July 2021

QIAstat-Dx® Respiratory SARS-CoV-2 Panel Instructions for Use (Handbook)

Version 1

For *in vitro* diagnostic use under Emergency Use Authorization Only

Rx Only

IVD

REF 691223

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R5

Sample to Insight

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Contents

Intended Use

The QIAstat-Dx Respiratory SARS-CoV-2 Panel is a multiplexed nucleic acid real-time PCR test intended for the qualitative detection and differentiation of nucleic acid from multiple respiratory viral and bacterial organisms, including the SARS-CoV-2 virus, in nasopharyngeal swabs (NPS) eluted in universal transport media collected from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity or moderate complexity tests.

The QIAstat-Dx Respiratory SARS-CoV-2 Panel is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following organism types and subtypes: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, SARS-CoV-2, Human Metapneumovirus A+B, Influenza A, Influenza A H1, Influenza A H3, Influenza A H1N1/pdm09, Influenza B, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Rhinovirus/Enterovirus, Respiratory Syncytial Virus A+B, *Bordetella pertussis*, *Chlamydophila 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 nasopharyngeal swabs (NPS) during the acute phase of infection. Positive results are indicative of the presence of the identified microorganism, but do not rule out co-infection with other pathogens not detected by the test, or lower respiratory tract infection that is not detected by a nasopharyngeal swab. The agent detected may not be the definite cause of disease.

For SARS-CoV-2 positive specimens; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status.

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

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions. Negative SARS-CoV-2 results must be combined with clinical observations, patient history, and epidemiological information. Negative results for other organisms identified 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 QIAstat Dx Respiratory SARS-CoV-2 Panel is intended for use by qualified and trained operators who are proficient in performing the tests using the QIAstat Dx Analyzer System. The QIAstat Dx Respiratory SARS-CoV-2 Panel is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation

QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge Description

The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge is a disposable plastic device that allows performance of fully automated molecular assays for the detection of respiratory pathogens. The main features of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge include compatibility with nasopharyngeal swab in transport medium (liquid samples), hermetical containment of the pre-loaded reagents necessary for testing, and true walk-away operation. All sample preparation and assay testing steps are performed within the cartridge.

All reagents required for the complete execution of a test run are pre-loaded and self-contained in the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge. The user does not need to come in contact with and/or manipulate any reagents. During the test, reagents are handled within the cartridge in the Analytical Module of the QIAstat-Dx Analyzer 1.0 by pneumatically-operated microfluidics and make no direct contact with the actuators. The QIAstat-Dx Analyzer 1.0 houses air filters for both incoming and outgoing air, further safeguarding the environment. After testing, the cartridge stays hermetically closed at all times, greatly enhancing its safe disposal.

Within the cartridge, multiple steps are automatically performed in sequence using pneumatic pressure to transfer samples and fluids via the transfer chamber to their intended destinations.

After the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge containing the sample is introduced into the QIAstat-Dx Analyzer 1.0, the following assay steps occur automatically:

- Resuspension of Internal Control
- Cell lysis using mechanical and/or chemical means
- Membrane-based nucleic acid purification
- Mixing of the purified nucleic acid with lyophilized master mix reagents
- Transfer of defined aliquots of eluate/master mix to different reaction chambers
- Performance of multiplex real-time RT-PCR testing within each reaction chamber.

  Note: An increase in fluorescence, indicating detection of the target analyte, is detected directly within each reaction chamber.

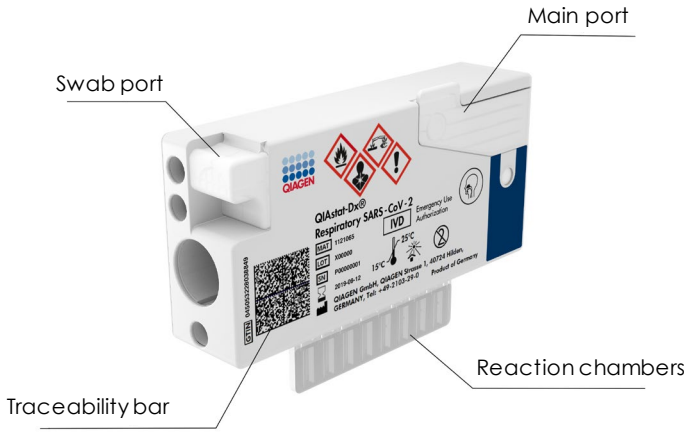

Figure 1. Layout of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge and its features.

Note: The swab port is not used for the QIAstat-Dx Respiratory SARS-CoV-2 Panel assay.

Pathogen Information

Acute respiratory infections can be caused by a variety of pathogens, including bacteria and viruses, and generally present with nearly indistinguishable clinical signs and symptoms. The rapid and accurate determination of the presence or absence of potential causative agent(s) helps make timely decisions regarding treatment, hospital admission, infection control, and return of the patient to work and family. It may also greatly support improved antimicrobial stewardship and other important public health initiatives.

The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge is a single-use cartridge that includes all reagents needed for nucleic acid extraction, nucleic acid amplification and detection of 22 bacteria and viruses (or their subtypes), including SARS-CoV-2 that cause respiratory symptoms. Testing requires a small sample volume and minimal hands-on time, and the results are available in approximately one hour.

The SARS-CoV-2 target in the QIAstat-Dx Respiratory SARS-CoV-2 Panel has been designed upon alignment of more than 170 genomic sequences available in public databases from the SARS-CoV-2, which was identified as the causative agent of the viral pneumonia (COVID-19) outbreak originated in Wuhan, Hubei, China. The SARS-CoV-2 in this panel targets 2 genes of the virus genome (Orf1b poly gene (Rdrp gene) and E genes) detected with the same fluorescence channel. The two gene targets are not differentiated and amplification of either or both gene targets leads to a fluorescence signal.

Pathogens (and subtypes) that can be detected and identified with the QIAstat-Dx Respiratory SARS-CoV-2 Panel are listed in Table 1 (next page).

Table 1. Pathogens detected by the QIAstat-Dx Respiratory SARS-CoV-2 Panel

Pathogen	Classification (genome type)
Influenza A	Orthomyxovirus (RNA)
Influenza A, subtype H1N1/2009/pdm09	Orthomyxovirus (RNA)
Influenza A subtype H1	Orthomyxovirus (RNA)
Influenza A subtype H3	Orthomyxovirus (RNA)
Influenza B	Orthomyxovirus (RNA)
Coronavirus 229E	Coronavirus (RNA)
Coronavirus HKU1	Coronavirus (RNA)
Coronavirus NL63	Coronavirus (RNA)
Coronavirus OC43	Coronavirus (RNA)
SARS-CoV-2	Coronavirus (RNA)
Parainfluenza virus 1	Paramyxovirus (RNA)
Parainfluenza virus 2	Paramyxovirus (RNA)
Parainfluenza virus 3	Paramyxovirus (RNA)
Parainfluenza virus 4	Paramyxovirus (RNA)
Respiratory Syncytial Virus A/B	Paramyxovirus (RNA)
Human Metapneumovirus A/B	Paramyxovirus (RNA)
Adenovirus	Adenovirus (DNA)
Rhinovirus/Enterovirus	Picornavirus (RNA)
Mycoplasma pneumoniae	Bacterium (DNA)
Chlamydophila pneumoniae	Bacterium (DNA)
Bordetella pertussis	Bacterium (DNA)

Note: Enterovirus and Rhinovirus are both detected, but not differentiated, with the QIAstat-Dx Respiratory SARS-CoV-2 Panel.

Principle of the Procedure

Description of the process

Diagnostic tests with the QIAstat-Dx Respiratory SARS-CoV-2 Panel are performed on the QIAstat-Dx Analyzer 1.0. All of the sample preparation and analysis steps are performed automatically by the QIAstat-Dx Analyzer 1.0. Samples are collected and loaded manually into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge:

A transfer pipette provided with the test kit is used for dispensing transport medium liquid sample into the main port (Figure 2).

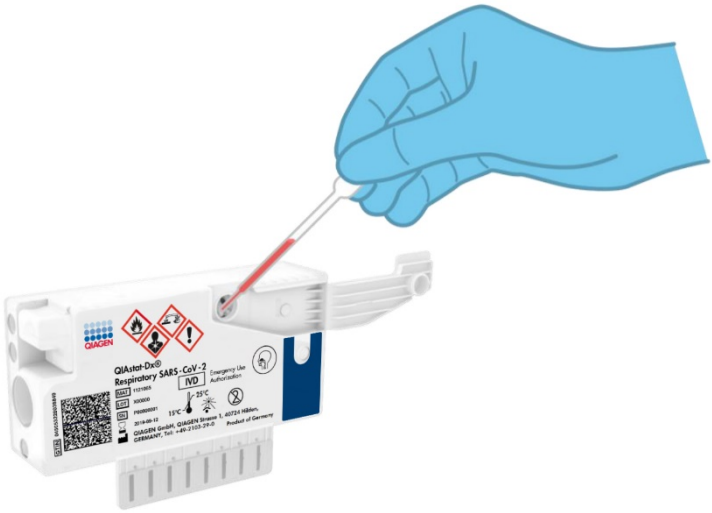

Figure 2. Dispensing transport medium liquid sample into the main port.

Sample collection and cartridge loading

The collection of samples and their subsequent loading into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge should be performed by personnel trained in safe handling of biological samples.

The following steps are involved and must be executed by the user:

1. A nasopharyngeal swab sample is collected.
2. The nasopharyngeal swab is placed into transport medium.
3. The sample information is manually written on or a sample label is affixed to the top of a QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.
4. Transport medium liquid sample is loaded manually into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

   300 µl of sample is transferred into the main port of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge using one of the included transfer pipettes.

   Note: When loading transport medium liquid sample, the user performs a visual check of the sample inspection window (see image below) to confirm that the liquid sample has been loaded (Figure 3, next page).

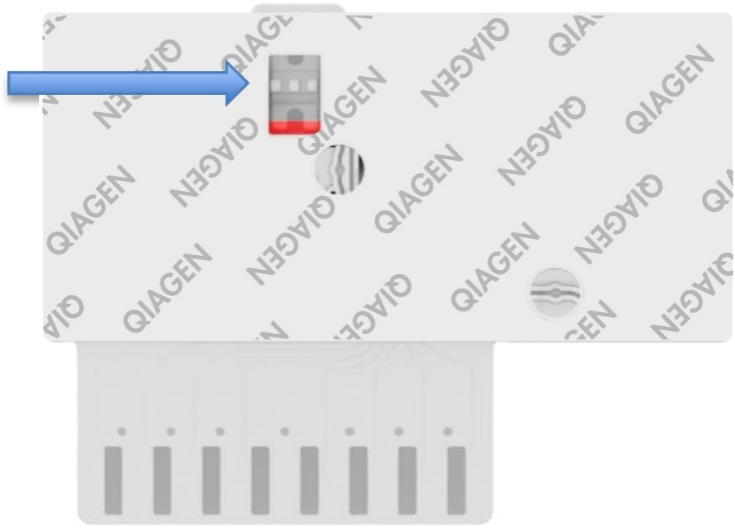

Figure 3. Sample inspection window (blue arrow).

5. The sample bar code and QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge QR code are scanned in the QIAstat-Dx Analyzer 1.0.
6. The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge is introduced into the QIAstat-Dx Analyzer 1.0.
7. The test is started on the QIAstat-Dx Analyzer 1.0.

Sample preparation, nucleic acid amplification and detection

The extraction, amplification, and detection of nucleic acids in the sample are performed automatically by the QIAstat-Dx Analyzer 1.0.

1. The liquid sample is homogenized and cells are lysed in the lysis chamber of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, which includes a rotor that turns at high speed.
2. Nucleic acids are purified from the lysed sample via binding to a silica membrane in the purification chamber of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge in the presence of chaotropic salts and alcohol.
3. The purified nucleic acids are eluted from the membrane in the purification chamber and are mixed with the lyophilized PCR chemistry in the dried-chemistry chamber of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.
4. The mixture of sample and PCR reagents is dispensed into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge PCR chambers, which contain lyophilized, assay-specific primers and probes.
5. The QIAstat-Dx Analyzer 1.0 creates the optimal temperature profiles to carry out effective multiplex real-time RT-PCR and performs real-time fluorescence measurements to generate amplification curves.
6. The QIAstat-Dx Analyzer 1.0 Software interprets the resulting data and process controls and delivers a test report.

Materials Provided

Kit contents

QIAstat-Dx Respiratory SARS-CoV-2 Panel **Catalog no.** **Number of tests**	 **691223** **6**
QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge*	6
Transfer pipettes†	6

* 6 individually packaged cartridges containing all reagents needed for sample preparation and multiplex real-time RT-PCR, plus Internal Control.

† 6 individually packaged transfer pipettes for dispensing liquid sample into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

Materials Required but Not Provided

The QIAstat-Dx Respiratory SARS-CoV-2 Panel is designed for use with the QIAstat-Dx Analyzer 1.0. Before beginning a test, make sure the following are available:

- QIAstat-Dx Analyzer 1.0 (at least one Operational Module and one Analytical Module) with software version 1.2 or higher
- *QIAstat-Dx Analyzer 1.0 User Manual* (for use with software version 1.2 or higher)
- QIAstat-Dx latest Assay Definition File software for Respiratory SARS-CoV-2 Panel installed on the Operational Module

Warnings and Precautions

For *in vitro* diagnostic use under Emergency Use Authorization only.

The QIAstat-Dx Respiratory SARS-CoV-2 Panel is to be used by laboratory professionals trained in the use of QIAstat-Dx Analyzer 1.0.

This device is restricted to sale by or on the order of a physician, or to a clinical laboratory; its use is restricted to, by, or on the order of a physician.

Pertussis is a nationally notifiable infectious disease in the U.S. If *Bordetella pertussis* is detected, notify state and/or local health departments.

Laboratories are required to report all positive SARS-CoV-2 results to the appropriate public health authorities.

For in vitro diagnostic use • For Prescription Use Only (Rx only) • For use under an Emergency Use Authorization (EUA) only • This test has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories; laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 U.S.C. §263a that meet the requirements to perform high complexity or moderate complexity tests. • This product has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms. • The emergency use of this product 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 declaration is terminated or authorization is revoked sooner.

Safety information

When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, consult the appropriate safety data sheets (SDSs). These are available online in PDF format at **www.qiagen.com/safety** where you can find, view and print the SDS for each QIAGEN kit and kit component.

Always wear appropriate personal protective equipment, including but not limited to disposable powder-free gloves, a lab coat, and protective eyewear. Protect skin, eyes, and mucus membranes. Change gloves often when handling samples.

Handle all samples, used cartridges and transfer pipettes as if they are capable of transmitting infectious agents. Always observe safety precautions as outlined in relevant guidelines, such as the Clinical and Laboratory Standards Institute® (CLSI) *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline* (M29), or other appropriate documents provided by:

- OSHA®: Occupational Safety and Health Administration (United States of America)
- ACGIH®: American Conference of Government Industrial Hygienists (United States of America)
- COSHH: Control of Substances Hazardous to Health (United Kingdom)

Follow your institution's safety procedures for handling biological samples. Dispose of samples, QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges, and transfer pipettes according to the appropriate regulations.

The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge is a closed, single-use device that contains all reagents needed for sample preparation and multiplex real-time RT-PCR within the QIAstat-Dx Analyzer 1.0. Do not use a QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge that is past its expiration date, appears damaged, or leaks fluid. Dispose

of used or damaged cartridges in accordance with all national, state, and local health and safety regulations and laws.

Observe standard laboratory procedures for keeping the working area clean and contamination-free. Guidelines are outlined in publications such as the *Biosafety in Microbiological and Biomedical Laboratories* from the Centers for Disease Control and Prevention and the National Institutes of Health (**https://www.cdc.gov/labs/BMBL.html**).

The following hazard and precautionary statements apply to components of the QIAstat-Dx Respiratory SARS-CoV-2 Panel.

QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge

Contains: ethanol; guanidine hydrochloride; guanidine thiocyanate; isopropanol; proteinase K; t-Octylphenoxypolyethoxyethanol. Danger! Highly flammable liquid and vapour. Harmful if swallowed or if inhaled. May be harmful in contact with skin. Causes severe skin burns and eye damage. May cause allergy or asthma symptoms or breathing difficulties if inhaled. May cause drowsiness or dizziness. Harmful to aquatic life with long lasting effects. Contact with acids liberates very toxic gas. Corrosive to the respiratory tract. Keep away from heat/sparks/open flames/hot surfaces. No smoking. Avoid breathing dust/fume/gas/mist/vapours/spray. Wear protective gloves/protective clothing/eye protection/face protection. Wear respiratory protection. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. IF exposed or concerned: Immediately call a POISON CENTER or doctor/ physician. Remove person to fresh air and keep comfortable for breathing.

Reagent Storage and Handling

Store the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges in a dry, clean storage space at room temperature (15–25°C). Do not remove the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges or the transfer pipettes from their individual packaging until actual use. Under these conditions, QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges can be stored until the expiration date printed on the individual packaging. The expiration date is also included in the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge bar code and is read by the QIAstat-Dx Analyzer 1.0 when the cartridge is inserted into the instrument to run a test.

Specimen Handling, Storage and Preparation

Nasopharyngeal samples should be collected and handled according to the manufacturer's recommended procedures.

Recommended storage conditions for NPS (nasopharyngeal swab) resuspended in UTM specimens are listed below:

- Room temperature up to 4 hours at 15–25°C
- Refrigerated up to 3 days at 2–8°C
- Frozen up to 30 days at –15 to –25°C

Procedure

Internal Control

The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge includes a full process Internal Control which is titered MS2 bacteriophage. The MS2 bacteriophage is a single-stranded RNA virus that is included in the cartridge in dried form and is rehydrated upon sample loading. This Internal Control material verifies all steps of the analysis process, including sample resuspension/homogenization, lysis, nucleic acid purification, reverse transcription and PCR.

A positive signal for the Internal Control indicates that all processing steps performed by the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge were successful.

A negative signal of the Internal Control does not negate any positive results for detected and identified targets, but it does invalidate all negative results in the analysis. Therefore, the test should be repeated if the Internal Control signal is negative.

Protocol: Transport medium liquid samples

Sample collection, transport and storage

Collect nasopharyngeal swab samples according to the swab manufacturer's recommended procedures and place the swab into Universal Transport Medium.

Loading a sample into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge

1. Open the package of a QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge using the tear notches on the sides of the packaging (Figure 4).

   IMPORTANT: After the package is open, sample should be introduced inside the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge and loaded into the QIAstat-Dx Analyzer 1.0 within 120 minutes.

Figure 4. Opening the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

2. Remove the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge from the packaging and position it so that the QR code on the label faces you.
3. Manually write the sample information or place a sample information label on the top of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge. Make sure that the label is properly positioned and does not block the lid opening (Figure 5).

Figure 5. Sample information placement on top of QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

4. Open the sample lid of the main port on the front of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge (Figure 6).

