcus salivarius	ATCC 13419	1 x 10^6 CFU/mL	Not observed
Varicella Zoster Virus	82	8.9 x 10^3 $TCID_{50}$/mL	Not observed

Reproducibility

A multisite reproducibility study of the **cobas® eplex** RP panel was performed to evaluate agreement with expected results across major sources of variability, such as site-to-site, lot-to-lot, day-to-day and operator-to-operator. Testing occurred at 3 sites (2 external, 1 internal) on one **cobas® eplex** system per site with either 3 or 4 towers. Two operators performed testing at each site on 6 days (5 nonconsecutive days) with 3 unique lots of RP panel cartridges. A reproducibility panel consisting of 3 panel members with 7 organisms (representing 8 RP panel targets) at 3 concentrations (moderate positive- 3x LoD, low positive- 1x LoD, and negative) was tested in triplicate. The 7 viral/bacterial organisms tested included adenovirus, coronavirus OC43, human metapneumovirus, influenza A H3, parainfluenza virus 1, RSV A, and *Bordetella pertussis;* organisms were diluted in natural clinical matrix (pooled, negative nasopharyngeal swab samples). Negative samples consisted of natural clinical matrix only. Each simulated sample was divided into aliquots and stored frozen (-70 °C) prior to testing. Each operator tested 9 samples (3 member reproducibility panel in triplicate) each day; each panel member was tested 108 times (3 replicates x 3 sites x 2 operators x 3 lots x 2 days of testing/operator/lot) for a minimum of 324 tests.

Percent agreement (95% CI) with expected results was 100% for all 8 targets for the moderate positive and negative panel, and 100% for 6 of 8 low positive panel targets (coronavirus OC43, human metapneumovirus, influenza A, influenza A H3, parainfluenza 1, and RSV A); percent agreement was 91.6% for adenovirus and 99.1% for *B. pertussis*. Summary results for the 8 **cobas® eplex** RP panel targets that correspond to the 7 organisms in the reproducibility panel are provided in **Table 28-Table 35** below.

Table 28: Percent agreement for adenovirus

Adenovirus concentration	Site	Agreement with expected results		
		Agreed / N	%	95% CI
Moderate Positive 3x LoD 6 x 10^0 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Adenovirus concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Low Positive 1x LoD 2×10^0 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	34/36	94.4	(81.9-98.5)
	3	28/35	80.0	(64.1-90.0)
	All	98/107	91.6	(84.8-95.5)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

CI=Confidence Interval

Table 29: Percent agreement for coronavirus OC43 (CoV OC43)

CoV OC43 concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 1.5×10^3 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 5×10^2 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 30: Percent agreement for human metapneumovirus (hMPV)

hMPV concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 6.75×10^2 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 2.25×10^2 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 31: Percent agreement for influenza A

Influenza A concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 1.5 x 10^2 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 5 x 10^1 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 32: Percent agreement for influenza A H3

Influenza A H3 concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 1.5 x 10^2 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 5 x 10^1 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 33: Percent agreement for parainfluenza virus (PIV) 1

PIV 1 concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 1.2 x 10^0 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 4 x 10^{-1} $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)

PIV 1 concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 34: Percent agreement for respiratory syncytial virus (RSV) A

RSV A concentration	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 4.5 x 10^0 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 1.5 x 10^0 $TCID_{50}$/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	35/35	100	(90.1-100)
	All	107/107	100	(96.5-100)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Table 35: Percent agreement for *Bordetella pertussis*

***B. pertussis* concentration**	**Site**	**Agreement with expected results**		
		Agreed / N	**%**	**95% CI**
Moderate Positive 3x LoD 1.5 x 10^5 CFU/mL	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Low Positive 1x LoD 5 x 10^4 CFU/mL	1	36/36	100	(90.4-100)
	2	35/36	97.2	(85.8-99.5)
	3	35/35	100	(90.1-100)
	All	106/107	99.1	(94.9-99.8)
Negative	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Samples with co-detected organisms

Detection of more than one clinically relevant viral and/or bacterial organism in a sample was evaluated with the **cobas®** **eplex** RP panel using a natural clinical matrix (pooled, negative nasopharyngeal swab samples) spiked with two RP panel organisms: one organism at a low concentration (1-3x LoD) and the second organism at a high concentration (1 x 10^5 $TCID_{50}$/mL for viruses and 1 x 10^6 CFU/mL for bacteria). **Table 36** contains the results of co-detection testing which demonstrated the ability of the **cobas®** **eplex** RP panel to detect 2 organisms in a sample at both high and low concentrations as indicated in the table.

