cobas® eplex

respiratory pathogen panel

Package Insert

For in vitro Diagnostic Use
For Professional Laboratory Use Only

IVD

P/N: 9554998001

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INTENDED USE

The **cobas**® **eplex** respiratory pathogen panel (RP) is a qualitative nucleic acid multiplex in vitro diagnostic test intended for use on the **cobas**® **eplex** system for simultaneous detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals exhibiting signs and symptoms of respiratory tract infection.

The following virus types, subtypes, and bacteria are identified using the **cobas**® **eplex** RP panel: adenovirus, coronavirus 229E, coronavirus HKU1, coronavirus NL63, coronavirus OC43, 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*, *Chlamydia pneumoniae, 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.

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** RP 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.

SUMMARY AND EXPLANATION OF TEST

The **cobas**® **eplex** RP 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 20 respiratory viral targets and four bacterial targets as summarized in Table 1. This test is performed on the **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]

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).[4] Less common causes of influenza-like illness include bacteria such as *Legionella pneumophila* and *Mycoplasma pneumoniae*.[4]

Table 1: Targets Detected by the **cobas**® **eplex** RP panel

Target	Classification (Genome Type)	Seasonal Prevalence*	Most Commonly Infected Demographic
Adenovirus	Adenovirus (DNA)	Late winter to early summer[5]	All ages, immunocompromised[6]
Coronavirus 229E	Coronavirus (RNA)	Winter, spring[7]	All ages[7]
Coronavirus HKU1			
Coronavirus NL63			
Coronavirus OC43			
Middle East Respiratory Syndrome Coronavirus		April through June[8]	All ages[8]
Human Bocavirus	Parvovirus (DNA)	No peak season identified[9]	Infants, children[9]
Human Metapneumovirus	Paramyxovirus (RNA)	Winter[10]	Children, elderly, immunocompromised[11]
Human Rhinovirus/ Enterovirus	Picornavirus (RNA)	Fall, spring[12]/ summer[13]	All ages, immunocompromised[12-14]
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[15]	All ages[16]
Parainfluenza Virus 2		Fall, early winter[15]	
Parainfluenza Virus 3		Spring, summer[15]	
Parainfluenza Virus 4		Fall, early winter[15]	
Respiratory Syncytial Virus A	Paramyxovirus (RNA)	Winter[17,18]	Infants, children, older adults[17,18]
Respiratory Syncytial Virus B			
Bordetella pertussis	Bacterium (DNA)	No peak season[19]	All ages[19]
Chlamydia pneumoniae	Bacterium (DNA)	No peak season[20]	All ages, most common in children[20]
Legionella pneumophila	Bacterium (DNA)	No peak season[21,22]	Older adults, smokers, immunocompromised[21,22]
Mycoplasma pneumoniae	Bacterium (DNA)	Late summer, fall[23]	Children, young adults[23]

* 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.[24] 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.[6,25] 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.[6,26] 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.[6,24] In addition to respiratory infections, adenovirus can also cause gastroenteritis, conjunctivitis, and cystitis.[6,24]

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).[27] Human coronaviruses usually cause mild to moderate upper respiratory infections, but can cause significant disease in the elderly, young children, and immunocompromised individuals.[27-29] 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.[30] 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%.[31]

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.[32,33] 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.[9,32] While most cases are mild, severe respiratory disease has been reported.[9]

Human Metapneumovirus: Human metapneumovirus is a member of the *Paramyxoviridae* virus family and is closely related to RSV.[11] 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.[11] 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.[34]

Human Rhinovirus and Enterovirus: Rhinovirus and enterovirus are closely related RNA viruses in the *Picornaviridae* family.[14] There are more than 100 different serotypes that all share high sequence homology.[35] 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.[12,36] 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.[12,13]

There are 62 non-polio enteroviruses that can cause disease in humans.[14] 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.[14] A 2014 outbreak of enterovirus D68 (EV-D68) resulted in severe respiratory infections, some of which were fatal.[37]

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.[3,38] 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.[39] The two most common Influenza A subtypes infecting humans are H1N1 (including the 2009 Pandemic H1N1 variant) and H3N2, and prevalence varies annually.[38] 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.[40] 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.[41]

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.[42] This strain replaced the H1N1 virus that was previously circulating in humans and is common in both Europe and the U.S.[3,38]

Parainfluenza Virus: The parainfluenza viruses are members of the paramyxovirus family that commonly cause respiratory infections in children.[43] 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.[44]

Respiratory Syncytial Virus: RSV is the most common cause of pediatric viral respiratory infections.[11] 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.[45] 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.[18,46]

***Bordetella pertussis*:** Pertussis, or whooping cough, is a highly contagious, acute respiratory illness that is caused by the gram-negative bacteria *Bordetella pertussis*.[19] Pertussis is known for severe, uncontrollable coughing that makes it hard to breathe, resulting in a "whooping" sound when the person tries to breathe.[47] 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.[48] 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.[47] 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.[49] *B. pertussis* is a notifiable infection in the US and in all EU and EEA member states.[50,51]