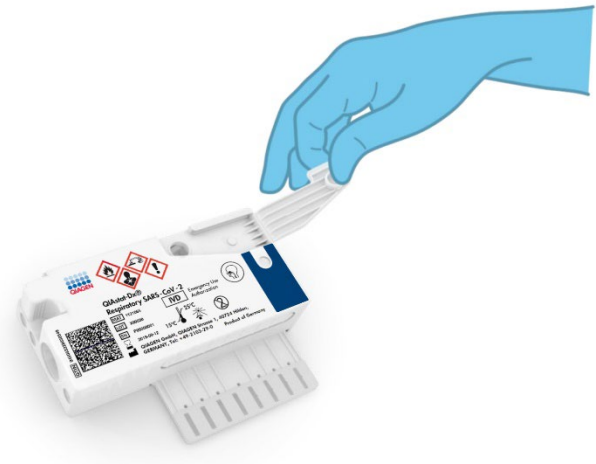

Figure 6. Opening the sample lid of main port.

5. Open the tube with the sample to be tested. Use the supplied transfer pipette to draw up fluid to the third fill line on the pipette (i.e., 300 µl) (Figure 7).

   IMPORTANT: Take care to avoid drawing air into the pipette. If Copan® UTM®, Universal Transport Medium is used as transport medium take care not to aspirate any of the beads present in the tube. If air or beads are drawn into the pipette, carefully expel the sample fluid in the pipette back into the sample tube and draw up fluid again.

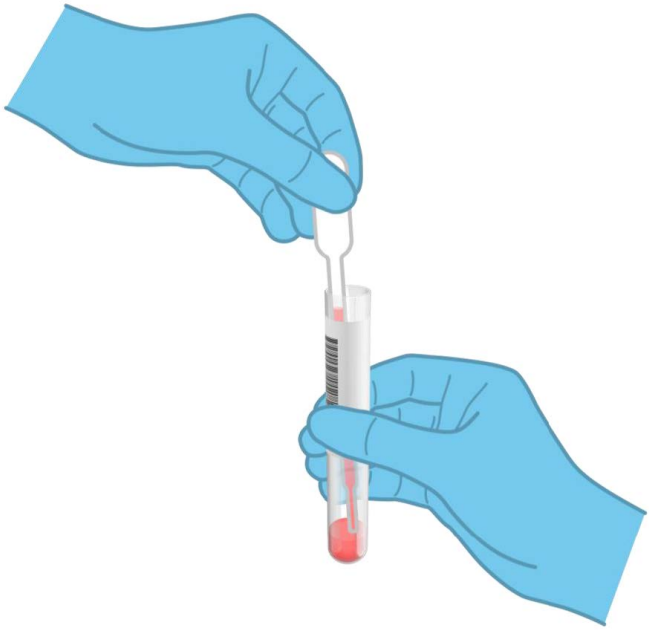

Figure 7. Drawing up sample into the supplied transfer pipette.

6. Carefully transfer 300 µl of sample volume into the main port of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge using the supplied single-use transfer pipette (Figure 8, next page).

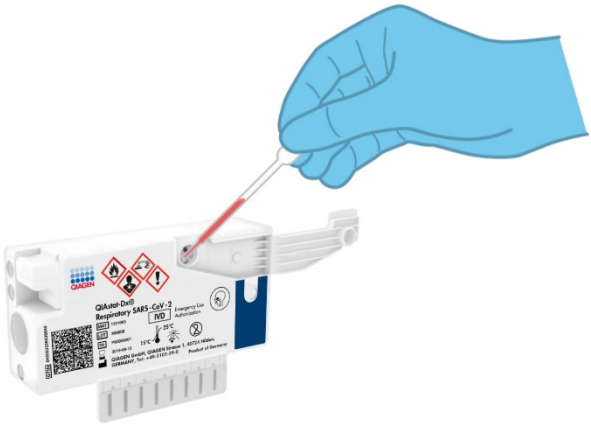

Figure 8. Transferring sample to main port of QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

7. Firmly close the sample lid of the main port until it clicks (Figure 9).

Figure 9. Closing the sample lid of the main port.

8. Visually confirm that the sample has been loaded by checking the sample inspection window of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge (Figure 10).

   IMPORTANT: After the sample is placed inside the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, the cartridge must be loaded into the QIAstat-Dx Analyzer 1.0 within 90 minutes.

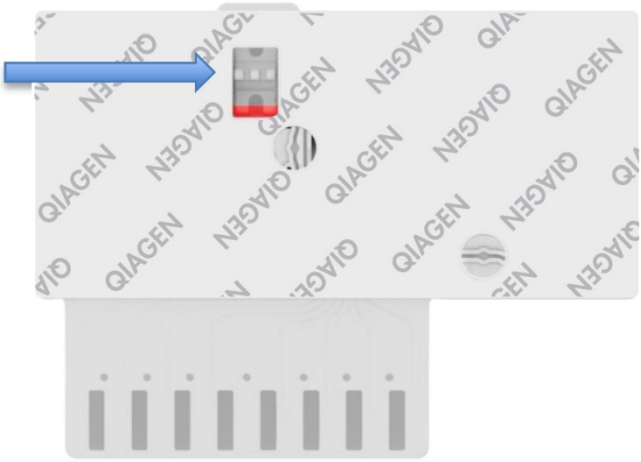

Figure 10. Sample inspection window (blue arrow).

Starting the QIAstat-Dx Analyzer 1.0

9. Power ON the QIAstat-Dx Analyzer 1.0 using the On/Off button on the front of the instrument.

   Note: The power switch on the back of the Analytical Module must be set in the "I" position. The QIAstat-Dx Analyzer 1.0 status indicators will turn blue.

10. Wait until the Main screen appears and the QIAstat-Dx Analyzer 1.0 status indicators turn green and stop blinking.
11. Log in to the QIAstat-Dx Analyzer 1.0 by entering the user name and password.

Note: The Login screen will appear if User Access Control is activated. If the User Access Control is disabled, no user name/password will be required and the Main screen will appear.

12. If the Assay Definition File software has not been installed on the QIAstat-Dx Analyzer 1.0, follow the installation instructions prior to running the test (see "Appendix A: Installing the Assay Definition File", page 127, for additional information).

Running a test

13. Press the Run Test button in the top right corner of the touchscreen of the QIAstat-Dx Analyzer 1.0.
14. When prompted, scan the sample ID bar code on the UTM tube containing the sample, or scan the specimen information bar code located on the top of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge (see step 3) using the integrated front bar code reader of the QIAstat-Dx Analyzer 1.0 (Figure 11).

    Note: It is also possible to enter the sample ID using the virtual keyboard of the touchscreen by selecting the Sample ID field.

    Note: Depending on the chosen system configuration, entering the patient ID may also be required at this point.

    Note: Instructions from the QIAstat-Dx Analyzer 1.0 appear in the Instructions Bar at the bottom of the touchscreen.

Figure 11. Scanning sample ID bar code.

15. When prompted, scan the bar code of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge to be used (Figure 12). The QIAstat-Dx Analyzer 1.0 automatically recognizes the assay to be run based on the cartridge bar code.

    Note: The QIAstat-Dx Analyzer 1.0 will not accept QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges with lapsed expiration dates, previously used cartridges, or cartridges for assays that have not been installed on the unit. An error message will be shown in these cases and the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge will be rejected. Refer to the *QIAstat-Dx Analyzer 1.0 User Manual* for further details on how to install assays.

Figure 12. Scanning QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge bar code.

16. The Confirm screen will appear. Review the entered data and make any necessary changes by selecting the relevant fields on the touchscreen and editing the information.
17. Press Confirm when all the displayed data are correct. If needed, select the appropriate field to edit its content, or press Cancel to cancel the test (Figure 13, next page).

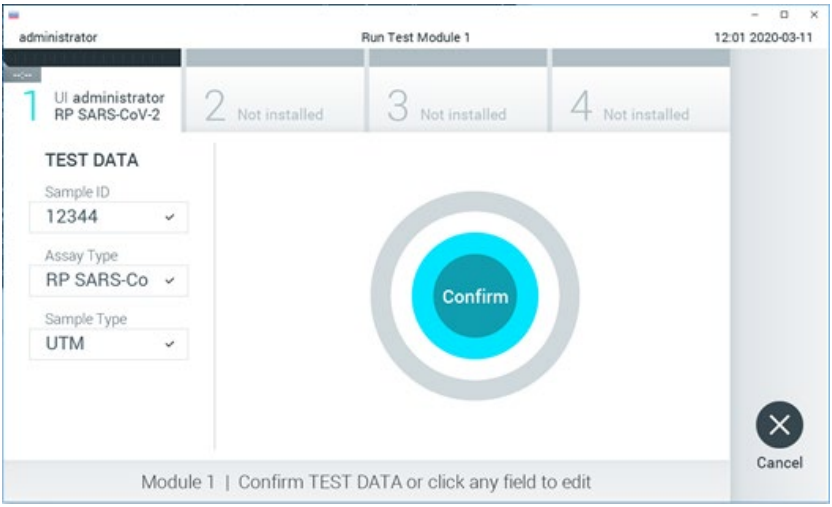

Figure 13. Confirming data entry.

18. Make sure that both sample lids of the swab port and main port of the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge are firmly closed. When the cartridge entrance port on the top of the QIAstat-Dx Analyzer 1.0 automatically opens, insert the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge with the bar code facing to the left and the reaction chambers facing down (Figure 14, next page).

    Note: There is no need to push the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge into the QIAstat-Dx Analyzer 1.0. Position it correctly into the cartridge entrance port and the QIAstat-Dx Analyzer 1.0 will automatically move the cartridge into the Analytical Module.

Figure 14. Inserting QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge into QIAstat-Dx Analyzer 1.0.

19. Upon detecting the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, the QIAstat-Dx Analyzer 1.0 will automatically close the lid of the cartridge entrance port and start the test run. No further action from the operator is required to start the run.

    Note: The QIAstat-Dx Analyzer 1.0 will not accept a QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge other than the one used and scanned during the test setup. If a cartridge other than the one scanned is inserted, an error will be generated and the cartridge will be automatically ejected.

    Note: Up to this point, it is possible to cancel the test run by pressing the Cancel button in the bottom right corner of the touchscreen.

    Note: Depending on the system configuration, the operator may be required to re-enter their user password to start the test run.

Note: The lid of the cartridge entrance port will close automatically after 30 seconds if a QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge is not positioned in the port. If this occurs, repeat the procedure starting with step 17.

20. While the test is running, the remaining run time is displayed on the touchscreen.
21. After the test run is completed, the Eject screen will appear (Figure 15) and the Module status bar will display the test result as one of the following options:

- **TEST COMPLETED**: The test was completed successfully
- **TEST FAILED**: An error occurred during the test
- **TEST CANCELED**: The user canceled the test

IMPORTANT: If the test fails, refer to the "Troubleshooting" section in the *QIAstat-Dx Analyzer 1.0 User Manual* for possible reasons and instructions on how to proceed.

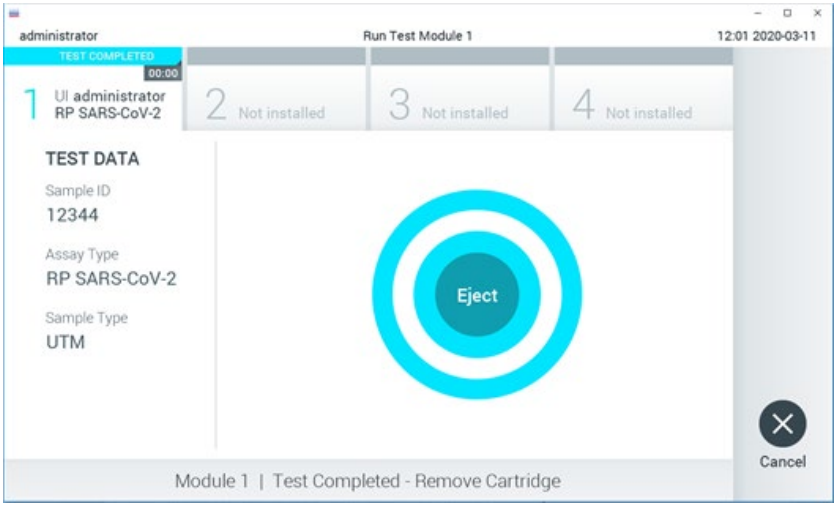

Figure 15. Eject screen display.

22. Press Eject on the touchscreen to remove the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge and dispose of it as biohazardous waste in accordance

with all national, state, and local health and safety regulations and laws. The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge should be removed when the cartridge entrance port opens and ejects the cartridge. If the cartridge is not removed after 30 seconds, it will automatically move back into the QIAstat-Dx Analyzer 1.0 and cartridge entrance port lid will close. If this occurs, press Eject to open the lid of the cartridge entrance port again and then remove the cartridge.

IMPORTANT: Used QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges must be discarded. It is not possible to re-use cartridges for tests for which the execution was started but then subsequently cancelled by the operator, or for which an error was detected.

23. After the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge has been ejected, the results Summary screen will appear. Refer to "Interpretation of Results", page, 37 for further details. To begin the process for running another test, press Run Test.

    Note: For further information on the use of the QIAstat-Dx Analyzer 1.0, refer to the *QIAstat-Dx Analyzer 1.0 User Manual*.

Viewing results

The QIAstat-Dx Analyzer 1.0 automatically interprets and saves test results. After ejecting the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, the results Summary screen is automatically displayed (Figure 16).

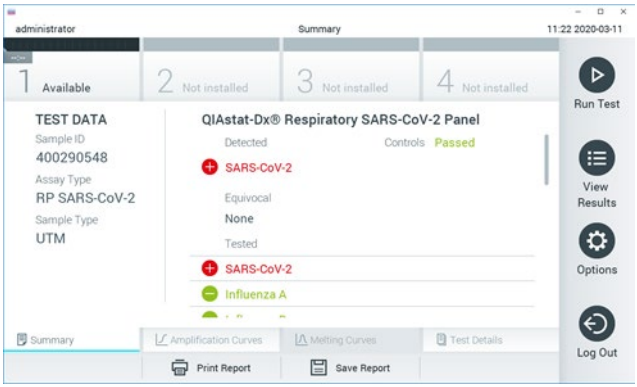

Figure 16. Results Summary screen example showing Test Data on the left panel and Test Summary in the main panel.

The main part of the screen provides the following three lists and uses color-coding and symbols to indicate the results:

- The first list includes all pathogens detected and identified in the sample, preceded by a ⊕ sign and are colored red.
- The second list includes all equivocal pathogens, preceded by a yellow question mark ?, in the event any of the subtypes H1, H3 and/or H1N1 pdm09 are detected and identified in the sample, but Influenza A is not detected.
- The third list includes all pathogens tested in the sample. Pathogens detected and identified in the sample are preceded by a ⊕ sign and are colored red. Pathogens that were tested but not detected are preceded by a ⊖ sign and are colored green. Equivocal pathogens are preceded by a ?.

Note: Pathogens detected and identified in the sample are shown in all lists.

If the test failed to complete successfully, a message will indicate "Failed", followed by the specific Error Code.

The following Test Data is shown on the left side of the screen:

- Sample ID
- Assay Type
- Sample Type

Further data about the assay is available, depending on the operator's access rights, through the tabs at the bottom of the screen (e.g., amplification plots and test details). For additional details, please see section below.

Interpretation of Results

Internal Control interpretation

Internal Control results are to be interpreted according to Table 2.

Table 2. Interpretation of Internal Control results

Control result	Explanation	Action
Passed	The Internal Control amplified successfully	The run was completed with success. All results are validated and can be reported. Detected pathogens are reported as "positive" and undetected pathogens are reported as "negative".
Failed	The Internal Control failed	Positively detected pathogen(s) are reported, but all negative results (tested but not detected pathogen[s]) are invalid. Repeat the testing using a new QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge.

Pathogen Result interpretation

Result interpretation information for SARS-CoV-2:

The SARS-CoV-2 in this panel targets two genes of the virus genome (Orf1b poly gen (Rdrp gene) and E genes) detected with the same fluorescence channel. The two targets are not differentiated, and amplification of either or both regions leads to a fluorescence signal.

Result Interpretation information for Influenza A

A result for a respiratory organism is interpreted as "Positive" when the corresponding PCR assay is positive (see exceptions for Influenza A below). The Influenza A assay in the QIAstat-Dx Respiratory SARS-CoV-2 Panel is designed to detect Influenza A as

well as Influenza A subtype H1N1/2009, Influenza A subtype H1, or Influenza A subtype H3. In particular, this means:

- If seasonal Influenza A H1 strain is detected by the QIAstat-Dx Respiratory SARS-CoV-2 Panel assay, two signals will be generated and displayed on the QIAstat-Dx Analyzer 1.0 screen: one for Influenza A and a second one for H1 strain.

  Note: It is acceptable if only the H1 signal is obtained, which would be indicated as "equivocal".

- If seasonal Influenza A H3 strain is detected by the QIAstat-Dx Respiratory SARS-CoV-2 Panel assay, two signals will be generated and displayed on the QIAstat-Dx Analyzer 1.0 screen: one for Influenza A and a second one for H3 strain.

  Note: It is acceptable if only the H3 signal is obtained, which would be indicated as "equivocal".

- If a pandemic Influenza A/H1N1/2009 strain is detected, two signals will be generated and displayed on the QIAstat-Dx Analyzer 1.0 screen: one for Influenza A and a second one for H1N1/2009.

  Note: It is acceptable if only the H1N1/2009 signal is obtained, which would be indicated as "equivocal".

  Note: It is acceptable if only the Influenza A signal is obtained, which would be indicated as "Influenza A (no subtype detected)".

IMPORTANT: If only an Influenza A signal is present and no additional signal for any of the subtypes is generated, it can be due to either low concentration or, in very rare cases, a new variant or any Influenza A strain other than H1 and H3 (e.g., H5N1, which can infect humans). See important precautions regarding possible detection of Influenza A with no subtype detected.

Result Interpretation for all other pathogens

For every other pathogen that can be detected with the QIAstat-Dx Respiratory SARS-CoV-2 Panel, only one signal will be generated if the pathogen is present in the sample.

Viewing amplification curves

To view test amplification curves of pathogens detected, press the Amplification Curves tab (Figure 17).

Figure 17. Amplification Curves screen (PATHOGENS tab).

Details about the tested pathogens and controls are shown on the left, and the amplification curves are shown in the center.

Note: If User Access Control is enabled on the QIAstat-Dx Analyzer 1.0, the Amplification Curves screen is only available for operators with access rights.

Press the PATHOGENS tab on the left side to display the plots corresponding to the tested pathogens. Press on the pathogen name to select which pathogens are

shown in the amplification plot. It is possible to select single, multiple, or no pathogens. Each pathogen in the selected list will be assigned a color corresponding to the amplification curve associated with the pathogen. Unselected pathogens will be shown in gray.

The corresponding C_T and endpoint fluorescence (EP) values are shown below each pathogen name.

Press the CONTROLS tab on the left side to view the controls in the amplification plot. Press the circle next to the control name to select or deselect it (Figure 18).

Figure 18. Amplification Curves screen (CONTROLS tab).

The amplification plot displays the data curve for the selected pathogens or controls. To alternate between logarithmic or linear scale for the Y-axis, press the Lin or Log button at the bottom left corner of the plot.

The scale of the X-axis and Y-axis can be adjusted using the ● blue pickers on each axis. Press and hold a blue picker and then move it to the desired location on the axis. Move a blue picker to the axis origin to return to the default values.