Table 36: Detection of co-infections

Organism 1	High titer	Organism 2	Low titer	Multiple of LoD
Influenza A H3	1 x 10^5 $TCID_{50}$/mL	Adenovirus B	2 x 10^0 $TCID_{50}$/mL	1x
Adenovirus	1 x 10^5 $TCID_{50}$/mL	Influenza A H3	5 x 10^1 $TCID_{50}$/mL	1x
Influenza A H3	1 x 10^5 $TCID_{50}$/mL	RSV A	1.5 x 10^0 $TCID_{50}$/mL	1x
RSV A	1 x 10^5 $TCID_{50}$/mL	Influenza A H3	5 x 10^1 $TCID_{50}$/mL	1x
Influenza A H1-2009	1 x 10^5 $TCID_{50}$/mL	RSV B	6 x 10^{-1} $TCID_{50}$/mL	3x
RSV B	1 x 10^5 $TCID_{50}$/mL	Influenza A H1-2009	1x 10^{-1} $TCID_{50}$/mL	1x
Influenza A H1-2009	1 x 10^5 $TCID_{50}$/mL	Rhinovirus	1.5 x 10^0 $TCID_{50}$/mL	1x
Rhinovirus	1 x 10^5 $TCID_{50}$/mL	Influenza A H1-2009	3 x 10^{-1} $TCID_{50}$/mL	3x
Influenza A H1-2009	1 x 10^5 $TCID_{50}$/mL	Parainfluenza Virus 3	5 x 10^0 $TCID_{50}$/mL	1x
Parainfluenza Virus 3	1 x 10^5 $TCID_{50}$/mL	Influenza A H1-2009	1 x 10^{-1} $TCID_{50}$/mL	1x
Influenza A H1-2009	1 x 10^5 $TCID_{50}$/mL	*Bordetella pertussis*	1.5 x 10^5 CFU/mL	3x
B. pertussis	1 x 10^6 CFU/mL	Influenza A H1-2009	1 x 10^{-1} $TCID_{50}$/mL	1x
Rhinovirus	1 x 10^5 $TCID_{50}$/mL	RSV A	1.5 x 10^0 $TCID_{50}$/mL	1x
RSV A	1 x 10^5 $TCID_{50}$/mL	Rhinovirus	1.5 x 10^0 $TCID_{50}$/mL	1x
Coronavirus NL63	1 x 10^5 $TCID_{50}$/mL	RSV A	1.5 x 10^0 $TCID_{50}$/mL	1x
RSV A	1 x 10^5 $TCID_{50}$/mL	Coronavirus NL63	7.5 x 10^0 $TCID_{50}$/mL	1x
Human Metapneumovirus	1 x 10^5 $TCID_{50}$/mL	Adenovirus	2 x 10^0 $TCID_{50}$/mL	1x
Adenovirus	1 x 10^5 $TCID_{50}$/mL	Human Metapneumovirus	2.25 x 10^2 $TCID_{50}$/mL	1x
Adenovirus	1 x 10^5 $TCID_{50}$/mL	RSV A	1.5 x 10^0 $TCID_{50}$/mL	1x
RSV A	1 x 10^5 $TCID_{50}$/mL	Adenovirus	2 x 10^0 $TCID_{50}$/mL	1x
B. pertussis	1 x 10^6 CFU/mL	RSV A	1.5 x 10^0 $TCID_{50}$/mL	1x
RSV A	1 x 10^5 $TCID_{50}$/mL	*B. pertussis*	5 x 10^4 CFU/mL	1x

Sample matrix equivalency

All analytical studies that utilized viral and bacterial cultures close to LoD were performed by spiking the viral and bacterial cultures into a pool of negative NPS as sample matrix. For analytical studies that used viral and bacterial cultures at a concentration which was at least 10x LoD or higher, the viral and bacterial cultures were spiked into MicroTest™ M5® transport media from Remel instead of negative pooled NPS for ease of use. A sample matrix equivalency study was performed to demonstrate equivalency of natural clinical matrix (pooled, negative nasopharyngeal swab samples) with clinically collected nasopharyngeal samples in viral transport media for targets spiked at a concentration of approximately 10x LoD. Quantified, representative viral and bacterial strains were diluted in a natural clinical matrix (pooled, negative nasopharyngeal swab samples) and in viral transport media. There was no difference observed in detection of targets in natural clinical matrix vs. viral transport media.