Chlamydia pneumoniae: *Chlamydia pneumoniae* is a common cause of upper respiratory infections including atypical pneumonia.[52] *C. pneumoniae* is transmitted person-to-person by respiratory secretions, and outbreaks are common in close contact settings.[20] Infection severity can be mild or result in more severe disease, particularly in high risk populations such as people with heart or lung disease, diabetes, and the elderly.[20,53] The true prevalence of *C. pneumoniae* infections is unknown, but the use of molecular diagnostics has improved detection of this organism, as it is difficult to identify using traditional laboratory methods.[52]

***Legionella pneumophila*:** *Legionella pneumophila* is a bacterium that is found naturally in fresh water, such as lakes, rivers and hot springs, around the world.[21,54] It also grows easily in warm, man-made water sources like hot tubs, cooling towers, and plumbing systems.[21,54] 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.[21] 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.[21,22] 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.[55] *L. pneumophila* is a notifiable infection in the US and in all EU and EEA member states.[56,57]

***Mycoplasma pneumoniae*:** *Mycoplasma pneumonia*e is a bacterium lacking a cell wall and is a major cause of respiratory disease.[23] *M. pneumonia*e is transmitted person-to-person by respiratory droplets and is a common cause of atypical, or walking pneumonia.[58] *M. pneumoniae* is frequently undiagnosed, but is estimated to be involved in up to 30% of respiratory infections.[23] Infection often results in mild illness such as tracheobronchitis, or a chest cold, and is most prevalent in young adults and school-aged

children.[23,58] Outbreaks of *M. pneumoniae* occur mostly in crowded environments, like schools, college dormitories, military barracks, and nursing homes.[58]

PRINCIPLES OF TECHNOLOGY

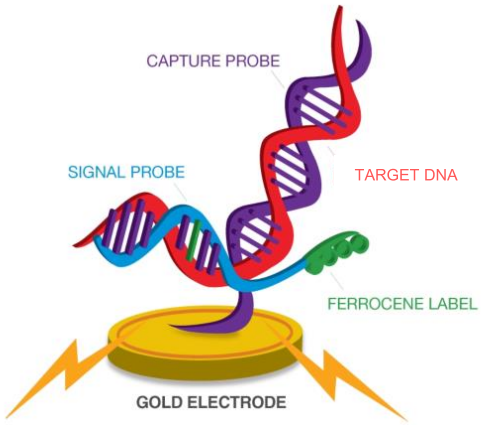
The **cobas**® **eplex** system automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and eSensor technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA hybridization and electrochemical 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 **cobas**® **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: The **cobas**® **eplex** respiratory pathogen panel kit contents

Product	Item number	Components (quantity)	Storage
cobas® **eplex** respiratory pathogen panel	Roche: 9554998001	**cobas**® **eplex** respiratory pathogen panel cartridge (12)	2 – 8 ºC
		Sample Delivery Device – RP panel (12)	2 – 8 ºC

Safety Data Sheets (SDS) for all reagents provided in this kit may be obtained at: https://dialog.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** RP panel cartridges

Composition of Reagents on the cobas® eplex RP 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
Dynol-604	Ribonuclease inhibitor
EDTA	SDS, pH adjusted with HCl
EGTA	Sodium perchlorate
Ethanol	Sorbitane trioleate
Glycerol	Super Q water
Guanidinium Hydrochloride	Trehalose
Lithium Dodecyl Sulfate	Trimethyl terminated, 5cSt
Magnesium Chloride ($MgCl_2$)	Tris-HCl
MTG, pH adjusted with sodium hydroxide + Tween-20	Tween-20
NaCl	Urea

REAGENT STORAGE, STABILITY, AND HANDLING

- Store the **cobas**® **eplex** RP panel kit components at 2 – 8 ºC.
- Do not use RP 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** RP 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** RP 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.
- 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.
- 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** RP panel cartridge contains chemicals that are classified as hazardous. Review the Safety Data Sheets (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 eLabDoc.

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.
- 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).

