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QIAstat-Dx®
Meningitis/Encephalitis (ME) Panel
Instructions for Use (Handbook)

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Version 1

For In Vitro Diagnostic Use

For use with QIAstat-Dx Analyzer 1.0 and QIAstat-Dx Analyzer 2.0

IVD

CE

REF 691611

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Sample to Insight

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Intended Use

The QIAstat-Dx Meningitis/Encephalitis (ME) Panel ("QIAstat-Dx ME Panel") is a qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for use with the QIAstat-Dx System. The QIAstat-Dx ME Panel is capable of simultaneous detection and identification of multiple bacterial, viral, and yeast nucleic acids from cerebrospinal fluid (CSF) specimens obtained via lumbar puncture from individuals with signs and/or symptoms of meningitis and/or encephalitis.

The following organisms are identified and differentiated using the QIAstat-Dx ME Panel: Escherichia coli K1, *Haemophilus influenzae*, *Listeria monocytogenes, Neisseria meningitidis (encapsulated), Streptococcus agalactiae, Streptococcus pneumoniae, Mycoplasma pneumoniae, Streptococcus pyogenes*, Herpes simplex virus 1, Herpes simplex virus 2, Human herpes virus 6, Enterovirus, Human parechovirus, *Varicella-zoster virus and Cryptococcus neoformans/gattii**.

*Cryptococcus neoformans and Cryptococcus gattii are not differentiated.

The QIAstat-Dx ME Panel is indicated as an aid in the diagnosis of specific agents of meningitis and/or encephalitis and results must be used in conjunction with other clinical, epidemiological, and laboratory data. Results from the QIAstat-Dx ME Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out co-infection with organisms not included in the QIAstat-Dx ME Panel. The agent or agents detected may not be the definite cause of the disease. Negative results do not preclude central nervous system (CNS) infection.

Not all agents of CNS infection are detected by this test, and sensitivity in clinical use may differ from that described in the package insert.

The QIAstat-Dx ME Panel is not intended for testing of specimens collected from indwelling CNS medical devices.

The QIAstat-Dx ME Panel is intended to be used in conjunction with standard of care (e.g., culture for organism recovery, serotyping, and antimicrobial susceptibility testing).

The QIAstat-Dx ME Panel is intended for in vitro diagnostic use by laboratory professionals only.

Summary and Explanation

QIAstat-Dx ME Panel Cartridge description

The QIAstat-Dx ME Panel Cartridge is a disposable plastic device that allows performance of fully automated molecular assays for the detection and identification of nucleic acids from multiple agents, directly from CSF samples. The main features of the QIAstat-Dx ME Panel Cartridge include compatibility with a liquid sample type, 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 ME 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 or the QIAstat-Dx Analyzer 2.0 by pneumatically operated microfluidics and make no direct contact with the actuators. The QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 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 ME Panel Cartridge containing the sample is introduced into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, the following assay steps occur automatically:

- Resuspension of Internal Control
- Cell lysis using mechanical and 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.

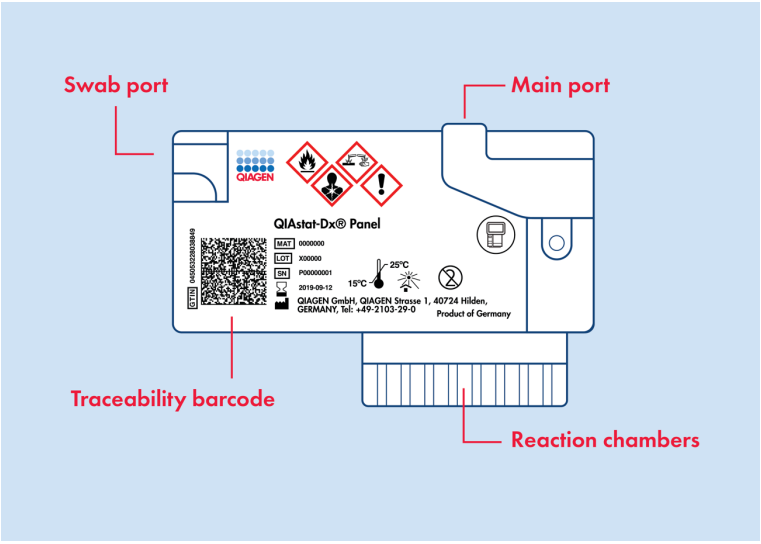


Figure 1. Layout of the QIAstat-Dx ME Panel Cartridge and its features.

Note: The swab port is not used for the QIAstat-Dx ME Panel assay.

Pathogen Information

Meningitis and encephalitis are potentially devastating conditions and can be associated with significant morbidity and mortality.(1) Meningitis is defined as inflammation of the meninges,

encephalitis is defined as inflammation of the brain parenchyma, and meningoencephalitis is defined as inflammation at both locations. All these conditions can be caused by bacteria, viruses, or fungi, with encephalitis being more commonly associated with a viral etiology.(2) Clinical presentations are usually nonspecific; as patients often experience headache, altered mental status, and, in the case of meningitis, nuchal rigidity. Early diagnosis is vital, as symptoms can appear suddenly and escalate to brain damage, hearing and/or speech loss, blindness, or even death. As treatment differs depending on the cause of the disease, identification of a specific causative agent is necessary to adjust treatment accordingly.

The QIAstat-Dx ME Panel Cartridge allows detection of 15 bacterial, viral, and fungal pathogenic targets that cause signs and/or symptoms of meningitis and/or encephalitis. Testing requires a small sample volume and minimal hands-on time, and the results are available in less than 80 minutes.

Pathogens that can be detected and identified with the QIAstat-Dx ME Panel are listed in Pathogens detected by QIAstat-Dx ME Panel.

Table 1. Pathogens detected by QIAstat-Dx ME Panel

Pathogen	Classification (genome type)
Escherichia coli K1	Bacterium (DNA)
Haemophilus influenzae	Bacterium (DNA)
Listeria monocytogenes	Bacterium (DNA)
Neisseria meningitidis (encapsulated)	Bacterium (DNA)
Streptococcus agalactiae	Bacterium (DNA)
Streptococcus pneumoniae	Bacterium (DNA)
Streptococcus pyogenes	Bacterium (DNA)
Mycoplasma pneumoniae	Bacterium (DNA)
Herpes simplex virus 1	Herpesvirus (DNA)

Table 1. Pathogens detected by QIAstat-Dx ME Panel (continued)

Pathogen	Classification (genome type)
Herpes simplex virus 2	Herpesvirus (DNA)
Human herpes virus 6	Herpesvirus (DNA)
Enterovirus	Picornavirus (RNA)
Human parechovirus	Picornavirus (RNA)
Varicella-zoster virus	Herpesvirus (DNA)
Cryptococcus gattii/Cryptococcus neoformans	Yeast (DNA)

Principle of the Procedure

Description of the process

Diagnostic tests with the QIAstat-Dx ME Panel are performed on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0. All of the sample preparation and analysis steps are performed automatically by the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0. Samples are collected and loaded manually into the QIAstat-Dx ME Panel Cartridge.

A transfer pipette is used for sample transfer into the main port (Dispensing sample into the main port.).

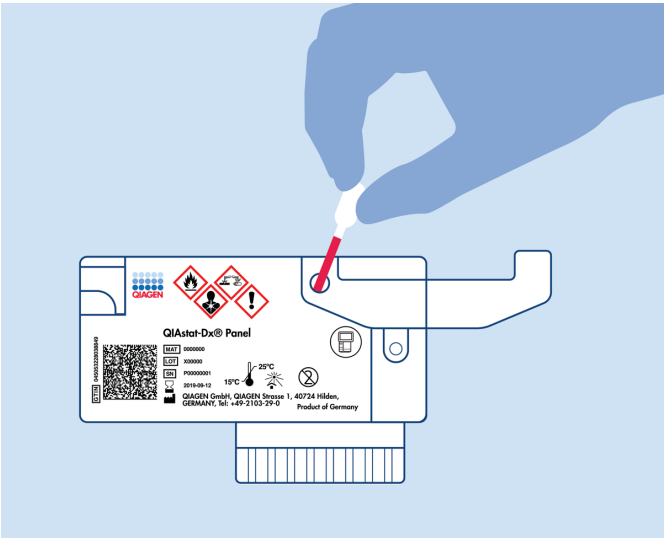


Figure 2. Dispensing sample into the main port.

