ePlex®
Respiratory Pathogen Panel 2
Package Insert

For Use Under the Emergency Use Authorization Only

EUA

For *in vitro* Diagnostic Use Only
For Prescription Use Only

Designed For the Patient, Optimized For the Lab®

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TABLE OF CONTENTS

Intended Use 4
Summary and Explanation of Test 5
Summary of Detected Organisms 6
Principles of Technology 8
Materials Provided 9
Reagent Storage, Stability, and Handling 9
Materials Not Provided 9
- Equipment 9
- Consumables 9

Warnings and Precautions 10
- General 10
- Safety 10
- Laboratory 11

Specimen Collection, Handling, and Storage 11
Procedure 12
- Procedural Notes 12
- Detailed Procedure 12

Quality Control 13
- Internal Controls 13
- External Controls 14

Results 14
- Influenza A Results 14

Test Reports 15
- Detection Report 15
- External Control Report 16
- Summary Report 16

Limitations of the Procedure 16
- Conditions of Authorization for the Laboratory 18

Performance Characteristics 18
- ePlex RP and RP2 Panels 18

Clinical performance 19
Expected values 19
Performance characteristics ..... **Error! Bookmark not defined.**
Clinical performance 21
- Clinical Performance of the ePlex RP2 Panel and SARS-CoV-2 21
- RP2 Clinical Study ePlex Instrument Performance 23
- Clinical Performance of the ePlex RP Panel 23
- Comparator Method 23
- Prospective Clinical Samples 23
- Prospective Clinical Performance 24
- Retrospective Clinical Samples 25
- Retrospective Clinical Performance 26
- Contrived Sample Performance 27
- Clinical and Contrived Sample Performance by Target 27
- Co-detections in Prospective Clinical Samples 31
- Clinical Study ePlex RP Panel Instrument Performance 34

Analytical Performance Characteristics 34
- Limit of Detection for SARS-CoV-2 34
- Limit of Detection for All other RP2 Panel Targets 34
- Analytical Reactivity (Inclusivity) 35
- Reactivity of SARS-CoV-2 Assays 35
- Inclusivity of All Other RP2 Targets 36
- Supplemental Analytical Reactivity (Inclusivity) for Influenza A 39
- Analytical Specificity (Cross-Reactivity and Exclusivity) 43
- In silico Analysis of the ePlex RP2 Panel SARS-CoV-2 Assays 44
- Analytical Specificity (Cross-Reactivity and Exclusivity) of Other RP2 Panel Targets 45
- Reproducibility 47
- Samples with Co-Detected Organisms 51
- Sample Matrix Equivalency 53
- Interfering Substances 53
- Carryover and Cross-contamination 54

Troubleshooting....54
Technical Support....55
Glossary of Symbols....56
References....56
Trademarks....59
Patent Information....59

INTENDED USE

The ePlex® Respiratory Pathogen Panel 2 (ePlex RP2 Panel) is a multiplexed nucleic acid in vitro diagnostic test intended for use on the ePlex Instrument for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms, including nucleic acid from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), in nasopharyngeal swabs (NPS) eluted in viral transport media obtained from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and the targeted respiratory viral and bacterial organisms can be similar. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform moderate or high complexity tests.

The ePlex RP2 Panel is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following virus types, subtypes, and bacteria: adenovirus, coronavirus (229E, HKU1, NL63, OC43), SARS-CoV-2, 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, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*.

SARS-CoV-2 RNA and nucleic acids from the other respiratory viral and bacterial organisms identified by this test are generally detectable in NPS specimens during the acute phase of infection. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and/or symptoms of respiratory infection aids in the diagnosis of respiratory infection when used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results are indicative of active infection with the identified respiratory pathogen but do not rule out infection or co-infection with non-panel organisms. The agent detected by the ePlex RP2 Panel may not be the definite cause of disease.

Laboratories within the United States and its territories are required to report all results for SARS-CoV-2 to the appropriate public health authorities.

Negative results for SARS-CoV-2 and other organisms on the ePlex RP2 Panel may be due to infection with pathogens that are not detected by this test, or lower respiratory tract infection that may not be detected by a nasopharyngeal swab specimen. Negative results do not preclude infection with SARS-CoV-2 or other organisms on the ePlex RP2 Panel and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

Negative results for other organisms detected by the test may require additional laboratory testing (e.g., bacterial and viral culture, immunofluorescence and radiography) when evaluating a patient with possible respiratory tract infection.

Testing with the ePlex RP2 Panel is intended for use by qualified laboratory personnel who have been trained and are proficient in performing testing on the ePlex system. The ePlex RP2 Panel is only for use under the Food and Drug Administration's Emergency Use Authorization.

Due to the genetic similarity between human rhinovirus and enterovirus, the ePlex RP2 Panel cannot reliably differentiate them. If differentiation is required, an ePlex RP2 Panel positive human

rhinovirus/enterovirus result should be followed-up using an alternative method (e.g., cell culture or sequence analysis).

Performance characteristics for influenza A were established when influenza A H1-2009 and A H3 were the predominant influenza A viruses in circulation. Performance of detecting influenza A may vary if other influenza A strains are circulating or a novel influenza A virus emerges. 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 departments for testing. Viral culture should not be attempted in these cases unless a BSL-3+ facility is available to receive and culture specimens.

SUMMARY AND EXPLANATION OF TEST

The ePlex RP2 Panel is an automated qualitative nucleic acid multiplex *in vitro* diagnostic test for simultaneous detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) collected in viral transport media (VTM). The test is able to detect 16 respiratory viral targets and 2 bacterial targets as summarized in **Table 1**. This test is performed on ePlex instrument.

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] Influenza viruses have a peak season in the winter months in the northern hemisphere and the severity of the flu season varies each year based on the particular strain or strains that are in circulation and how effective the vaccine is for that year.[2] Globally, seasonal influenza results in about 3-5 million severe cases and 250,000 – 500,000 deaths annually.[3] In late 2019, a novel coronavirus was identified in Wuhan, China. The disease caused by this novel coronavirus was initially called “2019 novel coronavirus” or “2019-nCoV” and was later renamed Coronavirus Disease 2019, or COVID-19.[4] As of July, 2020, cases have been identified in 188 countries around the world with over 16 million cases and 655,000 deaths.[5]

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).[6] Less common causes of influenza-like illness include bacteria such as *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*.[6]

Table 1: Targets Detected by the ePlex RP2 Panel

Target	Classification (Genome Type)	Seasonal Prevalence*	Most Commonly Infected Demographic
Adenovirus (A-F)	Adenovirus (DNA)	Late winter to early summer[7]	All ages, immunocompromised[8]
Coronavirus (229E, HKU1, NL63, OC43)	Coronavirus (RNA)	Winter, spring[9]	All ages[9]
SARS-CoV-2	Coronavirus (RNA)	Unknown[4]	Not established[4]
Human Metapneumovirus	Paramyxovirus (RNA)	Winter[10]	Children, elderly, immunocompromised[11]

Target	Classification (Genome Type)	Seasonal Prevalence*	Most Commonly Infected Demographic
Human Rhinovirus/ Enterovirus	Picornavirus (RNA)	Fall, spring[12]/ Summer[13]	All ages, immunocompromised[12, 13, 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			
Chlamydia pneumoniae	Bacterium (DNA)	No peak season[19]	All ages, most common in children[19]
Mycoplasma pneumoniae	Bacterium (DNA)	Late summer, fall[20]	Children, young adults[21]

* 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.[22] 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.[8] 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.[8, 23] Adenovirus infections generally cause mild illness but can result in severe disease in infants or in immunocompromised patients, particularly in hematopoietic stem cell transplant recipients.[8, 22] In addition to respiratory infections, adenovirus can also cause gastroenteritis, conjunctivitis, and cystitis.[8, 22] Adenovirus species A, D, and F are not typically associated with respiratory infections.

Coronavirus: Human coronaviruses usually cause mild to moderate upper respiratory infections but can cause significant disease in the elderly, young children, and immunocompromised individuals.[24, 25] Infection with coronaviruses 229E, HKU1, NL63, and OC43 is common worldwide.

SARS-CoV-2: In late 2019, a novel coronavirus was identified in Wuhan, China. The disease caused by this novel coronavirus was initially called “2019 novel coronavirus” or “2019-nCoV” and was later renamed Coronavirus Disease 2019, or COVID-19.[4] This novel coronavirus was named Severe Acute Respiratory Syndrome Coronavirus, or SARS-CoV-2 due to genetic similarity to the coronavirus responsible for an outbreak in 2003.[26] As of July 2020, cases have been identified in 188 countries around the world with over 16 million cases and 655,000 deaths.[5]

Human Metapneumovirus: Human metapneumovirus is a member of the paramyxovirus 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 HIV or cardiac disease; it can also cause more severe disease in immunocompromised adults, especially those with COPD (chronic obstructive pulmonary disease), asthma, cancer, or in transplant patients.[26]

Human Rhinovirus and Enterovirus: Rhinovirus and enterovirus are closely related RNA viruses in the *Picornaviridae* family.[13, 14] There are more than 100 different serotypes that all share high sequence homology.[25] 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, 29] 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.[30]

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, 31] 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.[32] The two most common influenza A subtypes infecting humans are H1N1 (including the 2009 Pandemic H1N1 variant) and H3N2, and prevalence varies annually.[33] 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.[33] 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.[34]

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.[31] This strain replaced the H1N1 virus that was previously circulating in humans and is common in both Europe and the U.S. [31, 33]

Parainfluenza Virus: The parainfluenza viruses are members of the paramyxovirus family that commonly cause respiratory infections in children.[35] 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 patients, such as those with cystic fibrosis or transplant recipients.[36]

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.[37] 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.[17, 38]

Chlamydia pneumoniae (formerly known as Chlamydophila pneumoniae): *Chlamydia pneumoniae* is a common cause of upper respiratory infections including atypical pneumonia.[39] *C. pneumoniae* is transmitted person-to-person by respiratory secretions and outbreaks are common in close contact settings.[19] 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.[19, 40] 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.[40]

***Mycoplasma pneumoniae*:** *Mycoplasma pneumonia*e is a bacterium lacking a cell wall and is a major cause of respiratory disease.[21] *M. pneumonia*e is transmitted person-to-person by respiratory droplets and is a common cause of atypical, or walking pneumonia.[41] *M. pneumoniae* is frequently undiagnosed but is estimated to be involved in up to 30% of respiratory infections.[120] Infection often results in mild illness such as tracheobronchitis, or a chest cold, and is most prevalent in young adults and school-aged children.[22, 41] Outbreaks of *M. pneumoniae* occur mostly in crowded environments, like schools, college dormitories, military barracks, and nursing homes.[41]

PRINCIPLES OF TECHNOLOGY

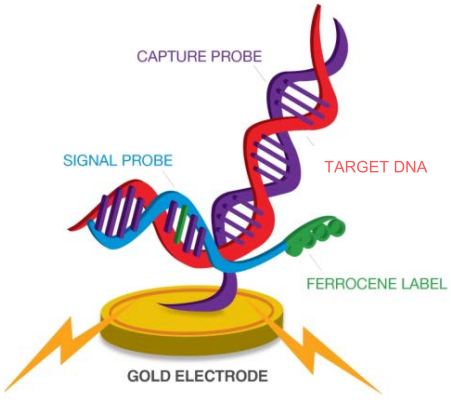
The True Sample-to-Answer Solution ePlex instrument automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and GenMark's eSensor® technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA hybridization and electrochemical detection, which is highly specific and is not based on fluorescent or optical detection.

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

A sample is loaded onto the 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 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 True Sample-to-Answer Solution*® ePlex Respiratory Pathogen Panel 2 Kit Contents

Product	Item number	Components (quantity)	Storage
ePlex Respiratory Pathogen Panel 2	EA001222	ePlex Respiratory Pathogen Panel 2 Cartridge (12)	2–8 ºC

The ePlex RP2 Panel reagents are shipped at room temperature; upon receipt, reagents should be stored at 2-8 °C. Safety Data Sheets (SDS) for all reagents provided in this kit may be obtained at https://www.genmarkdx.com/support/safety-data-sheets-sds/. For paper copies, please contact GenMark Customer Service at CustomerService@genmarkdx.com.

REAGENT STORAGE, STABILITY, AND HANDLING

- Store the ePlex RP2 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

- GenMark ePlex instrument and Software
- Pipettes calibrated to deliver 200 µL
- Vortex mixer
- Printer (optional) - See ePlex Operator Manual for compatibility guidelines

Consumables

- Pipette tips, aerosol resistant, RNase/DNase-free
- Disposable, powder free gloves

- 10% bleach for decontamination of appropriate surfaces
- 70% ethanol or isopropyl alcohol

WARNINGS AND PRECAUTIONS

General

- For use under Emergency Use Authorization Only.
- For *in vitro* diagnostic use only.
- This test has not been FDA cleared or approved.
- This test has been authorized by FDA under an EUA for use by authorized laboratories.
- This test has been authorized only for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms, including nucleic acid from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2).
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
- A trained healthcare professional should carefully interpret the results from the ePlex RP2 Panel in conjunction with a patient's signs, 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 diagnosis of respiratory infection.
- Laboratories within the United States and its territories are required to report all results for SARS-CoV-2 to the appropriate public health authorities.
- Do not reuse ePlex RP2 Panel kit components.
- Do not use reagents beyond the expiration date printed on the labeling.
- Do not use a reagent that is damaged.
- Follow the procedure as described in this package insert. Read all instructions before starting the test. Any deviation from the procedures and guidelines may affect optimal test performance.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.