SPECIMEN COLLECTION, HANDLING, AND STORAGE

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 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 universal 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.
- 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 onto the **cobas**® **eplex** RP panel cartridge, the sample should be processed within 2 hours.
- Do not re-use cartridges or Sample Delivery Devices.
- Do not use a Sample Delivery Device that is empty. Visually verify that the vial contains liquid prior to use by tapping vial on the benchtop. Presence of liquid in the vial indicates that the vial can be used for testing. To prevent damage to the Sample Delivery Device, do not centrifuge the Sample Delivery Device.
- 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** RP 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** RP panel with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove one RP panel cartridge pouch and one Sample Delivery Device from kit packaging.
3. Open RP panel cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the RP panel cartridge.
5. Write the accession ID or place a barcode label with accession ID on the Sample Delivery Device.
6. Vortex the sample for 3-5 seconds.
7. Gently tap the Sample Delivery Device on the counter or benchtop surface to collect liquid that may have adhered to the sides of the vial.
   NOTE: Contents of vial may adhere to side of vial and inside cap during transit. Visually verify presence of liquid inside vial after tapping vial.
8. Unscrew the purple cap from the Sample Delivery Device.
9. Use a calibrated pipette to aspirate 200 µL of sample and pipette into the Sample Delivery Device.
10. Replace purple cap on Sample Delivery Device. Ensure that cap is securely fastened on the Sample Delivery Device.
11. Vortex the Sample Delivery Device for 10 seconds.
    NOTE: This step should be done immediately before loading sample onto cartridge.
12. Remove the white cover from the tip of the Sample Delivery Device cap.
13. Invert the Sample Delivery Device and dispense the entire volume (~350 µL) by squeezing the vial and dispensing the drops into the sample loading port of the RP panel cartridge.
    NOTE: Minimize dispensing of bubbles into sample loading port.

14. Close the sample loading port by sliding the cap over the port and firmly pushing down on the cap to securely seal the sample delivery port.
    NOTE: Bubbles can be present when closing the cap.
15. Scan the RP 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.
16. Insert the RP 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 **cobas**® **eplex** RP 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 RP 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 RP 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 RP panel Detection Report. Test is valid, report results.

Internal Control Result	Explanation	Action
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 RP panel Detection Report. Test is not valid, repeat the test using a new cartridge.

External Controls

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** RP 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 RP 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 RP 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 RP 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 RP panel Detection Report. Test is not valid, repeat test.

Influenza A Results

The **cobas**® **eplex** RP 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.	If subtyping is required, repeat test. If a novel influenza A strain is suspected, repeat test. If result repeats, contact public health or follow laboratory procedures for handling potentially novel influenza A strains.
Influenza A Detected and more than one subtype (H1, H1-2009, or H3) reported as detected.	Sample is co-infected with multiple influenza subtypes. Infection with multiple subtypes of influenza are possible but rare. Contamination has occurred.	Result reported as influenza A and multiple subtypes detected.	Retest recommended to confirm result.

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 RP 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 RP panel External Control Report is generated for an external control that has been pre-defined in the **cobas**® **eplex** RP 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** RP panel cannot reliably differentiate them. If a poliovirus infection is suspected, an **cobas**® **eplex** RP 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** RP panel cannot reliably differentiate them. If differentiation is required, a positive human rhinovirus/enterovirus result may be followed-up using an alternative method.
- 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 without signs and symptoms of respiratory infection.
- Results from this test must be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- 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.
- A result of No Targets Detected on the **cobas**® **eplex** RP panel does not exclude the possibility of viral or bacterial infection. A sample with a result of No Targets Detected may contain respiratory viruses or bacteria not targeted by the **cobas**® **eplex** RP panel.

- Not Detected results may occur due to 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** RP panel should not be used as the sole basis for diagnosis, treatment or other patient management decisions.
- If four or more organisms are detected in a sample, retesting is recommended to confirm polymicrobial result.
- The **cobas**® **eplex** RP panel influenza A subtyping reagents target the influenza A hemagglutinin gene only. The **cobas**® **eplex** RP panel does not detect or differentiate the influenza A neuraminidase gene.
- The performance of this test has not been established for monitoring treatment of seasonal influenza A H1, H3, 2009 H1N1, or RSV infections.
- The performance of this test has not been established for screening of blood or blood products for the presence of seasonal influenza A H1, H3 or 2009 H1N1 viruses.
- 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.
- Recent administration of a live intranasal influenza virus vaccine may cause false positive results for influenza A, H1, H3, 2009 H1N1, and/or influenza B.
- Detection of variant influenza A H3N2 virus (H3N2v) is sequence-dependent based on in silico analysis. For more information, refer to the Analytical Reactivity (Inclusivity) data in this package insert.

ANALYTICAL PERFORMANCE CHARACTERISTICS

Limit of Detection

The limit of detection (LoD), or analytical sensitivity was identified and verified for each viral and bacterial target on the **cobas**® **eplex** RP panel using quantified reference strains or synthetic transcripts. Serial dilutions were prepared in a natural clinical matrix (pooled, negative nasopharyngeal swab 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** RP panel organism is shown in Table 7.

Table 7: 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

Target	Strain	LoD Concentration
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
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
Chlamydia pneumoniae	AR-39	3 x 10^2 $TCID_{50}$/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)

A panel of 115 strains/isolates representing the genetic, temporal, and geographic diversity of each target on the **cobas**® **eplex** RP 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** RP panel organisms.

All of the 115 strains/isolates tested for inclusivity were detected by the **cobas**® **eplex** RP panel. Results of analytical reactivity are shown in Table 8 to Table 22.