Viewing test details

Press Test Details in the Tab Menu bar at the bottom of the touchscreen to review the results in more detail. Scroll down to see the complete report. The following Test Details are shown in the center of the screen (Figure 19, next page):

- User ID
- Cartridge SN (serial number)
- Cartridge Expiration Date
- Module SN (serial number)
- Test Status (Completed, Failed, or Canceled by operator)
- Error Code (if applicable)
- Test Start Date and Time
- Test Execution Time
- Assay Name
- Test ID
- Test Result:
  - Positive (if at least one respiratory pathogen is detected/identified)
  - Positive with warning (at least one respiratory pathogen is detected but the Internal Control failed)
  - Negative (no respiratory pathogen is detected)
  - Invalid
- List of analytes tested in the assay, with C_T and endpoint fluorescence in the event of a positive signal
- Internal Control, with C_T and endpoint fluorescence

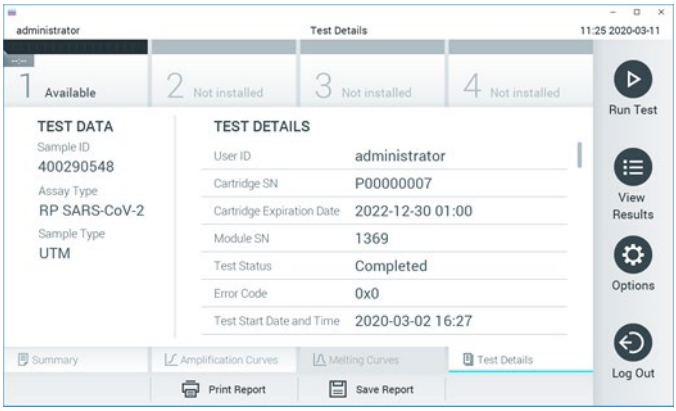

Figure 19. Example screen showing Test Data on the left panel and Test Details in the main panel.

Browsing results from previous tests

To view results from previous tests that are stored in the results repository, press View Results on the Main Menu bar (Figure 20).

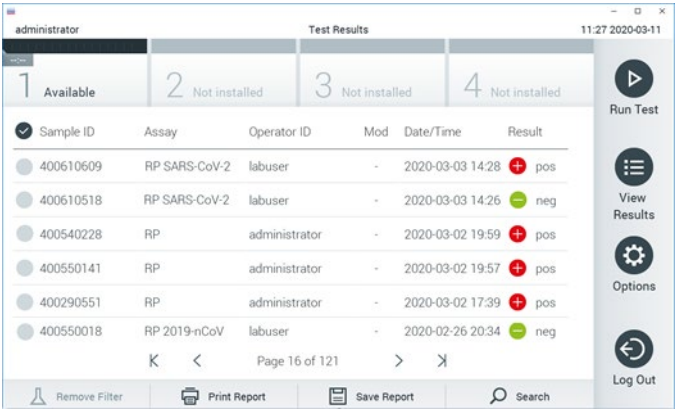

Figure 20. Example View Results screen.

The following information is available for every executed test (Figure 21):

- Sample ID
- Assay (name of test assay)
- Operator ID
- Mod (Analytical Module on which the test was executed)
- Date/Time (date and time when the test was finished)
- Result (outcome of the test: positive [pos], positive with warning [pos*], negative [neg], failed [fail] or successful [suc])

Note: If User Access Control is enabled on the QIAstat-Dx Analyzer 1.0, the data for which the user has no access rights will be hidden with asterisks.

Select one or more test results by pressing the gray circle to left of the sample ID. A checkmark will appear next to selected results. Unselect test results by pressing this checkmark. The entire list of results can be selected by pressing the checkmark circle in the top row (Figure 21).

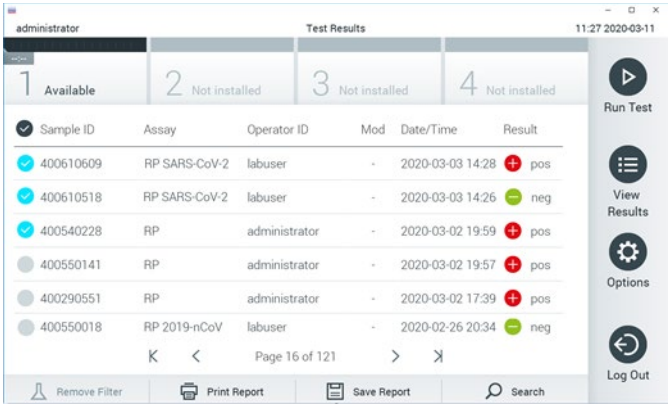

Figure 21. Example of selecting Test Results in the View Results screen.

Press anywhere in the test row to view the result for a particular test.

Press a column headline (e.g., Sample ID) to sort the list in ascending or descending order according to that parameter. The list can be sorted according to only one column at a time.

The Result column shows the outcome of each test (Table 3):

Table 3. Descriptions of test results

Outcome	Result	Description
Positive	pos	At least one pathogen is positive.
Positive with warning	pos*	At least one pathogen is positive but the Internal Control failed.
Negative	neg	No pathogens were detected.
Failed	fail	The test failed because either an error occurred or the test was canceled by the user.
Successful	suc	The test is either positive or negative, but the user does not have the access rights to view the test results

Make sure a printer is connected to the QIAstat-Dx Analyzer 1.0 and the proper driver is installed. Press Print Report to print the report(s) for the selected result(s).

Press Save Report to save the report(s) for the selected result(s) in PDF format to an external USB storage device.

Select the report type: List of Tests or Test Reports.

Press Search to search the test results by Sample ID, Assay and Operator ID. Enter the search string using the virtual keyboard and press Enter to start the search. Only the records containing the search text will be displayed in the search results.

If the results list has been filtered, the search will only apply to the filtered list.

Press and hold a column headline to apply a filter based on that parameter. For some parameters, such as Sample ID, the virtual keyboard will appear so the search string for the filter can be entered.

For other parameters, such as Assay, a dialog will open with a list of assays stored in the repository. Select one or more assays to filter only the tests that were performed with the selected assays.

The  symbol to the left of a column headline indicates that the column's filter is active.

A filter can be removed by pressing Remove Filter in the Submenu bar.

Exporting results to a USB drive

From any tab of the View Results screen, select Save Report to export and save a copy of the test results in PDF format to a USB drive. The USB port is located on the front of the QIAstat-Dx Analyzer 1.0.

Printing results

Make sure a printer is connected to the QIAstat-Dx Analyzer 1.0 and the proper driver is installed. Press Print Report to send a copy of the test results to the printer.

Quality Control

In accordance with QIAGEN's ISO-certified Quality Management System, each lot of QIAstat-Dx Respiratory SARS-CoV-2 Panel is tested against predetermined specifications to ensure consistent product quality. External controls are not provided with the QIAstat-Dx Respiratory SARS-CoV-2 Panel. Quality control requirements should be performed in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's standard quality control procedures.

The following external controls are available:

- ZeptoMetrix® Inc. NATtrol™ Respiratory Verification Panel (Cat. No. NATRVP-QIA)
- ZeptoMetrix Inc. NATtrol SARS-CoV-2 E/ORF1ab recombinant (Cat. No. 0831043)

Limitations

- For prescription use only.
- The use of this assay as an in vitro diagnostic under FDA Emergency Use Authorization (EUA) is limited to laboratories that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high or moderate complexity tests.
- Results from the QIAstat-Dx Respiratory SARS-CoV-2 Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions.
- Laboratories are required to report all SARS-CoV-2 results to the appropriate public health authorities.
- Primers and probes for this kit target highly conserved regions within the genome of SARS- CoV-2. Mutations occurring in these highly conserved regions (although rare) may result in RNA being undetectable.
- The clinical performance for SARS-CoV-2 has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- The E gene target is homologous to sequences from multiple bat SARS viruses. These viruses are unlikely to be found in nasopharyngeal swabs and their potential to infect human hosts is unknown.
- 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.

- Positive results do not rule out co-infection with organisms not included in the QIAstat-Dx Respiratory SARS-CoV-2 Panel. The agent detected may not be the definitive cause of the disease.
- Negative results do not preclude infection of the upper respiratory tract. Not all agents of acute respiratory infection are detected by this assay and sensitivity in some clinical settings may differ from that described in the package insert.
- A negative result with the QIAstat-Dx Respiratory SARS-CoV-2 Panel does not exclude the infectious nature of the syndrome. Negative assay results may originate from several factors and their combinations, including sample handling mistakes, variation in the nucleic acid sequences targeted by the assay, infection by organisms not included in the assay, organism levels of included organisms that are below the limit of detection for the assay, and use of certain medications, therapies, or agents.
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel is not intended for testing of samples other than those described in these Instructions for Use. Test performance characteristics have been established only with nasopharyngeal swab samples collected in universal transport media (UTM) from individuals with acute respiratory symptoms.
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel is intended to be used in conjunction with standard of care culture for organism recovery, serotyping, and/or antimicrobial susceptibility testing where applicable.
- The results from the QIAstat-Dx Respiratory SARS-CoV-2 Panel must be interpreted by a trained healthcare professional within the context of all relevant clinical, laboratory, and epidemiological findings.
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel can be used only with the QIAstat-Dx Analyzer 1.0.
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel is a qualitative assay and does not provide a quantitative value for detected organisms.

- Viral and bacterial nucleic acids may persist in vivo, even if the organism is not viable or infectious. Detection of a target marker does not imply that the corresponding organism is the causative agent of the infection or the clinical symptoms.
- Detection of viral and bacterial nucleic acids depends on proper sample collection, handling, transportation, storage and loading into the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge. Improper operations for any of the aforementioned processes can cause incorrect results, including false-positive or false-negative results.
- The performance of this test has not been established for screening of blood or blood products.
- The performance of this test has not been established in individuals who received influenza vaccine. Recent administration of a nasal influenza vaccine may cause false positive results for Influenza A and/or Influenza B.
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel may not be able to distinguish between existing viral strains and new variants as they emerge. For example, the QIAstat-Dx Respiratory SARS-CoV-2 Panel can detect seasonal H3N2 Influenza but may not be able to distinguish seasonal H3N2 from H3N2 variant (H3N2v).
- The QIAstat-Dx Respiratory SARS-CoV-2 Panel detects the multi-copy IS481 insertion sequence present in multiple *Bordetella* species. False positive *B. pertussis* results are possible if the specimen is contaminated with non-pertussis *Bordetella* species.
- The assay sensitivity and specificity, for the specific organisms and for all organisms combined, are intrinsic performance parameters of a given assay and do not vary depending on prevalence. In contrast, both the negative and positive predictive values of a test result are dependent on the disease/organism 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 or low.

Conditions of Authorization for the Laboratory

The QIAstat-Dx Respiratory SARS-CoV-2 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/in-vitro-diagnostics-euas**

However, to assist clinical laboratories using the QIAstat-Dx Respiratory SARS-CoV-2 Panel ("your product" in the conditions below), the relevant Conditions of Authorization are listed below:

- Authorized laboratories * using your product must include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product must use your product as outlined in the authorized labelling. 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 your product are not permitted.

* The letter of authorization refers to, "United States (U.S.) laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high or moderate complexity tests" as "authorized laboratories."

- Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

- Authorized laboratories must collect information on the performance of your product and will report to DMD/OHT7-OIR/OPEQ/CDRH (via email: **CDRH-EUA-Reporting@fda.hhs.gov**) and QIAGEN (**https://www.qiagen.com/us/service-and-support/technical-support/technical-support-form/**) any suspected occurrence of false positive or false negative results, and significant deviations from the established performance characteristics of your product of which they become aware.
- All laboratory personnel using your product must be appropriately trained in RT-PCR techniques, use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.
- QIAGEN GmbH, authorized distributors, and authorized laboratories using your product must 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.

Performance Characteristics

The QIAstat-Dx Respiratory SARS-CoV-2 Panel (Cat. No. 691223) assay was developed by introducing the reagents required to detect the SARS-CoV-2 target in a separate reaction chamber of the QIAstat-Dx Respiratory Panel assay (Cat. No. 691221), leaving all other targets unchanged. As a result of this and/or availability of SARS-CoV-2 clinical samples, certain studies shown below were not done or repeated using the QIAstat-Dx Respiratory SARS-CoV-2 Panel.

SARS-CoV-2 Target

Clinical performance

The performance of SARS-CoV-2 target in the QIAstat-Dx Respiratory SARS-CoV-2 Panel was evaluated using retrospective nasopharyngeal swab clinical specimens in transport medium. Specifically, 30 individual negative nasopharyngeal specimens and a total of 30 positive samples consisting of:

- 10 positive clinical samples tested with a validated molecular comparator assay obtained from a Hospital in Barcelona (Spain)
- 20 contrived positive clinical samples at 1-2x LoD

All clinical samples were collected from patients with signs and symptoms of upper respiratory infection by qualified personnel according to the package insert of the collection device and stored frozen until use.

Low positive contrived clinical samples were prepared by spiking a quantified clinical sample obtained from a Hospital in Barcelona (Spain) into individual negative clinical samples to approximately 1x- 2x LoD (20 samples).

Overall results are shown on Table 4:

Table 4. Overall clinical performance results of SARS-CoV-2 target

Sample	Sample Type	N	SARS-CoV-2 Target			
			% Positive	(95% CI)	% Negative	**(95% CI)**
Positives	Positive clinical sample	10	(10/10) 100%	N/A	0/0	N/A
	Low positive contrived sample (1x-2xLoD)	20	(20/20) 100%	N/A	0/0	N/A
	Total Positive Samples	30	(30/30) 100%	85.8 -100	0/0	N/A
Negative	**Total Negative Samples**	30	0/0	N/A	(30/30) 100%	85.8 -100

Performance of the SARS-CoV-2 target in the QIAstat-Dx Respiratory SARS-CoV-2 Panel against the expected results are:

Positive Percent Agreement (PPA%): 30/30 = 100 % (95% CI: 85.8% - 100%)

Negative Percent Agreement (NPA%): 30/30 = 100% (95% CI: 85.8% - 100%)

Analytical performance

Sensitivity (Limit of Detection)

The Analytical Sensitivity, or Limit of Detection (LoD), is defined as the lowest concentration at which ≥95% of the tested samples generate a positive call.

The LoD of the SARS-CoV-2 target was assessed by analyzing serial dilutions of analytical samples prepared from a quantified clinical sample obtained from a Hospital from Barcelona (Spain). Dilutions were preformed using simulated matrix consisting of UTM and HeLa cells. Four (4) replicates were tested of each serial dilution. The lowest concentration at which all replicates were positive was interpreted as the tentative LoD. The LoD was then confirmed by testing twenty (20) replicates with concentrations at the tentative limit of detection. To confirm the

established LoD concentration, the detection rate of all replicates must be ≥95% (at least 19/20 replicates must generate a positive signal).

Table 5. LoD value obtained for the SARS-CoV-2 target tested with the QIAstat-Dx Respiratory SARS-CoV-2 Panel

Pathogen	Strain	Source	Concentration	Detection rate
SARS-CoV-2	Clinical Sample	Hospital from Barcelona (Spain)	500 copies/mL	20/20

The final LoD for the SARS-CoV-2 target in the QIAstat-Dx Respiratory SARS-CoV-2 panel according to the assay results interpretation, is 500 copies/ml.

FDA SARS-CoV-2 reference panel testing

The evaluation of sensitivity and MERS-CoV cross-reactivity was performed using reference material (T1), blinded samples, and a standard protocol provided by the FDA. The study included a range-finding study and a confirmatory study for LoD. Blinded sample testing was used to establish specificity and to confirm the LoD. All the reagents required for the complete execution of the test are pre-loaded and self-contained in the QIAstat-Dx Respiratory SARS-CoV-2 Panel cartridge. The instrument used was the QIAstat-Dx Analyzer 1.0. The results are summarized in Table 6 .

Table 6. Summary of LoD confirmation result using the FDA SARS-CoV-2 Reference Panel

Reference Materials Provided by FDA	Specimen Type	Product LoD	Cross-Reactivity
SARS-CoV-2	Nasopharyngeal swab	$1.8x10^5$ NDU/ml	N/A
MERS-CoV		N/A	ND

Abbreviations: NDU/ml = RNA NAAT detectable units/ml; ND = not detected; N/A = not applicable.

Exclusivity (Cross-reactivity and Exclusivity)

The analytical specificity study was carried out by *in silico* analysis and *in vitro* * testing to assess the cross-reactivity and exclusivity of the SARS-CoV-2 target. On-panel organisms were tested to assess the potential for intra-panel cross-reactivity and off-panel organisms were tested to evaluate panel exclusivity. The off-panel organisms selected were clinically relevant organisms (colonizing the upper respiratory tract or causing respiratory symptoms), common skin flora, or laboratory contaminants, or microorganisms for which much of the population may have been infected.

* Only a limited number of organisms were tested *in vitro* (shown in Table 7).

Samples were prepared by spiking potential cross-reactive organisms into simulated nasopharyngeal swab sample matrix at the highest concentration possible based on the organism stock – at least 10^5 $TCID_{50}$/ml for viral targets and 10^6 CFU/ml for bacterial and fungal targets. These concentrations represent levels approximately 800–1,000,000-fold higher than the LoD of the SARS-CoV-2 Target.

Table 7. List of Analytical Specificity pathogens tested *in vitro*

Type	Pathogen
On-panel bacteria	*Chlamydophila pneumoniae*
Off-panel bacteria	*Haemophilus influenzae* *Streptococcus pyogenes* *Streptococcus pneumoniae* *Mycobacterium tuberculosis*
Off-panel viruses	**MERS Coronavirus** **SARS Coronavirus***

* SARS Coronavirus was tested using custom gBlocks from the two regions targeted by the SARS-CoV-2 designs.

In silico, sequence hits were analyzed together in order to detect unique specific sequences matching with all primers and probes to be considered as positive amplifications. Primers and probes were considered as reactive if the following parameters were fulfilled:

- At least one forward, one probe, and one reverse primer of the SARS-CoV-2 assay match with the target BLAST hit sequence.
- At least 70% of query cover/identity between the BLAST hit sequence and every single primer/probe sequence.
- A maximum of 500 bp of amplicon size.

This analysis of the SARS-CoV-2 designs show that a potential unspecific signal can be produced by a cross-reaction with a group of coronaviruses found in bats. These coronaviruses have only been detected in bats and have not been reported to

infect or colonize humans. No unspecific signals were generated with critical off-panel human targets.

No cross-reactivity was observed, both *in silico* and *in vitro*, with any clinically relevant pathogens (colonizing the upper respiratory tract or causing respiratory symptoms), or common sin flora or laboratory contaminants, or microorganisms.

Inclusivity (Analytical Reactivity)

In silico analysis shows that the SARS-CoV-2 assays in the QIAstat-Dx Respiratory SARS-CoV-2 panel show a 100% sequence identity to 1,988,986 out of the 2,059,693 (96.6%) SARS-CoV-2 genomes available in the public databases.

For those genomes with any mismatch in any oligonucleotide, 65,278 genomes (3.17%) showed any mismatch in non-critical positions with no expected impact in the PCR, whereas only 5,515 genomes (0.27%) presented mismatches with potentially critical impact.

However, the influence of those most abundant critical mismatches has been flagged for experimental check with no impact on assay performance detected. These single mismatches are tolerated by the PCR workflow in the QIAstat-Dx system.

As a conclusion, no safety and performance issues with the QIAstat-Dx Respiratory SARS-CoV-2 assay were identified among all SARS-CoV-2 genomic sequences available as of June 2021, including all Variants of Concern (VOCs), Variants of Interest (VOIs) and Variants Under Investigation (VUIs) described up to this date.

Additional Targets included in the QIAstat-Dx SARS-CoV-2 Panel

The performance of the other targets in the panel (Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus A+B, Influenza A, Influenza A H1, Influenza A H3, Influenza A H1N1/pdm09, Influenza B,

Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Rhinovirus/Enterovirus, Respiratory Syncytial Virus A+B, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*) has been previously established and is presented below.