Safety

- Handle all specimens and waste materials as if they were capable of transmitting infectious agents in accordance with Universal Precautions. Observe safety guidelines such as those outlined in CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories,* CLSI Document M29 *Protection of Laboratory Workers from Occupationally Acquired Infections*, or other appropriate guidelines.
- Do not eat, smoke, drink, apply cosmetics, or handle contact lenses in areas where reagents or human specimens are handled.
- Follow national biological safety procedures for handling biological samples. (*e.g.*, do not pipette by mouth, wear appropriate protective clothing and eye protection).
- 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 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 ePlex instrument 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 ePlex cartridge. Reagents may cause irritation to skin, eyes, and respiratory tract. Harmful if swallowed or inhaled. Contains oxidizing liquids.
- The ePlex RP2 Panel cartridge contains chemicals that are classified as hazardous. Review the Safety Data Sheet (SDS) before use, and in cases of exposure, refer to the SDS for more information.
- Observe safety guidelines such as wearing proper protective equipment including laboratory coats, gowns, gloves, eye protection, and a biological safety cabinet as outlined in Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition https://www.cdc.gov/labs/BMBL.html.
- If infection with SARS-CoV-2 is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent) prior to processing a specimen.
- Immediately clean up any spill containing potentially infections material with a 0.5-1% (w/v) sodium hypochlorite (20% v/v bleach).
- Performance characteristics have been determined with nasopharyngeal swab samples from human patients with signs and symptoms of respiratory infection.
- Specimens should be processed in a Class II (or higher) biological safety cabinet.
- To mitigate the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.
- Contamination of the sample may occur if the sample is loaded in an area where PCR amplicons for respiratory pathogens are generated. Avoid loading sample in areas that are potentially contaminated with PCR amplicon.

Laboratory

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

SPECIMEN COLLECTION, HANDLING, AND STORAGE

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 ºC for up to 10 days after collection in transport media. Specimens can also be stored at -20 ºC or -80 ºC for 12 months with up to 2 freeze/thaw cycles.

Inadequate or inappropriate specimen collection, storage, and transport are likely to yield false test results. Training in specimen collection is highly recommended due to the importance of specimen quality. CLSI MM13-A may be referenced as an appropriate resource.

PROCEDURE

Procedural Notes

- All frozen samples should be thawed completely before testing.
- Samples should be nasopharyngeal swabs in viral transport media.
- 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 into the ePlex RP2 Panel cartridge, the sample should be tested as soon as possible or within 2 hours.
- Do not re-use cartridges.
- Use a new, sterile pipette tip for loading each sample.
- Do not insert a wet cartridge into the ePlex instrument. If the cartridge or sample has leaked, dispose of cartridge in accordance with all federal, state, and local regulations.
- Samples should be transferred into the ePlex RP2 Panel cartridge in an amplicon-free, clean environment.
- Samples, consumables, and lab areas should be protected from aerosol or direct contamination with amplicon. Decontaminate laboratory areas and affected equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
- Samples and cartridges should be handled and/or tested one at a time. To mitigate the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.
- 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 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 ePlex RP2 Panel with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove one RP2 Panel cartridge pouch from kit packaging.
3. Open the RP2 Panel cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the RP2 Panel cartridge.
5. Vortex the sample for 3-5 seconds.
6. Use a calibrated pipette to aspirate 200 µL of sample and dispense into the sample loading port of the ePlex RP2 Panel cartridge.
7. 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.
8. Scan the RP2 Panel cartridge using the barcode reader provided with the ePlex instrument.
   NOTE: If an accession ID barcode label is not used, manually enter accession ID with the on-screen keyboard.

NOTE: The barcode scanner will read both the accession ID barcode (if placed on the cartridge by the operator) and the 2D barcode printed on the cartridge label; however, the barcode scanner will only beep once to indicate that both barcodes have been read.

9. Insert the RP2 Panel cartridge into any available bay, indicated by a flashing, white LED light. The test will begin automatically when the cartridge has been inserted into the bay and the pre-run check (cartridge initialization) is completed, indicated by a blue LED light.

QUALITY CONTROL

Internal Controls

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

Each amplification reaction on the cartridge has at least one internal control and in each reaction either the internal control or a target must generate signal above the defined threshold for a valid test result. Internal control results are interpreted by the ePlex software and displayed on ePlex RP Panel Reports as Internal Control with a result of PASS, FAIL, N/A or INVALID. **Table 3** includes details on the interpretation of Internal Control results.

Table 3: Internal Control Results

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

External Controls

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

RESULTS

Table 4: Interpretation of Results on the ePlex RP2 Panel Detection Report

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

Influenza A Results

The ePlex RP2 Panel detects Influenza A and the H1, H1-2009, and H3 subtypes using unique assays for each. Interpretation of results for Influenza A are described in **Table 5**.

Table 5: 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

Results for Influenza A and Subtypes	Explanation	Results on Report	Recommended Action
Influenza A detected, all subtypes (H1, H1-2009, and H3) reported as not detected	Low virus titers can result in detection of influenza A matrix without a subtype. Detection of influenza A matrix without a subtype can also indicate the presence of a novel strain.	Result reported as influenza A detected. No Influenza A subtype detected.	Re-test to confirm result. If the original result is confirmed, contact the appropriate public health authorities for additional testing. If the re-test provides a different result, test the sample a third time to ensure the accuracy of the result.
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. A live intranasal multivalent influenza virus vaccine may cause false positive results for influenza A, A/H1, A/H3, A/H1-2009, and/or influenza B. Contamination has occurred.	Result reported as influenza A and multiple subtypes detected.	Re-test to confirm result. If the re-test result confirms the original result, it is recommended that the sample be further investigated using a different FDA-cleared influenza A subtyping assay.
Influenza A not detected, at least one subtype (H1, H1-2009, or H3) reported as detected.	Low virus titers can result in detection of influenza A subtype without the influenza A matrix. Detection of influenza A subtype without the influenza A matrix can also indicate the presence of a novel strain.	Influenza A (subtype) detected. Re-testing of this sample to confirm Influenza A (subtype) is recommended. Refer to package insert for additional information.	Re-test to confirm result. If the re-test result confirms the original result, the influenza A subtype is considered positive. It is recommended that the sample be further investigated using a different FDA-cleared influenza A subtyping assay and/or sending the residual sample to local public health laboratory for further testing.

TEST REPORTS

There are several different reports that are available on the ePlex instrument. 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 ePlex reports, refer to the ePlex Operator Manual.

Detection Report

The RP2 Panel Detection Report includes the results for each individual sample run on the ePlex instrument.

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 RP2 Panel External Control Report is generated for an external control that has been pre-defined in the ePlex RP2 Panel software. For more information on defining external controls on ePlex RP2 Panel, refer to the ePlex Operator 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 defined 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 ePlex Operator Manual.

LIMITATIONS OF THE PROCEDURE

- This product can be used only with the GenMark ePlex instrument.
- At high titers, cross-reactivity with SARS-CoV-1 was observed with the ePlex RP2 Panel.
- Due to the genetic similarity between human rhinovirus and enterovirus, this test cannot reliably differentiate them. An ePlex RP2 Panel Rhinovirus/Enterovirus positive result should be followed-up using an alternate method (e.g. cell culture or sequence analysis) if differentiation between the viruses is required.
- 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 samples in viral transport media.
- 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.
- The effect of antibiotic treatment on test performance has not been evaluated.
- The performance of this test has not been established for screening of blood or blood products.

- 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 specimen 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 positive or false negative values resulting from improperly collected, transported, or handled samples.
- There is a risk of false negative values due to the presence of sequence variants in the viral or bacterial targets of the test, the presence of inhibitors, technical error, sample mix-up, or an infection caused by an organism not detected by the panel. Test results may be affected by concurrent antibacterial or antiviral therapy or levels of bacteria or virus in the sample that are below the limit of detection for the test. A result of No Targets Detected on the ePlex RP2 Panel should not be used as the sole basis for diagnosis, treatment or other patient management decisions.
- A result of No Targets Detected on the ePlex RP2 Panel in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or lower respiratory tract infection that is not detected by a nasopharyngeal swab sample.
- There is a risk of false positive results due to contamination of the sample with target organisms, their nucleic acids, or amplicons. Particular attention should be given to the Laboratory precautions noted under the *Warnings and Precautions* section.
- There is a risk of false positive results due to non-specific amplification and cross-reactivity with organisms found in the respiratory tract. Erroneous results due to cross-reactivity with organisms that were not specifically evaluated or new variant sequences that emerge are possible.
- If four or more organisms are detected in a sample, retesting is recommended to confirm polymicrobial result.
- The ePlex RP2 Panel influenza A subtyping reagents target the influenza A hemagglutinin gene only. The ePlex RP2 Panel does not detect or differentiate the influenza A neuraminidase gene.
- The performance of this test has not been established for monitoring treatment of infection with any of the panel organisms.
- Positive and negative predictive values are highly dependent on prevalence. False negative test results are more likely during peak activity when prevalence of disease is high. False positive test results are more likely during periods when prevalence is moderate to low.
- Clinical performance was established when influenza A H3 and influenza A H1-2009 were the predominant influenza A viruses in circulation. When other influenza A viruses emerge, performance may vary.
- Due to the small number of positive samples collected for *Chlamydia pneumoniae* during the prospective and retrospective clinical studies, performance characteristics for *Chlamydia pneumoniae* were established primarily with contrived clinical specimens. Performance characteristics for Influenza A H1 were established using contrived clinical specimens only.
- Clinical evaluation indicates a lower sensitivity for the detection of coronavirus OC43. If infection with coronavirus OC43 is suspected, negative samples should be confirmed using an alternative method.
- 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% weight/volume in the sample, tobramycin was found to inhibit assay performance.
- The performance of this test has not been specifically evaluated for specimens collected from individuals who recently received influenza vaccine. Recent administration of a live intranasal influenza virus vaccine may cause false positive results for influenza A, H1, H3, H1-2009, and/or influenza B.
- The ePlex RP2 Panel cannot differentiate variant viruses, such as H3N2v, from seasonal influenza A viruses. If variant virus infection is suspected, clinicians should contact their state or local health department to arrange specimen transport and request a timely diagnosis at a state public health laboratory.

Conditions of Authorization for the Laboratory

The ePlex RP2 Panel Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas.

However, to assist clinical laboratories using the ePlex RP2 Panel, the relevant Conditions of Authorization are listed below:

A. Authorized laboratories[1] using the ePlex RP2 Panel will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

B. Authorized laboratories using the ePlex RP2 Panel will use the ePlex RP2 Panel as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the ePlex RP2 Panel are not permitted.

C. Authorized laboratories that receive the ePlex RP2 Panel will notify the relevant public health authorities of their intent to run the ePlex RP2 Panel prior to initiating testing.

D. Authorized laboratories using the ePlex RP2 Panel will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

E. Authorized laboratories will collect information on the performance of the ePlex RP2 Panel and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and GenMark Diagnostics, Inc. (via email: technicalsupport@genmarkdx.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the ePlex RP2 Panel Test of which they become aware.

F. All laboratory personnel using the ePlex RP2 Panel must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the ePlex RP2 Panel in accordance with the labeling.

G. Genmark Diagnostics, Inc., authorized distributors, and authorized laboratories using the ePlex RP2 Panel will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

[1] The letter of authorization refers to, “laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests” as “authorized laboratories.”

PERFORMANCE CHARACTERISTICS

ePlex RP and RP2 Panels

The ePlex RP2 Panel was developed by incorporating the reagents required to detect the SARS-CoV-2 targets from the ePlex SARS-CoV-2 Test into the existing ePlex Respiratory Pathogen Panel (RP Panel).

The assays for detection of SARS-CoV-2 were added into PCR pools that contain additional targets. The targets that are now co-amplified with SARS-CoV-2 are influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, and adenovirus; assays for all other targets were unchanged. Studies were conducted to demonstrate that the performance characteristics of the RP Panel were not affected by the addition of the SARS-CoV-2 assays. Additional studies to support the addition of SARS-CoV-2 are included in the sections below. The original studies from the RP Panel are still relevant for the RP2 Panel.

CLINICAL PERFORMANCE

EXPECTED VALUES

A prospective, multicenter clinical study was conducted to evaluate the clinical performance of the ePlex RP Panel in nasopharyngeal swab samples. 2462 nasopharyngeal swab samples were prospectively-collected at 8 collection sites in 2 phases from patients of all ages and genders presenting with signs and/or symptoms of respiratory infection. In the first phase from March 2013 through August 2014, 1951 samples were prospectively-collected and frozen; from September 2016 through October 2016, 511 samples were prospectively-collected and tested fresh (never frozen). The expected values of individual analytes based on ePlex RP Panel results in prospective samples for each phase are summarized in **Tables 6-9**. **NOTE:** Expected values for SARS-CoV-2 have not been determined.