Table 8: Analytical Reactivity (Inclusivity) Results for Adenovirus

Note: Adenovirus species B, C, and E are respiratory 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	Ch.79 Type 16	2 x 10^2 $TCID_{50}$/mL	100x
	Compton Type 34	6 x 10^0 $TCID_{50}$/mL	3x
	De Wit Type 14	6 x 10^0 $TCID_{50}$/mL	3x
	Holden Type 35	6 x 10^0 $TCID_{50}$/mL	3x
	Type 3	6 x 10^0 $TCID_{50}$/mL	3x
	Type 11	6 x 10^0 $TCID_{50}$/mL	3x
	Type 21	6 x 10^0 $TCID_{50}$/mL	3x
	WanType 50	2 x 10^1 $TCID_{50}$/mL	10x
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
E	Type 4	2 x 10^0 $TCID_{50}$/mL	1x
F	Type 40 Dugan	3 x 10^3 $TCID_{50}$/mL	3x
	Type 41/ Strain Tak	3 x 10^3 $TCID_{50}$/mL	3x

Table 9: 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 10: 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 11: Analytical Reactivity (Inclusivity) Results for Human Metapneumovirus

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

Table 12: Analytical Reactivity (Inclusivity) Results for Human Rhinovirus/Enterovirus

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

Table 13: 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 a Flu 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/FM/1/47	9 x 10^0 $TCID_{50}$/mL	10x (Influenza A matrix) 10000x (H1 subtype)
	A/New Caledonia/20/1999		3x
	A/NewJersey/8/76		3x Not detected (H1 subtype)[a]
	A/NWS/33		10x (Influenza A matrix) Not detected (H1 subtype)[b]
	A/PR/8/34		3x (Influenza A matrix) Not detected (H1 subtype)[c]
	A/Solomon Islands/3/2006		3x
	A/Taiwan/42/06		30x
Influenza A H3	A/Hong Kong/8/68	1.5 x 10^2 $TCID_{50}$/mL	3x
	A/PortChalmers/1/73		3x
	A/Nanchang/933/95		3x
	A/Victoria/3/75		3x
	A/Wisconsin/67/05		3x
Influenza A H1-2009	A/California/7/2009	1 x 10^0 $TCID_{50}$/mL	10x
	A/Mexico/4108/09	3 x 10^{-1} $TCID_{50}$/mL	3x
	A/NY/02/2009	1 x 10^0 $TCID_{50}$/mL	10x
	A/Swine NY/03/2009	3 x 10^{-1} $TCID_{50}$/mL	3x
	A/Swine/Iowa/15/30	3 x 10^{-1} $TCID_{50}$/mL	3x (Influenza A matrix) 100,000x (H1-2009 subtype)[d]
	A/Virginia/ATCC1/2009	1 x 10^0 $TCID_{50}$/mL	10x
	A/Virginia/ATCC2/2009	1 x 10^1 $TCID_{50}$/mL	100x[e]
	A/Virginia/ATCC3/2009	1 x 10^2 $TCID_{50}$/mL	1,000x[e]

[a] H1-2009 subtype was detected in this seasonal Influenza A H1 strain at 30x LoD

[b] *In silico* analysis revealed little homology between this non-contemporary influenza strain sequence and the H1 Signal Probe/Capture Probe sequences.

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

[d] *In silico* analysis revealed little homology between the influenza strain sequence and the H1 or H1-2009 primers, signal probes and capture probes sequences.

[e] No sequence data was available to investigate poor inclusivity of the influenza A H1-2009 A/Virginia/ATCC2/2009 and A/Virginia/ATTC3/2009 strains.

Table 14: 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/Denver/1/57	1.6 x 10^2 $CEID_{50}$/mL (Influenza A matrix) 1.6 x 10^8 $CEID_{50}$/mL (H1 subtype)
	A/Mal/302/54	1.58 x 10^2 $CEID_{50}$/mL (Influenza A matrix) 1.58 x 10^5 $CEID_{50}$/mL (H1 subtype)
Influenza A H3	A/Aichi/2/68 H3N2	1.58 x 10^3 $CEID_{50}$/mL
	Alice (vaccine) A/England/42/72	5 x 10^0 EID_{50}/mL (Influenza A matrix) 5 x 10^1 EID_{50}/mL (H3 subtype)
	MRC-2 Recombinant Strain	8.89 x 10^2 $CEID_{50}$/mL (Influenza A matrix) 8.89 x 10^3 $CEID_{50}$/mL (H3 subtype)
Influenza A H1N1	A/Washington/24/2012 (A/H1 pdm09)	3.16 x 10^3 EID_{50}/mL (Influenza A matrix) 3.16 x 10^2 EID_{50}/mL (H1-2009 subtype)
Influenza A H1N2	Kilbourne F63: A/NWS/34 (HA) x A/Rockefeller Institute/5/57 (NA), Reassortant NWS-F- Matrix	8.89 x 10^1 $CEID_{50}$/mL (Influenza A matrix) Not detected (H1-2009 subtype)[a]
Influenza A H5N8	A/Gyrfalcon/Washington/41088-6/2014 BPL	1.58 x 10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[b]
Influenza A H5N2	A/Northern Pintail/Washington/40964/2014 BPL	2.51 x 10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[b]
Influenza A H7N9	A/ANHUI/1/2013	7.94 x 10^3 EID_{50}/mL (Influenza A matrix) No subtype detected[c]
Influenza A H3N2v	A/Indiana/21/2012	2.51 x 10^4 EID_{50}/mL (Influenza A matrix and H3 subtype)