Interfering substances

Substances commonly found in respiratory specimens, substances that could be introduced during specimen collection or medications commonly used to treat congestion, allergies, or asthma symptoms that could potentially interfere with the **cobas® eplex** RP panel were individually evaluated. To simulate clinical samples, quantified representative viral and bacterial strains were diluted to 1x LoD in a natural clinical matrix (pooled, negative nasopharyngeal swab specimens) and tested in triplicate. Natural clinical matrix (pooled, negative nasopharyngeal swab samples) with no organisms added was used as a control. All substances and organisms tested for interference were shown to be compatible with the **cobas® eplex** RP panel. No potentially interfering substances were found to inhibit the **cobas® eplex** RP panel at the concentrations tested in **Table 37.**

Table 37: List of substances for testing

Potentially interfering substance	Active ingredient	Testing concentration
Control sample matrix[a]	Becton Dickinson UVT	N/A
Transport medium[a]	Copan eSwab (Liquid Amies media)	N/A
Viral transport medium[a]	MicroTest M4	N/A
	MicroTest M4-RT	N/A
	MicroTest M5	N/A
	MicroTest M6	N/A
Flocked swabs	Copan Minitip in UVT	N/A
	Copan Regular Tip in UVT	N/A
Blood (human)	Blood	2% v/v
	Human gDNA	50 ng/rxn
Throat lozenges, oral anesthetic and analgesic	Benzocaine, menthol	26% w/v
Mucin	Purified mucin protein	1% w/v
Nasal sprays or drops	Phenylephrine HCl (Neo-Synephrine®)[b]	1.0% v/v
	Oxymetazoline HCl (Afrin®)	1% v/v
	Sodium chloride	0.8% w/v
Antibacterial, systemic	Tobramycin[c]	1% w/v
Antibiotic, nasal ointment	Mupirocin	2% w/v
Nasal corticosteroids	Beclomethasone	1.5% w/v
	Dexamethasone	1.5% w/v
	Flunisolide	1.5% w/v
	Budesonide (Rhinocort®)	0.9% v/v
	Triamcinolone (Nasacort®)	1.5% w/v
	Fluticasone (Flonase®)	1.5% w/v
ZICAM® Allergy Relief Nasal Gel	Luffa opperculata	1% v/v
	Sulfur	
	Galphimia glauca	

Potentially interfering substance	Active ingredient	Testing concentration
	Histaminum hydrochloricum	
Anti-viral drugs	Zanamivir	550 ng/mL
	Oseltamivir	142 ng/mL
Virus	Cytomegalovirus	1 x 10^5 $TCID_{50}$/mL
Bacteria	*Bordetella parapertussis*	1 x 10^6 CFU/mL
	Corynebacterium diptheriae	
	Haemophilus influenzae	
	Neisseria meningitides	
	Staphylococcus aureus	
	Streptococcus pneumoniae	

[a] Testing of media was done by adding a negative NPS collected in the specified media and diluting in the natural clinical matrix.

[b] At concentrations greater than 1.0% volume/volume in the sample, Phenylephrine HCl was found to inhibit assay performance.

[c] At concentrations greater than 1% weight/volume in the sample, Tobramycin was found to inhibit assay performance.

Supplemental testing of additional potentially interfering substances

Additional performance testing was done on potentially interfering substances which are commonly used for sample collection and transport. To simulate clinical samples, quantified representative viral and bacterial strains were diluted to a concentration near the LoD in a natural clinical matrix (pooled, negative nasopharyngeal swab specimens) and 20 replicates were tested for each substance. Organisms in natural clinical matrix prepared in Viral Transport media were used as a control. All collection/transport media tested for interference as listed in **Table 38** were shown to be compatible with the **cobas® eplex** RP panel.

Table 38: Collection and transport media tested for interference

Potentially Interfering Substance	Result
1x PBS	No interference observed
0.9% Saline	No interference observed
PrimeStore® Molecular Transport Media	No interference observed

Carryover and cross-contamination

The carryover/cross-contamination rate of the **cobas® eplex** RP panel and **cobas® eplex** system was tested in a checkerboard approach by running high positive and negative samples interspersed in all bays of a four-tower **cobas® eplex** system over 5 separate runs on 5 separate days. Quantified parainfluenza virus 3 was prepared in viral transport media at a high concentration (1 x 10^5 $TCID_{50}$/mL, 20,000x LoD) to simulate a clinically relevant high positive and was tested as a representative target organism. Transport media was used to represent negative samples. On each round of testing, 24 **cobas® eplex** RP panel cartridges were evaluated. 100% of parainfluenza 3-positive samples generated a result of Detected and 100% of parainfluenza 3-negative samples generated a parainfluenza 3 result of No Target Detected, indicating no carryover or cross-contamination was observed within bays or between bays with the **cobas® eplex** RP panel when testing consecutively or in adjacent bays.