Table 6: Expected Value (As Determined by ePlex RP Panel) Summary By Age Group in the Prospective Clinical Evaluation (Phase 1: March 2013 – August 2014)

Organism	All Ages (N=1951) n (%)	Age 0-1 (N=315) n (%)	Age >1-5 (N=250) n (%)	Age >5-21 (N=246) n (%)	Age >21-65 (N=745) n (%)	Age >65 (N=395) n (%)
Adenovirus	72 (3.7)	31 (9.8)	24 (9.6)	7 (2.8)	7 (0.9)	3 (0.8)
Coronavirus (229E, HKU1, NL63, OC43)	102 (5.2)	19 (6.0)	18 (7.2)	16 (6.5)	32 (4.3)	17 (4.3)
Human Metapneumovirus	113 (5.8)	22 (7.0)	28 (11.2)	6 (2.4)	31 (4.2)	26 (6.6)
Human Rhinovirus/Enterovirus	388 (19.9)	113 (35.9)	94 (37.6)	58 (23.6)	87 (11.7)	36 (9.1)
Influenza A	110 (5.6)	6 (1.9)	18 (7.2)	20 (8.1)	49 (6.6)	17 (4.3)
Influenza A H1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1-2009	76 (3.9)	4 (1.3)	13 (5.2)	14 (5.7)	37 (5.0)	8 (2.0)
Influenza A H3	34 (1.7)	1 (0.3)	5 (2.0)	6 (2.4)	12 (1.6)	10 (2.5)
Influenza B	62 (3.2)	4 (1.3)	9 (3.6)	10 (4.1)	24 (3.2)	15 (3.8)
Parainfluenza Virus 1	24 (1.2)	4 (1.3)	12 (4.8)	4 (1.6)	3 (0.4)	1 (0.3)
Parainfluenza Virus 2	10 (0.5)	4 (1.3)	4 (1.6)	0 (0.0)	2 (0.3)	0 (0.0)
Parainfluenza Virus 3	99 (5.1)	31 (9.8)	20 (8.0)	3 (1.2)	27 (3.6)	18 (4.6)
Parainfluenza Virus 4	7 (0.4)	3 (1.0)	2 (0.8)	1 (0.4)	1 (0.1)	0 (0.0)
RSV A	28 (1.4)	13 (4.1)	6 (2.4)	3 (1.2)	2 (0.3)	4 (1.0)
RSV B	83 (4.3)	33 (10.5)	19 (7.6)	6 (2.4)	15 (2.0)	10 (2.5)
Chlamydia pneumoniae	3 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.1)	1 (0.3)
Mycoplasma pneumoniae	5 (0.3)	1 (0.3)	1 (0.4)	2 (0.8)	1 (0.1)	0 (0.0)

Table 7: Expected Value (As Determined by ePlex RP Panel) Summary By Age Group in the Prospective Clinical Evaluation (Phase 2: September 2016 – October 2016)

Organism	All Ages (N=511) n (%)	Age 0-1 (N=73) n (%)	Age >1-5 (N=75) n (%)	Age >5-21 (N=75) n (%)	Age >21-65 (N=181) n (%)	Age >65 (N=107) n (%)
Adenovirus	10 (2.0)	3 (4.1)	4 (5.3)	1 (1.3)	1 (0.6)	1 (0.9)
Coronavirus (229E, HKU1, NL63, OC43)	8 (1.6)	2 (2.7)	0 (0.0)	1 (1.3)	4 (2.2)	1 (0.9)
Human Metapneumovirus	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Human Rhinovirus/Enterovirus	188 (36.8)	37 (50.7)	40 (53.3)	33 (44.0)	58 (32.0)	20 (18.7)
Influenza A	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1-2009	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza B	2 (0.4)	0 (0.0)	0 (0.0)	1 (1.3)	1 (0.6)	0 (0.0)
Parainfluenza Virus 1	1 (0.2)	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
Parainfluenza Virus 2	13 (2.5)	3 (4.1)	4 (5.3)	3 (4.0)	2 (1.1)	1 (0.9)
Parainfluenza Virus 3	5 (1.0)	2 (2.7)	1 (1.3)	1 (1.3)	1 (0.6)	0 (0.0)
Parainfluenza Virus 4	8 (1.6)	1 (1.4)	4 (5.3)	2 (2.7)	1 (0.6)	0 (0.0)
RSV A	8 (1.6)	5 (6.8)	3 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)
RSV B	9 (1.8)	3 (4.1)	4 (5.3)	0 (0.0)	2 (1.1)	0 (0.0)
Chlamydia pneumoniae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mycoplasma pneumoniae	4 (0.8)	0 (0.0)	1 (1.3)	2 (2.7)	1 (0.6)	0 (0.0)

Table 8: Expected Value (As Determined by ePlex RP Panel) Summary By Sample Collection Site in the Prospective Clinical Evaluation (Phase 1: March 2013 – August 2014)

Organism	All Sites (N=1951) n (%)	Site 1 (N=165) n (%)	Site 2 (N=248) n (%)	Site 3 (N=350) n (%)	Site 4 (N=892) n (%)	Site 5 (N=296) n (%)
Adenovirus	72 (3.7)	4 (2.4)	8 (3.2)	28 (8.0)	23 (2.6)	9 (3.0)
Coronavirus (229E, HKU1, NL63, OC43)	102 (5.2)	8 (4.8)	11 (4.4)	32 (9.1)	29 (3.3)	22 (7.4)
Human Metapneumovirus	113 (5.8)	10 (6.1)	23 (9.3)	27 (7.7)	30 (3.4)	23 (7.8)
Human Rhinovirus/Enterovirus	388 (19.9)	27 (16.4)	33 (13.3)	61 (17.4)	185 (20.7)	82 (27.7)
Influenza A	110 (5.6)	5 (3.0)	21 (8.5)	48 (13.7)	19 (2.1)	17 (5.7)
Influenza A H1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1-2009	76 (3.9)	3 (1.8)	22 (8.9)	31 (8.9)	5 (0.6)	15 (5.1)
Influenza A H3	34 (1.7)	2 (1.2)	0 (0.0)	18 (5.1)	12 (1.3)	2 (0.7)
Influenza B	62 (3.2)	9 (5.5)	9 (3.6)	9 (2.6)	19 (2.1)	16 (5.4)
Parainfluenza Virus 1	24 (1.2)	0 (0.0)	0 (0.0)	5 (1.4)	2 (0.2)	17 (5.7)
Parainfluenza Virus 2	10 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	10 (1.1)	0 (0.0)
Parainfluenza Virus 3	99 (5.1)	13 (7.9)	3 (1.2)	28 (8.0)	41 (4.6)	14 (4.7)
Parainfluenza Virus 4	7 (0.4)	0 (0.0)	0 (0.0)	1 (0.3)	4 (0.4)	2 (0.7)
RSV A	28 (1.4)	4 (2.4)	6 (2.4)	7 (2.0)	4 (0.4)	7 (2.4)
RSV B	83 (4.3)	6 (3.6)	15 (6.0)	24 (6.9)	15 (1.7)	23 (7.8)
Chlamydia pneumoniae	3 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.2)	0 (0.0)
Mycoplasma pneumoniae	5 (0.3)	1 (0.6)	0 (0.0)	3 (0.9)	0 (0.0)	1 (0.3)

Table 9: Expected Value (As Determined by ePlex RP Panel) Summary By Sample Collection Site in the Prospective Clinical Evaluation (Phase 2: September 2016 – October 2016)

Organism	All Sites (N=511) n (%)	Site 5 (N=49) n (%)	Site 6 (N=101) n (%)	Site 7 (N=161) n (%)	Site 8 (N=200) n (%)
Adenovirus	10 (2.0)	2 (4.1)	3 (3.0)	3 (1.9)	2 (1.0)
Coronavirus (229E, HKU1, NL63, OC43)	8 (1.6)	0 (0.0)	2 (2.0)	4 (2.5)	2 (1.0)
Human Metapneumovirus	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Human Rhinovirus/Enterovirus	188 (36.8)	24 (49.0)	49 (48.5)	62 (38.5)	53 (26.5)
Influenza A	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H1-2009	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza A H3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza B	2 (0.4)	1 (2.0)	0 (0.0)	0 (0.0)	1 (0.5)
Parainfluenza Virus 1	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Parainfluenza Virus 2	13 (2.5)	2 (4.1)	4 (4.0)	3 (1.9)	4 (2.0)
Parainfluenza Virus 3	5 (1.0)	2 (4.1)	2 (2.0)	0 (0.0)	1 (0.5)
Parainfluenza Virus 4	8 (1.6)	1 (2.0)	1 (1.0)	4 (2.5)	2 (1.0)
RSV A	8 (1.6)	0 (0.0)	8 (7.9)	0 (0.0)	0 (0.0)
RSV B	9 (1.8)	1 (2.0)	4 (4.0)	0 (0.0)	4 (2.0)
Chlamydia pneumoniae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mycoplasma pneumoniae	4 (0.8)	0 (0.0)	3 (3.0)	0 (0.0)	1 (0.5)

CLINICAL PERFORMANCE

Clinical Performance of the ePlex RP2 Panel and SARS-CoV-2

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

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

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

Positive percent agreement (PPA) was calculated by dividing the number of true positive (TP) results by the sum of TP and false negative (FN) results, while negative percent agreement (NPA) was calculated by dividing the number of true negative (TN) results by the sum of TN and false positive (FP) results. A TP result was one where the detected ePlex RP2 Panel result matched the detected comparator method result, while a TN result was one where a negative ePlex RP2 Panel result matched a presumed negative result. Since archived negative samples were not tested by the comparator method, false positives are

calculated based on a presumed negative clinical truth. The two-sided 95% confidence interval was also calculated. Results are shown in **Table 10** below.

Table 10. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for SARS-CoV-2 in the ePlex RP2 Panel Clinical Study

ePlex RP2 Test	Comparator Result		
	Positive	Negative	Total
Positive	59	0	59
Negative	0	111	111
Total	59	111	170

PPA: 59/59 100% (95% CI: 93.9-100)
NPA: 111/111 100% (95% CI: 96.7-100)

In the second arm of the study, testing was done to evaluate the performance of ePlex RP2 Panel targets co-amplified with the SARS-CoV-2 assays (assays for SARS-CoV-2 were incorporated into PCR pools that also include influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, and adenovirus; assays for all other targets were unchanged). Samples were tested with the ePlex RP2 Panel and the original ePlex Respiratory Pathogen Panel; or to the known contrived organism. For the Influenza A H1 target only, contrived samples were evaluated. Results are shown in **Tables 11-12** below.

Table 11: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) of the ePlex RP2 Panel with the ePlex RP Panel in Nasopharyngeal Swab Samples

Organism	Positive % Agreement		Negative % Agreement	
	TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Adenovirus	25/25	100 (86.7-100)	83/86[a]	96.5 (90.2-98.8)
Influenza A	56/57[b]	98.2 (90.7-99.7)	54/54	100 (93.4-100)
Influenza A H1	0/0	---	111/111	100 (96.7-100)
Influenza A H1-2009	26/27[c]	96.3 (81.7-99.3)	84/84	100 (95.6-100)
Influenza A H3	29/30[b]	96.7 (83.3-99.4)	81/81	100 (95.5-100)
Influenza B	28/29[d]	96.6 (82.8-99.4)	82/82	100 (95.5-100)

[a] 3 FP Adenovirus results were detected by the ePlex RP Panel (IUO) in the original clinical study.
[b] 1 FN Influenza A H3 result was not detected by the RP Panel (IUO) in the original clinical study.
[c] 1 FN Influenza A 2009 H1N1 result was detected by the RP Panel (IUO) in the original clinical study.
[d] 1 FN Influenza B result was detected by the RP Panel (IUO) in the original clinical study.

Table 12: Positive Percent Agreement (PPA) for the ePlex RP2 Panel with the ePlex RP Panel with Contrived Samples

Organism	Positive % Agreement	
	TP/TP+FN	PPA (95% CI)
Influenza A	15/15	100 (79.6-100)
Influenza A H1	15/15	100 (79.6-100)

RP2 Clinical Study ePlex Instrument Performance

A total of 189 samples (174 NPS and 15 contrived) were initially tested with the ePlex RP2 Panel and 183/189 = 96.8% (95% CI: 93.2% - 98.5%) generated valid results on the first attempt. Two samples were re-tested and both had valid results. The remaining invalid samples did not have sufficient volume for repeat testing.

Clinical Performance of the ePlex RP Panel

Comparator Method

The performance of the ePlex RP Panel was compared to an FDA-cleared multiplexed molecular respiratory pathogen panel and analytically validated PCR tests with bi-directional sequencing for confirmation of RSV subtypes. Details of the comparator method are described in **Table 13**.

Table 13: Comparator Methods Used to Assess ePlex RP Panel Clinical Performance

Target	Comparator Method
Adenovirus	FDA-cleared multiplexed molecular respiratory pathogen panel
Coronavirus (229E, HKU1, NL63, OC43)	
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 A	FDA-cleared multiplexed molecular respiratory pathogen panel followed by a PCR test with bi-directional sequencing confirmation
Respiratory Syncytial Virus B	
Chlamydia pneumoniae	FDA-cleared multiplexed molecular respiratory pathogen panel
Mycoplasma pneumoniae	

Prospective Clinical Samples

Clinical performance was evaluated in clinical nasopharyngeal swab samples in VTM prospectively-collected at 8 clinical sites in 2 phases. From March 2013 through August 2014, 2218 samples were prospectively-collected and frozen; from September 2016 through October 2016, 514 samples were prospectively-collected and tested fresh (never frozen). A total of 2732 samples were collected across the 2 phases. Prior to the start of investigational testing, 263 samples were withdrawn (251 had sample handling deviations, 9 were tested outside of protocol timelines, 2 had insufficient volume, and 1 had incomplete documentation). Of the 2469 prospectively-collected samples eligible for testing, 2462 were evaluable. Samples with final, valid results and a valid comparator result were considered evaluable. Seven prospectively-collected samples were not evaluable because they did not have final, valid ePlex RP Panel results and were excluded from performance evaluations. Demographic information for prospectively-collected samples is described in **Table 14**. Subjects enrolled in this study were from a diverse demographic distribution and represent the intended patient population.