Sample collection and cartridge loading

The collection of samples and their subsequent loading into the QIAstat-Dx ME 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 Cerebral Spinal Fluid (CSF) sample is collected.
2. The sample information is manually written on or a sample label is affixed to the top of a QIAstat-Dx ME Panel Cartridge.
3. CSF sample is loaded manually into the QIAstat-Dx ME Panel Cartridge.

   200 µL of sample is transferred into the main port of the QIAstat-Dx ME Panel Cartridge using one of the included transfer pipettes. Use alternative sterile and graduated pipettes in case all six pipettes provided with the kit have been used.

   Note: When loading a CSF 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).

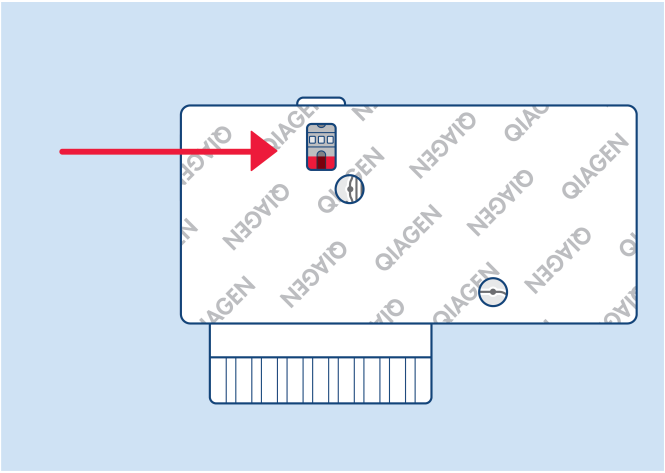


Figure 3. Sample inspection window (blue arrow).

4. The sample bar code and QIAstat-Dx ME Panel Cartridge QR code are scanned in the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.
5. The QIAstat-Dx ME Panel Cartridge is introduced into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.
6. The test is started on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.

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 or the QIAstat-Dx Analyzer 2.0.

1. The sample is homogenized, and cells are lysed in the lysis chamber of the QIAstat-Dx ME 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 ME 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 ME Panel Cartridge.
4. The mixture of sample and PCR reagents is dispensed into the QIAstat-Dx ME Panel Cartridge PCR chambers, which contain lyophilized assay-specific primers and probes.
5. The QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 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 or the QIAstat-Dx Analyzer 2.0 Software interprets the resulting data and process controls and delivers a test report.

Materials Provided

Kit contents

QIAstat-Dx ME Panel Catalog no. **Number of tests**	**691611** **6**
QIAstat-Dx ME 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 ME Panel Cartridge.

Materials Required But Not Provided

The QIAstat-Dx ME Panel is designed for use with the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0. Before beginning a test, make sure the following are available:

- QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 (at least one Operational Module and one Analytical Module) with software version from 1.4 or higher OR QIAstat-Dx Analyzer 2.0 (at least Operational Module PRO and one Analytical Module) with software version 1.6 or higher)
- QIAstat-Dx Analyzer 1.0 User Manual (for use with software version from 1.4 or higher) OR QIAstat-Dx Analyzer 2.0 User Manual (for use with version 1.6 or higher)
- QIAstat-Dx latest Assay Definition File software for the QIAstat-Dx ME Panel installed in the Operational Module or Operational Module PRO.

Note: Application Software version 1.6 or higher cannot be installed on QIAstat-Dx Analyzer 1.0.

Warnings and Precautions

For in vitro diagnostic use.

The QIAstat-Dx ME Panel is to be used by laboratory professionals trained in the use of QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.

Safety information

When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. Protect the skin, eyes, and mucus membranes, and change gloves often when handling samples. 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.

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.

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

The QIAstat-Dx ME 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 or the QIAstat-Dx 2.0. Do not use a QIAstat-Dx ME Panel Cartridge if it 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 (**www.cdc.gov/od/ohs/biosfty/biosfty.htm**).

The following hazard and precautionary statements apply to components of the QIAstat-Dx ME Panel.

Contains: ethanol; guanidine hydrochloride; guanidine thiocyanate; isopropanol; proteinase K; t-Octylphenoxypolyethoxyethanol. Danger! Highly flammable liquid and vapor. 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/vapors/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.

Laboratory precautions

To guard against possible contamination of the specimen and work area standard laboratory safety and cleaning procedures should be used, including the following precautions:

- Samples should be processed in a biosafety cabinet or a similar clean surface ensuring the user's protection. If a biosafety cabinet is not used, a dead air box (e.g., AirClean PCR workstation), a splash shield (e.g., Bel-Art Scienceware Splash Shields), or a face shield should be used when preparing samples.
- A biosafety cabinet that is used for performing CSF pathogen testing (e.g. culture) should not be used for sample preparation or cartridge loading.

- Prior to processing samples, thoroughly clean the work area using a suitable cleaner such as freshly prepared 10% bleach or a similar disinfectant. To avoid residue buildup and potential damage to the specimen or interference from disinfectants, wipe disinfected surfaces with water.
- Samples and cartridges should be handled one at a time.
- Use clean gloves to remove materials from bulk packaging bags and reseal bulk packaging bags when not in use.
- Change gloves and clean the work area between each sample.
- Discard used cartridges in an appropriate biohazard container immediately after the run has been completed.
- Avoid excessive handling of cartridges after test runs.

  Avoid damaging the cartridge.*

  *Refer to Safety Information for handling of damaged cartridges
- Use clean gloves to remove materials from bulk packaging boxes, and close bulk packaging when not in use.

  Due to sensitive nature of the pathogen detection by QIAStat-Dx Meningitis/Encephalitis Panel and to prevent contamination of the specimen, it is key to follow standard microbiological laboratory practices. Clinical laboratory personnel could be the source of pathogens (e.g. *S. pneumoniae, H. influenza*, HSV-1, etc.) that are detectable by the QIAstat-Dx Meningitis/Encephalitis Panel.

  Contamination of the specimen could happen while the specimen is being collected, transported, or tested. Adherence to best practice sample handling and testing procedures is recommended to minimize the risk of contamination that could lead to false positive results. Additional precautions may include extra PPE, such as face mask, especially when

experiencing signs or symptoms of a respiratory infection or an active herpes sore/fever blister.

Cartridge Storage and Handling

Store the QIAstat-Dx ME Panel Cartridges in a dry, clean storage space at room temperature (15–25°C). Do not remove the QIAstat-Dx ME Panel Cartridges or the transfer pipettes from their individual packaging until actual use. Under these conditions, the QIAstat-Dx ME Panel Cartridges can be stored until the expiration date printed on the individual packaging. The expiration date is also included in the QIAstat-Dx ME Panel Cartridge bar code and is read by the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 when the cartridge is inserted into the instrument to run a test.

For handling of damaged cartridge, refer to chapter Safety information.

Specimen Handling, Storage and Preparation

The CSF specimen should be collected via lumbar puncture and should not be centrifuged or diluted.

Recommended storage condition for CSF is room temperature (15–25°C) up to 12 hours.

Procedure

Internal Control

The QIAstat-Dx ME Panel Cartridge includes a full process Internal Control, which is titered *Schizosaccharomyces pombe*, a yeast (fungi) 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 homogenization, lysis of viral and cellular structures (by means of chemical and mechanical disruption), nucleic acid purification, reverse transcription, and real-time PCR.

A positive signal for the Internal Control indicates that all processing steps performed by the QIAstat-Dx ME 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.

Loading a sample into the QIAstat-Dx ME Panel Cartridge

1. Thoroughly clean the work area with freshly prepared 10% bleach (or a suitable disinfectant) followed by a water rinse.
2. Open the package of a QIAstat-Dx ME Panel Cartridge using the tear notches on the sides of the packaging (Figure 4).

   IMPORTANT: After the package is opened, sample should be loaded inside the QIAstat-Dx ME Panel Cartridge and loaded into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 within 120 minutes.