Clinical performance

The clinical performance of the QIAstat-Dx Respiratory Panel (Cat. No. 691221) was established during a multi-center study conducted at six (6) geographically diverse study sites: five (5) U.S. sites and one (1) international site. Each study location was representative of the intended use setting (clinical laboratories), and testing was performed by trained clinical laboratory personnel. Residual nasopharyngeal swab (NPS) samples were collected from subjects with signs and symptoms of respiratory infection for QIAstat-Dx Respiratory Panel and comparator testing.

Residual NPS specimens in UTM were tested with the QIAstat-Dx Respiratory Panel (Cat. No. 691221) and an FDA-cleared molecular comparator, in accordance with product instructions for use. Specimens tested in the clinical study were collected using the Universal Transport Medium (UTM) (Copan Diagnostics [Brescia, Italy and CA, USA]), MicroTest™ M4®, M4RT®, M5®, M6® (Thermo Fisher Scientific®, MA, USA), BD™ Universal Viral Transport (UVT) System (Becton Dickinson, NJ, USA), Universal Transport Medium (UTM) System (HealthLink® Inc., FL, USA), Universal Transport Medium (Diagnostic Hybrids®, OH, USA), V-C-M Medium (Quest Diagnostics®, NJ, USA) and UniTranz-RT® Universal Transport Media (Puritan® Diagnostics, ME, USA) collection kits.

A total of 2304 residual NPS specimens (1994 prospective, 310 archived) were tested in this comparison study. Between December 2017 to April 2019, specimens were prospectively collected from all comers meeting the study inclusion criteria and immediately frozen for later testing by the study site as frozen prospective specimens (N=1093). No frozen samples were distributed amongst sites. At time of testing,

specimens were thawed and tested on both the QIAstat-Dx Respiratory Panel and comparator method.

Between February and August 2018, specimens were prospectively collected from all comers meeting the study eligibility criteria and tested fresh (N=901) on both the QIAstat-Dx Respiratory Panel and comparator method in accordance with product instructions as fresh prospective specimens. One specimen was withdrawn from the study due to an incorrect specimen type.

Table 8 provides the summary of demographic information for the 1994 subjects that participated in the prospective study.

Table 8. Demographic summary for the prospective study arm

		Overall	Site 1 Copenhagen, Denmark	Site 2 Minneapolis, MN	Site 3 Indianapolis, IN	Site 4 Liverpool, NY	Site 5 Columbus, OH	Site 6 Albuquerque, NM
SEX	Male	924 (46.3%)	186	0	196	177	170	195
	Female	1070 (53.7%)	232	0	230	271	133	204
AGE	≤5 years	627 (31.4%)	126	0	103	49	216	133
	6–21 years	239 (11.9%)	34	0	40	38	79	48
	22–49 years	330 (16.5%)	110	0	56	107	7	50
	50+ years	798 (40.0%)	148	0	227	254	1	168
STATUS	Outpatient	788 (39.5%)	272	0	50	44	145	277
	Hospitalized	686 (34.4%)	145	0	318	0	101	122
	Emergency	67 (3.4%)	0	0	9	34	24	0
	ICU	153 (7.7%)	1	0	49	70	33	0
	Not provided/ unknown	300 (15.0%)	0	0	0	300	0	0
	Total	1994	418	0	426	448	303	399

A total of 1994 specimens were evaluated for all panel members in the prospective study. The performance of the QIAstat-Dx Respiratory Panel was evaluated by comparing the QIAstat-Dx Respiratory Panel test results with those from an FDA-cleared multiplexed respiratory pathogen panel.

Positive Percent Agreement (PPA) for each analyte was calculated as 100% x (TP/[TP+FN]). True Positive (TP) indicates that both the QIAstat-Dx Respiratory Panel and the comparator method yielded a "Detected" result of that specific analyte. A False Negative (FN) indicates that the QIAstat-Dx Respiratory Panel was "Not Detected" while the comparator method was "Detected" for the analyte in question. Negative Percent Agreement (NPA) was calculated as 100% x (TN/[TN+FP]). True Negative (TN) indicates that both the QIAstat-Dx Respiratory Panel and the comparator method resulted in "Not Detected" for that specific analyte. A False Positive (FP) indicates that the QIAstat-Dx Respiratory Panel was "Detected" while the comparator method was "Not Detected" for the specific pathogen.

Binomial two-sided 95% Confidence Intervals were calculated using the Wilson Score Method.

The QIAstat-Dx Respiratory Panel prospective performance data in positive percent and negative percent agreements against the comparator methods are presented by analyte in Table 9, next page.

Table 9. QIAstat-Dx Respiratory Panel prospective clinical performance summary

Analyte		TP/(TP+FN)	Sensitivity/PPA	95% CI	TN/(TN+FP)	Specificity/NPA	95% CI
Viruses							
Adenovirus[a]	Fresh	55/58	94.8%	85.9–98.2	833/839	99.3%	98.4–99.7
	Frozen	31/32	96.9%	84.3–99.4	1047/1057	99.1%	98.3–99.5
	Overall	86/90	95.6%	89.1–98.3	1880/1896	99.2%	98.6–99.5
Coronavirus 229E	Fresh	8/9	88.9%	56.5–98.0	886/886	100.0%	99.6–100.0
	Frozen	0/0	N/A	N/A	1089/1089	100.0%	99.6–100.0
	Overall	8/9	88.9%	56.5–98.0	1975/1975	100.0%	99.8–100.0
Coronavirus HKU1[b]	Fresh	3/3	100.0%	43.8–100.0	890/892	99.8%	99.2–99.9
	Frozen	48/49	98.0%	89.3–99.6	1035/1040	99.5%	98.9–99.8
	Overall	51/52	98.1%	89.9–99.7	1925/1932	99.6%	99.3–99.8
Coronavirus NL63[c]	Fresh	4/5	80.0%	37.6–96.4	890/890	100.0%	99.6–100.0
	Frozen	36/42	85.7%	72.2–93.3	1046/1048	99.8%	99.3–99.9
	Overall	40/47	85.1%	72.3–92.6	1936/1938	99.9%	99.6–100.0
Coronavirus OC43[d]	Fresh	3/3	100.0%	43.8–100.0	892/892	100.0%	99.6–100.0
	Frozen	23/26	88.5%	71.0–96.0	1059/1063	99.6%	99.0–99.9
	Overall	26/29	89.7%	73.6–96.4	1951/1955	99.8%	99.5–99.9

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Table 9 (continued)

Analyte		TP/(TP+FN)	Sensitivity/PPA	95% CI	TN/(TN+FP)	Specificity/NPA	95% CI
Viruses (continued)							
Human Meta-pneumovirus[e]	Fresh	62/67	92.5%	83.7–96.8	828/829	99.9%	99.3–100.0
	Frozen	53/55	96.4%	87.7–99.0	1030/1034	99.6%	99.0–99.8
	Overall	115/122	94.3%	88.6–97.2	1858/1863	99.7%	99.4–99.9
Rhinovirus/ Enterovirus[f]	Fresh	144/157	91.7%	86.3–95.1	715/739	96.8%	95.2–97.8
	Frozen	124/137	90.5%	84.4–94.4	941/953	98.7%	97.8–99.3
	Overall	268/294	91.2%	87.4–93.9	1656/1692	97.9%	97.1–98.5
Influenza A[g]	Fresh	132/133	99.2%	95.8–99.9	753/757	99.5%	98.6–99.8
	Frozen	110/111	99.1%	95.1–99.8	972/977	99.5%	98.8–99.8
	Overall	242/244	99.2%	97.0–99.8	1725/1734	99.5%	99.0–99.7
Influenza A H1[h]	Fresh	0/1	0.0%	0.0–79.3	894/894	100.0%	99.6–100.0
	Frozen	0/0	N/A	N/A	1089/1089	100.0%	99.6–100.0
	Overall	0/1	0.0%	0.0–79.3	1983/1983	100.0%	99.8–100.0
Influenza A H1N1/pdm09[i]	Fresh	62/63	98.4%	91.5–99.7	826/831	99.4%	98.6–99.7
	Frozen	18/18	100.0%	82.4–100.0	1071/1071	100.0%	99.6–100.0
	Overall	80/81	98.8%	93.3–99.8	1897/1902	99.7%	99.4–99.9

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Table 9 (continued)

Analyte		TP/(TP+FN)	Sensitivity/PPA	95% CI	TN/(TN+FP)	Specificity/NPA	95% CI
Viruses (continued)							
Influenza A H3[j]	Fresh	67/67	100.0%	94.5–100.0	825/826	99.9%	99.3–100.0
	Frozen	89/90	98.9%	82.4–100.0	992/998	99.4%	98.7–99.7
	Overall	156/157	99.4%	93.3–99.8	1817/1824	99.6%	99.2–99.8
Influenza B[k]	Fresh	64/67	95.5%	87.6–98.5	827/828	99.9%	99.3–100.0
	Frozen	58/62	93.5%	84.6–97.5	1026/1026	100.0%	99.6–100.0
	Overall	122/129	94.6%	89.2–97.3	1853/1854	99.9%	99.7–100.0
Parainfluenza virus 1[l]	Fresh	3/3	100.0%	43.8–100.0	892/892	100.0%	99.6–100.0
	Frozen	13/14	92.9%	68.5–98.7	1072/1075	99.7%	99.2–99.9
	Overall	16/17	94.1%	73.0–99.0	1964/1967	99.8%	99.6–99.9
Parainfluenza virus 2	Fresh	2/2	100.0%	34.2–100.0	893/893	100.0%	99.6–100.0
	Frozen	0/0	N/A	N/A	1089/1089	100.0%	99.6–100.0
	Overall	2/2	100.0%	34.2–100.0	1982/1982	100.0%	99.8–100.0
Parainfluenza virus 3[m]	Fresh	102/104	98.1%	93.3–99.5	788/793	99.4%	98.5–99.7
	Frozen	9/9	100.0%	70.1–100.0	1081/1081	100.0%	99.6–100.0
	Overall	111/113	98.2%	93.8–99.5	1869/1874	99.7%	99.4–99.9

(continued on next page)

Table 9 (continued)

Analyte		TP/(TP+FN)	Sensitivity/PPA	95% CI	TN/(TN+FP)	Specificity/NPA	95% CI
Viruses (continued)							
Parainfluenza virus 4[n]	Fresh	3/3	100.0%	43.8–100.0	892/892	100.0%	99.6–100.0
	Frozen	0/0	N/A	N/A	1087/1089	99.8%	99.3–99.9
	Overall	3/3	100.0%	43.8–100.0	1979/1981	99.9%	99.6–100.0
Respiratory Syncytial Virus (RSV)[o]	Fresh	73/76	96.1%	88.9–98.6	819/820	99.9%	99.3–100.0
	Frozen	139/144	96.5%	92.1–98.5	941/945	99.6%	98.9–99.8
	Overall	212/220	96.4%	93.0–98.1	1760/1765	99.7%	99.3–99.9
Bacteria							
Bordetella pertussis[p]	Fresh	2/2	100.0%	34.2–100.0	893/893	100.0%	99.6–100.0
	Frozen	1/1	100.0%	20.7–100.0	1082/1088	99.4%	98.8–99.7
	Overall	3/3	100.0%	43.8–100.0	1975/1981	99.7%	99.3–99.9
Chlamydophila pneumoniae[q]	Fresh	4/4	100.0%	51.0–100.0	891/891	100.0%	99.6–100.0
	Frozen	1/1	100.0%	20.7–100.0	1087/1088	99.9%	99.5–100.0
	Overall	5/5	100.0%	56.6–100.0	1978/1979	99.9%	99.7–100.0
Mycoplasma pneumoniae[r]	Fresh	18/18	100.0%	82.4–100.0	875/877	99.8%	99.2–100.0
	Frozen	1/1	100.0%	20.7–100.0	1085/1088	99.7%	99.2–99.9
	Overall	19/19	100.0%	83.2–100.0	1960/1965	99.7%	99.4–99.9

[a] Adenovirus was detected in 3/4 FN specimens using an independent molecular method. Adenovirus was detected in 6/16 FP specimens using an independent molecular method.
[b] The single FN specimen was negative for Coronavirus HKU1 when tested using an independent molecular method. Coronavirus HKU1 was detected 0/7 FP specimens using an independent molecular method.
[c] Coronavirus NL63 was detected in 7/7 FN specimens using an independent molecular method. Coronavirus NL63 was detected in 1/2 FP specimens using an independent molecular method.
[d] The 3 FN specimens were negative for Coronavirus OC43 when tested using an independent molecular method. Coronavirus OC43 was detected in 3/4 FP specimens using an independent molecular method.
[e] Human metapneumovirus (hMPV) was detected in 4/7 FN specimens using an independent molecular method. hMPV was detected in 3/5 FP specimens using an independent molecular method.
[f] Rhinovirus was detected in 18/26 FN specimens using an independent molecular method. Rhinovirus was detected in 14/36 FP specimens using an independent molecular method.
[g] Influenza A was detected in 1/2 FN specimens by an independent molecular method. Three (3) FP samples were not available for testing. Influenza A was detected in the 3/6 remaining FP samples by an independent molecular method.
[h] Influenza A H1 was detected in 1/1 FN specimen by an independent molecular method. Note: Non-2009 H1 has not been in circulation since being replaced by the 2009 H1 and thus this discrepancy test result is likely false.
[i] Influenza A H1N1 pdm09 was detected in 1/1 FN by an independent molecular method. Influenza A H1 was detected in 3/5 FP specimens by an independent molecular method.
[j] Influenza A H3 was detected in 1/1 FN by an independent molecular method. Influenza H3 was detected in 7/7 FP specimens by an independent molecular method.
[k] Influenza B was detected in 6/6 FN specimens available for testing by an independent molecular method; one discordant sample was not tested by an independent molecular method. Influenza B was detected in 1/1 FP specimens available for testing by an independent molecular method.
[l] The single FN specimen was negative for Parainfluenza virus 1 by an independent molecular method. Parainfluenza virus 1 was detected in 3/3 FP specimens by an independent molecular method.
[m] Parainfluenza virus 3 was detected in 1/2 FN specimens by an independent molecular method. Parainfluenza 3 was detected in 3/5 FP specimens by an independent molecular method.
[n] Parainfluenza virus 4 was detected in 2/2 FP specimens by an independent molecular method.
[o] Respiratory Syncytial Virus was detected in 2/8 FN specimens by an independent molecular method. Respiratory Syncytial Virus was detected in 3/5 FP specimens by an independent molecular method.
[p] *Bordetella pertussis* was detected in 1/6 FP specimens by an independent molecular method.
[q] *Chlamydophila pneumoniae* was detected in 1/1 FP specimens by an independent molecular method.
[r] *Mycoplasma pneumoniae* was detected in 1/4 specimens by an independent molecular method.

The QIAstat-Dx Respiratory Panel detected a total of 191 specimens with distinctive multiple organism detections (9.6% of all specimens) in the prospective study.

All distinct co-infection combinations, as detected by the QIAstat-Dx Respiratory Panel during the prospective clinical study, are presented in Table 10 (next page).

Table 10. Distinct co-infection combinations detected by QIAstat-Dx Respiratory Panel in the prospective study

Distinct co-infection combinations detected by the QIAstat-Dx Respiratory Panel				Total co-infections	Number of discrepant co-infections	Discrepant analyte(s)
Analyte 1	Analyte 2	Analyte 3	Analyte 4			
Adenovirus	Rhinovirus/ Enterovirus	Coronavirus NL63		2	0	N/A
Adenovirus	Rhinovirus/ Enterovirus			12	3	Rhinovirus/Enterovirus (1); Adenovirus (2)
Adenovirus	Respiratory Syncytial Virus			11	1	Respiratory Syncytial Virus (1)
Adenovirus	*Mycoplasma pneumoniae*			2	1	*Mycoplasma pneumoniae* (1)
Adenovirus	Coronavirus HKU1			3	1	Coronavirus HKU1 (1)
Coronavirus HKU1	Adenovirus	Respiratory Syncytial Virus		1	1	Coronavirus HKU1 (1)
Coronavirus HKU1	Human Metapneumovirus			3	1	Human Metapneumovirus (1)
Coronavirus HKU1	Parainfluenza virus 3	Rhinovirus/ Enterovirus		1	0	N/A
Coronavirus HKU1	Parainfluenza virus 4			1	1	Coronavirus HKU1, Parainfluenza virus 4 (1)
Coronavirus HKU1	Respiratory Syncytial Virus			8	1	Coronavirus HKU1 (1)
Coronavirus HKU1	Rhinovirus/ Enterovirus	Respiratory Syncytial Virus		1	0	N/A
Coronavirus HKU1	Rhinovirus/ Enterovirus			4	1	Rhinovirus/Enterovirus (1)
Coronavirus NL63	Adenovirus	Respiratory Syncytial Virus		1	0	N/A
Coronavirus NL63	Adenovirus			1	1	Adenovirus (1)
Coronavirus NL63	*Bordetella pertussis*			2	2	*Bordetella pertussis* (2)

(continued on next page)

Table 10 (continued)

Distinct co-infection combinations detected by the QIAstat-Dx Respiratory Panel				Total co-infections	Number of discrepant co-infections	Discrepant analyte(s)
Analyte 1	Analyte 2	Analyte 3	Analyte 4			
Coronavirus NL63	Parainfluenza virus 1			1	0	N/A
Coronavirus NL63	Respiratory Syncytial Virus			2	0	N/A
Coronavirus NL63	Rhinovirus/ Enterovirus			2	0	N/A
Coronavirus OC43	Adenovirus			2	0	N/A
Coronavirus OC43	Human Metapneumovirus			2	0	N/A
Coronavirus OC43	Parainfluenza virus 3	Rhinovirus/ Enterovirus		1	0	N/A
Coronavirus OC43	Respiratory Syncytial Virus			4	0	N/A
Coronavirus OC43	Rhinovirus/ Enterovirus	Respiratory Syncytial Virus		2	0	N/A
Coronavirus OC43	Rhinovirus/ Enterovirus			2	2	Rhinovirus/ Enterovirus (2)
Coronavirus 229E	Respiratory Syncytial Virus			1	0	N/A
Human Metapneumovirus	Adenovirus			2	1	Adenovirus (1)
Human Metapneumovirus	Respiratory Syncytial Virus			2	0	N/A
Human Metapneumovirus	Rhinovirus/ Enterovirus			9	3	Rhinovirus/ Enterovirus (3)
Human Metapneumovirus	Rhinovirus/ Enterovirus	Adenovirus	Coronavirus 229E	1	1	Adenovirus, Rhinovirus/ Enterovirus (1)
Influenza A (no subtype)	Respiratory Syncytial Virus	Adenovirus		1	1	Influenza A, Adenovirus (1)

(continued on next page)

Table 10 (continued)