Table 14: Subject Demographic Data for Prospectively-Collected Samples by Collection Site (N=2462)

	All Sites N=2462 n (%)	Site 1 N=165 n (%)	Site 2 N=248 n (%)	Site 3 N=350 n (%)	Site 4 N=892 n (%)	Site 5 N=345 n (%)	Site 6 N=101 n (%)	Site 7 N=161 n (%)	Site 8 N=200 n (%)
Sex									
Male	1247 (50.6)	96 (58.2)	118 (47.6)	186 (53.1)	450 (50.4)	188 (54.5)	43 (42.6)	84 (52.2)	82 (41.0)
Female	1215 (49.4)	69 (41.8)	130 (52.4)	164 (46.9)	442 (49.6)	157 (45.5)	58 (57.4)	77 (47.8)	118 (59.0)
Age (years)									
0–1	388 (15.8)	17 (10.3)	21 (8.5)	74 (21.1)	164 (18.4)	45 (13.0)	28 (27.7)	3 (1.9)	36 (18.0)
> 1–5	325 (13.2)	12 (7.3)	22 (8.9)	62 (17.7)	64 (7.2)	100 (29.0)	39 (38.6)	16 (9.9)	10 (5.0)
> 5–21	321 (13.0)	15 (9.1)	6 (2.4)	38 (10.9)	82 (9.2)	116 (33.6)	34 (33.7)	18 (11.2)	12 (6.0)
> 21–65	926 (37.6)	87 (52.7)	131 (52.8)	98 (28.0)	385 (43.2)	55 (15.9)	0 (0.0)	92 (57.1)	78 (39.0)
> 65	502 (20.4)	34 (20.6)	68 (27.4)	78 (22.3)	197 (22.1)	29 (8.4)	0 (0.0)	32 (19.9)	64 (32.0)

Prospective Clinical Performance

Positive percent agreement (PPA) was calculated by dividing the number of true positive (TP) results by the sum of TP and false negative (FN) results, while negative percent agreement (NPA) was calculated by dividing the number of true negative (TN) results by the sum of TN and false positive (FP) results. A TP result was one where the detected ePlex RP Panel result matched the detected comparator method result, while a TN result was one where a negative ePlex RP Panel result matched a negative comparator method result. The two-sided 95% confidence interval was also calculated.

A total of 2462 prospectively-collected samples (511 tested fresh and 1951 tested after previously frozen) were evaluated for 17 ePlex RP Panel organisms. PPA and NPA results are summarized by target in **Tables 15 and 16** below.

Table 15: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) in the ePlex RP Panel Clinical Study (Fresh)

Organism	Prevalence	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Adenovirus	1.6%	6/8[a]	75.0 (40.9-92.9)	499/503[a]	99.2 (98.0-99.7)
Coronavirus (229E, HKU1, NL63, OC43)	1.4%	7/7	100 (64.6-100)	503/504	99.8 (98.9-100)
Human Metapneumovirus	0.0%	0/0	---	511/511	100 (99.3-100)
Human Rhinovirus/Enterovirus	35.8%	176/183[b]	96.2 (92.3-98.1)	316/328[b]	96.3 (93.7-97.9)
Influenza A	0.0%	0/0	---	511/511	100 (99.3-100)
Influenza A H1	0.0%	0/0	---	511/511	100 (99.3-100)
Influenza A H1-2009	0.0%	0/0	---	511/511	100 (99.3-100)
Influenza A H3	0.0%	0/0	---	511/511	100 (99.3-100)
Influenza B	0.2%	1/1	100 (20.7-100)	509/510	99.8 (98.9-100)
Parainfluenza Virus 1	0.2%	1/1	100 (20.7-100)	510/510	100 (99.3-100)
Parainfluenza Virus 2	2.5%	12/13	92.3 (66.7-98.6)	497/498	99.8 (98.9-100)
Parainfluenza Virus 3	1.0%	5/5	100 (56.6-100)	506/506	100 (99.2-100)
Parainfluenza Virus 4	0.6%	3/3	100 (43.9-100)	503/508[c]	99.0 (97.7-99.6)
RSV A	1.8%	8/9	88.9 (56.5-98.0)	501/501	100 (99.2-100)
RSV B	2.0%	9/10	90.0 (59.6-98.2)	500/500	100 (99.2-100)

Organism	Prevalence	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Chlamydia pneumoniae	0.0%	0/0	---	511/511	100 (99.3-100)
Mycoplasma pneumoniae	0.6%	3/3	100 (43.9-100)	507/508[d]	99.8 (98.9-100)

[a] Adenovirus was not detected in 2 of 2 FN samples and detected in 4 of 4 FP samples using PCR/sequencing.
[b] Human rhinovirus/enterovirus was not detected in 1 of 7 FN samples and detected in 9 of 12 FP samples using PCR/sequencing.
[c] Parainfluenza virus 4 was detected in 3 of 5 FP samples using PCR/sequencing.
[d] *M. pneumoniae* was detected in the 1 FP sample using PCR/sequencing.

Table 16: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) in the ePlex RP Panel Clinical Study (After Previously Frozen)

Organism	Prevalence	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Adenovirus	2.7%	48/53[a]	90.6 (79.7-95.9)	1874/1898[a]	98.7 (98.1-99.1)
Coronavirus (229E, HKU1, NL63, OC43)	5.6%	89/110[b]	80.9 (72.6-87.2)	1828/1841[b]	99.3 (98.8-99.6)
Human Metapneumovirus	5.8%	107/113[c]	94.7 (88.9-97.5)	1832/1838[c]	99.7 (99.3-99.9)
Human Rhinovirus/Enterovirus	17.2%	317/336[d]	94.3 (91.3-96.4)	1544/1615[d]	95.6 (94.5-96.5)
Influenza A[e]	5.7%	106/111[f]	95.5 (89.9-98.1)	1836/1840[f]	99.8 (99.4-99.9)
Influenza A H1	0.0%	0/0	---	1951/1951	100 (99.8-100)
Influenza A H1-2009	3.6%	70/71	98.6 (92.4-99.8)	1874/1880[g]	99.7 (99.3-99.9)
Influenza A H3	1.9%	34/37[h]	91.9 (78.7-97.2)	1914/1914	100 (99.8-100)
Influenza B	3.3%	58/65[i]	89.2 (79.4-94.7)	1882/1886[i]	99.8 (99.5-99.9)
Parainfluenza Virus 1	1.2%	23/24	95.8 (79.8-99.3)	1926/1927	99.9 (99.7-100)
Parainfluenza Virus 2	0.5%	9/9	100 (70.1-100)	1941/1942	99.9 (99.7-100)
Parainfluenza Virus 3	5.3%	94/104[j]	90.4 (83.2-94.7)	1842/1847[j]	99.7 (99.4-99.9)
Parainfluenza Virus 4	0.3%	5/5	100 (56.6-100)	1944/1946	99.9 (99.6-100)
RSV A	1.6%	27/31	87.1 (71.1-94.9)	1917/1918	99.9 (99.7-100)
RSV B	4.4%	81/86	94.2 (87.1-97.5)	1861/1863[k]	99.9 (99.6-100)
Chlamydia pneumoniae	0.3%	2/5[l]	40.0 (11.8-76.9)	1945/1946[l]	99.9 (99.7-100)
Mycoplasma pneumoniae	0.3%	4/5[m]	80.0 (37.6-96.4)	1945/1946	99.9 (99.7-100)

[a] Adenovirus was not detected in 1 of 5 FN samples and detected in 9 of 24 FP samples using PCR/sequencing.
[b] Coronavirus was not detected in 2 of 21 FN samples and detected in 3 of 13 FP samples using PCR/sequencing.
[c] Human Metapneumovirus was not detected in 1 of 6 FN samples and detected in 4 of 6 FP samples using PCR/sequencing.
[d] Human rhinovirus/enterovirus was not detected in 6 of 19 FN samples and detected in 33 of 71 FP samples using PCR/sequencing.
[e] Influenza A comparator results contain 71 samples with A H1-2009, 37 samples with A H3, and 3 samples with no subtype detected.
[f] Influenza A was not detected in 1 of 3 FN samples (2 samples were not tested by PCR/sequencing) and detected in 1 of 4 FP samples using PCR/sequencing.
[g] Influenza A H1-2009 was detected in 4 of 6 FP samples using PCR/sequencing.
[h] Influenza A H3 was not detected in 1 of 3 FN samples using PCR/sequencing.
[i] Influenza B was not detected in 3 of 7 FN samples and detected in 2 of 4 FP samples using PCR/sequencing.
[j] Parainfluenza virus 3 was not detected in 3 of 10 FN samples and detected in 4 of 5 FP samples using PCR/sequencing.
[k] RSV B was detected in 1 of 2 FP samples using PCR/sequencing.
[l] *C. pneumoniae* was not detected in 1 of 3 FN samples and detected in the 1 FP sample using PCR/sequencing.
[m] *M. pneumoniae* was not detected in the 1 FN sample using PCR/sequencing.

Retrospective Clinical Samples

To supplement the number of positives for targets that were not sufficiently represented in the prospective collection, additional nasopharyngeal swab in VTM samples were retrospectively collected from 6 sites. A total of 535 nasopharyngeal swab samples that had previously tested positive for one or more of the

target organisms during standard-of-care (SOC) testing were collected and stored frozen. Prior to the start of investigational testing, 11 samples were withdrawn due to noncompliance with the study protocol, and 52 samples were withdrawn because the organisms present had sufficient representation in other samples. In addition, the composition and integrity of the retrospective samples were confirmed with the same comparator method employed in the prospective clinical study (i.e., an FDA-cleared multiplexed respiratory pathogen panel). As the result of this confirmation testing using the comparator method, 26 additional samples were withdrawn because the original SOC testing positive results for the intended organisms were not confirmed when tested with the comparator method. Of the remaining 446 retrospectively-collected samples eligible for testing, all 446 were evaluable. Demographic information for retrospectively-collected samples is described in **Table 17**. Subjects enrolled in this study were from a diverse demographic distribution and represent the intended patient population.

Table 17: Subject Demographic Data for Retrospectively-Collected Samples by Collection Site (N=446)

	All Sites N=446 n (%)	Site 1 N=1 n (%)	Site 2 N=1 n (%)	Site 3 N=129 n (%)	Site 4 N=18 n (%)	Site 5 N=131 n (%)	Site 6 N=166 n (%)
Sex							
Male	232 (52.0)	0 (0.0)	1 (100)	76 (58.9)	11 (61.1)	68 (51.9)	76 (45.8)
Female	214 (48.0)	1 (100)	0 (0.0)	53 (41.1)	7 (38.9)	63 (48.1)	90 (54.2)
Age (years)							
0 – 1	122 (27.4)	0 (0.0)	0 (0.0)	24 (18.6)	5 (27.8)	56 (42.7)	37 (22.3)
> 1 – 5	107 (24.0)	0 (0.0)	1 (100)	51 (39.5)	3 (16.7)	16 (12.2)	36 (21.7)
> 5 – 21	59 (13.2)	0 (0.0)	0 (0.0)	9 (7.0)	2 (11.1)	19 (14.5)	29 (17.5)
> 21 – 65	99 (22.2)	1 (100)	0 (0.0)	11 (8.5)	8 (44.4)	31 (23.7)	48 (28.9)
> 65	59 (13.2)	0 (0.0)	0 (0.0)	34 (26.4)	0 (0.0)	9 (6.9)	16 (9.6)

Retrospective Clinical Performance

A total of 446 retrospectively-collected samples were evaluated for 17 ePlex RP Panel organisms. The following specimens with the original positive SOC results for the unintended organisms that were not confirmed by the comparator method were excluded from the performance calculation for the respective organism: 1 coronavirus positive specimen, 3 human rhinovirus/enterovirus positive specimens, 1 influenza A positive specimen, 1 influenza A H3 positive specimen, 1 parainfluenza virus positive specimen. In addition, 5 unintended RSV positive specimens by the comparator method were not confirmed by PCR/sequencing with regard to determining RSV subtypes and therefore were excluded from the performance calculations for RSV A and RSV B. PPA and NPA results are summarized by target in **Table 18** below.