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

[b] Detection of the H5 Subtype not expected

[c] Detection of the H7 Subtype not expected

NOTE: $CEID_{50}$/mL= Chicken Embryo Infectious Dose; EID_{50}/mL= Egg Infectious Dose

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 15: 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

Influenza A Subtype	Host	Strain	GenBank ID	Simulated cobas® eplex Result
		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
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

Influenza A Subtype	Host	Strain	GenBank ID	Simulated cobas® eplex Result
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	
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

Influenza A Subtype	Host	Strain	GenBank ID	Simulated cobas® eplex Result
			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 16: Analytical Reactivity (Inclusivity) Results for Influenza B

Influenza B Subtype	Strain	Concentration	Multiple of LoD Detected
Influenza B	B/Allen/45	1×10^{0} $TCID_{50}$/mL	10x
	B/GL/1739/54	3×10^{-1} $TCID_{50}$/mL	3x
	B/Hong Kong/5/72	1×10^{1} $TCID_{50}$/mL	100x
	B/Lee/40	3×10^{-1} $TCID_{50}$/mL	3x
	B/Malaysia/2506/04	3×10^{-1} $TCID_{50}$/mL	3x
	B/Maryland/1/59	1×10^{1} $TCID_{50}$/mL	100x
	B/Taiwan/2/62	1×10^{1} $TCID_{50}$/mL	100x

Table 17: Analytical Reactivity (Inclusivity) Results for Parainfluenza Virus

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

Table 18: Analytical Reactivity (Inclusivity) Results for Respiratory Syncytial Virus

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

Table 19: Analytical Reactivity (Inclusivity) Results for Bordetella pertussis

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

Table 20: Analytical Reactivity (Inclusivity) Results for Chlamydia pneumoniae

	Strain	Concentration	Multiple of LoD Detected
Chlamydia pneumoniae	CWL-029	9×10^2 $TCID_{50}$/mL	3x
	TWAR strain 2043		3x

Table 21: Analytical Reactivity (Inclusivity) Results for Legionella pneumophila

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

Table 22: Analytical Reactivity (Inclusivity) Results for Mycoplasma pneumoniae

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

Analytical Specificity (Cross-Reactivity and Exclusivity)

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) of quantified strains diluted in transport media. Table 23 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 23: 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
Parainfluenza Virus 4	Type 4a	1 x 10^5 $TCID_{50}$/mL	Not observed

Target	Strain	Concentration	Cross-Reactivity Results
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
Chlamydia pneumoniae	AR-39	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 or CCU/mL for bacterial strains, or 1 x 10^6 copies/mL) by diluting quantified strains in transport media. Table 24 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 24: 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 PFU/mL	Not observed
Candida glabrata	ATCC 15126	1 x 10^6 PFU/mL	Not observed
Corynebacterium diphtheriae	ATCC 13812	1 x 10^6 PFU/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
*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

Target	Strain	Concentration	Cross-Reactivity Results
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 25 to Table 32 below.

Table 25: 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)
Low Positive 1x LoD 2 x 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 26: 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 x 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 x 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 27: Percent Agreement for Human Metapneumovirus (hMPV)

hMPV Concentration	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Moderate Positive 3x LoD 6.75 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 2.25 x 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 28: 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 29: Percent Agreement for Influenza A H3

Influenza A H3 Concentration	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Moderate Positive 3x LoD 1.5×10^2 $TCID_{50}$/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 5×10^1 $TCID_{50}$/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 30: Percent Agreement for Parainfluenza Virus (PIV) 1

PIV 1 Concentration	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Moderate Positive 3x LoD 1.2×10^0 $TCID_{50}$/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 4×10^{-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 31: Percent Agreement for Respiratory Syncytial Virus (RSV) A

RSV A Concentration	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Moderate Positive 3x LoD 4.5×10^0 $TCID_{50}$/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 1.5×10^0 $TCID_{50}$/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 32: 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)