Distinct co-infection combinations detected by the QIAstat-Dx Respiratory Panel				Total co-infections	Number of discrepant co-infections	Discrepant analyte(s)
Analyte 1	**Analyte 2**	**Analyte 3**	**Analyte 4**			
Influenza A (no subtype)	Respiratory Syncytial Virus			1	0	N/A
Influenza A H1N1/pdm09	Coronavirus NL63			1	0	N/A
Influenza A H1N1/pdm09	Coronavirus OC43	Adenovirus		1	1	Adenovirus (1)
Influenza A H1N1/pdm09	Rhinovirus/ Enterovirus			2	0	N/A
Influenza A H1N1/pdm09	Rhinovirus/ Enterovirus	*Bordetella pertussis*		1	0	N/A
Influenza A H1N1/pdm09	Respiratory Syncytial Virus			1	0	N/A
Influenza A H3	Adenovirus			2	1	Adenovirus (1)
Influenza A H3	Coronavirus NL63	Parainfluenza virus 1		1	0	N/A
Influenza A H3	Coronavirus NL63	*Bordetella pertussis*		1	1	*Bordetella pertussis* (1)
Influenza A H3	Coronavirus NL63			1	1	NL63 (1)
Influenza A H3	Coronavirus OC43	Adenovirus	Respiratory Syncytial Virus	1	1	Coronavirus OC43, Adenovirus (1)
Influenza A H3	Rhinovirus/ Enterovirus			4	2	Rhinovirus/ Enterovirus (2)
Influenza A H3	Parainfluenza virus 1			2	0	N/A
Influenza A H3	Parainfluenza virus 3			2	0	N/A
Influenza A H3	Respiratory Syncytial Virus			1	0	N/A
Influenza A H3	Coronavirus 229E			1	0	N/A
Influenza B	Coronavirus HKU1			3	0	N/A

Influenza B	Coronavirus NL63	1	0	N/A

(continued on next page)

Table 10 (continued)

Distinct co-infection combinations detected by the QIAstat-Dx Respiratory Panel				Total co-infections	Number of discrepant co-infections	Discrepant analyte(s)
Analyte 1	Analyte 2	Analyte 3	Analyte 4			
Influenza B	Respiratory Syncytial Virus			2	0	N/A
Influenza B	Rhinovirus/ Enterovirus			7	4	Rhinovirus/ Enterovirus (4)
Mycoplasma pneumoniae	Coronavirus HKU1			1	1	Coronavirus HKU1 (1)
Mycoplasma pneumoniae	Rhinovirus/ Enterovirus			1	0	N/A
Parainfluenza virus 1	Adenovirus			1	0	N/A
Parainfluenza virus 1	Respiratory Syncytial Virus			1	1	Parainfluenza virus 1 (1)
Parainfluenza virus 1	Rhinovirus/ Enterovirus			2	0	N/A
Parainfluenza virus 1	Rhinovirus/ Enterovirus	*Mycoplasma pneumoniae*		1	1	Rhinovirus/ Enterovirus (1)
Parainfluenza virus 3	Adenovirus			3	2	Adenovirus (2)
Parainfluenza virus 3	Adenovirus	Rhinovirus/ Enterovirus		3	1	Parainfluenza virus 3 (1)
Parainfluenza virus 3	Human Metapneumovirus			2	1	Human Metapneumovirus (1)
Parainfluenza virus 3	Respiratory Syncytial Virus			2	1	Parainfluenza virus 3 (1)
Parainfluenza virus 3	Rhinovirus/ Enterovirus			14	3	Rhinovirus/ Enterovirus (2), Parainfluenza virus 3 (1)
Parainfluenza virus 4	Respiratory Syncytial Virus			1	0	N/A
Parainfluenza virus 4	Rhinovirus/ Enterovirus			2	0	N/A

(continued on next page)

Table 10 (continued)

Distinct co-infection combinations detected by the QIAstat-Dx Respiratory Panel				Total co-infections	Number of discrepant co-infections	Discrepant analyte(s)
Analyte 1	Analyte 2	Analyte 3	Analyte 4			
Respiratory Syncytial Virus	Human Metapneumovirus	Rhinovirus/ Enterovirus	Adenovirus	1	0	N/A
Respiratory Syncytial Virus	Human Metapneumovirus	Rhinovirus/ Enterovirus		2	1	Human Metapneumovirus, Rhinovirus/ Enterovirus (1)
Respiratory Syncytial Virus	Rhinovirus/ Enterovirus			29	6	Rhinovirus/ Enterovirus (5), Respiratory Syncytial Virus (1)
Rhinovirus/ Enterovirus	Respiratory Syncytial Virus	Adenovirus		2	0	N/A
Total co-infections				191	51	
Total double infections				166	42	
Total triple infections				22	7	
Total quadruple infections				3	2	

The three organisms most prevalent in multiple detections by the QIAstat-Dx Respiratory Panel in the prospective study were Rhinovirus/Enterovirus (108/191, 56.5%), Respiratory Syncytial Virus (77/191, 40.8%), and Adenovirus (53/191, 27.7%). The prevalence of individual organisms in each multiple detection are shown in Table 11 (next page).

Table 11. The prevalence of individual organisms in each QIAstat-Dx multiple detection

Analyte	Prevalence in multiple detections (N=191)
Viruses	
Adenovirus	53 (27.7%)
Coronavirus 229E	3 (1.6%)
Coronavirus HKU1	26 (13.6%)
Coronavirus NL63	16 (8.4%)
Coronavirus OC43	15 (7.9%)
Human Metapneumovirus	24 (12.6%)
Rhinovirus/Enterovirus	108 (56.5%)
Influenza A H1	0 (0.0%)
Influenza A H1N1/pdm09	6 (3.1%)
Influenza A H3	16 (8.4%)
Influenza B	13 (6.8%)
Parainfluenza virus 1	9 (4.7%)
Parainfluenza virus 2	0 (0.0%)
Parainfluenza virus 3	28 (14.7%)
Parainfluenza virus 4	4 (2.1%)
Respiratory Syncytial Virus	78 (40.8%)
Bacteria	
Bordetella pertussis	4 (2.1%)
Chlamydophila pneumoniae	0 (0.0%)
Mycoplasma pneumoniae	5 (2.6%)

Additional distinct co-infection combinations detected by the comparator method but not detected by the QIAstat-Dx Respiratory Panel in the prospective clinical trial are presented in Table 12 (next page).

Table 12. Additional distinct co-infection combinations detected by the comparator method but not by the QIAstat-Dx Respiratory Panel in the prospective study

Distinct co-infection combinations detected by the comparator method			Total co-infections
Analyte 1	**Analyte 2**	**Analyte 3**	
Adenovirus	Coronavirus HKU1	Respiratory Syncytial Virus	1
Adenovirus	Coronavirus OC43	Coronavirus NL63	1
Adenovirus	Respiratory Syncytial Virus	Coronavirus NL63	1
Adenovirus	Rhinovirus/Enterovirus	Respiratory Syncytial Virus	1
Coronavirus HKU1	Coronavirus OC43		1
Coronavirus HKU1	Respiratory Syncytial Virus		1
Coronavirus HKU1	Coronavirus NL63	Respiratory Syncytial Virus	1
Coronavirus HKU1	Coronavirus NL63		1
Coronavirus HKU1	Parainfluenza virus 1	Rhinovirus/Enterovirus	1
Coronavirus NL63	Respiratory Syncytial Virus		1
Coronavirus NL63	Rhinovirus/Enterovirus		1
Coronavirus NL63	Influenza A H3		1
Coronavirus OC43	Respiratory Syncytial Virus		1
Human Metapneumovirus	Parainfluenza virus 3	Rhinovirus/Enterovirus	1
Human Metapneumovirus	Rhinovirus/Enterovirus		1
Rhinovirus/Enterovirus	Adenovirus		1
Rhinovirus/Enterovirus	Influenza A H3		2
Rhinovirus/Enterovirus	Parainfluenza virus 3		1
Rhinovirus/Enterovirus	Parainfluenza virus 3	Respiratory Syncytial Virus	1
Rhinovirus/Enterovirus	Parainfluenza virus 4		2
Influenza A H3	Respiratory Syncytial Virus		1
Influenza B	Influenza A (Equivocal)		1
		Total co-infections	**24**
		Total double infections	**16**
		Total triple infections	**8**

A total of 1994 prospective clinical specimens were tested and analyzed during the prospective clinical evaluation. Of these, 95.88% (1912/1994) yielded valid results on the first attempt (i.e., first loaded cartridge). Invalid or no result were obtained for the remaining 82 specimens (4.11%). Forty-two (42) specimens were invalid due to cartridge internal control failure (2.11%). Of these, 20 (1.00%) provided a result for positively detected targets and 22 (1.10%) had no detections. For 40 (2.00%) specimens, no results were obtained due to incomplete runs. Of these, 1 specimen was aborted by users (0.05%), 21 were due to instrument errors (1.05%), and 18 were due to cartridge-related errors (0.90%). Seventy-two (72) of the 82 initially failed (no result or invalid); specimens yielded valid results after a single retesting using a new cartridge/sample. The remaining 10 specimens failed on the second attempt (2 due to cartridge failures, 1 due to instrument errors, and 7 due to internal control failures). Of these internal control failures, detected pathogens were reported for 4 specimens.

Preselected archived specimens

Some of the analytes on the QIAstat-Dx Respiratory Panel were of low prevalence and were not encountered in sufficiently large numbers during the prospective study to adequately demonstrate clinical performance. To supplement the results of the prospective clinical study, an evaluation of preselected frozen archived retrospective specimens was performed. The specimens selected for testing had previously tested positive for one of the following targets at the clinical laboratory by their standard of care method: *Bordetella pertussis*, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Influenza A H1N1 2009, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, Parainfluenza virus 1, Parainfluenza virus 2, and Parainfluenza virus 4. Testing was performed by operators who were blinded to the expected test result. A total of 310 clinical samples were included within the frozen archived retrospective sample tested arm. Samples were tested by both the comparator method and QIAstat-Dx Respiratory Panel. If the comparator method

did not confirm the preselected target as positive, it was excluded from the data analysis for that target.

A summary of the demographic information available for the archived specimens is provided in Table 13 (next page).

Table 13. Demographic summary for the retrospective study arm

		Overall (%)
SEX	Male	158 (50.8%)
	Female	152 (49.2%)
AGE	≤5 years	139 (44.9%)
	6–21 years	85 (27.4%)
	22–49 years	53 (17.1%)
	50+ years	33 (10.7%)
STATUS	Outpatient	224 (72.3%)
	Hospitalized	68 (21.9%)
	Emergency	8 (2.6%)
	ICU	8 (2.6%)
	Other	2 (0.6%)
	Total	**310**

The QIAstat-Dx Respiratory Panel retrospective specimens testing performance data against the comparator method are provided in Table 14 (next page) by analyte.

Table 14. Overall retrospective clinical study performance

Analyte	TP/(TP+FN)	Sensitivity/PPA	95% CI	TN/(TN+FP)	Specificity/NPA	95% CI
Viruses						
Adenovirus[a]	9/9	100.0%	70.1–100.0	297/304	97.8%	95.4–98.9
Coronavirus 229E	26/27	96.3%	81.7–99.3	286/286	100.0%	98.7–100.0
Coronavirus HKU1[b]	14/14	100.0%	78.5–100.0	298/299	99.7%	98.1–99.9
Coronavirus NL63[c]	24/24	100.0%	86.2–100.0	286/288	99.3%	97.5–99.8
Coronavirus OC43	28/29	96.6%	82.8–99.4	279/279	100.0%	98.6–100.0
Human Metapneumovirus	2/2	100.0%	34.2–100.0	311/311	100.0%	98.7–100.0
Rhinovirus/ Enterovirus[d]	44/49	89.8%	78.2–95.5	254/264	96.2%	93.2–97.9
Influenza A	17/17	100.0%	81.5–100.0	296/296	100.0%	98.7–100.0
Influenza A H1	0/0	N/A	N/A	313/313	100.0%	98.8–100.0
Influenza A H1N1/pdm09[e]	7/8	87.5%	52.9–97.8	304/304	100.0%	98.8–100.0
Influenza A H3	8/8	100.0%	67.5–100.0	305/305	100.0%	98.8–100.0
Influenza B	1/1	100.0%	20.7–100.0	312/312	100.0%	98.8–100.0
Parainfluenza virus 1	40/40	100.0%	91.2–100.0	267/267	100.0%	98.6–100.0
Parainfluenza virus 2	3/3	100.0%	43.8–100.0	309/309	100.0%	98.8–100.0
Parainfluenza virus 3[f]	1/4	25.0%	4.6–69.9	309/309	100.0%	98.8–100.0
Parainfluenza virus 4[g]	22/24	91.7%	74.2–97.7	278/278	100.0%	98.6–100.0
Respiratory Syncytial Virus (RSV)[h]	11/12	91.7%	64.6–98.5	300/301	99.7%	98.4–99.9
Bacteria						
Bordetella pertussis	33/33	100.0%	89.6–100.0	261/261	100.0%	98.5–100.0
Chlamydophila pneumoniae[i]	54/61	88.5%	78.2–94.3	250/250	100.0%	98.5–100.0
Mycoplasma pneumoniae	25/25	100.0%	86.7–100.0	287/288	99.7%	98.1–99.9

[a] Adenovirus was detected in 3/5 FP specimens using an independent molecular method. 2 FP did not undergo discordant analysis.

[b] The single FP Coronavirus HKU1 specimen was negative when tested using an independent molecular method.

[c] The single FP Coronavirus NL63 specimen was negative when tested using an independent molecular method.
[d] Rhinovirus was detected in 1/2 FN when tested using an independent molecular method. Rhinovirus was detected in 4/10 FP specimens using an independent molecular method.
[e] Influenza H1N1 pdm09 was detected in the single FN specimen.
[f] Parainfluenza virus 3 was detected in 1/3 FN specimens by an independent molecular method.
[g] Parainfluenza virus 4 was detected in 1/2 FN specimens by an independent molecular method.
[h] The single FN Respiratory Syncytial Virus was negative for that target by an independent molecular method. The single FP Respiratory Syncytial Virus was negative for that target by an independent molecular method.
[i] *Chlamydophila pneumoniae* was detected in 4/5 FN specimens by an independent molecular method.

Testing of contrived specimen

Influenza A H1, Parainfluenza virus 2, Parainfluenza virus 4, Coronavirus 229E and *Chlamydophila pneumoniae*, despite all prospective and retrospective testing efforts, were insufficient to demonstrate system performance. Therefore, contrived specimens were used as surrogate clinical specimens to supplement and test the sensitivity and specificity of the above analytes. Residual negative clinical specimens were spiked with the pathogens at 3x, 5x and 10x LoD levels (50 of each).

Contrived samples were provided a unique study identification number and the individual who contrived the samples did not test them therefore the status of each contrived specimen was unknown at the time of testing. Results of contrived specimen testing are provided in Table 15 (next page).

Table 15. Contrived specimen results

	Positive Predictive Agreement			
Analyte	**x LoD**	**TP/(TP + FN)**	**%**	**95% CI**
Influenza A H1*	3	24/24	100%	86.2–100
	5	27/27	100%	87.5–100
	10	24/24	100%	86.2–100
Coronavirus 229E	3	16/16	100%	80.6–100
	5	18/18	100%	82.4–100
	10	16/16	100%	80.6–100
Parainfluenza virus 2	3	16/16	100%	80.6–100
	5	18/18	100%	82.4–100
	10	16/16	100%	80.6–100
Parainfluenza virus 4	3	15/16	93.8%	71.7–98.9
	5	18/18	100%	82.4–100
	10	16/16	100%	80.6–100
Chlamydophila pneumoniae	3	16/16	100%	80.6–100
	5	18/18	100%	82.4–100
	10	16/16	100%	80.6–100

* One Influenza A H1 strain [VR-897] was initially spiked incorrectly, yielding unexpected results across all LoD concentrations [3x LoD = 4/8 (50%), 5x LoD = 2/9 (22.2%) and 10x LoD = 6/8 (75.0%). A replacement strain [0810244CFHI] was sent to the testing site for spiking and strain VR-897 was also repeated to confirm that the issue was isolated to a procedural error and not an instrument failure.

Expected values

During the prospective QIAstat-Dx Respiratory Panel (Cat. No. 691221) clinical study, 1994 eligible prospective nasopharyngeal swab (NPS) specimens were collected and tested at five (5) sites across the U.S. (4) and Europe (1) from December 2017 through June 2018. The number and percentage of positive cases, as determined by the QIAstat-Dx Respiratory Panel, calculated by testing site or by age group are presented in Table 16, Table 17, and Table 18 (following pages).

Table 16. Expected value (EV) (as determined by the QIAstat Dx Respiratory Panel) summary overall and by site for the prospective clinical evaluation (N = number)

	Overall (n=1994)		Site 1 (n=418)		Site 2 (n=426)		Site 3 (n=448)		Site 4 (n=303)		Site 5 (n=399)	
Organism	**N**	**EV**	**N**	**EV**	**N**	**EV**	**N**	**EV**	**N**	**EV**	**N**	**EV**
Viruses												
Adenovirus	102	5.1%	44	10.5%	9	2.1%	12	2.7%	30	9.9%	7	1.8%
Coronavirus 229E	8	0.4%	1	0.2%	0	0.0%	0	0.0%	7	2.3%	0	0.0%
Coronavirus HKU1	58	2.9%	4	1.0%	11	2.6%	14	3.1%	12	4.0%	17	4.3%
Coronavirus NL63	42	2.1%	4	1.0%	1	0.2%	15	3.3%	11	3.6%	11	2.8%
Coronavirus OC43	30	1.5%	0	0.0%	5	1.2%	6	1.3%	12	4.0%	7	1.8%
Human Metapneumovirus	120	6.0%	42	10.0%	24	5.6%	14	3.1%	14	4.6%	26	6.5%
Human Rhinovirus/Enterovirus	304	15.2%	59	14.1%	78	18.3%	39	8.7%	53	17.5%	75	18.8%
Influenza A	251	12.6%	120	28.7%	0	0.0%	58	12.9%	38	12.5%	35	8.8%
Influenza A H1	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Influenza A H1N1 pdm 2009	85	4.3%	67	16.0%	0	0.0%	4	0.9%	10	3.3%	4	1.0%
Influenza H3	163	8.2%	52	12.4%	0	0.0%	52	11.6%	28	9.2%	31	7.8%
Influenza B	123	6.2%	58	13.9%	0	0.0%	32	7.1%	7	2.3%	26	6.5%
Parainfluenza virus 1	19	1.0%	2	0.5%	1	0.2%	2	0.4%	4	1.3%	10	2.5%
Parainfluenza virus 2	2	0.1%	2	0.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Parainfluenza virus 3	116	5.8%	23	5.5%	19	4.5%	16	3.6%	23	7.6%	35	8.8%
Parainfluenza virus 4	5	0.3%	1	0.2%	0	0.0%	1	0.2%	0	0.0%	3	0.8%
Respiratory Syncytial Virus	217	10.9%	64	15.3%	40	9.4%	35	7.8%	40	13.2%	38	9.5%
Bacteria												
Bordetella pertussis	9	0.5%	2	0.5%	1	0.2%	0	0.0%	6	2.0%	0	0.0%
Chlamydophila pneumoniae	6	0.3%	2	0.5%	1	0.2%	1	0.2%	1	0.3%	1	0.3%
Mycoplasma pneumoniae	24	1.2%	19	4.5%	0	0.0%	2	0.4%	1	0.3%	2	0.5%

Table 17. Expected value (EV) (as determined by the QIAstat Dx Respiratory Panel) summary by age category for the prospective clinical evaluation (N = number)

Organism	Overall (n=1994)			≤5 years (n=627)		6–21 years (n=239)		22–49 years (n=330)		>49 years (n=798)	
	N	EV	**N**	N	EV	N	EV	N	EV	N	EV
Viruses											
Adenovirus	102	5.1%	78	12.4%	7	2.9%	11	3.3%	6	0.8%	
Coronavirus 229E	8	0.4%	4	0.6%	4	1.7%	0	0.0%	0	0.0%	
Coronavirus HKU1	58	2.9%	29	4.6%	5	2.1%	8	2.4%	16	2.0%	
Coronavirus NL63	42	2.1%	25	4.0%	3	1.3%	5	1.5%	9	1.1%	
Coronavirus OC43	30	1.5%	20	3.2%	2	0.8%	4	1.2%	4	0.5%	
Human Metapneumovirus	120	6.0%	46	7.3%	3	1.3%	17	5.2%	54	6.8%	
Human Rhinovirus/Enterovirus	304	15.2%	186	29.7%	35	14.6%	22	6.7%	61	7.6%	
Influenza A	251	12.6%	47	7.5%	36	15.1%	64	19.4%	104	13.0%	
Influenza A H1	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	
Influenza A H1N1 pdm 2009	85	4.3%	20	3.2%	6	2.5%	30	9.1%	29	3.6%	
Influenza H3	163	8.2%	25	4.0%	30	12.6%	35	10.6%	73	9.1%	
Influenza B	123	6.2%	11	1.8%	22	9.2%	27	8.2%	63	7.9%	
Parainfluenza virus 1	19	1.0%	11	1.8%	0	0.0%	4	1.2%	4	0.5%	
Parainfluenza virus 2	2	0.1%	1	0.2%	0	0.0%	0	0.0%	1	0.1%	
Parainfluenza virus 3	116	5.8%	70	11.2%	4	1.7%	6	1.8%	36	4.5%	
Parainfluenza virus 4	5	0.3%	4	0.6%	0	0.0%	0	0.0%	1	0.1%	
Respiratory Syncytial Virus	217	10.9%	135	21.5%	11	4.6%	17	5.2%	54	6.8%	
Bacteria											
Bordetella pertussis	9	0.5%	5	0.8%	2	0.8%	0	0.0%	2	0.3%	
Chlamydophila pneumoniae	6	0.3%	1	0.2%	3	1.3%	2	0.6%	0	0.0%	
Mycoplasma pneumoniae	24	1.2%	4	0.6%	6	2.5%	11	3.3%	3	0.4%	

The number and percentage of co-infection cases, as determined by the QIAstat-Dx Respiratory Panel, calculated by age group are presented in Table 18, next page.