Table 18: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) of the ePlex RP Panel With Comparator Methods (Retrospective Collection)

Organism	Positive % Agreement		Negative % Agreement	
	TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Adenovirus	55/56[a]	98.2 (90.6-99.7)	386/390[a]	99.0 (97.4-99.6)
Coronavirus (229E, HKU1, NL63, OC43)	121/138[b]	87.7 (81.2-92.2)	307/307	100 (98.8-100)
Human Metapneumovirus	5/7	71.4 (35.9-91.8)	439/439	100 (99.1-100)
Human Rhinovirus/Enterovirus	37/41	90.2 (77.5-96.1)	384/402	95.5 (93.0-97.1)
Influenza A[c]	75/82[d]	91.5 (83.4-95.8)	363/363	100 (99.0-100)

Organism	Positive % Agreement		Negative % Agreement	
	TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Influenza A H1	0/0	---	446/446	100 (99.1-100)
Influenza A H1-2009	27/31[e]	87.1 (71.1-94.9)	415/415	100 (99.1-100)
Influenza A H3	45/51[f]	88.2 (76.6-94.5)	394/394	100 (99.0-100)
Influenza B	1/1	100 (20.7-100)	445/445	100 (99.1-100)
Parainfluenza Virus 1	43/48[g]	89.6 (77.8-95.5)	396/397	99.7 (98.6-100)
Parainfluenza Virus 2	46/51	90.2 (79.0-95.7)	395/395	100 (99.0-100)
Parainfluenza Virus 3	2/2	100 (34.2-100)	444/444	100 (99.1-100)
Parainfluenza Virus 4	18/20	90.0 (69.9-97.2)	426/426	100 (99.1-100)
RSV A	25/27	92.6 (76.6-97.9)	414/414	100 (99.1-100)
RSV B	21/22	95.5 (78.2-99.2)	419/419	100 (99.1-100)
Chlamydia pneumoniae	1/1	100 (20.7-100)	445/445	100 (99.1-100)
Mycoplasma pneumoniae	7/7	100 (64.6-100)	439/439	100 (99.1-100)

[a] Adenovirus was not detected in the 1 FN sample and detected in 2 of 4 FP samples using PCR/sequencing.
[b] Coronavirus was not detected in 2 of 16 FN samples using PCR/sequencing (1 sample was not tested by PCR/sequencing).
[c] Influenza A comparator results contain 31 samples with A H1-2009 and 51 samples with A H3 detected.
[d] Influenza A was not detected in 3 of 7 FN samples using PCR/sequencing.
[e] Influenza A H1-2009 was not detected in 2 of 4 FN samples using PCR/sequencing.
[f] Influenza A H3 was not detected in 1 of 6 FN samples using PCR/sequencing.
[g] Parainfluenza virus 1 was not detected in 2 of 5 FN samples using PCR/sequencing.

Contrived Sample Performance

There were 327 contrived samples created and tested to supplement the low prevalence targets on the RP Panel; 104 contained one or more low prevalence organisms and 223 were negative for the contrived organisms. All 327 contrived samples were tested with the ePlex RP Panel and 326 were evaluable. PPA and NPA results are summarized for these low prevalence organisms in **Table 19** below.

Table 19: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) of the ePlex RP Panel With Comparator Method (Contrived Samples)

Organism	Positive % Agreement		Negative % Agreement	
	TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Chlamydia pneumoniae	52/52	100 (93.1-100)	274/274	100 (98.6-100)
Influenza A H1	51/51	100 (93.0-100)	275/275	100 (98.6-100)

Clinical and Contrived Sample Performance by Target

Tables 20-36 below include the clinical performance by pathogen of prospective samples tested fresh (shown in **Table 15**), prospective samples tested after previously freezing (shown in **Table 16**), retrospective samples (shown in **Table 18**), and contrived samples (shown in **Table 1**).

Table 20: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Adenovirus in the ePlex RP Panel Clinical Study

Adenovirus	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	6/8[a]	75.0 (40.9-92.9)	499/503[a]	99.2 (98.0-99.7)
	Frozen	48/53[b]	90.6 (79.7-95.9)	1874/1898[b]	98.7 (98.1-99.1)
	Total	54/61	88.5 (78.2-94.3)	2373/2401	98.8 (98.3-99.2)

Adenovirus	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Retrospectively-Collected Samples		55/56[c]	98.2 (90.6-99.7)	386/390[c]	99.0 (97.4-99.6)

[a] Adenovirus was not detected in 2 of 2 FN samples and detected in 4 of 4 FP samples using PCR/sequencing.
[b] Adenovirus was not detected in 1 of 5 FN samples and detected in 9 of 24 FP samples using PCR/sequencing.
[c] Adenovirus was not detected in the 1 FN sample and detected in 2 of 4 FP samples using PCR/sequencing.

Table 21: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Coronavirus (229E, HKU1, NL63, OC43) in the ePlex RP Panel Clinical Study

Coronavirus (229E, HKU1, NL63, OC43)	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples[a]	Fresh	7/7	100 (64.6-100)	503/504	99.8 (98.9-100)
	Frozen	89/110[b]	80.9 (72.6-87.2)	1828/1841[b]	99.3 (98.8-99.6)
	Total	96/117	82.1 (74.1-88.0)	2331/2345	99.4 (99.0-99.6)
Retrospectively-Collected Samples[c]		121/138[d]	87.7 (81.2-92.2)	307/307	100 (98.8-100)

[a] 20 FN prospectively-collected frozen samples were repeat tested with the comparator method and 12 had coronavirus detected. Of these 12 samples, 11 were repeat tested with the ePlex RP Panel and 3 had coronavirus detected.
[b] Coronavirus was not detected in 2 of 21 FN samples and detected in 3 of 13 FP samples using PCR/sequencing.
[c] 10 FN retrospectively-collected samples were repeat tested with the comparator method and all 10 had coronavirus detected. Of these 10 samples, 9 were repeat tested with the ePlex RP Panel and 5 had coronavirus detected.
[d] Coronavirus was not detected in 2 of 16 FN samples using PCR/sequencing (1 sample was not tested by PCR/sequencing).

Table 22: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Human Metapneumovirus in the ePlex RP Panel Clinical Study

Human Metapneumovirus	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	107/113[a]	94.7 (88.9-97.5)	1832/1838[a]	99.7 (99.3-99.9)
	Total	107/113	94.7 (88.9-97.5)	2343/2349	99.7 (99.4-99.9)
Retrospectively-Collected Samples		5/7	71.4 (35.9-91.8)	439/439	100 (99.1-100)

[a] Human Metapneumovirus was not detected in 1 of 6 FN samples and detected in 4 of 6 FP samples using PCR/sequencing.

Table 23: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Human Rhinovirus/Enterovirus in the ePlex RP Panel Clinical Study

Human Rhinovirus/Enterovirus	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	176/183[a]	96.2 (92.3-98.1)	316/328[a]	96.3 (93.7-97.9)
	Frozen	317/336[b]	94.3 (91.3-96.4)	1544/1615[b]	95.6 (94.5-96.5)
	Total	493/519	95.0 (92.8-96.6)	1860/1943	95.7 (94.7-96.5)
Retrospectively-Collected Samples		37/41	90.2 (77.5-96.1)	384/402	95.5 (93.0-97.1)

[a] Human rhinovirus/enterovirus was not detected in 1 of 7 FN samples and detected in 9 of 12 FP samples using PCR/sequencing.
[b] Human rhinovirus/enterovirus was not detected in 6 of 19 FN samples and detected in 33 of 71 FP samples using PCR/sequencing.

Table 24: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Influenza A in the ePlex RP Panel Clinical Study

Influenza A	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples[a]	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	106/111[b]	95.5 (89.9-98.1)	1836/1840[b]	99.8 (99.4-99.9)
	Total	106/111	95.5 (89.9-98.1)	2347/2351	99.8 (99.6-99.9)
Retrospectively-Collected Samples[c]		75/82[d]	91.5 (83.4-95.8)	363/363	100 (99.0-100)

[a] Influenza A comparator results contain 71 samples with A H1-2009, 37 samples with A H3, and 3 samples with no subtype detected.
[b] Influenza A was not detected in 1 of 3 FN samples (2 samples were not tested by PCR/sequencing) and detected in 1 of 4 FP samples using PCR/sequencing.
[c] Influenza A comparator results contain 31 samples with A H1-2009 and 51 samples with A H3 detected.
[d] Influenza A was not detected in 3 of 7 FN samples using PCR/sequencing.

Table 25: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Influenza A H1 in the ePlex RP Panel Clinical Study

Influenza A H1	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	0/0	---	1951/1951	100 (99.8-100)
	Total	0/0	---	2462/2462	100 (99.8-100)
Retrospectively-Collected Samples		0/0	---	446/446	100 (99.1-100)
Contrived Samples		51/51	100 (93.0-100)	275/275	100 (98.6-100)

Table 26: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Influenza A H1-2009 in the ePlex RP Panel Clinical Study

Influenza A H1-2009	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	70/71	98.6 (92.4-99.8)	1874/1880[a]	99.7 (99.3-99.9)
	Total	70/71	98.6 (92.4-99.8)	2385/2391	99.7 (99.5-99.9)
Retrospectively-Collected Samples		27/31[b]	87.1 (71.1-94.9)	415/415	100 (99.1-100)

[a] Influenza A H1-2009 was detected in 4 of 6 FP samples using PCR/sequencing.
[b] Influenza A H1-2009 was not detected in 2 of 4 FN samples using PCR/sequencing.

Table 27: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Influenza A H3 in the ePlex RP Panel Clinical Study

Influenza A H3	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	34/37[a]	91.9 (78.7-97.2)	1914/1914	100 (99.8-100)
	Total	34/37	91.9 (78.7-97.2)	2425/2425	100 (99.8-100)
Retrospectively-Collected Samples		45/51[b]	88.2 (76.6-94.5)	394/394	100 (99.0-100)

[a] Influenza A H3 was not detected in 1 of 3 FN samples using PCR/sequencing.
[b] Influenza A H3 was not detected in 1 of 6 FN samples using PCR/sequencing.

Table 28: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Influenza B in the ePlex RP Panel Clinical Study

Influenza B	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	1/1	100 (20.7-100)	509/510	99.8 (98.9-100)
	Frozen	58/65[a]	89.2 (79.4-94.7)	1882/1886[a]	99.8 (99.5-99.9)
	Total	59/66	89.4 (79.7-94.8)	2391/2396	99.8 (99.5-99.9)
Retrospectively-Collected Samples		1/1	100 (20.7-100)	445/445	100 (99.1-100)

[a] Influenza B was not detected in 3 of 7 FN samples and detected in 2 of 4 FP samples using PCR/sequencing.

Table 29: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Parainfluenza Virus 1 in the ePlex RP Panel Clinical Study

Parainfluenza Virus 1	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	1/1	100 (20.7-100)	510/510	100 (99.3-100)
	Frozen	23/24	95.8 (79.8-99.3)	1926/1927	99.9 (99.7-100)
	Total	24/25	96.0 (80.5-99.3)	2436/2437	100 (99.8-100)
Retrospectively-Collected Samples		43/48[a]	89.6 (77.8-95.5)	396/397	99.7 (98.6-100)

[a] Parainfluenza virus 1 was not detected in 2 of 5 FN samples using PCR/sequencing.

Table 30: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Parainfluenza Virus 2 in the ePlex RP Panel Clinical Study

Parainfluenza Virus 2	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	12/13	92.3 (66.7-98.6)	497/498	99.8 (98.9-100)
	Frozen	9/9	100 (70.1-100)	1941/1942	99.9 (99.7-100)
	Total	21/22	95.5 (78.2-99.2)	2438/2440	99.9 (99.7-100)
Retrospectively-Collected Samples		46/51	90.2 (79.0-95.7)	395/395	100 (99.0-100)

Table 31: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Parainfluenza Virus 3 in the ePlex RP Panel Clinical Study

Parainfluenza Virus 3	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	5/5	100 (56.6-100)	506/506	100 (99.2-100)
	Frozen	94/104[a]	90.4 (83.2-94.7)	1842/1847[a]	99.7 (99.4-99.9)
	Total	99/109	90.8 (83.9-94.9)	2348/2353	99.8 (99.5-99.9)
Retrospectively-Collected Samples		2/2	100 (34.2-100)	444/444	100 (99.1-100)

[a] Parainfluenza virus 3 was not detected in 3 of 10 FN samples and detected in 4 of 5 FP samples using PCR/sequencing.

Table 32: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Parainfluenza Virus 4 in the ePlex RP Panel Clinical Study

Parainfluenza Virus 4	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	3/3	100 (43.9-100)	503/508[a]	99.0 (97.7-99.6)
	Frozen	5/5	100 (56.6-100)	1944/1946	99.9 (99.6-100)
	Total	8/8	100 (67.6-100)	2447/2454	99.7 (99.4-99.9)
Retrospectively-Collected Samples		18/20	90.0 (69.9-97.2)	426/426	100 (99.1-100)

[a] Parainfluenza virus 4 was detected in 3 of 5 FP samples using PCR/sequencing.

Table 33: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Respiratory Syncytial Virus A in the ePlex RP Panel Clinical Study

Respiratory Syncytial Virus A	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	8/9	88.9 (56.5-98.0)	501/501	100 (99.2-100)
	Frozen	27/31	87.1 (71.1-94.9)	1917/1918	99.9 (99.7-100)
	Total	35/40	87.5 (73.9-94.5)	2418/2419	100 (99.8-100)
Retrospectively-Collected Samples		25/27	92.6 (76.6-97.9)	414/414	100 (99.1-100)

Table 34: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for Respiratory Syncytial Virus B in the ePlex RP Panel Clinical Study

Respiratory Syncytial Virus B	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	9/10	90.0 (59.6-98.2)	500/500	100 (99.2-100)
	Frozen	81/86	94.2 (87.1-97.5)	1861/1863[a]	99.9 (99.6-100)
	Total	90/96	93.8 (87.0-97.1)	2361/2363	99.9 (99.7-100)
Retrospectively-Collected Samples		21/22	95.5 (78.2-99.2)	419/419	100 (99.1-100)

[a] RSV B was detected in 1 of 2 FP samples using PCR/sequencing.