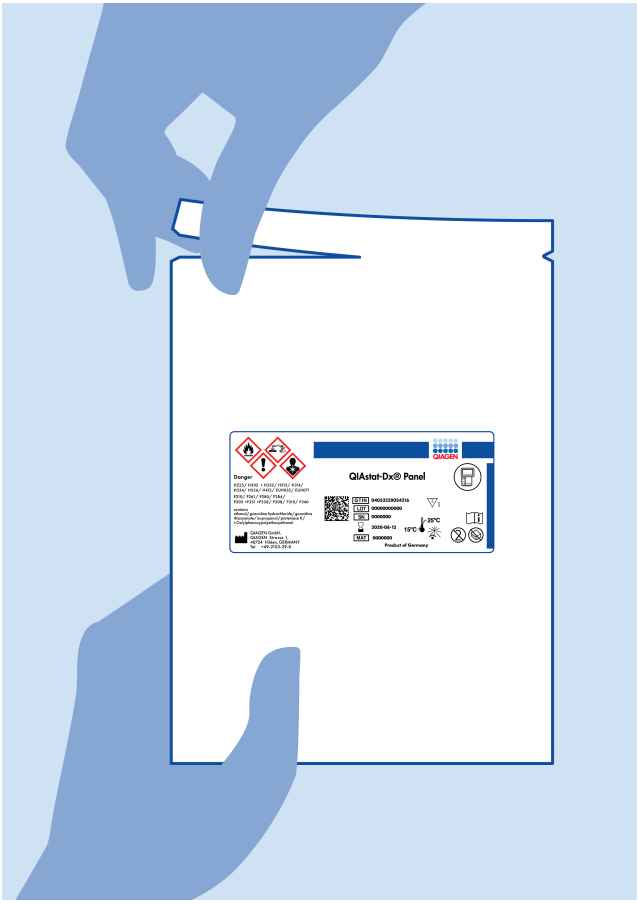


Figure 4. Opening the QIAstat-Dx ME Panel Cartridge.

3. Remove the QIAstat-Dx ME Panel Cartridge from the packaging and position it so that the bar code on the label faces you.

4. Manually write the sample information or place a sample information label on the top of the QIAstat-Dx ME Panel Cartridge. Make sure that the label is properly positioned and does not block the lid opening (Figure 5).

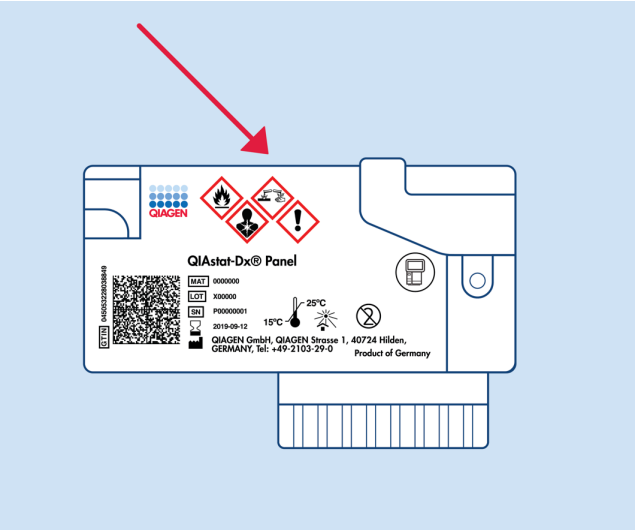


Figure 5. Sample information placement on top of QIAstat-Dx Meningitis/Encephalitis Panel Cartridge.

5. Open the sample lid of the main port on the front of the QIAstat-Dx ME Panel Cartridge (Figure 6).

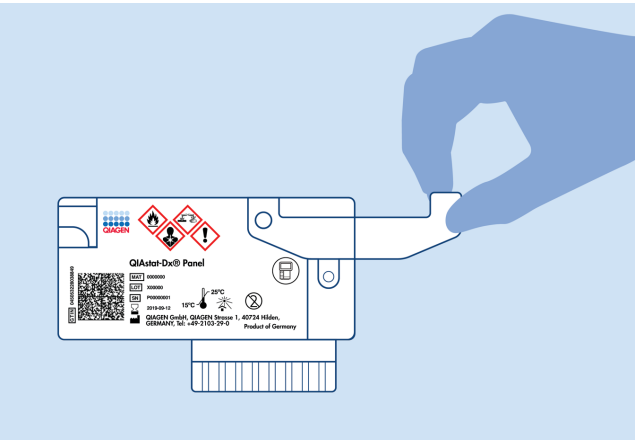


Figure 6. Opening the sample lid of main port.

6. Open the tube with the sample to be tested. Use the supplied transfer pipette to draw fluid up to the second fill line on the pipette (i.e., 200 µL) (Figure 7).

   IMPORTANT: Do not draw air into the pipette. If air is drawn into the pipette, carefully expel the sample fluid in the pipette back into the sample tube and draw up fluid again.

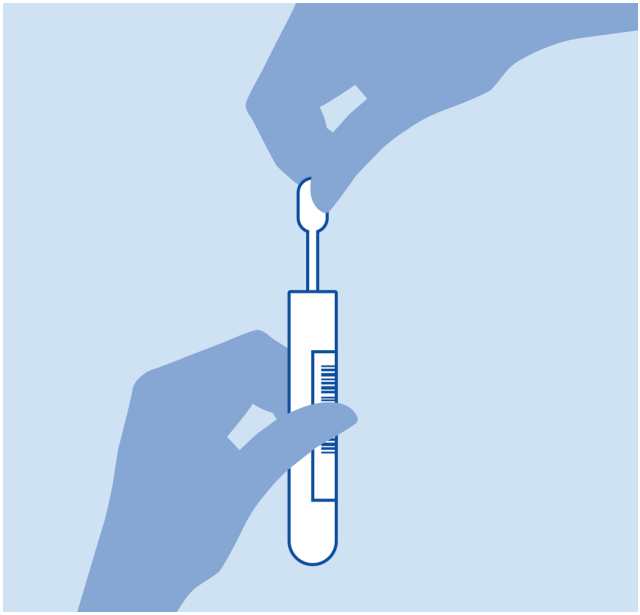


Figure 7. Drawing sample into the supplied transfer pipette.

7. Carefully transfer 200 µL of sample into the main port of the QIAstat-Dx ME Panel Cartridge using the supplied single-use transfer pipette (Figure 8).

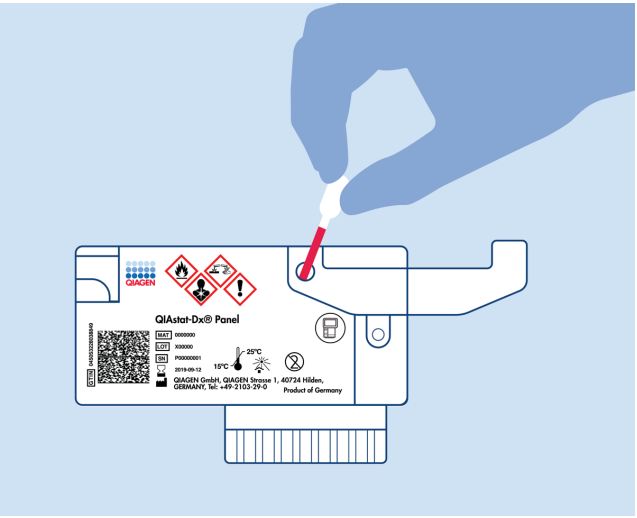


Figure 8. Transferring sample to main port of QIAstat-Dx ME Panel Cartridge.

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

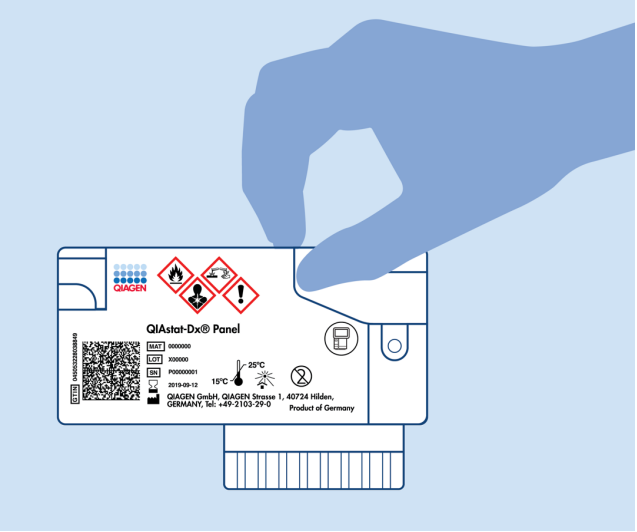


Figure 9. Closing the lid of the main port.