Table 18. Expected value (co-infections as determined by the QIAstat-Dx Respiratory Panel) summary by age group

Co-infection	Number (expected value) overall (n=191)	<6 years (n=151)	6–21 years (n=12)	22–49 years (n=14)	>49 years (n=14)
AdV + HRV/EV + CoV NL63	2 (1.05%)	2	0	0	0
AdV + HRV/EV	12 (6.28%)	9	2	1	0
AdV + RSV	11 (5.82%)	11	0	0	0
AdV + *M. pneumoniae*	2 (1.05%)	1	1	0	0
AdV + CoV HKU1	3 (1.57%)	3	0	0	0
CoV HKU1+ AdV+ RSV	1 (0.52%)	1	0	0	0
CoV HKU1 + HMPV	3 (1.57%)	3	0	0	0
CoV HKU1 + PIV 3 + HRV/EV	1 (0.52%)	1	0	0	0
CoV HKU1 + PIV 4	1 (0.52%)	1	0	0	0
CoV HKU1 + RSV	8 (4.28%)	5	1	1	1
CoV HKU1 + HRV/EV + RSV	1 (0.52%)	1	0	0	0
CoV HKU1 + HRV/EV	4 (2.09%)	2	0	0	2
CoV NL63 + AdV+ RSV	1 (0.52%)	1	0	0	0
CoV NL63 + AdV	1 (0.52%)	1	0	0	0
CoV NL63 + *B. pertussis*	2 (1.05%)	1	1	0	0
CoV NL63 + PIV 1	1 (0.52%)	0	0	1	0
CoV NL63 + RSV	2 (1.05%)	2	0	0	0
CoV NL63 + HRV/EV	2 (1.05%)	2	0	0	0
CoV OC43 + AdV	2 (1.05%)	2	0	0	0
CoV OC43 + HMPV	2 (1.05%)	2	0	0	0
CoV OC43 + PIV 3 + HRV/EV	1 (0.52%)	1	0	0	0
CoV OC43 + RSV	4 (2.09%)	3	1	0	0
CoV OC43 + HRV/EV + RSV	2 (1.05%)	2	0	0	0
CoV OC43 + HRV/EV	2 (1.05%)	1	1	0	0
CoV 229E + RSV	1 (0.52%)	1	0	0	0
HMPV + AdV	2 (1.05%)	1	0	1	0
HMPV + RSV	2 (1.05%)	1	0	0	1

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Table 18 (continued)

Co-infection	Number (expected value) overall (n=191)	<6 years (n=151)	6–21 years (n=12)	22–49 years (n=14)	>49 years (n=14)
HMPV + HRV/EV	9 (4.71%)	6	0	2	1
HMPV + HRV/EV + AdV + CoV 229E	1 (0.52%)	1	0	0	0
Influenza A (no subtype) + RSV + AdV	1 (0.52%)	1	0	0	0
Influenza A (no subtype) + RSV	1 (0.52%)	1	0	0	0
Influenza A H1N1/pdm09 + CoV NL63	1 (0.52%)	0	0	1	0
Influenza A H1N1/pdm09 + CoV OC43 + AdV	1 (0.52%)	1	0	0	0
Influenza A H1N1/pdm09 + HRV/EV	2 (1.05%)	1	1	0	0
Influenza A H1N1/pdm09 + HRV/EV + *B. pertussis*	1 (0.52%)	1	0	0	0
Influenza A H1N1/pdm09 + RSV	1 (0.52%)	1	0	0	0
Influenza A H3 + AdV	2 (1.05%)	0	0	1	1
Influenza A H3 + CoV NL63 + PIV 1	1 (0.52%)	1	0	0	0
Influenza A H3 + CoV NL63 + *B. pertussis*	1 (0.52%)	1	0	0	0
Influenza A H3 + CoV NL63	1 (0.52%)	0	0	0	1
Influenza A H3 + CoV OC43 + AdV + RSV	1 (0.52%)	1	0	0	0
Influenza A H3 + HRV/EV	4 (2.09%)	2	0	1	1
Influenza A H3 + PIV 1	2 (1.05%)	2	0	0	0
Influenza A H3 + PIV 3	2 (1.05%)	1	0	0	1
Influenza A H3 + RSV	1 (0.52%)	0	0	1	0
Influenza A H3 + CoV 229E	1 (0.52%)	0	1	0	0
Influenza B + CoV HKU1	3 (1.57%)	1	0	0	2
Influenza B + CoV NL63	1 (0.52%)	0	1	0	0

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Table 18 (continued)

Co-infection	Number (expected value) overall (n=191)	<6 years (n=151)	6–21 years (n=12)	22–49 years (n=14)	>49 years (n=14)
Influenza B + RSV	2 (1.05%)	2	0	0	0
Influenza B + HRV/EV	7 (3.67%)	4	1	1	1
M. pneumoniae + CoV HKU1	1 (0.52%)	0	1	0	0
M. pneumoniae + HRV/EV	1 (0.52%)	0	0	1	0
PIV 1 + AdV	1 (0.52%)	1	0	0	0
PIV 1 + RSV	1 (0.52%)	1	0	0	0
PIV 1 + HRV/EV	2 (1.05%)	2	0	0	0
PIV 1 + HRV/EV + *M. pneumoniae*	1 (0.52%)	1	0	0	0
PIV 3 + AdV	3 (1.57%)	3	0	0	0
PIV 3 + AdV + HRV/EV	3 (1.57%)	3	0	0	0
PIV 3 + HMPV	2 (1.05%)	2	0	0	0
PIV 3 + RSV	2 (1.05%)	2	0	0	0
PIV 3 + HRV/EV	14 (7.33%)	14	0	0	0
PIV 4 + RSV	1 (0.52%)	1	0	0	0
PIV 4 + HRV/EV	2 (1.05%)	2	0	0	0
RSV + HMPV + HRV/EV + AdV	1 (0.52%)	1	0	0	0
RSV + HMPV + HRV/EV	2 (1.05%)	1	0	0	1
RSV + HRV/EV	29 (15.18%)	26	0	2	1

Analytical performance

Sensitivity (Limit of Detection)

The Analytical Sensitivity, or Limit of Detection (LoD), is defined as the lowest concentration at which ≥95% of the tested samples generate a positive call.

The LoD for each QIAstat-Dx Respiratory Panel pathogen was assessed by analyzing serial dilutions of analytical samples prepared from high-titer stocks obtained from commercial suppliers (ZeptoMetrix and ATCC®) or artificial samples for commercially unavailable target analytes.

The LoD concentration was determined for a total of 51 pathogen strains. The LoD per analyte was determined using selected strains representing individual pathogens that are possible to detect with the QIAstat-Dx Respiratory Panel. To confirm the established LoD concentration, the detection rate of all replicates must be ≥95% (at least 19/20 replicates must generate a positive signal).

At least three different cartridge lots and at least three different QIAstat-Dx Analyzers were used for LoD determination for every pathogen.

Individual LoD values for each QIAstat-Dx Respiratory Panel target is shown in Table 19 (next page).

Table 19. LoD values obtained for the different respiratory target strains tested with the QIAstat-Dx Respiratory SARS-CoV-2 Panel

Pathogen	Strain	Source	Concentration	Detection rate
Influenza A H1N1	A/New Jersey/8/76	ATCC VR-897	341 $CEID_{50}$/ml	Flu A: 20/20 H1: 20/20
	A/Brisbane/59/07	ZeptoMetrix 0810244CFHI	4 $TCID_{50}$/ml	Flu A: 20/20 H1: 20/20
	A/New Caledonia/20/99	ZeptoMetrix 0810036CFHI	15 $TCID_{50}$/ml	Flu A: 20/20 H1: 19/20
Influenza A H3N2	A/Virginia/ATCC6/2012*	ATCC VR-1811	0.1 PFU/ml	Flu A: 20/20 H3: 20/20
	A/Wisconsin/67/2005*	ZeptoMetrix 0810252CFHI	3.8 $TCID_{50}$/ml	Flu A: 20/20 H3: 20/20
	A/Port Chalmers/1/73	ATCC VR-810	499.3 $CEID_{50}$/ml	Flu A: 20/20 H3: 20/20
Influenza A, subtype H1N1/2009/pdm09	A/Virginia/ATCC1/2009	ATCC VR-1736	67 PFU/ml	Flu A: 20/20 H1N1: 20/20
	A/SwineNY/03/2009	ZeptoMetrix 0810249CFHI	56 $TCID_{50}$/ml	Flu A: 20/20 H1N1: 20/20
Influenza B	B/Virginia/ATCC5/2012*	ATCC VR-1807	0.03 PFU/ml	20/20
	B/FL/04/06	ATCC VR-1804	1080 $CEID_{50}$/ml	20/20
	B/Taiwan/2/62	ATCC VR-295	5000 $CEID_{50}$/ml	19/20
Coronavirus 229E	–	ATCC VR-740	0.2 $TCID_{50}$/ml	20/20
	–*	ZeptoMetrix 0810229CFHI	3.6 $TCID_{50}$/ml	20/20
Coronavirus OC43	–	ATCC VR-1558	0.1 $TCID_{50}$/ml	20/20
	–*	ZeptoMetrix 0810024CFHI	0.1 $TCID_{50}$/ml	20/20
Coronavirus NL63	–	ZeptoMetrix 0810228CFHI	0.01 $TCID_{50}$/ml	20/20
Coronavirus HKU1	–*	Clinical sample S510	40,000 copies/ml	20/20

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Table 19 (**continued)**

Pathogen	Strain	Source	Concentration	Detection rate
Parainfluenza virus 1 (PIV 1)	C35*	ATCC VR-94	0.2 $TCID_{50}$/ml	19/20
	–	ZeptoMetrix 0810014CFHI	0.2 $TCID_{50}$/ml	19/20
Parainfluenza virus 2 (PIV 2)	Greer	ATCC VR-92	7.3 $TCID_{50}$/ml	20/20
	–*	ZeptoMetrix 0810015CFHI	1.3 $TCID_{50}$/ml	19/20
Parainfluenza virus 3 (PIV 3)	C 243	ATCC VR-93	2.3 $TCID_{50}$/ml	20/20
	–*	ZeptoMetrix 0810016CFHI	11.5 $TCID_{50}$/ml	20/20
Parainfluenza virus 4a (PIV 4a)	M-25	ATCC VR-1378	0.5 $TCID_{50}$/ml	20/20
Parainfluenza virus 4b (PIV 4b)	–*	ZeptoMetrix 0810060BCFHI	9.5 $TCID_{50}$/ml	20/20
Respiratory Syncytial Virus A	A2*	ATCC VR-1540	12.0 PFU/ml	20/20
	Long*	ATCC VR-26	33.0 PFU/ml	20/20
Respiratory Syncytial Virus B	18537*	ATCC VR-1580	0.03 PFU/ml	20/20
	CH93(18)-18	ZeptoMetrix 0810040CFHI	0.4 $TCID_{50}$/ml	20/20
Human Metapneumovirus	Peru6-2003 (type B2)*	ZeptoMetrix 0810159CFHI	0.01 $TCID_{50}$/ml	19/20
	hMPV-16, IA10-2003 (A1)	ZeptoMetrix 0810161CFHI	0.5 $TCID_{50}$/ml	20/20
	hMPV-20, IA14-2003 (A2)*	ZeptoMetrix, 0810163CFHI	0.4 $TCID_{50}$/ml	19/20
	hMPV-3, Peru2-2002 (B1)*	ZeptoMetrix, 0810156CFHI	1479.9 $TCID_{50}$/ml	19/20
Adenovirus	GB (Adenovirus B3)	ATCC VR-3	4993.0 $TCID_{50}$/ml	20/20
	RI-67 (Adenovirus E4)*	ATCC VR-1572	15.8 $TCID_{50}$/ml	20/20
	Adenoid 75 (Adenovirus C5)*	ATCC VR-5	7331.0 $TCID_{50}$/ml	20/20
	Adenoid 71 (Adenovirus C1)*	ATCC VR-1	69.5 $TCID_{50}$/ml	20/20
	Adenoid 6 (Adenovirus C2)*	ATCC VR-846	28.1 $TCID_{50}$/ml	20/20
	Tonsil 99 (Adenovirus C6)*	ATCC VR-6	88.8 $TCID_{50}$/ml	20/20

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Table 19 (**continued)**

Pathogen	Strain	Source	Concentration	Detection rate
Enterovirus	/US/IL/14-18952 (Enterovirus D68)	ATCC VR-1824	8.9 $TCID_{50}$/ml	19/20
	Echovirus 6*	ATCC VR-241	0.9 $TCID_{50}$/ml	19/20
Rhinovirus	1059 (Rhinovirus B14)*	ATCC VR-284	8.9 $TCID_{50}$/ml	20/20
	HGP (Rhinovirus A2)	ATCC VR-482	8.9 $TCID_{50}$/ml	19/20
	11757 (Rhinovirus C16)*	ATCC VR-283	50.0 $TCID_{50}$/ml	20/20
	Type 1A*	ATCC VR-1559	8.9 $TCID_{50}$/ml	20/20
Mycoplasma pneumoniae	M129-B7 (type 1)*	ATCC 29342	0.1 CCU/ml	20/20
	PI 1428	ATCC 29085	1.0 CCU/ml	20/20
Chlamydia pneumoniae	TW183	ATCC VR-2282	14.2 IFU/ml	20/20
	CWL-029*	ATCC VR-1310	120.0 IFU/ml	19/20
Bordetella pertussis	I028	ATCC BAA-2707	0.3 CFU/ml	20/20
	18323*	ATCC 9797	2.6 CFU/ml	19/20

* The LoD has been obtained in simulated matrix.

Exclusivity (Cross-reactivity and Exclusivity)

The analytical specificity study was carried out by *in silico* analysis and *in vitro* testing to assess the cross-reactivity and exclusivity of the QIAstat-Dx Respiratory Panel. On-panel organisms were tested to assess the potential for intra-panel cross-reactivity and off-panel organisms were tested to evaluate panel exclusivity. The off-panel organisms selected were clinically relevant organisms (colonizing the upper respiratory tract or causing respiratory symptoms), common skin flora or laboratory contaminants, or microorganisms for which much of the population may have been infected. The on-panel organisms tested are shown in Table 20 (next page).

Samples were prepared by spiking potential cross-reactive organisms into simulated nasopharyngeal swab sample matrix at the highest concentration possible based on the organism stock – at least 10^5 $TCID_{50}$/ml for viral targets and 10^6 CFU/ml for

bacterial and fungal targets. These concentrations represent levels approximately 800–1,000,000-fold higher than the LoD of the QIAstat-Dx Respiratory Panel.

Bordetella pertussis detection in the QIAstat-Dx Respiratory SARS-CoV-2 Panel targets the IS481 region. As a consequence, a certain level of cross-reactivity with off-panel *Bordetella* species and *Bordetella pertussis* was predicted by preliminary sequence analysis and was observed when high concentrations of *Bordetella holmesii* were tested. In concordance with the CDC guidelines for assays that use the IS481 as a target region, when using QIAstat-Dx Respiratory SARS-CoV-2 Panel if the C_T value for *Bordetella pertussis* is C_T>29, a confirmatory specificity test is recommended.

Table 20. List of Analytical Specificity pathogens tested

Type	Pathogen
On-panel bacteria	*Mycoplasma pneumoniae* *Bordetella pertussis* *Chlamydia pneumoniae*
Off-panel bacteria	*Acinetobacter calcoaceticus* *Bordetella avium* *Bordetella bronchiseptica* *Bordetella hinzii* *Bordetella holmesii* *Bordetella parapertussis* *Chlamydia trachomatis* *Corynebacterium diphteriae* *Enterobacter aerogenes* *Escherichia coli* (O157) *Haemophilus influenzae* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Lactobacillus acidophilus* *Lactobacillus plantarum* *Legionella bozemanii* *Legionella dumofii* *Legionella feeleii* *Legionella longbeacheae* *Legionella micdadei* *Legionella pneumophila* *Moraxella catarrhalis*

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Table 20 (continued)

Type	Pathogen
Off-panel bacteria (continued)	*Mycobacterium tuberculosis**
	Mycoplasma genitalium
	Mycoplasma hominis
	Mycoplasma orale
	Neisseria elongata
	Neisseria gonorrhoeae
	Neisseria meningitidis
	Proteus mirabilis
	Pseudomonas aeruginosa
	Serratia marcescens
	Staphylococcus aureus
	Staphylococcus epidermidis
	Stenotrophomonas maltophilia
	Streptococcus agalactiae
	Streptococcus pneumoniae
	Streptococcus pyogenes
	Streptococcus salivarus
	Ureaplasma urealyticum
On-panel viruses	Influenza A H1N1
	Influenza A H3N2
	Influenza A H1N1/pdm09
	Influenza B
	Coronavirus 229E
	Coronavirus OC43
	Coronavirus NL63
	Coronavirus HKU1†
	Parainfluenza virus 1
	Parainfluenza virus 2
	Parainfluenza virus 3
	Parainfluenza virus 4a
	RSV A
	hMPV A
	Adenovirus C
	Adenovirus B

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Table 20 (continued)

Type	Pathogen
On-panel viruses (continued)	Enterovirus Rhinovirus
Off-panel viruses	Bocavirus‡ Cytomegalovirus Epstein-Barr Virus Herpes Simplex Virus 1 Herpes Simplex Virus 2 Measles Virus Middle East Respiratory Syndrome Coronavirus§ Mumps
Off-panel fungi	*Aspergillus flavus* *Aspergillus fumigatus* *Candida albicans* *Cryptococcus neoformans*

* *Mycobacterium tuberculosis* genomic DNA tested.
† Coronavirus HKU1 clinical specimen tested.
‡ Bocavirus Type 1 clinical specimens tested.
§ Middle East Respiratory Syndrome Coronavirus synthetic RNA tested.