Table 35: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for *Chlamydia pneumoniae* in the ePlex RP Panel Clinical Study

Chlamydia pneumoniae	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	0/0	---	511/511	100 (99.3-100)
	Frozen	2/5[a]	40.0 (11.8-76.9)	1945/1946[a]	99.9 (99.7-100)
	Total	2/5	40.0 (11.8-76.9)	2456/2457	100 (99.8-100)
Retrospectively-Collected Samples		1/1	100 (20.7-100)	445/445	100 (99.1-100)
Contrived Samples		52/52	100 (93.1-100)	274/274	100 (98.6-100)

[a] *C. pneumoniae* was not detected in 1 of 3 FN samples and detected in the 1 FP sample using PCR/sequencing.

Table 36: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for *Mycoplasma pneumoniae* in the ePlex RP Panel Clinical Study

Mycoplasma pneumoniae	Sample Type	Positive % Agreement		Negative % Agreement	
		TP/TP+FN	PPA (95% CI)	TN/TN+FP	NPA (95% CI)
Prospectively-Collected Samples	Fresh	3/3	100 (43.9-100)	507/508[a]	99.8 (98.9-100)
	Frozen	4/5[b]	80.0 (37.6-96.4)	1945/1946	99.9 (99.7-100)
	Total	7/8	87.5 (52.9-97.8)	2452/2454	99.9 (99.7-100)
Retrospectively-Collected Samples		7/7	100 (64.6-100)	439/439	100 (99.1-100)

[a] *M. pneumoniae* was detected in the 1 FP sample using PCR/sequencing.

[b] *M. pneumoniae* was not detected in the 1 FN sample using PCR/sequencing.

Co-detections in Prospective Clinical Samples

The ePlex RP Panel identified a total of 135 prospective samples with multiple organisms detected, or 5.5% of all prospectively-collected samples. Of these, 118 (4.8%) had two organisms, 14 (0.6%) had three organisms, and 3 (0.1%) had four organisms detected. Of the 135 co-detected samples, 58 included 1 or more organisms that had not been detected by the comparator method(s). Results are summarized in **Table 37 and 38**.

Table 37: Distinct Co-Detection Combinations Detected by the ePlex RP Panel in the Prospective Clinical Samples

Distinct Co-Detection Combinations Detected by the ePlex RP Panel				Total Number Of Co-detections (% of samples)	Number of Discrepant Co-detections	Discrepant Organism(s)[a]
Organism 1	Organism 2	Organism 3	Organism 4			
ADV	CoV			2 (0.08%)	0	
ADV	CoV	HRV/EV		2 (0.08%)	1	ADV (1)
ADV	Flu A (unk)	Flu B	HRV/EV	1 (0.04%)	1	ADV (1), Flu A (unk) (1), Flu B (1), HRV/EV (1)
ADV	Flu AH3			1 (0.04%)	0	

Distinct Co-Detection Combinations Detected by the ePlex RP Panel				Total Number Of Co-detections (% of samples)	Number of Discrepant Co-detections	Discrepant Organism(s) [a]
Organism 1	Organism 2	Organism 3	Organism 4			
ADV	Flu B	HRV/EV	RSV B	1 (0.04%)	1	ADV (1), Flu B (1)
ADV	FluA09H1			1 (0.04%)	1	ADV (1), FluA09H1 (1)
ADV	FluA09H1	HRV/EV		1 (0.04%)	0	
ADV	FluA09H1	PIV 3		1 (0.04%)	1	PIV 3 (1)
ADV	HMPV			3 (0.12%)	2	ADV (2)
ADV	HMPV	HRV/EV	RSV A	1 (0.04%)	1	RSV A (1)
ADV	HRV/EV			18 (0.73%)	7	ADV (6), HRV/EV (1)
ADV	HRV/EV	Mpneum		1 (0.04%)	0	
ADV	HRV/EV	PIV 1		1 (0.04%)	1	PIV 1 (1)
ADV	HRV/EV	PIV 4		1 (0.04%)	1	ADV (1), PIV 4 (1)
ADV	HRV/EV	RSV B		1 (0.04%)	0	
ADV	PIV 2			2 (0.08%)	1	ADV (1)
ADV	PIV 3			2 (0.08%)	1	ADV (1)
ADV	PIV 4			1 (0.04%)	1	ADV (1)
ADV	RSV B			2 (0.08%)	2	ADV (2)
CPneum	HRV/EV			1 (0.04%)	0	
CoV	FluA09H1			1 (0.04%)	0	
CoV	HMPV			4 (0.16%)	0	
CoV	HMPV	HRV/EV		2 (0.08%)	0	
CoV	HRV/EV			12 (0.49%)	4	CoV (1), HRV/EV (4)
CoV	HRV/EV	RSV B		1 (0.04%)	1	CoV (1)
CoV	PIV 1			1 (0.04%)	0	
CoV	RSV A			3 (0.12%)	0	
CoV	RSV B			3 (0.12%)	2	CoV (2)
Flu A (unk)	HRV/EV			1 (0.04%)	1	Flu A (unk) (1)
Flu AH3	HRV/EV			2 (0.08%)	1	HRV/EV (1)
Flu AH3	RSV B			1 (0.04%)	0	
Flu B	HRV/EV			4 (0.16%)	2	HRV/EV (2)
Flu B	HRV/EV	RSV B		1 (0.04%)	0	
Flu B	PIV 3			1 (0.04%)	0	
FluA09H1	HMPV	HRV/EV		1 (0.04%)	1	HRV/EV (1)
FluA09H1	HRV/EV			2 (0.08%)	1	HRV/EV (1)
HMPV	HRV/EV			5 (0.20%)	1	HRV/EV (1)
HMPV	HRV/EV	RSV B		1 (0.04%)	1	HRV/EV (1)
HMPV	PIV 3			1 (0.04%)	0	
HRV/EV	PIV 1			3 (0.12%)	0	
HRV/EV	PIV 2			7 (0.28%)	3	HRV/EV (1), PIV 2 (2)
HRV/EV	PIV 3			11 (0.45%)	5	HRV/EV (5)
HRV/EV	PIV 4			4 (0.16%)	4	PIV 4 (4)
HRV/EV	RSV A			5 (0.20%)	0	
HRV/EV	RSV B			11 (0.45%)	6	HRV/EV (6)
PIV 1	PIV 4			1 (0.04%)	1	PIV 4 (1)

Distinct Co-Detection Combinations Detected by the ePlex RP Panel				Total Number Of Co-detections (% of samples)	Number of Discrepant Co-detections	Discrepant Organism(s) [a]
Organism 1	Organism 2	Organism 3	Organism 4			
PIV 3	RSV B			1 (0.04%)	0	
RSV A	RSV B			1 (0.04%)	1	RSV B (1)
Total Number of Co-Detections				135 (5.5%)	57	64/290[b]
Total Number with 2 Organisms Detected				118 (4.8%)	47	49/236
Total Number with 3 Organisms Detected				14 (0.6%)	7	8/42
Total Number with 4 Organisms Detected				3 (0.1%)	3	7/12

Note: ADV= adenovirus, CoV= coronavirus (229E, HKU1, NL63, OC43), HMPV= human metapneumovirus, HRV/EV= human rhinovirus/enterovirus, Flu= Influenza, (unk)= unknown subtype, PIV= parainfluenza, RSV= respiratory syncytial virus, Cpneum= *C. pneumoniae*, Mpneum= *M. pneumoniae*

[a] A discrepant organism is defined as one that was detected by the ePlex RP Panel but not by the comparator method(s).

[b] 64/64 discrepant organisms were investigated using PCR/sequencing; the discrepant organism was detected in 20/64 cases:
-In 8/18 samples, adenovirus was detected by PCR/sequencing.
-In 1/4 samples, coronavirus was detected by PCR/sequencing.
-In 7/25 samples, human rhinovirus/enterovirus was detected by PCR/sequencing.
-In 1/1 sample, influenza A H1-2009 was detected by PCR/sequencing.
-In 1/1 sample, parainfluenza virus 3 was detected by PCR/sequencing.
-In 2/6 samples, parainfluenza virus 4 was detected by PCR/sequencing.

Table 38: Additional Co-Detection Combinations Detected by the Comparator Method in the Prospective Clinical Samples

Distinct Co-Detection Combinations Detected by the Comparator Method			Total Number Of Co-detections (% of samples)	Number of Discrepant Co-detections	Discrepant Organism(s) [a,b]
Organism 1	Organism 2	Organism 3			
ADV	CoV		1 (0.04%)	1	ADV (1), CoV (1)
ADV	HRV/EV		4 (0.16%)	4	ADV (4)
ADV	HRV/EV	PIV 3	1 (0.04%)	1	HRV/EV (1), PIV 3 (1)
ADV	HRV/EV	RSV A	1 (0.04%)	1	ADV (1)
CPneum	HRV/EV		1 (0.04%)	1	CPneum (1)
CPneum	PIV 3		1 (0.04%)	1	CPneum (1)
CoV	FluA09H1		2 (0.08%)	2	CoV (2)
CoV	HMPV		1 (0.04%)	1	CoV (1)
CoV	HRV/EV		6 (0.24%)	6	CoV (4), HRV/EV (2)
CoV	PIV 3		1 (0.04%)	1	CoV (1)
CoV	RSV B		3 (0.12%)	3	CoV (2), RSV B (1)
Flu AH3	HRV/EV	PIV 3	1 (0.04%)	1	Flu AH3 (1), PIV 3 (1)
Flu AH3	PIV 3		1 (0.04%)	1	PIV 3 (1)
FluA09H1	HMPV	HRV/EV	1 (0.04%)	1	HMPV (1), HRV/EV (1)
HMPV	HRV/EV		1 (0.04%)	1	HRV/EV (1)
HRV/EV	PIV 1		1 (0.04%)	1	HRV/EV (1)
HRV/EV	PIV 3		2 (0.08%)	2	HRV/EV (2)
HRV/EV	PIV 3	RSV B	1 (0.04%)	1	PIV 3 (1)
HRV/EV	RSV A		2 (0.08%)	2	RSV A (2)

[a] A discrepant organism is defined as one that was detected by the comparator method(s) but not by the ePlex RP Panel.

[b] 36/36 discrepant organisms were investigated using PCR/sequencing; the discrepant organism was not detected in 10/36 cases:
-In 2/6 samples, adenovirus was not detected by PCR/sequencing.
-In 1/2 samples, *Chlamydia pneumoniae* was not detected by PCR/sequencing.
-In 1/11 samples, coronavirus was not detected by PCR/sequencing.
-In 5/8 samples, human rhinovirus/enterovirus was not detected by PCR/sequencing.
-In 1/1 sample, influenza A H3 was not detected by PCR/sequencing.

Clinical Study ePlex RP Panel Instrument Performance

A total of 3281 samples (including prospective, retrospective, and contrived samples) were initially tested in the clinical evaluations and 3127/3281 = 95.3% (95% CI: 94.5%-96.0%) generated valid results on the first attempt. After re-test, 8 samples had invalid results; final validity rate was 3273/3281 = 99.8% (95% CI: 99.5%-99.9%).

ANALYTICAL PERFORMANCE CHARACTERISTICS

Limit of Detection for SARS-CoV-2

The limit of detection (LoD), or analytical sensitivity was identified and verified for SARS-CoV-2 using commercially available heat inactivated quantified virus. Serial dilutions were prepared in a natural clinical matrix (pooled, negative nasopharyngeal swab in VTM) and at least 20 replicates per concentration were tested in the study. The limit of detection was defined as the lowest concentration at which SARS-CoV-2 is detected at least 95% of the time. The confirmed LoD for detection of SARS-CoV-2 is shown in **Table 39**.

Table 39: SARS-CoV-2 LoD Results Summary

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

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

Limit of Detection for All other RP2 Panel Targets

The limit of detection (LoD), or analytical sensitivity was identified and verified for each viral and bacterial target on the ePlex RP2 Panel using quantified reference strains/isolates. Serial dilutions were prepared in a natural clinical matrix (pooled, negative nasopharyngeal swab in VTM samples) with one or more organisms per series, and at least 20 replicates per target were tested in the study. The limit of detection was defined as the lowest concentration at which each target is detected at least 95% of the time. The confirmed LoD for each ePlex RP2 Panel organism is shown in **Table 40.**

Table 40: LoD Results Summary

Target	Strain	LoD Concentration
Adenovirus	Type 1 (C)	1×10^{3} $TCID_{50}$/mL
	Type 4 (E)	2×10^{0} $TCID_{50}$/mL
	Type 7 (B)	2×10^{0} $TCID_{50}$/mL
Coronavirus 229E	229E	1×10^{0} $TCID_{50}$/mL
Coronavirus HKU1	HKU1[a]	5×10^{4} copies/mL
Coronavirus NL63	NL63	7.5×10^{0} $TCID_{50}$/mL
Coronavirus OC43	OC43	5×10^{2} $TCID_{50}$/mL
Human Metapneumovirus	A1 IA3-2002	2×10^{-1} $TCID_{50}$/mL
	A2 IA14-2003	2×10^{3} $TCID_{50}$/mL
	B1 Peru2-2002	2×10^{2} $TCID_{50}$/mL
	B2 Peru1-2002	2.25×10^{2} $TCID_{50}$/mL

Target	Strain	LoD Concentration
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)	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	4a	3 x 10^1 $TCID_{50}$/mL
Respiratory Syncytial Virus A	2006 Isolate	1.5 x 10^0 $TCID_{50}$/mL
Respiratory Syncytial Virus B	CH93(18)-18	2 x 10^{-1} $TCID_{50}$/mL
Chlamydia pneumoniae	AR-39	3 x 10^2 $TCID_{50}$/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.