9. Visually confirm that the sample has been loaded by checking the sample inspection window of the QIAstat-Dx ME Panel Cartridge (Figure 10).

   IMPORTANT: After the sample is placed inside the QIAstat-Dx ME Panel Cartridge, the cartridge must be loaded into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 within 90 minutes.

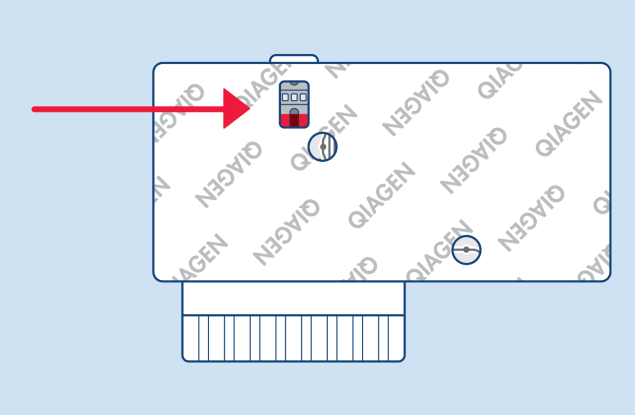


Figure 10. Sample inspection window (blue arrow).

Starting the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0

1. Power ON the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 by pressing 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 or the QIAstat-Dx Analyzer 2.0 status indicators will turn blue.

2. Wait until the Main screen appears and the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 status indicators turn green and stop blinking.

3. Log in to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 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.

4. If the Assay Definition File software has not been installed on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, follow the installation instructions prior to running the test (see Appendix A: Installing the Assay Definition File, page 92, for additional information).

Running a test

1. Press the Run Test button in the top-right corner of the touchscreen of the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.
2. When prompted, scan the sample ID bar code on the CSF tube containing the sample, or scan the specimen information barcode located on the top of the QIAstat-Dx ME Panel Cartridge (see step 3) using the integrated front bar code reader of the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 (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 or the QIAstat-Dx Analyzer 2.0 appear in the Instructions Bar at the bottom of the touchscreen.

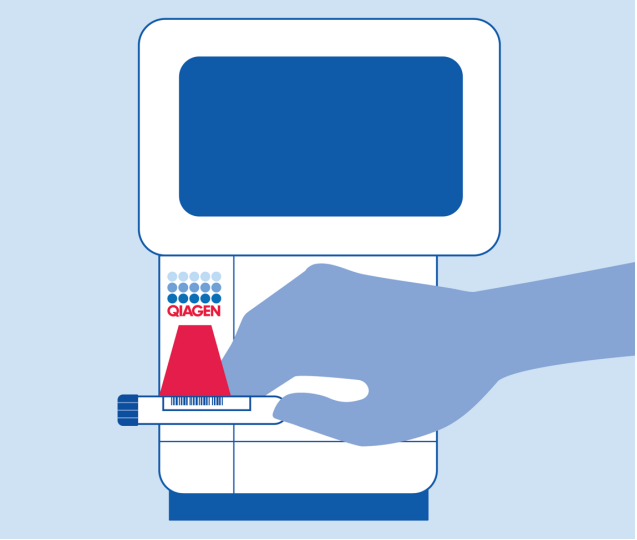


Figure 11. Scanning sample ID bar code.

3. When prompted, scan the bar code of the QIAstat-Dx ME Panel Cartridge to be used (Figure 12). The QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 automatically recognizes the assay to be run based on the cartridge bar code.

   Note: The QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 will not accept QIAstat-Dx ME 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 ME Panel Cartridge will be rejected. Refer to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 User Manual for further details on how to install assays.

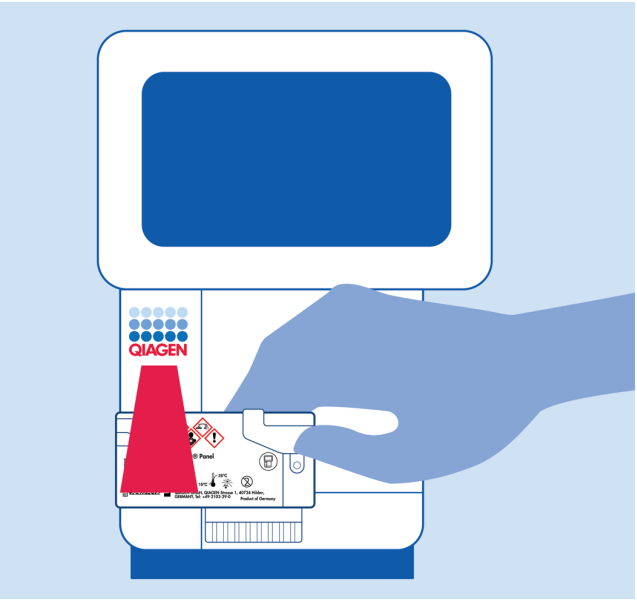


Figure 12. Scanning QIAstat-Dx Meningitis/Encephalitis Panel Cartridge bar code.

4. 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.
5. 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).

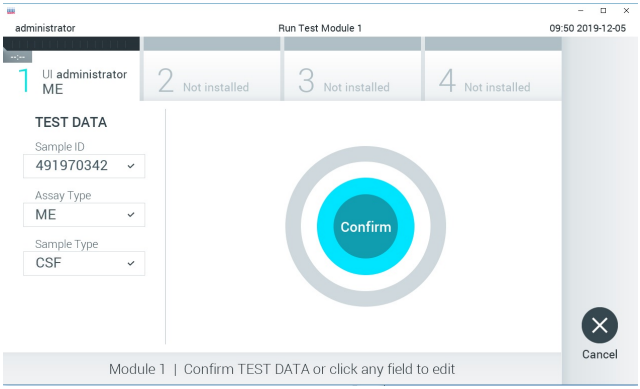


Figure 13. Confirming data entry.

6. Make sure that both sample lids of the swab port and main port of the QIAstat-Dx ME Panel Cartridge are firmly closed. When the cartridge entrance port on the top of the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 automatically opens, insert the QIAstat-Dx ME Panel Cartridge with the bar code facing to the left and the reaction chambers facing down (Figure 14).

   Note: There is no need to push the QIAstat-Dx ME Panel Cartridge into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0. Position it correctly into the cartridge entrance port and the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 will automatically move the cartridge into the Analytical Module.

   Note: The swab port is not used for the QIAstat-Dx ME Panel assay.

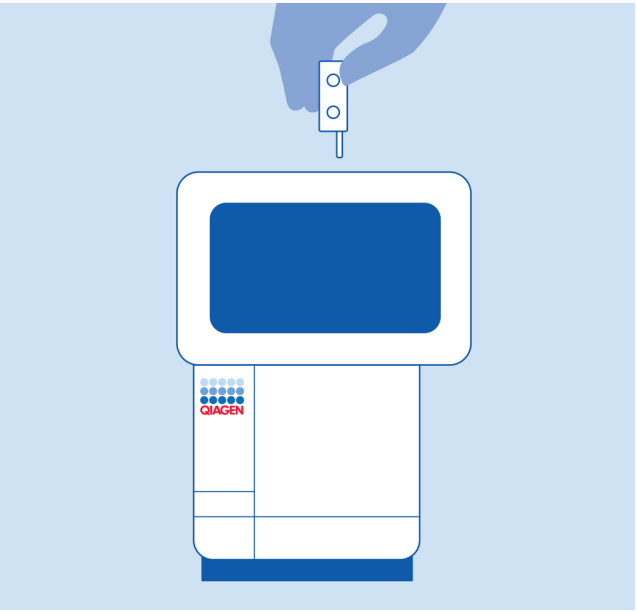


Figure 14. Inserting QIAstat-Dx ME Panel Cartridge into QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.

7. Upon detecting the QIAstat-Dx ME Panel Cartridge, the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 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 or the QIAstat-Dx Analyzer 2.0 will not accept a QIAstat-Dx ME 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 ME Panel Cartridge is not positioned in the port. If this occurs, repeat the procedure starting with step 18.