TROUBLESHOOTING

Table 39: Troubleshooting table

For a complete list of all **cobas® eplex** error messages, please refer to the **cobas® eplex** User Assistance Manual.

Error	Error messages	Description	Re-test recommendations
Test did not start	Cartridge failure The cartridge initialization test failed Cartridge not present Bay heater failure Unknown error Bay main / fluid motor failure Bay over pressured Bay temperature out of range The system was unable to read the cartridge Cartridge inserted doesn't match the serial number of the cartridge scanned The system is not ready to accept the cartridge The system failed to prepare the cartridge for processing	An error that occurs during pre-run checks (cartridge initialization) of the cartridge upon insertion into the bay. Cartridge initialization occurs when the cartridge is first inserted into the bay and takes approximately 90 seconds. Upon completion of cartridge initialization, the cartridge cannot be restarted, but prior to this point, the cartridge can be restarted. To verify cartridge initialization has completed, examine the cartridge label upon removal. If RP cartridge label has been pierced, initialization started and cartridge cannot be re-tested. If the label has not been pierced, follow the recommendation as stated.	1. Remove cartridge from bay. a. Reset bay to clear the error b. Restart cartridge in any available bay 2. If the cartridge is not able to be run on the second try and again generates an error during pre-flight initialization, this indicates an issue with the cartridge. This cartridge should be discarded following laboratory procedures and the sample should be repeated using a new cartridge. Bay(s) should be reset to clear the errors. Please contact Technical support to alert them of the issue If the bay remains in an error state (flashing red) after the cartridge has been removed, then the bay must be reset through the Bay Configuration menu before it can be used to run cartridges.
Test did not finish	Bay heater failure Bay main / fluid motor failure Bay voltage failure Bay sub-system communication timeout Cartridge failure “Bay over pressured Bay auto-calibration failure Bay temperature out of range The system was unable to eject the cartridge from the bay	This type of error occurs during the run, after pre-run checks (cartridge initialization) have finished, and prevents the cartridge from being processed to completion.	Reagents have been consumed and the cartridge cannot be reused. Contact Technical Support and proceed with repeat testing of the sample using a new cartridge. If the bay remains in an error state (flashing red) after the cartridge has been removed, then the bay must be reset through the Bay Configuration menu before it can be used to run cartridges.
Invalid		This is an error that results in no valid results being generated. A test report will be generated, but all targets and internal control will be invalid.	Reagents have been consumed and the cartridge cannot be reused. Contact Technical Support and proceed with repeat testing the sample using a new cartridge.

Technical Support

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

GLOSSARY OF SYMBOLS

Symbol	Description	Symbol	Description
LOT	Batch Code	⌛	Use by date YYYY-MM-DD
⚠	Caution	SN	Serial number
Σ	Contains sufficient for <n> tests	REF	Catalog number
CE	European Union Conformity	☣	Biological risks
IVD	In vitro diagnostic medical device	🌡	Upper limit of temperature
🕮 i	Consult instructions for use	🌡	Lower limit of temperature
EC REP	Authorized representative in the European Community	🌡	Temperature range
🏭	Manufacturer	❗	Irritant, dermal sensitizer, acute toxicity (harmful), narcotic effects, respiratory tract irritation
C. LOT	Cartridge Lot	🔥	Oxidizers
UK CA	UK Conformity Assessed	②	Single Use
UDI	Unique Device Identifier	GTIN	Global Trade Identification Number
🌐	Importer	Roche PN	Roche Part Number

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DOCUMENT REVISION

Document Revision Information	
Doc Rev. 2.0 01/2025	Updated cover page to **cobas**® branding. Correct error in Composition of reagents table. Updated sample loading delivery port to sample inlet in procedure. Clarify language for storage of reagents at up to 25°C. Updated website address to navifyportal.roche.com. Updated phone number. Please contact your local Roche Representative if you have any questions.
Doc Rev. 1.0 09/2024	First publishing for Branchburg based on IFU PI121-F. Updated SDS website information in **Safety** section. Updated references. Removed “All rights reserved.” from the copyright statement. Please contact your local Roche Representative if you have any questions.

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