Analytical Reactivity (Inclusivity)

Reactivity of SARS-CoV-2 Assays

Inclusivity was evaluated using RNA for SARS-CoV-2 (Hong Kong/VM20001061/2020) at 750 copies/mL. Three replicates were tested and all replicates were detected as expected as shown in **Table 41.**

Table 41: Analytical Reactivity (Inclusivity) Results for SARS-CoV-2

Target	Test Material	Concentration	Percent Detected (positive replicates / total)
SARS-CoV-2	Hong Kong/VM20001061/2020 (BEI Resource – Isolated RNA)	750 copies/mL	100% (3/3)

Predicted (*in silico*) Reactivity (Inclusivity) Results for SARS-CoV-2

In silico analysis of >118,000 sequences from GISAID was conducted to assess the ability of the ePlex RP2 Panel to detect the most recent COVID-19 strains (analysis was conducted on October 5, 2020). The results of these analyses show that the sequences are ≥99% identical.

Inclusivity of All Other RP2 Targets

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

All of the strains/isolates tested for inclusivity were detected by the ePlex RP2 Panel. Results of analytical reactivity are shown in **Tables 42-52**.

Table 42: Analytical Reactivity (Inclusivity) Results for Adenovirus

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

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

Table 43: Analytical Reactivity (Inclusivity) Results for Human Metapneumovirus

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

Table 44: Analytical Reactivity (Inclusivity) Results for Human Rhinovirus/Enterovirus

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

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

Table 45: Analytical Reactivity (Inclusivity) Results for Influenza A

Note: Due to different assays for influenza A matrix and influenza A subtypes on the ePlex RP Panel, if different LoDs are observed for inclusivity for a Flu A matrix vs. HA 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	3 x 10^0 $TCID_{50}$/mL	10x (Influenza A matrix)[a] 10000x H1 subtype[b]
	A/New Caledonia/20/1999	9 x 10^{-1} $TCID_{50}$/mL	3x
	A/New Jersey/8/76	9 x 10^{-1} $TCID_{50}$/mL	3x H1 subtype not detected[c]

Influenza A Subtype	Strain	Concentration	Multiple of LoD Detected
	A/NWS/33	3 x 10^0 $TCID_{50}$/mL	10x (Influenza A matrix)[a] H1 subtype not detected[d]
	A/PR/8/34	9 x 10^{-1} $TCID_{50}$/mL	3x (Influenza A matrix) H1 subtype not detected[e]
	A/Solomon Islands/3/2006	9 x 10^0 $TCID_{50}$/mL	30x
	A/Taiwan/42/06	9 x 10^0 $TCID_{50}$/mL	30x[f]
Influenza A H3	A/Hong Kong/8/68	1.5 x 10^2 $TCID_{50}$/mL	3x
	A/Port Chalmers/1/73		
	A/Nanchang/933/95		
	A/Victoria/3/75		
	A/Wisconsin/67/05		
Influenza A 2009 H1N1	A/California/7/2009	1 x 10^0 $TCID_{50}$/mL	10x[g]
	A/Mexico/4108/09	3 x 10^{-1} $TCID_{50}$/mL	3x
	A/NY/02/2009	1 x 10^0 $TCID_{50}$/mL	10x[h]
	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)[i]
	A/Virginia/ATCC1/2009	1 x 10^0 $TCID_{50}$/mL	10x[j]
	A/Virginia/ATCC2/2009	1 x 10^1 $TCID_{50}$/mL	100x[j]
	A/Virginia/ATCC3/2009	1 x 10^2 $TCID_{50}$/mL	1,000x[j]

[a] *In silico* analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles).
[b] *In silico* analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.
[c] H1-2009 subtype was detected in this seasonal influenza A H1 strain at 30x LoD.
[d] *In silico* analysis revealed little homology between this non-contemporary strain sequence and the H1 signal probe/capture probe sequences.
[e] *In silico* analysis revealed little homology between this non-contemporary influenza strain sequence and the H1 primer sequences.
[f] For Influenza A matrix, *in silico* analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles). For H1 subtype, *in silico* analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.
[g] For Influenza A matrix, *in silico* analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes. For H1 subtype, *in silico* analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles).
[h] For Influenza A matrix, *in silico* analysis revealed good homology to primers and probes. Lower sensitivity is likely the result of incorrect estimation of genetic material present in the culture of this or the reference strain ($TCID_{50}$ value is based only on infectious virus particles). For H1-2009 subtype, *in silico* analysis revealed that lower sensitivity may be a result of mismatches in the assay primers and/or probes.
[i] *In silico* analysis revealed little homology between the strain sequence and the H1 or H1-2009 primer, signal probe and capture probe sequences.
[j] No sequence data was available to investigate lower sensitivity of the influenza A 2009 H1N1 A/Virginia/ATCC1/2009, A/Virginia/ATCC2/2009 and A/Virginia/ATTC3/2009 strains.

Table 46: Analytical Reactivity (Inclusivity) Results for Influenza A Strains Titered with Methods Different From the Reference Strain

Influenza A Subtype	Strain	Concentration Detected
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 Subtype	Strain	Concentration Detected
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) No subtype detected[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 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= Chick Embryo Infectious Dose; EID_{50}/mL= Egg Infectious Dose

Supplemental Analytical Reactivity (Inclusivity) for Influenza A

For human, avian, and swine influenza strains not available for testing on the ePlex RP Panel, *in silico* analysis was performed. Bioinformatics analysis was used to predict a result based on the number and location of mismatches in the primers, capture probes, and signal probes found in the ePlex RP Panel relative to an alignment of GenBank sequences.

Table 47: Predicted (*in silico*) Reactivity (Inclusivity) Results for Influenza A

Influenza A Subtype	Host	Strain	GenBank ID	Predicted ePlex Result
H2N2	Human	A/Albany/20/1957(H2N2)	CY022014	Influenza A
		Kilbourne F38: A/Korea/426/68 (HA, NA) x A/Puerto Rico/8/34	CY037296	Influenza A
	Avian	A/chicken/New York/13828-3/1995(H2N2)	CY014822	Influenza A
		A/Japan/305/1957(H2N2)	CY014977	Influenza A
		A/Korea/426/1968(H2N2)	CY031596	Influenza A
H4N6	Avian	A/Blue-winged teal/Minnesota/Sg-00043/2007(H4N6)	CY063978	Influenza A
H5N1		A/Peregrine falcon/Aomori/7/2011	AB629716	Influenza A
		A/Chicken/West Bengal/239022/2010	CY061305	Influenza A
		A/Chicken/West Bengal/193936/2009	GU272009	Influenza A
		A/Chicken/Hunan/1/2009	HM172150	Influenza A
		A/Chicken/Hunan/8/2008	GU182162	Influenza A
		A/Chicken/West Bengal/106181/2008	GU083632	Influenza A
		A/Chicken/Primorsky/85/2008	FJ654298	Influenza A
		A/Chicken/West Bengal/82613/2008	GU083648	Influenza A
		A/Duck/France/080036/2008	CY046185	Influenza A

Influenza A Subtype	Host	Strain	GenBank ID	Predicted ePlex Result
		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
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

Influenza A Subtype	Host	Strain	GenBank ID	Predicted ePlex Result
		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
			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	

Influenza A Subtype	Host	Strain	GenBank ID	Predicted ePlex Result
		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 48: Analytical Reactivity (Inclusivity) Results for Influenza B

Influenza B Subtype	Strain	Concentration	Multiple of LoD Detected
Influenza B (Yamagata Lineage)	B/Lee/40	3 x 10^{-1} $TCID_{50}$/mL	3x
	B/Allen/45	1 x 10^{0} $TCID_{50}$/mL	10x[a]
	B/Maryland/1/59	1 x 10^{1} $TCID_{50}$/mL	100x[a]
	B/Taiwan/2/62	1 x 10^{1} $TCID_{50}$/mL	100x[a]
Influenza B (Victoria Lineage)	B/Hong Kong/5/72	1 x 10^{1} $TCID_{50}$/mL	100x[b]
	B/Malaysia/2506/04	3 x 10^{-1} $TCID_{50}$/mL	3x
Influenza B (Lineage unknown)	B/GL/1739/54	3 x 10^{-1} $TCID_{50}$/mL	3x

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

Table 49: Analytical Reactivity (Inclusivity) Results for Parainfluenza Virus

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

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

Table 50: Analytical Reactivity (Inclusivity) Results for Respiratory Syncytial Virus

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

Table 51: Analytical Reactivity (Inclusivity) Results for *Chlamydia pneumoniae*

	Strain	Concentration	Multiple of LoD Detected
Chlamydia pneumoniae	CWL-029	9 x 10^2 CFU/mL	3x
	TWAR strain 2043	9 x 10^2 CFU/mL	3x

Table 52: 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	9 x 10^2 CCU/mL	3x
	M129-B7	9 x 10^2 CCU/mL	3x
	[M52]	9 x 10^2 CCU/mL	3x
	[Mac]	9 x 10^2 CCU/mL	3x
	Mutant 22	3 x 10^4 CCU/mL	100x[a]
	PI 1428	3 x 10^4 CCU/mL	100x[b]

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

Analytical Specificity (Cross-Reactivity and Exclusivity)

Cross-Reactivity of the SARS-CoV-2 Assays

Cross-reactivity of the SARS-CoV-2 assays was evaluated using both *in silico* analysis and by testing quantified analytes for organisms likely to be found in circulation and other pathogens in the same genetic family. Synthetic constructs were used for analytes where high-titer cultures were not available (SARS-CoV-1, MERS-CoV, and Coronavirus HKU1). A pool of two to four analytes were tested in triplicate. Viral analytes were diluted to testing concentrations ranging from 1x10^4 - 1x10^6 $TCID_{50}$/mL. Bacterial and fungal analytes were diluted to a testing concentration of 1x10^8 CFU/mL. Synthetic constructs were tested at a concentration of 1x10^6 copies/mL. A summary of the results of cross-reactivity testing are shown in **Table 53** below. At high titers, cross-reactivity with SARS-CoV-1 was observed with the ePlex RP2 Panel.

Table 53: Cross-Reactivity of SARS-CoV-2 Assays with On and Off-Panel Organisms

Virus/Bacteria	Strain	Concentration	Cross-Reactivity
Adenovirus C	1	1 x 10^4 $TCID_{50}$/mL	Not observed
Coronavirus	229E	1 x 10^4 $TCID_{50}$/mL	Not observed
Coronavirus	HKU1[a]	5 x 10^4 $TCID_{50}$/mL	Not observed
Coronavirus	NL63	1 x 10^4 $TCID_{50}$/mL	Not observed
Coronavirus	OC43	1 x 10^6 $TCID_{50}$/mL	Not observed
Coronavirus	MERS-CoV[a]	1 x 10^4 copies/µL	Not observed
Coronavirus	SARS-CoV-1[a]	1 x 10^6 copies/µL	Observed
Echovirus T	30	1 x 10^5 $TCID_{50}$/mL	Not observed
Enterovirus	68	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza A	H1N1/NY01/2009	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza B	Yamagata	1 x 10^5 $TCID_{50}$/mL	Not observed
Metapneumovirus	B2 Peru1-2002	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	1	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	2	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	3	1 x 10^5 $TCID_{50}$/mL	Not observed
Parainfluenza	4a	1 x 10^5 $TCID_{50}$/mL	Not observed
Respiratory Syncytial Virus A	2006	1 x 10^5 $TCID_{50}$/mL	Not observed
Rhinovirus	B14	1 x 10^5 $TCID_{50}$/mL	Not observed
Bordetella pertussis	ATCC53894	1 x 10^8 CFU/mL	Not observed
Candida albicans	ATCC24433	1 x 10^8 CFU/mL	Not observed
Corynebacterium diphtheriae	ATCC53281	1 x 10^8 CFU/mL	Not observed
Haemophilus influenzae	ATCC43065	1 x 10^8 CFU/mL	Not observed
Legionella pneumophila	ATCC35096	1 x 10^8 CFU/mL	Not observed
Mycobacterium tuberculosis	H37Rv	1 x 10^8 CFU/mL	Not observed
Moraxella catarrhalis	ATCC23246	1 x 10^8 CFU/mL	Not observed
Neisseria meningitidis	NCTC10026	1 x 10^8 CFU/mL	Not observed
Pseudomonas aeruginosa	ATCC BAA-1744	1 x 10^8 CFU/mL	Not observed
Staphylococcus aureus	ATCC25923	1 x 10^8 CFU/mL	Not observed
Staphylococcus epidermidis	ATCC700567	1 x 10^8 CFU/mL	Not observed
Staphylococcus salivarius	ATCC25975	1 x 10^8 CFU/mL	Not observed
Streptococcus pneumoniae	ATCC49136	1 x 10^8 CFU/mL	Not observed
Streptococcus pyogenes	ATCC49399	1 x 10^8 CFU/mL	Not observed
Pooled Nasal Swab	Human Clinical Sample	N/A	Not observed

[a] in vitro transcript

In silico Analysis of the ePlex RP2 Panel SARS-CoV-2 Assays

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

SARS-CoV-2.

Cross-Reactivity and Exclusivity of Other RP2 Panel Targets

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

Cross-reactivity of each viral and bacterial target on the ePlex RP Panel was evaluated at high concentrations ($1 \times 10^4 – 1 \times 10^6$ $TCID_{50}$/mL for viruses, 1×10^8 CFU/mL for bacterial and fungal isolates, or $1 \times 10^4 – 1 \times 10^6$ copies/mL for *in vitro* transcripts) of quantified strains/isolates diluted in viral transport media. *In vitro* transcript for coronavirus HKU1 was diluted in PBS. **Table 54** summarizes the results of the on-panel viral and bacterial strains/isolates tested. No cross-reactivity was observed between any of the on-panel viruses or bacteria.