8. While the test is running, the remaining run time is displayed on the touchscreen.
9. 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, contact Technical Service.

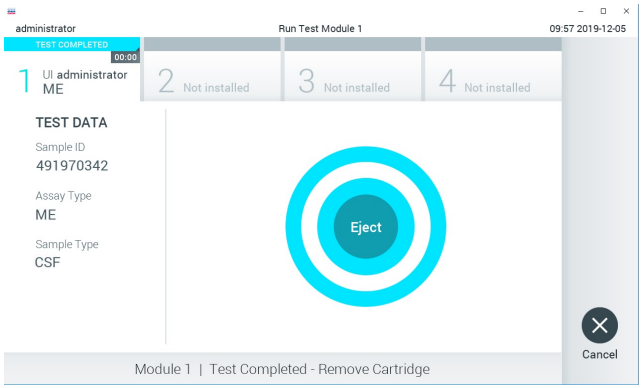


Figure 15. Eject screen display.

10. Press  Eject on the touchscreen to remove the QIAstat-Dx ME 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 ME 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 or the QIAstat-Dx Analyzer 2.0, and the 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 ME Panel Cartridges must be discarded. It is not possible to re-use cartridges for tests for which the execution was started but then subsequently canceled by the operator, or for which an error was detected.

11. After the QIAstat-Dx ME Panel Cartridge has been ejected, the results Summary screen will appear. 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 or the QIAstat-Dx Analyzer 2.0, refer to the *QIAstat-Dx Analyzer 1.0 User Manual*. For further information on the use of the QIAstat-Dx Analyzer 2.0, refer to the *QIAstat-Dx Analyzer 2.0 User Manual*.

Interpretation of Results

Note: Images of the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 screen in this section are meant as an example and may not represent the specific pathogen results provided for the QIAstat-Dx ME Panel.

Viewing results

The QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 automatically interprets and saves test results. After ejecting the QIAstat-Dx ME Panel Cartridge, the results Summary screen is automatically displayed (Figure 16) shows the screen for the QIAstat-Dx Analyzer 1.0.

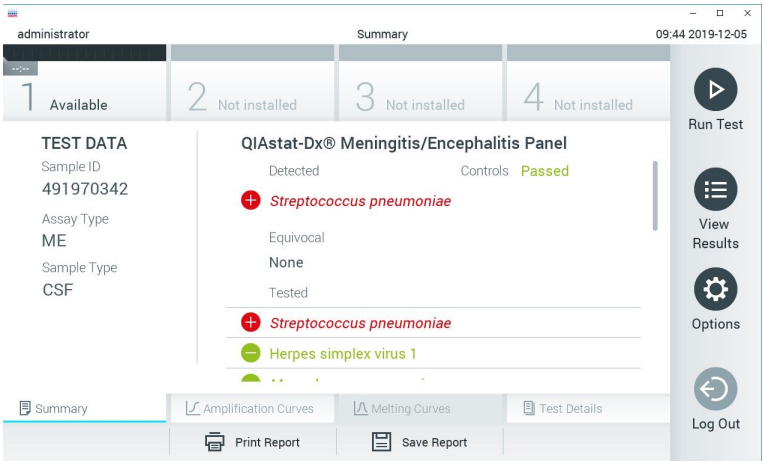


Figure 16. Results Summary screen example showing Test Data on the left panel and Test Summary in the main panel in the QIAstat-Dx Analyzer 1.0.

From this screen, other tabs with more information, which will be explained in the following chapters, are available:

- Amplication curves
- Melting Curves. This tab disabled for the QIAstat ME panel.
- Test Details

Figure 17 shows the screen for the QIAstat-Dx Analyzer 2.0.

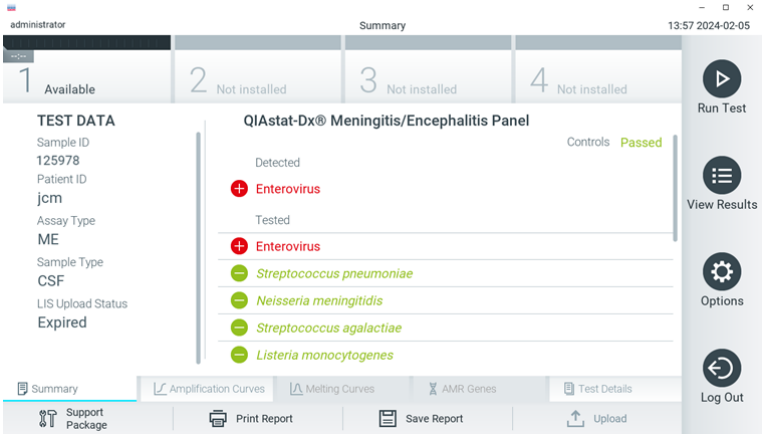


Figure 17. Results Summary screen example showing Test Data on the left panel and Test Summary in the main panel in the QIAstat-Dx Analyzer 2.0.

QIAstat-Dx Analyzer 2.0 includes an additional tab:

- AMR Genes. It is disabled for the QIAstat-Dx ME Panel.

Note: From this point forward, example screen shots will be used when referring to the QIAstat-Dx Analyzer 1.0 and/or QIAstat-Dx Analyzer 2.0 where the functions being explained are the same.

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

- The first list, under the heading Detected, includes all pathogens detected and identified in the sample, which are preceded by a  sign and are colored red.
- The second list, under the heading Equivocal is not used. Equivocal results are not applicable for the QIAstat-Dx ME Panel, therefore, the Equivocal list will always be empty.
- The third list, under the heading Tested, 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. Invalid pathogens are also displayed in this list.

Note: Pathogens detected and identified in the sample are shown in both the Detected and Tested 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
- Patient ID (if available)
- 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).

A report with the assay data can be exported to an external USB storage device. Insert the USB storage device into one of the USB ports of the QIAstat-Dx Analyzer 1.0 and press Save Report in the bottom bar of the screen. This report can be exported later at any time by selecting the test from the View Result List.

The report can also be sent to the printer by pressing Print Report in the bottom bar of the screen.

Viewing amplification curves

To view test amplification curves of pathogens detected, press the Amplification Curves tab (Figure 18).

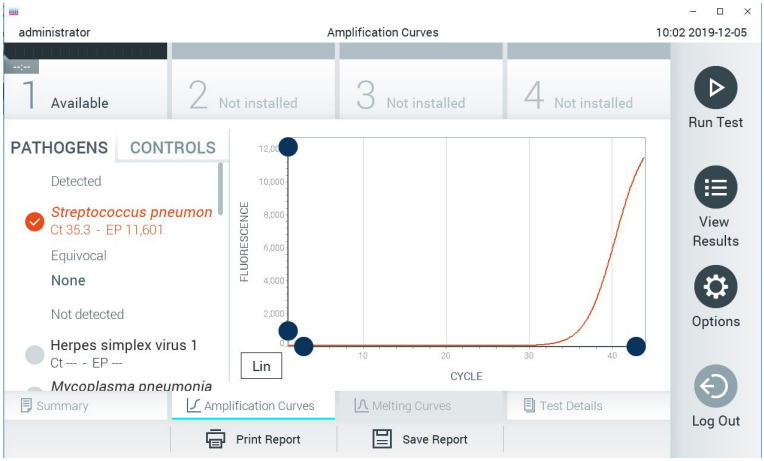


Figure 18. Amplification Curves screen (PATHOGENS tab).

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 and the QIAstat-Dx Analyzer 2.0, 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 19).