Inclusivity (Analytical Reactivity)

Analytical reactivity (Inclusivity) was evaluated with a collection of 127 respiratory pathogen isolates/strains that were selected based on clinical relevance and temporal/geographical diversity. Based on wet testing and *in silico* analysis, the QIAstat-Dx Respiratory SARS-CoV-2 Panel primers and probes are specific and inclusive for clinically prevalent and relevant strains for each pathogen. Wet testing has been done with the strains listed in Table 20. Every strain has been tested in triplicate with a 100% detection rate for concentrations listed.

Table 21 (following pages) provides details of the respiratory pathogens tested in this study.

Table 21. List of Analytical Reactivity pathogens tested

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Influenza A	H1N1	A/PR/8/34	ATCC VR-1469	3x	Influenza A H1
		A/New Jersey/8/76*	ATCC VR-897	1x	Influenza A H1
		A/Brisbane/59/07*	ZeptoMetrix 0810244CFHI	1x	Influenza A H1
		A/New Caledonia/20/99*	ZeptoMetrix 0810036CFHI	0.3x	Influenza A H1
		A/Denver/1/57	ATCC VR-546	0.1x	Influenza A H1
		A/Weiss/43	ATCC VR-96	0.1x	Influenza A H1
		A/Fort Monmouth/1/1947	ATCC VR-1754	0.1x	Influenza A H1
		A/WS/33	ATCC VR-1520	0.1x	Influenza A H1
		A/Swine/Iowa/15/1930	ATCC VR-333	1x	Influenza A H1
		A/Mal/302/54	ATCC VR-98	1x	Influenza A H1
	H3N2	A/Virginia/ATCC6/2012*	ATCC VR-1811	1x	Influenza A H3
		A/Wisconsin/67/2005*	ZeptoMetrix 0810252CFHI	1x	Influenza A H3
		A/Port Chalmers/1/73*	ATCC VR-810	1x	Influenza A H3
		A/Victoria/3/75	ATCC VR-822	1x	Influenza A H3
		A/Aichi/2/68	ATCC VR-1680	10x	Influenza A H3
		A/Hong Kong/8/68	ATCC VR-1679	10x	Influenza A H3
		A/Alice (recombinant, carries A/England/42/72)	ATCC VR-776	10x	Influenza A H3
		MRC-2 (recombinant A/England/42/72 and A/PR/8/34 strains)	ATCC VR-777	100x	Influenza A H3
		A/Switzerland/ 9715293/2013	ATCC VR-1837	1x	Influenza A H3
		A/Wisconsin/15/2009	ATCC VR-1882	1x	Influenza A H3

* Strain tested during LoD verification study.

Note: Influenza A/Brisbane/59/07 (ZeptoMetrix, 0810244CFHI) taken as reference strain to calculate the x-fold LoD detected.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Influenza A	H1N1 (pandemic)	A/Virginia/ATCC1/2009*	ATCC VR-1736	1x	Influenza A H1N1/pdm09
		A/SwineNY/03/2009*	ZeptoMetrix 0810249CFHI	1x	Influenza A H1N1/pdm09
		Canada/6294/09	ZeptoMetrix 0810109CFJHI	3x	Influenza A H1N1/pdm09
		Mexico/4108/09	ZeptoMetrix 0810166CFHI	0.1x	Influenza A H1N1/pdm09
		Netherlands/2629/2009	BEI Resources NR-19823	0.3x	Influenza A H1N1/pdm09
		A/Virginia/ATCC2/2009	ATCC VR-1737	0.1x	Influenza A H1N1/pdm09
		A/Virginia/ATCC3/2009	ATCC VR-1738	100x	Influenza A H1N1/pdm09
		Swine NY/01/2009	ZeptoMetrix 0810248CFHI	0.3x	Influenza A H1N1/pdm09
		Swine NY/02/2009	ZeptoMetrix 0810109CFNHI	10x	Influenza A H1N1/pdm09
		A/California/07/2009 NYMC X-179A	ATCC VR-1884	0.1x	Influenza A H1N1/pdm09
	H2N2	Japan/305/1957 (nucleic acid)	BEI Resources NR-2775	1x	Influenza A (no subtype)
		Korea/426/1968xPuerto Rico/8/1934 [isolate ID/source=recombinant] (nucleic acid)	BEI Resources NR-9679	0.3x	Influenza A (no subtype)
	H5N3	A/Duck/Singapore/645/ 1997 [isolate ID/source=avian]	BEI Resources NR-9682	1x	Influenza A (no subtype)

* Strain tested during LoD verification study.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Influenza A	H10N7	Chicken/Germany/N/49 [isolate ID/source=avian] (nucleic acid)	BEI Resources NR-2765	10x	Influenza A (no subtype)
	H1N2	Recombinant Kilbourne F63, A/NWS/1934 (HA) x A/Rockefeller Institute/5/1957 (NA) [isolate ID/source=recombinant] (nucleic acids)	BEI Resources NR-9677	100x	Influenza A H1
Influenza B	Not available	B/Virginia/ATCC5/2012*	ATCC VR-1807	1x	Influenza B
		B/FL/04/06*	ATCC VR-1804	1x	Influenza B
		B/Taiwan/2/62*	ATCC VR-295	0.3x	Influenza B
		B/Allen/45	ATCC VR-102	Not detected†	Negative
		B/Hong Kong/5/72	ATCC VR-823	Not detected†	Negative
		B/Maryland/1/59	ATCC VR-296	0.1x	Influenza B
		B/GL/1739/54	ATCC VR-103	1x	Influenza B
		B/Wisconsin/1/2010	ATCC VR-1883	0.1x	Influenza B
		B/Massachusetts/2/2012	ATCC VR-1813	3x	Influenza B
		B/Florida/02/06	ZeptoMetrix 0810037CFHI	Impaired detect-ability‡	Influenza B or Negative
		B/Brisbane/60/2008	BEI Resources NR-42005	0.1x	Influenza B
		B/Malaysia/2506/2004	BEI Resources NR-9723	0.3x	Influenza B

* Strain tested during LoD verification study.

† Both strains are derivative from B/Lee/40 ancestral lineage and, according to *in silico* analysis, they were predicted to be detected by the QIAstat-Dx Respiratory Panel.

‡ *In silico* analysis showed that this strain should be detected by QIAstat-Dx Respiratory Panel.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Coronavirus 229E	Not available	Not available*	ZeptoMetrix 0810229CFHI	1x	Coronavirus 229E
		Not available*	ATCC VR-740	0.3x	Coronavirus 229E
Coronavirus OC43	Not available	Not available*	ATCC VR-1558	1x	Coronavirus OC43
		Not available*	ZeptoMetrix 0810024CFHI	1x	Coronavirus OC43
Coronavirus NL63	Not available	Not available*	ZeptoMetrix 0810228CFHI	1x	Coronavirus NL63
	Not available	Not available	BEI Resources NR-470	1x	Coronavirus NL63
Coronavirus HKU1	Not available	Not available*	ZeptoMetrix NATRVP-IDI	1x	Coronavirus HKU1
		Not available	QIAGEN Barcelona (STAT-Dx) Clinical sample S510†	0.3x	Coronavirus HKU1
		Not available	QIAGEN Barcelona (STAT-Dx) Clinical sample S501†	1x	Coronavirus HKU1
		Not available	QIAGEN Barcelona (STAT-Dx) Clinical sample 496†	1x	Coronavirus HKU1

* Strain tested during LoD verification study.

† Stock titer not available according to manufacturer.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Para-influenza virus 1	Not available	Not available*	ZeptoMetrix 0810014CFHI	1x	Parainfluenza virus 1
		C35*	ATCC VR-94	1x	Parainfluenza virus 1
		Not available	ZeptoMetrix NATRVP-IDI†	10x	Parainfluenza virus 1
Para-influenza virus 2	Not available	Greer*	ATCC VR-92	1x	Parainfluenza virus 2
		Not available*	ZeptoMetrix 0810015CFHI	0.3x	Parainfluenza virus 2
		Not available	ZeptoMetrix 0810504CFHI	0.1x	Parainfluenza virus 2
Para-influenza virus 3	Not available	Not available*	ZeptoMetrix 0810016CFHI	1x	Parainfluenza virus 3
		C 243*	ATCC VR-93	1x	Parainfluenza virus 3
		Not available*	ZeptoMetrix NATRVP-IDI†	0.1x	Parainfluenza virus 3
Para-influenza virus 4	Not available	M-25*	ATCC VR-1378	1x	Parainfluenza virus 4
		Not available*	ZeptoMetrix 0810060BCFHI	0.3x	Parainfluenza virus 4
		Not available	ZeptoMetrix 0810060CFHI	0.1x	Parainfluenza virus 4
		CH 19503	ATCC VR-1377	0.3x	Parainfluenza virus 4

* Strain tested during LoD verification study.
† Stock titer not available according to manufacturer.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Respiratory Syncytial Virus A+B	Not available	18537*	ATCC VR-1580	1x	Respiratory Syncytial virus A+B
		A2*	ATCC VR-1540	0.3x	Respiratory Syncytial virus A+B
		Long*	ATCC VR-26	1x	Respiratory Syncytial virus A+B
		CH93(18)-18*	ZeptoMetrix 0810040CFHI	1x	Respiratory Syncytial virus A+B
		Not available	ZeptoMetrix 0810040ACFHI	0.1x	Respiratory Syncytial virus A+B
		B WV/14617/85	ATCC VR-1400	1x	Respiratory Syncytial virus A+B
Human Meta-pneumovirus	Not available	IA10-2003*	ZeptoMetrix 0810161CFHI	1x	Human Meta-pneumovirus A+B
		IA14-2003*	ZeptoMetrix 0810163CFHI	1x	Human Meta-pneumovirus A+B
		Peru2-2002*	ZeptoMetrix 0810156CFHI	1x	Human Meta-pneumovirus A+B
		Peru6-2003*	ZeptoMetrix 0810159CFHI	1x	Human Meta-pneumovirus A+B
		IA3-2002	ZeptoMetrix 0810160CFHI	3x	Human Metapneumovirus A+B
		IA27-2004	ZeptoMetrix 0810164CFHI	1x	Human Meta-pneumovirus A+B
		Peru3-2003	ZeptoMetrix 0810158CFHI	1x	Human Meta-pneumovirus A+B
		IA18-2003	ZeptoMetrix 0810162CFHI	1x	Human Meta-pneumovirus A+B
		Peru1-2002	ZeptoMetrix 0810157CFHI	10x	Human Meta-pneumovirus A+B

* Strain tested during LoD verification study.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Adenovirus	Not available	Tonsil 99*	ATCC VR-6	1x	Adenovirus
		GB*	ATCC VR-3	0.3x	Adenovirus
		Adenoid 71*	ATCC VR-1	1x	Adenovirus
		Adenoid 6*	ATCC VR-846	0.3x	Adenovirus
		Adenoid 75*	ATCC VR-5	0.3x	Adenovirus
		RI-67*	ATCC VR-1572	0.3x	Adenovirus
		Huie	ATCC VR-863	0.3x	Adenovirus
		Gomen	ATCC VR-7	0.1x	Adenovirus
		Slobitski	ATCC VR-12	10x	Adenovirus
		AV-1645 [128]	ATCC VR-256	0.3x	Adenovirus
		Compton	ATCC VR-716	0.3x	Adenovirus
		Holden	ATCC VR-718	0.3x	Adenovirus
		Trim	ATCC VR-1815	0.3x	Adenovirus
		Dugan	ATCC VR-931	0.1x	Adenovirus
		Tak (73-3544)	ATCC VR-930	3x	Adenovirus

* Strain tested during LoD verification study.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
Enterovirus	Not available	/US/IL/14-18952*	ATCC VR-1824	1x	Rhinovirus/Enterovirus
		D-1 (Cox)*	ATCC VR-241	0.3x	Rhinovirus/Enterovirus
		H	ATCC VR-1432	1x	Rhinovirus/Enterovirus
		M.K. (Kowalik)	ATCC VR-168	10x	Rhinovirus/Enterovirus
		Gregory	ATCC VR-41	10x	Rhinovirus/Enterovirus
		Bastianni	ATCC VR-1660	1x	Rhinovirus/Enterovirus
		Griggs	ATCC VR-1311	0.3x	Rhinovirus/Enterovirus
		Conn-5	ATCC VR-28	0.3x	Rhinovirus/Enterovirus
		Ohio-1	ATCC VR-29	3x	Rhinovirus/Enterovirus
		Nancy	ATCC VR-30	0.3x	Rhinovirus/Enterovirus
		CHHE-29	ATCC VR-47	10x	Rhinovirus/Enterovirus
		Kuykendall [V-024-001-012]	ATCC VR-850	10x	Rhinovirus/Enterovirus
Rhinovirus	Not available	1059*	ATCC VR-284	1x	Rhinovirus/Enterovirus
		2060*	ATCC VR-1559	0.1x	Rhinovirus/Enterovirus
		HGP*	ATCC VR-482	1x	Rhinovirus/Enterovirus
		11757*	ATCC VR-283	0.3x	Rhinovirus/Enterovirus
		FEB	ATCC VR-483	1x	Rhinovirus/Enterovirus
		33342	ATCC VR-1663	3x	Rhinovirus/Enterovirus

* Strain tested during LoD verification study.

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Table 21 (continued)

Pathogen	Subtype/ serotype	Strain	Source	x LoD Detected	Result
M. pneumoniae	Not available	PI 1428*	ATCC 29085	1x	*Mycoplasma pneumoniae*
		M129-B7*	ATCC 29342	1x	*Mycoplasma pneumoniae*
		FH strain of Eaton Agent [NCTC 10119]	ATCC 15531	0.1x	*Mycoplasma pneumoniae*
B. pertussis	Not available	I028*	ATCC BAA-2707	1x	*Bordetella pertussis*
		19323*	ATCC 9797	1x	*Bordetella pertussis*
		10-536	ATCC 10380†	0.3x	*Bordetella pertussis*
C. pneumoniae	Not available	TW183*	ATCC VR-2282	1x	*Chlamydophila pneumoniae*
		CWL-029*	ATCC VR-1310	1x	*Chlamydophila pneumoniae*
		AR-39	ATCC 53592	0.3x	*Chlamydophila pneumoniae*

* Strain tested during LoD verification study.

† Stock titer not available according to manufacturer.

Interfering substances

The effect of potentially interfering substances on the detectability of the QIAstat-Dx Respiratory Panel organisms was evaluated. Thirty (30) potentially interfering substances were added to contrived samples at a level predicted to be above the concentration of the substance likely to be found in an authentic NPS specimen. The contrived samples (also referred to as combined samples) were each comprised of a mix of organisms tested at a concentration of 5x LoD.

Endogenous substances such as whole blood, human genomic DNA and several pathogens were tested alongside exogenous substances like antibiotics, nasal sprays and different workflow contaminants.

The combined samples were tested with and without addition of an inhibitory substance allowing direct sample-to-sample comparison. Combined samples not spiked with any test substance served as a positive control. Additionally, for substances that may contain genetic material (such as blood, mucin, DNA and microorganisms), negative specimens (blank sNPS sample matrix with no organism mix) were spiked with only the test substance to evaluate the potential for false positive results due to the test substance itself.

Combined samples not spiked with any test substance served as a positive control and blank sNPS sample matrix with no organism mix as negative controls.

All pathogen-containing samples without spiked interferent generated positive signals for all pathogens present in the respective combined sample. Negative signals were obtained for all pathogens not present in the same sample but detected by the QIAstat-Dx Respiratory Panel.

None of the substances tested showed inhibition, except for the nasal influenza vaccines. This was due to the fact that the selection of substances concentration was higher than the concentrations expected to be present in a sample. In addition, nasal influenza vaccines (Fluenz Tetra and FluMist®) were predicted to be reactive with the QIAstat-Dx Respiratory Panel Influenza A (subtype) and Influenza B assays. Final dilution without observable interfering effect was 0.000001% v/v for both vaccines.

No impact on performance is expected when clinical liquid samples are examined in the presence of the substances tested.

Clinically relevant co-infections testing demonstrated that when at least two QIAstat-Dx Respiratory Panel pathogens of different concentrations are simultaneously present in one sample all targets can be detected by the assay.

The results of interfering substance testing are provided in Table 22 (next page).

Table 22. Final highest concentration without observable inhibitory effect

Substance tested	Concentration tested	Results
Endogenous substances		
Human genomic DNA 200 ng/µL	20 ng/µl	No Interference
Human blood (+NaCitrate)	1% v/v	No Interference
Mucin from bovine submaxillary	1% v/v	No Interference
Competitive microorganisms		
Staphylococcus aureus	1.00E+06 CFU/ml	No Interference
Neisseria meningitidis	5.00E+04 CFU/ml	No Interference
Corynebacterium diphtheriae	5.00E+03 CFU/ml	No Interference
Human Cytomegalovirus	1.00E+05 $TCID_{50}$/ml	No Interference
Exogenous substances		
Tobramycin	0.6 mg/ml	No Interference
Mupirocin	2% w/v	No Interference
Saline nasal spray with preservatives	1% v/v	No Interference
Afrin®, severe congestion nasal spray (Oxymetazoline HCl)	1% v/v	No Interference
Analgesic ointment (Vicks® VapoRub®)	1% w/v	No Interference
Petroleum Jelly (Vaseline®)	1% w/v	No Interference
FluMist nasal influenza vaccine	0.00001% v/v	Interference
FluMist nasal influenza vaccine	0.000001% v/v	No Interference
Fluenz Tetra nasal influenza vaccine	0.00001% v/v	Interference
Fluenz Tetra nasal influenza vaccine	0.000001% v/v	No Interference
Disinfecting/cleaning substances		
Disinfecting wipes	½ $inches^2$/1 ml UTM	No Interference
DNAZap™	1% v/v	No Interference
RNaseOUT™	1% v/v	No Interference
Bleach	5% v/v	No Interference
Ethanol	5% v/v	No Interference

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Table 22 (continued)

Substance tested	Concentration tested	Results
Specimen collection materials		
Swab Copan 168C	1 swab/1 ml UTM	No Interference
Swab Copan FloQ	1 swab/1 ml UTM	No Interference
Swab Copan 175KS01	1 swab/1 ml UTM	No Interference
Swab Puritan 25-801 A 50	1 swab/1 ml UTM	No Interference
VTM Sigma Virocult	100%	No Interference
VTM Remel® M4RT	100%	No Interference
VTM Remel M4	100%	No Interference
VTM Remel M5	100%	No Interference
VTM Remel M6	100%	No Interference
BD Universal Viral Transport	100%	No Interference

Reproducibility

Reproducibility testing of contrived samples was performed at three test sites including two external sites (LACNY [Laboratory Alliance of Central New York] and INDIANA [Indiana University]) and one internal site (STAT). The study incorporated a range of potential variation introduced by sites, days, replicates, cartridge lots, operators, and QIAstat-Dx analyzers. For each site, testing was performed across 5 days with 4 replicates per day (leading to a total of 20 replicates per target, concentration and site), a minimum of 2 different QIAstat-Dx Analyzers per site, and at least 2 operators on each testing day.