Chlamydia pneumoniae Performance

To demonstrate performance of *C. pneumoniae*, 6 clinical NPS samples with *C. pneumoniae* detected by the comparator method, 52 contrived samples with *C. pneumoniae* spiked into individual negative clinical NPS samples at or above the limit of detection, and 274 contrived samples that did not contain *C. pneumoniae* were tested with the **cobas**® **eplex** RP panel at 5 external testing sites. Percent positive agreement was calculated by dividing the number of true positive (TP) results by the sum of TP and false negative (FN) results. A true positive result was one where the detected **cobas**® **eplex** RP panel result matched the known contrived result or the result of the comparator method (an FDA cleared multiplexed molecular respiratory pathogen panel). The **cobas**® **eplex** RP panel detected *C. pneumoniae* in 55 of 58 samples resulting in positive percent agreement of 94.8% (95% Confidence Interval: 85.9% - 98.2%). Negative percent agreement was calculated by dividing the number of true negative (TN) results by the sum of TN and false positive (FP) results. The negative percent agreement was 100% (95% Confidence Interval: 98.6%-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 33 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 33: 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

C. pneumoniae Co-Detections

Detection of *C. pneumoniae* in samples when more than one clinically relevant viral and/or bacterial organism is present was evaluated with the **cobas**® **eplex** RP panel using a natural clinical matrix (pooled, negative nasopharyngeal swab samples) spiked with *C. pneumoniae* at a low concentration (3x LoD) and the second organism at a high concentration (1 x 10^5 $TCID_{50}$/mL for virus and 1 x 10^6 CFU/mL for bacteria). Table 34 contains the results of *C. pneumoniae* co-detection testing which demonstrated the ability of the **cobas**® **eplex** RP panel to detect C. pneumoniae at low concentrations when a second viral or bacterial pathogen is present at high concentration.

Table 34: C. pneumoniae Detection in Co-Infections

Organism 1	Low Titer	Multiple of LoD	Organism 2	High Titer
Chlamydia pneumoniae	9 x 10^2 $TCID_{50}$/mL	3x	*Legionella pneumophila*	1 x 10^6 CFU/mL
Chlamydia pneumoniae	9 x 10^2 $TCID_{50}$/mL	3x	*Bordetella pertussis*	1 x 10^6 CFU/mL
Chlamydia pneumoniae	9 x 10^2 $TCID_{50}$/mL	3x	*Mycoplasma pneumoniae*	1 x 10^6 CCU/mL
Chlamydia pneumoniae	9 x 10^2 $TCID_{50}$/mL	3x	Human Rhinovirus	1 x 10^5 $TCID_{50}$/mL
Chlamydia pneumoniae	9 x 10^2 $TCID_{50}$/mL	3x	Influenza A H3	1 x 10^5 $TCID_{50}$/mL

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 35.

Table 35: 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

Potentially Interfering Substance	Active Ingredient	Testing Concentration
	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	
	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.

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 36: 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 MAS or 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
	Batch Code		Use by date YYYY-MM-DD
	Caution		Serial number
	Contains sufficient for <n> tests		Catalog number
	European Union Conformity		Biological risks
	In vitro diagnostic medical device		Upper limit of temperature
	Consult instructions for use		Lower limit of temperature
	Authorized representative in the European Community		Temperature range
	Manufacturer		Irritant, dermal sensitizer, acute toxicity (harmful), narcotic effects, respiratory tract irritation
	Cartridge Lot		Oxidizers
	UK Conformity Assessed		Single Use
	Unique Device Identifier		Global Trade identification Number
	Importer		Roche Part Number