Figure 19. 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):

- 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:
    a. Positive (if at least one meningitis/encephalitis pathogen is detected/identified)
    b. Negative (if no meningitis/encephalitis pathogen is detected)

c. Failed (an error occurred or the test was canceled by the user)

- 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

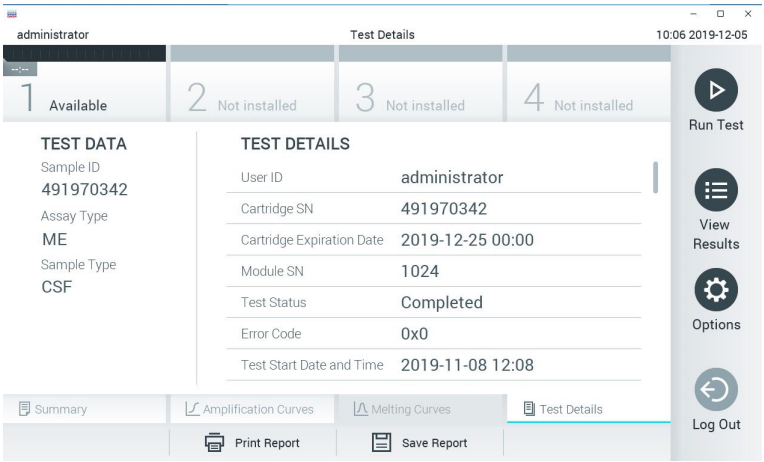


Figure 20. Example screen showing Test Data on the left panel and Test Details in the main panel.

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).

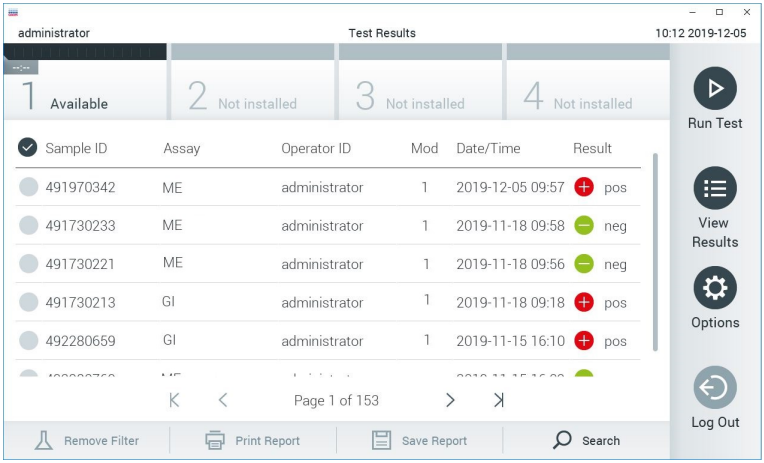


Figure 21. Example View Results screen.

The following information is available for every executed test (Figure 22):

- Sample ID
- Assay (name of test assay which is "ME" for Meningitis/Encephalitis Panel)
- 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], negative [neg], failed [fail] or successful [suc])

Note: If User Access Control is enabled on the QIAstat-Dx Analyzer 1.0 and the QIAstat-Dx Analyzer 2.0, 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).

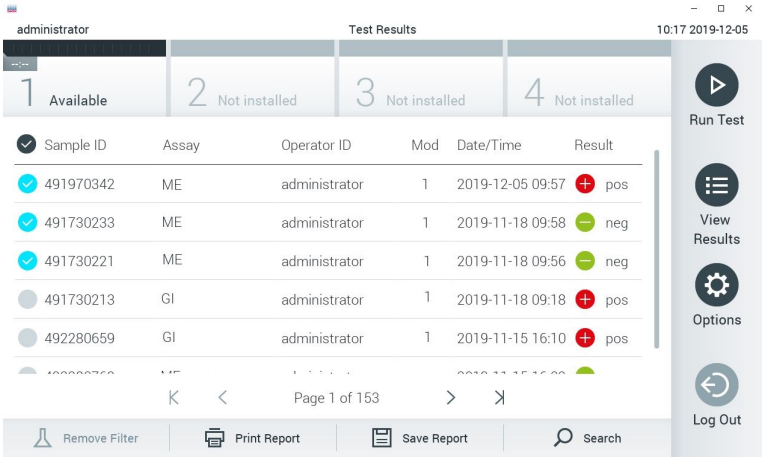


Figure 22. Example of selecting Test Results in the View Results screen.

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 2).

Table 2. Descriptions of the test results in View Results Screen

Outcome	Result	Description	Action
Positive	pos	At least one pathogen is positive	Refer to the Summary Result Screen or Result Printout for pathogen specific results.
Positive with warning	pos*	At least one pathogen is positive, but the Internal Control failed	Refer to the Summary Result Screen or Result Printout for pathogen specific results.

Table 2. Descriptions of the test results in View Results Screen (continued)

Outcome	Result	Description	Action
Negative	neg	No analytes were detected	Refer to the Summary Result Screen or Result Printout for pathogen specific results.
Failed	fail	The test failed because either an error occurred, the test was canceled by the user, or no pathogens were detected and the internal control failed.	Repeat the test using a new cartridge. Accept the results of the repeat testing. If the error persists, contact QIAGEN Technical Services for further instructions.
Successful	Suc	The test is either positive or negative, but the user does not have the access rights to view the test results.	Login from a user profile with rights to view the results.

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.

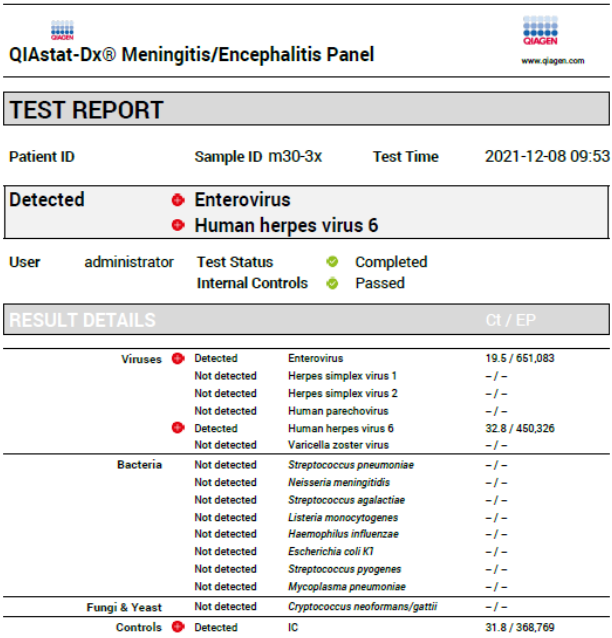
A filter can be removed by pressing Remove Filter in the Submenu bar.

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 (Figure 23 to Figure 25). The USB port is located on the front of the QIAstat-Dx Analyzer 1.0 and the QIAstat-Dx Analyzer 2.0. The interpretation of the results in the PDF file is shown on Table below.

Table 3. Interpretation of test results on PDF reports.

	Outcome	Symbol	Description
Pathogen result	Detected		Pathogen detected
	Not Detected	No symbol	Pathogen not detected
	Invalid	No symbol	The Internal Control failed there is not valid result for this target and the sample should be retested
Test Status	Completed		The test was completed and the Internal Control and/or one or more targets were detected
	Failed		The test failed
Internal Controls	Passed		The Internal Control passed
	Failed		The Internal Control failed



QIAstat-Dx® Meningitis/Encephalitis Panel

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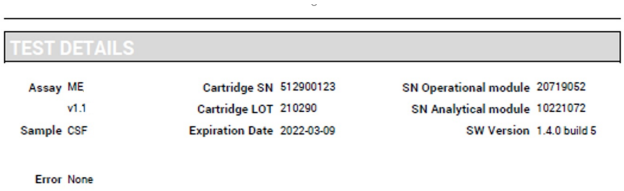
TEST REPORT

Patient ID		Sample ID m30-3x	Test Time 2021-12-08 09:53
Detected	Enterovirus		
	Human herpes virus 6		
User	administrator	Test Status	Completed
		Internal Controls	Passed

RESULT DETAILS — Ct / EP

Viruses	Detected	Enterovirus	19.5 / 651,083
	Not detected	Herpes simplex virus 1	– / –
	Not detected	Herpes simplex virus 2	– / –
	Not detected	Human parechovirus	– / –
	Detected	Human herpes virus 6	32.8 / 450,326
	Not detected	Varicella zoster virus	– / –
Bacteria	Not detected	*Streptococcus pneumoniae*	– / –
	Not detected	*Neisseria meningitidis*	– / –
	Not detected	*Streptococcus agalactiae*	– / –
	Not detected	*Listeria monocytogenes*	– / –
	Not detected	*Haemophilus influenzae*	– / –
	Not detected	*Escherichia coli K1*	– / –
	Not detected	*Streptococcus pyogenes*	– / –
	Not detected	*Mycoplasma pneumoniae*	– / –
Fungi & Yeast	Not detected	*Cryptococcus neoformans/gattii*	– / –
Controls	Detected	IC	31.8 / 368,769

Figure 23. Sample test report.