A total of 12 sample mixes were prepared with at least 3 replicates tested per sample mix. Each pathogen was spiked into HeLa in UTM combined samples in a final concentration of 0.1x LoD, 1x LoD or 3x LoD, respectively. A summary of results for each analyte is provided in Table 23 (next page).

Table 23 summarizes the results for 0.1x LoD concentration where it is observed that the detection rate for 24 of the 24 targets was <95% and therefore the acceptance criteria is met.

Reproducibility and repeatability will impact the SARS-CoV-2 target in the same manner as other target organisms verified in the QIAstat-Dx Respiratory Panel.

Table 23. Detection rate per target at 0.1x LoD concentration for each site of reproducibility study and 2-sided 95% Confidence Interval by target

Target (0.1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Adenovirus (ATCC VR-3)	STAT	10/20	50.0%	29.9–70.1%
	LACNY	9/19	47.4%	27.3–68.3%
	INDIANA	10/19	52.6%	31.7–72.7%
	All sites (overall)	29/58	50.0%	37.5–62.5%
B. pertussis (BAA-2707)	STAT	9/20	45.0%	25.8–65.8%
	LACNY	7/19	36.8%	19.1–59.0%
	INDIANA	9/20	45.0%	25.8–65.8%
	All sites (overall)	25/59	42.4%	30.6–55.1%
C. pneumoniae (ATCC VR-2282)	STAT	11/20	55.0%	34.2–74.2%
	LACNY	11/19	57.9%	36.3–76.9%
	INDIANA	14/20	70.0%	48.1–85.5%
	All sites (overall)	36/59	61.0%	48.3–72.4%
Coronavirus 229E (ATCC VR-740)	STAT	9/20	45.0%	25.8–65.8%
	LACNY	12/19	63.2%	41.0–80.9%
	INDIANA	5/20	25.0%	11.2–46.9%
	All sites (overall)	26/59	44.1%	32.2–56.7%
Coronavirus HKU1 (NATRVP-IDI)	STAT	17/20	85.0%	64.0–94.8%
	LACNY	10/19	52.6%	31.7–72.7%
	INDIANA	9/20	45.0%	25.8–65.8%
	All sites (overall)	36/59	61.0%	48.3–72.4%
Coronavirus NL63 (0810228CFHI)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	12/19	63.2%	41.0–80.9%
	INDIANA	14/19	73.7%	51.2–88.2%
	All sites (overall)	39/58	67.2%	54.4–77.9%

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Table 23 (continued)

Target (0.1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Coronavirus OC43 (ATCC VR-1558)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	15/20	75.0%	53.1–88.8%
	INDIANA	15/20	75.0%	53.1–88.8%
	All sites (overall)	43/60	71.7%	59.2–81.5%
Enterovirus (ATCC VR-1824)	STAT	8/20	40.0%	21.9–61.3%
	LACNY	6/19	31.6%	15.4–54.0%
	INDIANA	7/20	35.0%	18.1–56.7%
	All sites (overall)	21/59	35.6%	24.6–48.3%
Human Metapneumovirus (0810161CF)	STAT	6/20	30.0%	14.5–51.9%
	LACNY	9/19	47.4%	27.3–68.3%
	INDIANA	9/20	45.0%	25.8–65.8%
	All sites (overall)	24/59	40.7%	29.1–53.4%
Influenza A (0810249CFHI)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	18/20	90.0%	69.9–97.2%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	57/60	95.0%	86.3–98.3%
Influenza A (ATCC VR-810)	STAT	10/20	50.0%	29.9–70.1%
	LACNY	9/19	47.4%	27.3–68.3%
	INDIANA	16/19	84.2%	62.4–94.5%
	All sites (overall)	35/58	60.3%	47.5–71.9%
Influenza A (ATCC VR-897)	STAT	14/20	70.0%	48.1–85.5%
	LACNY	9/19	47.4%	27.3–68.3%
	INDIANA	12/20	60.0%	38.7–78.1%
	All sites (overall)	35/59	59.3%	46.6–70.9%

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Table 23 (continued)

Target (0.1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Influenza A H1 (ATCC VR-897)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	13/19	68.4%	46.0–84.6%
	INDIANA	15/20	75.0%	53.1–88.8%
	All sites (overall)	41/59	69.5%	56.9–79.7%
Influenza B (ATCC VR-295)	STAT	7/20	35.0%	18.1–56.7%
	LACNY	9/19	47.4%	27.3–68.3%
	INDIANA	8/20	40.0%	21.9–61.3%
	All sites (overall)	24/59	40.7%	29.1–53.4%
Influenza H1N1 (pdm09) (0810249CFHI)	STAT	14/20	70.0%	48.1–85.5%
	LACNY	16/20	80.0%	58.4–91.9%
	INDIANA	15/20	75.0%	53.1–88.8%
	All sites (overall)	45/60	75.0%	62.8–84.2%
Influenza H3 (ATCC VR-810)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	16/19	84.2%	62.4–94.5%
	INDIANA	17/19	89.5%	68.6–97.1%
	All sites (overall)	46/58	79.3%	67.2–87.7%
Mycoplasma pneumoniae (29085)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	14/20	70.0%	48.1–85.5%
	INDIANA	14/20	70.0%	48.1–85.5%
	All sites (overall)	41/60	68.3%	55.8–78.7%
Parainfluenza virus 1 (0810014CFHI)	STAT	14/20	70.0%	48.1–85.5%
	LACNY	12/19	63.2%	41.0–80.9%
	INDIANA	9/19	47.4%	27.3–68.3%
	All sites (overall)	35/58	60.3%	47.5–71.9%

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Table 23 (continued)

Target (0.1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Parainfluenza virus 2 (ATCC VR-92)	STAT	9/20	45.0%	25.8–65.8%
	LACNY	11/19	57.9%	36.3–76.9%
	INDIANA	12/20	60.0%	38.7–78.1%
	All sites (overall)	32/59	54.2%	41.7–66.3%
Parainfluenza virus 3 (ATCC VR-93)	STAT	13/20	65.0%	43.3–81.9%
	LACNY	17/20	85.0%	64.0–94.8%
	INDIANA	17/20	85.0%	64.0–94.8%
	All sites (overall)	47/60	78.3%	66.4–86.9%
Parainfluenza virus 4 (ATCC VR-1378)	STAT	10/20	50.0%	29.9–70.1%
	LACNY	11/19	57.9%	36.3–76.9%
	INDIANA	9/20	45.0%	25.8–65.8%
	All sites (overall)	30/59	50.9%	38.4–63.2%
RSVA (ATCC VR-1540)	STAT	6/20	30.0%	14.5–51.9%
	LACNY	7/20	35.0%	18.1–56.7%
	INDIANA	9/20	45.0%	25.8–65.8%
	All sites (overall)	22/60	36.7%	25.6–49.3%
Respiratory Syncytial Virus B (0810040CF)	STAT	14/20	70.0%	48.1–85.5%
	LACNY	15/19	79.0%	56.7–91.5%
	INDIANA	10/20	50.0%	29.9–70.1%
	All sites (overall)	39/59	66.1%	53.4–76.9%
Rhinovirus (ATCC VR-482)	STAT	15/20	75.0%	53.1–88.8%
	LACNY	15/20	75.0%	53.1–88.8%
	INDIANA	18/20	90.0%	69.9–97.2%
	All sites (overall)	48/60	80.0%	68.2–88.2%

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Table 24 summarizes the results for 1x LoD concentration where it is observed that the detection rate for 24 of the 24 targets was ≥95% and therefore the acceptance criteria is met.

Table 24. Detection rate per target at 1x LoD concentration for each site of reproducibility study and 2-sided 95% Confidence Interval by target

Target (1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Adenovirus (ATCC VR-3)	STAT	20/20	100%	83.9–100%
	LACNY	18/18	100%	82.4–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/58	100%	93.8–100%
B. pertussis (BAA-2707)	STAT	18/20	90.0%	69.9–97.2%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/60	96.7%	88.6–99.1%
C. pneumoniae (ATCC VR-2282)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%
Coronavirus 229E (ATCC VR-740)	STAT	18/20	90.0%	69.9–97.2%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/60	96.7%	88.6–99.1%
Coronavirus HKU1 (NATRVP-IDI)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%

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Table 24 (continued)

Target (1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Coronavirus NL63 (0810228CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	18/18	100%	82.4–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/58	100%	93.8–100%
Coronavirus OC43 (ATCC VR-1558)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Enterovirus (ATCC VR-1824)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	19/20	95.0%	76.4–99.1%
	All sites (overall)	58/60	96.7%	88.6–99.1%
Human Metapneumovirus (0810161CF)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Influenza A (0810249CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Influenza A (ATCC VR-810)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	18/18	100%	82.4–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	57/58	98.3%	90.9–99.7%
Influenza A (ATCC VR-897)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%

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Table 24 (continued)

Target (1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Influenza A H1 (ATCC VR-897)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	19/20	95.0%	76.4–99.1%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Influenza B (ATCC VR-295)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Influenza H1N1 (pdm09) (0810249CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Influenza H3 (ATCC VR-810)	STAT	20/20	100%	83.9–100%
	LACNY	18/18	100%	82.4–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/58	100%	93.8–100%
Mycoplasma pneumoniae (29085)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Parainfluenza virus 1 (0810014CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	18/18	100%	82.4–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/58	100%	93.8–100%

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Table 24 (continued)

Target (1x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Parainfluenza virus 2 (ATCC VR-92)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	19/20	95.0%	76.4–99.1%
	All sites (overall)	58/60	96.7%	88.6–99.1%
Parainfluenza virus 3 (ATCC VR-93)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Parainfluenza virus 4 (ATCC VR-1378)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%
RSVA (ATCC VR-1540)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Respiratory Syncytial Virus B (0810040CF)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%
Rhinovirus (ATCC VR-482)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%

Table 25 summarizes the results for 3x LoD concentration where it is observed that detection rate for 24 of the 24 targets was ≥95% and therefore the acceptance criteria has been met.

Table 25. Detection rate per target at 3x LoD concentration for each site of reproducibility study and 2-sided 95% Confidence Interval by target

Target (3x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Adenovirus (ATCC VR-3)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
B. pertussis (BAA-2707)	STAT	20/20	100%	83.9—100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
C. pneumoniae (ATCC VR-2282)	STAT	20/20	100%	83.9–100%
	LACNY	19/20	95.0%	76.4–99.1%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Coronavirus 229E (ATCC VR-740)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Coronavirus HKU1 (NATRVP-IDI)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%

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Table 25 (continued)

Target (3x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Coronavirus NL63 (0810228CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Coronavirus OC43 (ATCC VR-1558)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Enterovirus (ATCC VR-1824)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Human Metapneumovirus (0810161CF)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Influenza A (0810249CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Influenza A (ATCC VR-810)	STAT	20/20	100%	83.9-–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Influenza A (ATCC VR-897)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%

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Table 25 (continued)

Target (3x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Influenza A H1 (ATCC VR-897)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Influenza B (ATCC VR-295)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	58/59	98.3%	91.0–99.7%
Influenza H1N1 (pdm09) (0810249CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Influenza H3 (ATCC VR-810)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
Mycoplasma pneumoniae (29085)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Parainfluenza virus 1 (0810014CFHI)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%

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Table 25 (continued)

Target (3x LoD)	Site	Detection rate (# positive)	% detection rate (# positive)	95% Confidence Interval
Parainfluenza virus 2 (ATCC VR-92)	STAT	19/20	95.0%	76.4–99.1%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/60	98.3%	91.1–99.7%
Parainfluenza virus 3 (ATCC VR-93)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Parainfluenza virus 4 (ATCC VR-1378)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	59/59	100%	93.9–100%
RSVA (ATCC VR-1540)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%
Respiratory Syncytial Virus B (0810040CF)	STAT	20/20	100%	83.9–100%
	LACNY	20/20	100%	83.9–100%
	INDIANA	20/20	100%	83.9–100%
	All sites (overall)	60/60	100%	94.0–100%
Rhinovirus (ATCC VR-482)	STAT	20/20	100%	83.9–100%
	LACNY	19/19	100%	83.2–100%
	INDIANA	19/19	100%	83.2–100%
	All sites (overall)	58/58	100%	93.8–100%

Appendices

Appendix A: Installing the Assay Definition File

The Assay Definition File of the QIAstat-Dx Respiratory SARS-CoV-2 Panel must be installed on the QIAstat-Dx Analyzer 1.0 prior to testing with QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges.

Note: Whenever a new version of the QIAstat-Dx Respiratory SARS-CoV-2 Panel assay is released, the new QIAstat-Dx Respiratory SARS-CoV-2 Panel Assay Definition File must be installed prior to testing.

Note: Assay Definition Files are available at www.qiagen.com. The Assay Definition File (*.asy) must be saved onto a USB Drive prior to installation on the QIAstat-Dx Analyzer 1.0. This USB Drive must be formatted with a FAT32 file system.

To import new assays from the USB to the QIAstat-Dx Analyzer 1.0, proceed with the following steps:

1. Insert the USB stick containing the Assay Definition File into one of the USB ports on the QIAstat-Dx Analyzer 1.0.
2. Press the Options button and then select Assay Management. The Assay Management screen appears in the Content area of the display (Figure 22, next page).

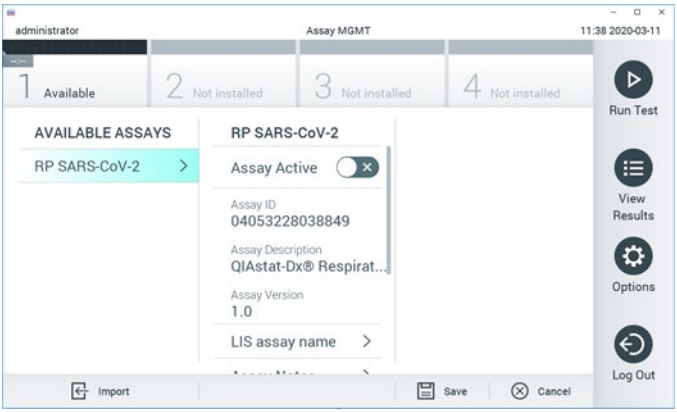

Figure 22. Assay Management screen.

3. Press the Import icon in the bottom left of the screen.
4. Select the file corresponding to the assay to be imported from the USB drive.
5. A dialog will appear to confirm upload of the file.
6. A dialog may appear to override the current version by a new one. Press yes to override.
7. The assay becomes active by selecting Assay Active (Figure 23).

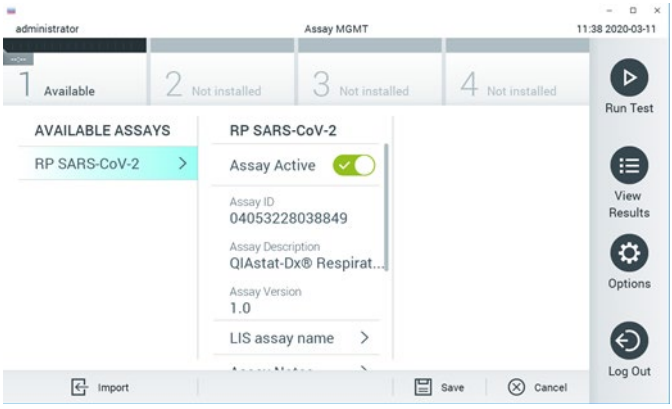

Figure 23. Activating the assay.

Appendix B: Glossary

Amplification curve: Graphical representation of the multiplex real-time RT-PCR amplification data.

Analytical Module (AM): The main QIAstat-Dx Analyzer 1.0 hardware module, in charge of executing tests on QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges. It is controlled by the Operational Module. Several Analytical Modules can be connected to one Operational Module.

QIAstat-Dx Analyzer 1.0: The QIAstat-Dx Analyzer 1.0 consists of an Operational Module and an Analytical Module. The Operational Module includes elements that provide connectivity to the Analytical Module and enables user interaction with the QIAstat-Dx Analyzer 1.0. The Analytical Module contains the hardware and software for sample testing and analysis.

QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge: A self-contained disposable plastic device with all pre-loaded reagents required for the complete execution of fully automated molecular assays for the detection of respiratory pathogens.

IFU: Instructions For Use.

Main port: In the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, inlet for transport medium liquid samples.

Nucleic acids: Biopolymers, or small biomolecules composed of nucleotides, which are monomers made of three components: a 5-carbon sugar, a phosphate group and a nitrogenous base.

Operational Module (OM): The dedicated QIAstat-Dx Analyzer 1.0 hardware that provides the user interface for 1–4 Analytical Modules (AM).

PCR: Polymerase Chain Reaction.

RT: Reverse Transcription.

Swab port: In the QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, inlet for dry swabs. The swab port is not used for the QIAstat-Dx Respiratory SARS-CoV-2 Panel assay.

User: A person who operates the QIAstat-Dx Analyzer 1.0/QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge in the intended way.

Appendix C: Disclaimer of warranties

EXCEPT AS PROVIDED IN QIAGEN TERMS AND CONDITIONS OF SALE FOR THE QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge, QIAGEN ASSUMES NO LIABILITY WHATSOEVER AND DISCLAIMS ANY EXPRESS OR IMPLIED WARRANTY RELATING TO THE USE OF THE QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge INCLUDING LIABILITY OR WARRANTIES RELATING TO MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR INFRINGEMENT OF ANY PATENT, COPYRIGHT, OR OTHER INTELLECTUAL PROPERTY RIGHT ANYWHERE IN THE WORLD.

Symbols

The following table describes the symbols that may appear on the labeling or in this document.

 <N>	Contains reagents sufficient for <N> reactions
	Use by
	*In vitro* diagnostic medical device
	Catalog number
	Lot number
	Material number (i.e., component labeling)
	Upper respiratory application
Rn	R is for revision of the Handbook and n is the revision number
	For prescription use only
	Temperature limitation
	Manufacturer
	Consult instructions for use
	Caution
	Serial number
	Do not reuse
	Keep away from sunlight
	Do not use if package is damaged

GTIN Global Trade Item Number

Ordering Information

Product	Contents	Cat. no.
QIAstat-Dx Respiratory SARS-CoV-2 Panel	For 6 tests: 6 individually packaged QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridges and 6 individually packaged transfer pipettes	691223
Related Products		
QIAstat-Dx Analyzer 1.0	1 QIAstat-Dx Analytical Module, 1 QIAstat-Dx Operational Module and related hardware and software to run molecular diagnostic QIAstat-Dx assay cartridges	9002824

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For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

Handbook Revision History

Date	Changes
Revision 3 06/2020	For with QIAstat-Dx Analyzer 1.0 software version 1.2 or higher. Update to the Coronavirus OC43 data in the overall retrospective clinical study performance table.
Revision 4 09/2020	Addition of FDA SARS-CoV-2 reference panel testing section.
Revision 5 07/2021	Updates to the Warnings and Precautions, Inclusivity (Analytical Reactivity), Limitations, and Conditions of Authorization for the Laboratory Sections.

QIAstat-Dx Respiratory SARS-CoV-2 Panel

Emergency Use Authorization (EUA) only

Please be advised:

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms; and;
- The emergency use of this product 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 Act, 21 U.S.C. § 360bbb-3 (b)(1), unless the declaration is terminated or authorization is revoked sooner.

This is not the complete instructions for use. Please find the instructions for use at the following web address:

https://www.qiagen.com/us/products/diagnostics-and-clinical-research/infectious-disease/qiastat-dx-syndromic-testing/qiastat-dx-eua-us/

Please contact QIAGEN Technical Services (1-800-426-8157) if you require a printed copy free of charge.