REFERENCES

1. John Hopkins Medicine. Upper respiratory infection (URI or common cold). Accessed: 27 Aug 2024. https://www.hopkinsmedicine.org/health/conditions-and-diseases/upper-respiratory-infection-uri-or-common-cold.
2. European Centre for Disease Prevention and Control. Seasonal influenza. Accessed: 27 Aug 2024. https://www.ecdc.europa.eu/en/seasonal-influenza.
3. World Health Organization. Influenza (seasonal). Published: 3 Oct 2023; Accessed: 27 Aug 2024. https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal).
4. Mossad SB. Upper respiratory tract infections. Published: Aug 2013; Accessed: 27 Aug 2024. https://teachmemedicine.org/cleveland-clinic-upper-respiratory-tract-infections/.
5. University of Rochester Medical Center. Adenovirus infections in children. Accessed: 27 Aug 2024. https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=90&contentid=p02508.
6. Centers for Disease Control and Prevention. About adenovirus. Updated: 14 May 2024; Accessed: 27 Aug 2024. https://www.cdc.gov/adenovirus/about/index.html.
7. Gaunt ER, Hardie A, Claas EC, Simmonds P, Templeton KE. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. *J Clin Microbiol*. 2010;48:2940-7. PMID: 20554810.
8. Sharif-Yakan A, Kanj SS. Emergence of MERS-CoV in the Middle East: Origins, transmission, treatment, and perspectives. *PLoS Pathog*. 2014;10:e1004457. PMID: 25474536.
9. Meriluoto M, Hedman L, Tanner L, et al. Association of human bocavirus 1 infection with respiratory disease in childhood follow-up study, Finland. *Emerg Infect Dis*. 2012;18:264-71. PMID: 22305021.
10. Centers for Disease Control and Prevention. About human metapneumovirus. Updated: 11 Apr 2024; Accessed: 27 Aug 2024. https://www.cdc.gov/human-metapneumovirus/about/index.html.
11. Fabre V, Auwaerter PG. Human metapneumovirus. Last updated: 8 Mar 2020; Accessed: 27 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540614/all/Metapneumovirus.
12. Anzueto A, Niederman MS. Diagnosis and treatment of rhinovirus respiratory infections. *Chest*. 2003;123:1664-72. PMID: 12740288.
13. Auwaerter P. Rhinovirus. Last updated: 18 Mar 2023; Accessed: 27 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540476/all/Rhinovirus?q=rhinovirus&ti=0#0.
14. Fabre V, Auwaerter P. Enterovirus. Last updated: 5 Sept 2020; Accessed: 27 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540204/all/Enterovirus?q=enterovirus&ti=0#0.
15. Henrickson KJ. Parainfluenza viruses. *Clin Microbiol Rev*. 2003;16:242-64. PMID: 12692097.
16. Schomacker H, Schaap-Nutt A, Collins PL, Schmidt AC. Pathogenesis of acute respiratory illness caused by human parainfluenza viruses. *Curr Opin Virol*. 2012;2:294-9. PMID: 22709516.
17. Mahony JB. Detection of respiratory viruses by molecular methods. *Clin Microbiol Rev*. 2008;21:716-47. PMID: 18854489.
18. Resch B, Kurath S, Manzoni P. Epidemiology of respiratory syncytial virus infection in preterm infants. *Open Microbiol J*. 2011;5:135-43. PMID: 22262986.
19. Havers FP, Moro PL, Hariri S, Skoff T. Chapter 16: Pertussis [14th edition of Pink Book published Aug 2021]. Reviewed: 12 Apr 2024; Accessed: 27 Aug 2024. https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-16-pertussis.html.
20. Centers for Disease Control and Prevention. *Chlamydia pneumoniae* infection: Causes and how it spreads. Updated: 30 Jan 2024; Accessed: 27 Aug 2024. https://www.cdc.gov/cpneumoniae/causes/index.html.
21. World Health Organization. Legionellosis. Published: 6 Sept 2022; Accessed: 27 Aug 2024. https://www.who.int/en/news-room/fact-sheets/detail/legionellosis.
22. Centers for Disease Control and Prevention. About Legionnaires' disease. Updated: 29 Jan 2024; Accessed: 27 Aug 2024. https://www.cdc.gov/legionella/about/index.html.
23. Auwaerter P. *Mycoplasma pneumoniae*. Last updated: 13 Jun 2024; Accessed: 27 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540373/all/Mycoplasma%20pneumoniae.
24. Spacek LA. Adenovirus. Updated: 5 Feb 2023; Accessed: 28 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540009/all/Adenovirus?q=adenovirus&ti=0#0.
25. Scott MK, Chommanard C, Lu X, et al. Human adenovirus associated with severe respiratory infection, Oregon, USA, 2013-2014. *Emerg Infect Dis*. 2016;22:1044-51. PMID: 27191834.
26. Radin JM, Hawksworth AW, Blair PJ, et al. Dramatic decline of respiratory illness among US military recruits after the renewed use of adenovirus vaccines. *Clin Infect Dis*. 2014;59:962-8. PMID: 24991024.
27. Centers for Disease Control and Prevention. Human coronavirus types. Last updated: 15 Feb 2020; Accessed: 28 Aug 2024. https://archive.cdc.gov/www_cdc_gov/coronavirus/types.html.