TEST DETAILS

Assay ME	Cartridge SN 512900123	SN Operational module 20719052	
v1.1	Cartridge LOT 210290	SN Analytical module 10221072	
Sample CSF	Expiration Date 2022-03-09	SW Version 1.4.0 build 5	
Error None			

Figure 24. Sample test report showing details about the test.

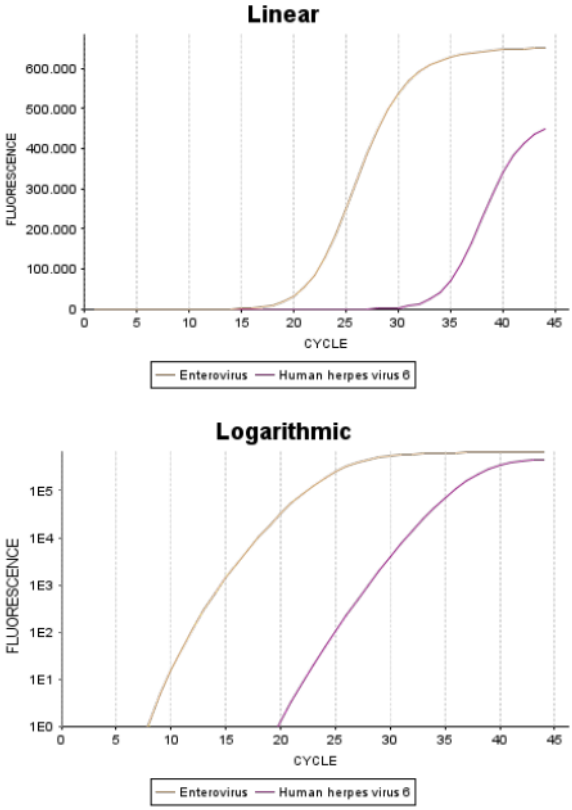


Figure 25. Sample test report showing assay data.

Printing results

Make sure a printer is connected to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 and the proper driver is installed. Press **Print Report** to send a copy of the PDF test results

to the printer.

Result interpretation

A result for a Meningitis/Encephalitis organism is interpreted as Positive when the corresponding PCR assay is positive.

Internal Control interpretation

Internal Control results are to be interpreted according to Table 4.

Table 4. Interpretation of Internal Control results

Control result	Explanation	Action
Passed	The Internal Control amplified successfully	The run was completed with success. All results are valid 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 Meningitis/Encephalitis Panel Cartridge.

Quality Control

In accordance with QIAGEN's ISO-certified Quality Management System, each lot of QIAstat-Dx ME Panel is tested against predetermined specifications to ensure consistent product quality.

Limitations

- Results from the QIAstat-Dx ME Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions.
- Positive results do not rule out co-infection with organisms not included in the QIAstat-Dx ME Panel. The agent or agents detected may not be the definite cause of the disease. Negative results do not preclude central nervous system (CNS) infection, as not all potential etiological agents are detected by this assay, and pathogens targeted by the QIAstat-Dx ME Panel may be present in lower concentrations below the limits of detection of the system
- Not all agents of CNS infection are detected by this test, and sensitivity in clinical use may differ from that described in the package insert.
- The QIAstat-Dx ME Panel is not intended for testing of specimens collected from indwelling CNS medical devices.
- A negative result with the ME 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 ME Panel is not intended for testing of samples other than those described in this Instructions for Use. Test performance characteristics have been established only with CSF.
- The QIAstat-Dx ME Panel is intended to be used in conjunction with standard of care (e.g., culture for organism recovery, serotyping, and antimicrobial susceptibility testing). The results from the QIAstat-Dx ME Panel must be interpreted by a trained healthcare professional within the context of all relevant clinical, laboratory, and epidemiological

findings.

- The QIAstat-Dx ME Panel can be used only with the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0*.

*DiagCORE Analyzer instruments running QIAstat-Dx software version 1.4 or higher can be used as an alternative to the QIAstat-Dx Analyzer 1.0.

- The QIAstat-Dx ME Panel is a qualitative assay and does not provide a quantitative value for detected organisms.
- Bacterial, viral, and fungal 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 bacterial, viral, and fungal nucleic acids depends on proper sample collection, handling, transportation, storage, and loading into the QIAstat-Dx ME Panel Cartridge. Improper operations for any of the aforementioned processes can cause incorrect results, including false-positive or false-negative results.
- 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. Please note that a higher prevalence favors the positive predictive value of a test result, while a lower prevalence favors the negative predictive value of a test result.
- Accidental contamination of the CSF sample with Propionibacterium acnes – a common commensal skin flora organism- can generate an unexpected signal (low positive) for Mycoplasma pneumoniae target in the QIAstat-Dx ME panel. Standard CSF sample handling should prevent this potential contamination.
- Results obtained during co-infection study in the analytical verification show a potential inhibition of HSV1 detection when S.pneumoniae is present in the same sample. As this effect was observed even with low concentrations of *S.pneumoniae*, negative results for

HSV1 in S.pneumoniae-positive samples should be interpreted with caution. The opposite effect (inhibition of *S.pneumoniae* when HSV1 is present in the same sample) was not observed at the highest tested concentration of HSV1 (1.00E+05 $TCID_{50}$/mL).

Performance Characteristics

Clinical performance

The clinical performance shown below was demonstrated using QIAstat-Dx Analyzer 1.0. The QIAstat-Dx Analyzer 2.0 use the same Analytical Modules as QIAstat-Dx Analyzer 1.0 therefore the performance is not impacted by the QIAstat-Dx Analyzer 2.0.

The performance characteristics of the QIAstat-Dx Meningitis/Encephalitis (ME) Panel was assessed by an observational, retrospective, clinical performance study, which included the testing of 585 eligible cerebrospinal fluid (CSF) residual specimens obtained by lumbar puncture from patients with signs and symptoms of meningitis and/or encephalitis using the QIAstat-Dx ME Panel across 3 clinical testing sites in Europe (Table 5).

Table 5. Number of participants per clinical testing site

Sites	Number or eligible specimens
Germany	200
France	194
Denmark	191
Overall/Total	585

Table 6 provides a summary of demographic information specimens included in the study.

Table 6. Summary of demographics for the clinical study

Variable	Subgroup	N	%
Age Group	< 2 years	9	1.54
	2-17 years	24	4.10
	18-64 years	322	55.04
	65+ years	212	36.58
	N.S.	16	2.74
Gender	Female	287	49.06
	Male	282	48.21
	N.S.	16	2.74

The performance of the QIAstat-Dx ME panel was evaluated by comparing the QIAstat-Dx ME Panel test result against the FilmArray Meningitis/Encephalitis Panel. Where there was disagreement between methods, the discordance was resolved by considering the standard of care testing result for the site (RT-PCR or culture).

Out of the 585 eligible clinical specimens, 579 produced an evaluable result, 6 samples which were considered in the analysis that had a positive with warning results. Contrived samples (n=367) were included to assess performance of pathogens with low prevalence (Neisseria meningitidis, Streptococcus agalactiae, Enterovirus, Herpes Virus Simplex 1, and Human Parechovirus) and for *Mycoplasma pneumoniae* and *Streptococcus pyogenes*. For each pathogen that was contrived, the chosen strains were spiked into negative clinical matrix in at least 10 different samples or pools of negative CSF. Once prepared, the contrived samples were randomized and blinded then sent to each of the clinical sites for testing within the standard workflow. Table 7 shows the samples included in the performance calculation.