Table 54: Cross-reactivity with ePlex RP Panel Target Organisms

Target	Strain	Concentration	Cross-Reactivity Results
Adenovirus A	Type 31	1×10^5 $TCID_{50}$/mL	Not observed
Adenovirus B	Type 7A	1×10^5 $TCID_{50}$/mL	Not observed
Adenovirus C	Type 1	1×10^5 $TCID_{50}$/mL	Not observed
Adenovirus D	Type 9	1×10^5 $TCID_{50}$/mL	Not observed
Adenovirus E	Type 4	1×10^5 $TCID_{50}$/mL	Not observed
Adenovirus F	Type 41	1×10^5 $TCID_{50}$/mL	Not observed
Coronavirus	229E	1×10^5 $TCID_{50}$/mL	Not observed
Coronavirus	HKU1 *in vitro* transcript	1×10^6 copies/mL	Not observed
Coronavirus	NL63	1×10^5 $TCID_{50}$/mL	Not observed
Coronavirus	OC43	1×10^5 $TCID_{50}$/mL	Not observed
Enterovirus	Type 68 2007 isolate	1×10^5 $TCID_{50}$/mL	Not observed
Human metapneumovirus	B1	1×10^5 $TCID_{50}$/mL	Not observed
Human rhinovirus	1A	1×10^5 $TCID_{50}$/mL	Not observed
Influenza A	A/Brisbane/59/07	1×10^5 $TCID_{50}$/mL	Not observed
Influenza A H1	A/Brisbane/59/07	1×10^5 $TCID_{50}$/mL	Not observed
Influenza A H1-2009	A/NY/01/2009	1×10^5 $TCID_{50}$/mL	Not observed
Influenza A H3	A/Brisbane/10/07	1×10^5 $TCID_{50}$/mL	Not observed
Influenza A H3N2v[a]	A/Indiana/21/2012	2.51×10^5 EID_{50}/mL	Not observed
Influenza A H5N2[b]	A/Northern Pintail Washington/40964/14BPL	2.51×10^5 EID_{50}/mL	Not observed
Influenza A H5N8[c]	A/Gyrfalcon/Washington /410886/2014 BPL	1.58×10^5 EID_{50}/mL	Not observed
Influenza A H7N9[d]	A/ANHUI/1/2013	7.94×10^5 EID_{50}/mL	Not observed

Target	Strain	Concentration	Cross-Reactivity Results
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
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
Chlamydia pneumoniae	AR-39	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

[a] Influenza A H3N2v detected as Influenza A, Influenza A H3
[b] Influenza A H5N2 detected as Influenza A
[c] Influenza A H5N8 detected as Influenza A
[d] Influenza A H7N9 detected as Influenza A

Cross-reactivity of viruses, bacteria, and fungi that are not targets on the ePlex RP Panel was evaluated at high concentrations (1 x 10^5 $TCID_{50}$/mL or copies/mL for viruses, 1 x 10^6 CFU/mL for bacterial and yeast isolates, or 1 x 10^6 copies/mL for plasmid DNA or genomic RNA) by diluting quantified strains in viral transport media. Plasmid for bocavirus and genomic RNA for MERS coronavirus (MERS-CoV) were diluted in PBS. **Table 55** summarizes the results of the strains tested. No cross-reactivity was observed between any of the off-panel viruses, bacteria or fungi with the ePlex RP Panel targets.

Table 55: Cross-reactivity with Organisms Not Detected by the ePlex RP Panel (Exclusivity)

Target	Strain	Concentration	Cross-Reactivity Results
Acinetobacter baumanii	ATCC® 19606	1 x 10^6 CFU/mL	Not observed
Bordetella pertussis	18323 [NCTC 10739]	1 x 10^6 CFU/mL	Not observed
Bordetella parapertussis	ATCC 15311	1 x 10^6 CFU/mL	Not observed
Burkholderia cepacia	ATCC 25416	1 x 10^6 CFU/mL	Not observed
Candida albicans	ATCC 10231	1 x 10^6 CFU/mL	Not observed
Candida glabrata	ATCC 15126	1 x 10^6 CFU/mL	Not observed
MERS Coronavirus (MERS-CoV)	EMC/2012[a]	1 x 10^5 copies/mL	Not observed
Corynebacterium diphtheriae	ATCC 13812	1 x 10^6 CFU/mL	Not observed
Cytomegalovirus	AD 169	1 x 10^5 $TCID_{50}$/mL	Not observed
Epstein Barr Virus	Strain B95-8	1 x 10^5 $TCID_{50}$/mL	Not observed
Escherichia coli	ATCC 10279	1 x 10^6 CFU/mL	Not observed
Haemophilus influenzae	ATCC 43065	1 x 10^6 CFU/mL	Not observed
Herpes Simplex Virus	Isolate 2	1 x 10^5 $TCID_{50}$/mL	Not observed
Human bocavirus	Bocavirus plasmid[b]	1 x 10^6 copies/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
Legionella pneumophila	Philadelphia-1	1 x 10^6 CFU/mL	Not observed
Measles	N/A	1 x 10^5 $TCID_{50}$/mL	Not observed

Target	Strain	Concentration	Cross-Reactivity Results
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
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

[a] Extracted genomic RNA

[b] Plasmid does not contain full length viral genome.

Reproducibility

A multisite reproducibility study of the 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 ePlex instrument 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 6 organisms (representing 7 RP Panel targets) at 3 concentrations (moderate positive- 3x LoD, low positive- 1x LoD, and negative) was tested in triplicate. The 6 organisms tested included adenovirus, coronavirus (229E, HKU1, NL63, OC43) , human metapneumovirus, influenza A H3, parainfluenza virus 1, and RSV A; 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 maximum of 324 tests. After completion of initial and repeat testing for invalid results, 1 low positive sample tested at Site 3 had an invalid result and was excluded from reproducibility performance analyses.

Percent agreement (95% CI) with expected results was 100% for all 7 targets for the moderate positive and negative panel, and 100% for 6 of 7 low positive panel targets (coronavirus, human metapneumovirus, influenza A, influenza A H3, parainfluenza 1, and RSV A); percent agreement was

91.6% for adenovirus. Summary results for the 7 ePlex RP Panel targets that correspond to the 6 organisms in the reproducibility panel are provided in **Tables 56-62**. Summary results for the 10 ePlex RP Panel targets that did not have organisms included in the reproducibility panel are provided in **Table 63**.

Table 56: 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 57: Percent Agreement for Coronavirus (229E, HKU1, NL63, OC43)

Coronavirus (229E, HKU1, NL63, 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 58: 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	1	36/36	100	(90.4-100)

hMPV Concentration	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
1x LoD 2.25 x 10^2 $TCID_{50}$/mL	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 59: 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 60: Percent Agreement for Influenza A H3

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

Table 61: 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 62: 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 63: Negative Percent Agreement with Organisms Not Included in the Reproducibility Panel

Target	Site	Agreement with Expected Negative Results		
		Agreed / N	%	95% CI
Human Rhinovirus/Enterovirus	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	104/107	97.2	(92.1-99.0)
	All	320/323	99.1	(97.3-99.7)
Influenza A H1	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
	1	108/108	100	(96.6-100)

Target	Site	Agreement with Expected Negative Results		
		Agreed / N	%	95% CI
Influenza A H1-2009	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Influenza B	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Parainfluenza Virus 2	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Parainfluenza Virus 3	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	106/107	99.1	(94.9-99.8)
	All	322/323	99.7	(98.3-99.9)
Parainfluenza Virus 4	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Respiratory Syncytial Virus B	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Chlamydia pneumoniae	1	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	107/107	100	(96.5-100)
	All	323/323	100	(98.8-100)
Mycoplasma pneumoniae	1	108/108	100	(96.6-100)
	2	107/108	99.1	(94.9-99.8)
	3	106/107	99.1	(94.9-99.8)
	All	321/323	99.4	(97.8-99.8)

Samples with Co-Detected Organisms

Co-Detection of SARS-CoV-2 with Other Organisms

Detection of SARS-CoV-2 in the presence of another clinically relevant organism was evaluated using a natural clinical matrix (pooled, negative nasopharyngeal swab samples) spiked with SARS-CoV-2 and a second organism co-amplified in the same PCR reaction. In this study, SARS-CoV-2 was tested at a low concentration (3x LoD) in combination with the second organism at a high concentration (1 x 10^6 copies/mL). SARS-CoV-2 was also tested a high concentration (2.5 x 10^6 copies/mL) in combination with the second organism at low concentration (3x LoD). **Table 64** contains the results of co-detection testing which demonstrated that there is no competitive inhibition when SARS-CoV-2 is co-amplified at low

concentrations in the presence of the indicated organisms at high concentrations or when SARS-CoV-2 at high concentration is co-amplified with the indicated organism at low concentration.

Table 64: Detection of Co-detections

Organism 1	High Titer	Organism 2	Multiple of LoD	% Positive of Organism 2
SARS-CoV-2	2.5 x 10^6 copies/mL	Influenza A H1-2009	3x	100%
SARS-CoV-2	2.5 x 10^6 copies/mL	Adenovirus	3x	100%
SARS-CoV-2	2.5 x 10^6 copies /mL	Influenza B	3x	100%
Influenza A H1-2009	1 x 10^6 copies /mL	SARS-CoV-2	3x	100%
Adenovirus	1 x 10^6 copies /mL	SARS-CoV-2	3x	100%
Influenza B	1 x 10^6 copies /mL	SARS-CoV-2	3x	100%

Samples with Co-Detected Organisms on the RP2 Panel

Detection of more than one clinically relevant viral organism in a sample was evaluated with the 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). **Table 65** contains the results of co-detection testing which demonstrated the ability of the ePlex RP Panel to detect 2 organisms in a sample at both high and low concentrations as indicated in the table.

Table 65: Detection of Co-detections

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
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 (229E, HKU1, NL63, OC43)	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 (229E, HKU1, NL63, OC43)	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

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 natural negative NPS in VTM 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 between natural clinical matrix (pooled, negative nasopharyngeal swab in VTM samples) and viral transport media when spiked with targets at a concentration of approximately 10x LoD. Quantified, representative viral and bacterial strains were diluted in a natural clinical matrix (pooled, negative nasopharyngeal swab in VTM samples) and in viral transport media. All samples were tested in duplicate. There was no difference observed in detection of targets in natural clinical matrix vs. viral transport media.

Interfering Substances

Substances commonly found in respiratory samples, 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 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 for negative and positive interference. 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 ePlex RP Panel. No potentially interfering substances were found to inhibit the ePlex RP Panel at the concentrations tested in **Table 66**.

Table 66: 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®)	1.5% v/v
	Oxymetazoline HCl (Afrin®)	1% v/v
	Sodium chloride	0.8% w/v
Antibacterial, systemic	Tobramycin[b]	1% w/v
Antibiotic, nasal ointment	Mupirocin	2% w/v
Nasal corticosteroids	Beclomethasone	1.5% w/v

Potentially Interfering Substance	Active Ingredient	Testing Concentration
	Dexamethasone	1.5% w/v
	Flunisolide	1.5% w/v
	Budesonide (Rhinocort®)	0.9% v/v
	Triamcinolone (Nasacort®)	1.5% v/v
	Fluticasone (Flonase®)	1.5% v/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	*Streptococcus pneumoniae*	1 x 10^6 CFU/mL
	Bordetella parapertussis	
	Haemophilus influenza	
	Staphylococcus aureus	
	Neisseria meningitides	
	Corynebacterium diptheriae	

[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% weight/volume in the sample, tobramycin was found to inhibit assay performance.

Carryover and Cross-contamination

The carryover/cross-contamination rate of the ePlex RP Panel and ePlex instrument was tested in a checkerboard approach by running high positive and negative samples interspersed in all bays of a four-tower ePlex instrument (24 bays total) 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 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 between bays or within bays with the ePlex RP Panel when testing consecutively or in adjacent bays.

TROUBLESHOOTING

Table 67: Troubleshooting Table

For a complete list of all ePlex error messages and a description of the messages, please refer to the ePlex Operator Manual.

Error	Error Messages	Description	Re-test Recommendations
Test did not start	Cartridge failure The cartridge initialization test failed	An error that occurs during pre-run checks (cartridge initialization) of the cartridge upon insertion into the bay. Cartridge initialization occurs	1. Remove cartridge from bay. a. Reset bay to clear the error b. Restart cartridge in any available bay

Error	Error Messages	Description	Re-test Recommendations
	Cartridge not present Bay heater failure Unknown error Bay main / fluid motor failure EEPROM 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 was unable to enable cartridge insertion for the bay The system failed to prepare the cartridge for processing	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 from the bay. If the cartridge label has been pierced, the test has already started and cartridge cannot be reused. If the label has not been pierced, follow the recommendation as stated.	2. If the cartridge is not able to be run on the second try and again generates an error during cartridge 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 GenMark 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 GenMark 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 the internal control will be invalid.	Reagents have been consumed and the cartridge cannot be reused. Contact GenMark Technical Support and proceed with repeat testing of the sample using a new cartridge.

Technical Support

GenMark Technical support is available 24 hours a day, 7 days a week to provide the highest level of customer support and satisfaction.

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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
Rx Only	For prescription use only		For Use Under the Emergency Use Authorization Only

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Effective Date: September 2020

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