28. European Centre for Disease Prevention and Control. Coronaviruses. Accessed: 28 Aug 2024. https://www.ecdc.europa.eu/en/coronaviruses.
29. Liu DX, Liang JQ, Fung TS. Human coronavirus-229E, -OC43, -NL63, and -HKU1 (*Coronaviridae*). *Encyclopedia of Virology*. 2021:428–40.
30. Centers for Disease Control and Prevention. Archived SARS-CoV page. Last reviewed: 6 Dec 2017; Accessed: 29 Aug 2024. https://archive.cdc.gov/www_cdc_gov/sars/index.html.
31. European Centre for Disease Prevention and Control. Factsheet about Middle East respiratory syndrome coronavirus (MERS-CoV). Accessed: 28 Aug 2024. https://www.ecdc.europa.eu/en/middle-east-respiratory-syndrome-coronavirus/factsheet.
32. Hustedt JW, Vazquez M. The changing face of pediatric respiratory tract infections: How human metapneumovirus and human bocavirus fit into the overall etiology of respiratory tract infections in young children. *Yale J Biol Med*. 2010;83:193-200. PMID: 21165338.
33. Milder E, Arnold JC. Human metapneumovirus and human bocavirus in children. *Pediatr Res*. 2009;65:78R-83R. PMID: 19190535.
34. Hermos CR, Vargas SO, McAdam AJ. Human metapneumovirus. *Clin Lab Med*. 2010;30:131-48. PMID: 20513544.
35. Tapparel C, Junier T, Gerlach D, et al. New respiratory enterovirus and recombinant rhinoviruses among circulating picornaviruses. *Emerg Infect Dis*. 2009;15:719-26. PMID: 19402957.
36. Jacobs SE, Lamson DM, St George K, Walsh TJ. Human rhinoviruses. *Clin Microbiol Rev*. 2013;26:135-62. PMID: 23297263.
37. European Centre for Disease Prevention and Control. Enterovirus 68 detected in the USA, Canada and Europe – Second update 25 November 2014. Stockholm: ECDC; 2014.
38. Centers for Disease Control and Prevention. Types of influenza viruses. Last reviewed: 30 Mar 2023; Accessed: 28 Aug 2024. http://www.cdc.gov/flu/about/viruses/types.htm.
39. European Centre for Disease Prevention and Control. Factsheet about seasonal influenza. Last updated: 12 Apr 2022; Accessed: 28 Aug 2024. https://www.ecdc.europa.eu/en/seasonal-influenza/facts/factsheet.
40. Short KR, Richard M, Verhagen JH, et al. One health, multiple challenges: The inter-species transmission of influenza A virus. *One Health*. 2015;1:1-13. PMID: 26309905.
41. Auwaerter PG. Influenza. Last updated: 10 Sept 2023; Accessed: 28 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540285/all/Influenza?q=influenza&ti=0#0.
42. Centers for Disease Control and Prevention. Update: influenza activity - United States, 2009-10 season. *MMWR Morb Mortal Wkly Rep*. 2010;59:901-8. PMID: 20671661.
43. Centers for Disease Control and Prevention. About human parainfluenza viruses (HPIVs). Reviewed: 5 Jun 2024; Accessed: 28 Aug 2024. https://www.cdc.gov/parainfluenza/about/index.html.
44. Auwaerter PG. Parainfluenza virus. Last updated: 8 Aug 2022; Accessed: 28 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540415/all/Parainfluenza_virus?q=parainfluenza&ti=0#0.
45. Centers for Disease Control and Prevention. Clinical overview of RSV. Reviewed: 3 Jul 2024; Accessed: 29 Aug 20024. https://www.cdc.gov/rsv/hcp/clinical-overview/index.html.
46. Walsh EE, McConnochie KM, Long CE, Hall CB. Severity of respiratory syncytial virus infection is related to virus strain. *J Infect Dis*. 1997;175:814-20. PMID: 9086135.
47. Centers for Disease Control and Prevention. Symptoms of whooping cough. Reviewed: 2 Apr 2024; Accessed: 29 Aug 2024. https://www.cdc.gov/pertussis/signs-symptoms/index.html.
48. Auwaerter P. *Bordetella* species. Last updated: 8 May 2023; Accessed: 28 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540061/all/Bordetella_species.
49. European Centre for Disease Prevention and Control. Expert consultation on pertussis. Published: 12 May 2014; Accessed 29 Aug 2024. https://www.ecdc.europa.eu/en/publications-data/expert-consultation-pertussis.
50. Centers for Disease Control and Prevention. Pertussis surveillance and trends. Updated: 28 Aug 2024; Accessed: 28 Aug 2024. https://www.cdc.gov/pertussis/php/surveillance/index.html.
51. European Centre for Disease Prevention and Control. Surveillance and disease data for pertussis. Accessed 29 Aug 2024. https://www.ecdc.europa.eu/en/pertussis/surveillance-and-disease-data.
52. Fabre V. *Chlamydia pneumoniae*. Last updated: 8 Feb 2023; Accessed: 28 Aug 2024. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540117/all/Chlamydophila%20pneumoniae.
53. Centers for Disease Control and Prevention. Risk factors for pneumonia. Accessed: 29 Aug 2024. https://www.cdc.gov/pneumonia/risk-factors/index.html.
54. European Centre for Disease Prevention and Control. Facts about Legionnaires' disease. Accessed: 28 Aug 2024. https://www.ecdc.europa.eu/en/legionnaires-disease/facts.
55. Centers for Disease Control and Prevention. How *Legionella* spreads. Reviewed: 29 Jan 2024; Accessed: 28 Aug 2024. https://www.cdc.gov/legionella/causes/index.html.

56. Centers for Disease Control and Prevention. Legionellosis surveillance and trends. Reviewed: 31 Jan 2024; Accessed: 28 Aug 2024. https://www.cdc.gov/legionella/php/surveillance/index.html.
57. European Centre for Disease Prevention and Control. Surveillance reports on Legionnaires' disease. Accessed: 29 Aug 2024. https://www.ecdc.europa.eu/en/legionnaires-disease/surveillance-and-disease-data/surveillance.
58. Centers for Disease Control and Prevention. *Mycoplasma pneumoniae* infection: Causes and how it spreads. Reviewed: 27 Dec 2023; Accessed: 29 Aug 2024. https://www.cdc.gov/mycoplasma/causes/index.html.

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