Table 7. Distribution of clinical and contrived samples analyzed

Variable	Subgroup	N	%
Sample Type	Clinical	585	61.45
	Contrived	367	38.55

Positive percent agreement (PPA) was calculated as 100% x (TP/(TP+FN)). True positive (TP) indicates that both the QIAstat-Dx ME Panel and reference/comparator method had a positive result for the specific analyte, and false negative (FN) indicates that the QIAstat-Dx result was negative while the comparator result was positive. Negative percent agreement (NPA) was calculated as 100% x (TN/(TN+FP)). True negative (TN) indicates that both QIAstat-Dx ME Panel and the reference/comparator method had negative results, and a false positive (FP) indicates that the QIAstat-Dx ME Panel result was positive but the comparator result was negative. The exact binomial two-sided 95% confidence interval was calculated. Table 8 shows the overall performance (PPA and NPA) for all pathogens in the QIAstat-Dx ME Panel adding clinical and contriving sample results. Table 8 lists the PPA and NPA results for the QIAstat-Dx ME Panel. For PPA, each target specifies if the performance calculation is based on clinical samples, contrived samples or a combination of both. NPA is reported only based on clinical samples.

Table 8. Clinical Performance acceptance criteria assessment for sensitivity and specificity – after discordant resolution to SoC Test

			PPA			NPA		
Pathogen Type	**Target**	**Testing Source**	**TP/ (TP+FN)**	**%**	**95% CI**	**TN/(TN+FP)**	**%**	**95% CI**
All	Overall	Clinical	140/147	95.24	90.50% - 97.67%	7381/7386	99.93%	99.84%-99.97%
Bacteria	*Escherichia coli K1*	Clinical	1/1	100.00%	20.65%-100.00%	579/579	100.00%	99.34%-100.00%
	Haemophilus influenzae	Clinical	4/4	100.00%	51.01%-100.00%	573/575	99.65%	98.74%-99.90%
	Listeria monocytogenes	Clinical	1/1	100.00%	20.65%-100.00%	578/578	100.00%	99.34%-100.00%
	Mycoplasma pneumoniae	Contrived	61/61	100.00%	94.08%-100.00%	NA	NA	NA
	Neisseria meningitidis	Combined	66/66	100.00%	94.5%-100.00%	578/578	100.00%	99.34%-100.00%
	Streptococcus agalactiae	Combined	63/64	98.44%	91.67%-99.72%	576/576	100.00%	99.34%-100.00%
	Streptococcus pneumoniae	Clinical	16/16	100.00%	80.64%-100.00%	563/563	100.00%	99.32%-100.00%
	Streptococcus pyogenes	Contrived	61/61	100.00%	94.08%-100.00%	NA	NA	NA
	Bacteria Overall	Clinical	26/26	100.00%	87.13%-100.00%	3447/3449	99.94%	99.79%-99.98%

Table 8. Clinical Performance acceptance criteria assessment for sensitivity and specificity – after discordant resolution to SoC Test (continued)

			PPA			NPA		
Pathogen Type	**Target**	**Testing Source**	**TP/ (TP+FN)**	**%**	**95% CI**	**TN/(TN+FP)**	**%**	**95% CI**
Virus	Enterovirus	Combined	66/69	95.65%	87.98%-98.51%	570/570	100.00%	99.33%-100.00%
	Herpes simplex virus 1 (HSV-1)	Clinical	20/20	100.00%	83.89%-100.00%	561/561	100.00%	99.32%-100.00%
	Herpes simplex virus 2 (HSV-2)	Clinical	23/25	92.00%	75.03%-97.78%	555/555	100.00%	99.31%-100.00%
	Human Parechovirus (HPeV)	Contrived	59/59	100.00%	93.89%-100.00%	579/579	100.00%	99.34%-100.00%
	Human herpes virus 6 (HHV-6)	Clinical	10/11	90.91%	62.26%-98.38%	568/569	99.82%	99.01%-99.97%
	Varicella zoster virus	Clinical	52/55	94.55%	85.15%-98.13%	523/525	99.62%	98.62%-99.90%
	Virus Overall	Clinical	113/120	94.17%	88.45%-97.15%	3356/3359	99.91%	99.74%-99.97%
Yeast	*Cryptococcus gattii/ Cryptococcus neoformans*	Clinical	1/1	100.00%	20.65%-100.00%	5578/5781	100.00%	99.34%-100.00%

There were eleven (11) cartridges (out of 597 cartridge runs, 596 samples) that failed to provide a valid result, yielding a 98.16% success rate on cartridge run.

Conclusion

The QIAstat-Dx Meningitis/Encephalitis Panel demonstrated robust clinical performance characteristics to aid in the diagnosis of specific agents of meningitis and/or encephalitis and results must be used in conjunction with other clinical, epidemiological, and laboratory data.

Analytical performance

The analytical performance shown below was demonstrated using QIAstat-Dx Analyzer 1.0. The QIAstat-Dx Analyzer 2.0 uses the same Analytical Module as QIAstat-Dx Analyzer 1.0 therefore the performance is not impacted by QIAstat-Dx Analyzer 2.0.

Sensitivity (Limit of detection)

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

The LoD for each QIAstat-Dx Meningitis/Encephalitis Panel pathogen was assessed by analyzing dilutions of analytical samples prepared from stocks obtained from commercial suppliers (ZeptoMetrix® and ATCC®).

The LoD concentration was determined for a total of 38 pathogen strains. The LoD of the QIAstat-Dx Meningitis/Encephalitis Panel was determined per analyte using selected strains representing individual pathogens that are possible to detect with the QIAstat-Dx Meningitis/Encephalitis Panel. All sample dilutions were prepared using negative clinical CSF. To confirm the established LoD concentration, the required detection rate of all replicates was ≥95% .

At least 4 different cartridge lots and at least 3 different QIAstat-Dx Analyzers were used for LoD determination for every pathogen.

Individual LoD values for each QIAstat-Dx ME Panel target is shown in Table 9.

Table 9. Limit of detection results

Pathogen	Strain	Supplier	Units	LoD
HSV1	HF	ATCC	TCID50/mL	2.81E+02
HSV1	Macintyre	ZeptoMetrix	TCID50/mL	3.38E+02
HSV2	G	ATCC	TCID50/mL	2.81E+01
HSV2	HSV-2. (Strain: MS)	ZeptoMetrix	U/mL	1.26E+01
Escherichia coli K1	Strain C5 [Bort]; O18ac:K1:H7	ATCC	CFU/mL	3.48E+02
Escherichia coli K1	NCTC 9001. Serovar O1:K1:H7	ATCC	CFU/mL	7.86E+02
Haemophilus influenzae	type b (cap)	ATCC	CFU/mL	3.16E+02
Haemophilus influenzae	Type e [strain AMC 36-A-7]	ATCC	CFU/mL	2.54E+03
Listeria monocytogenes	Type 1/2b	ZeptoMetrix	CFU/mL	5.89E+02
Listeria monocytogenes	Type 4b. Strain Li 2	ATCC	CFU/mL	6.64E+03
Neisseria meningitidis (encapsulated)	Serotype B. M2092	ATCC	CFU/mL	8.28E-02
Neisseria meningitidis (encapsulated)	Serotype Y. M-112 [BO-6]	ATCC	CFU/mL	1.33E+01
Streptococcus agalactiae	Z019	ZeptoMetrix	CFU/mL	1.75E+03
Streptococcus agalactiae	G19 group B	ATCC	CFU/mL	3.38E+03
Streptococcus pneumoniae	19F	ZeptoMetrix	CFU/mL	7.14E+02
Streptococcus pneumoniae	Serotype 1. NCTC 7465	ATCC	CFU/mL	6.22E-01
Streptococcus pyogenes	Z472; Serotype M1	ZeptoMetrix	CFU/mL	1.80E+03
Streptococcus pyogenes	Bruno [CIP 104226]	ATCC	CFU/mL	9.10E+01
Mycoplasma pneumoniae	PI 1428	ATCC	CFU/mL	9.48E+01
Mycoplasma pneumoniae	M129	ZeptoMetrix	CFU/mL	9.99E+01
Enterovirus A	Coxsackievirus A16	ZeptoMetrix	TCID50/mL	3.79E+00

Table 9. Limit of detection results (continued)

Pathogen	Strain	Supplier	Units	LoD
Enterovirus A	A6, species A. Strain Gdula	ATCC	TCID50/mL	1.60E+02
Enterovirus B	Coxsackievirus B5	ZeptoMetrix	TCID50/mL	8.91E+01
Enterovirus B	Coxsackievirus A9, species B	ZeptoMetrix	TCID50/mL	4.36E+01
Enterovirus C	Coxsackievirus A17, species C. Strain G-12	ATCC	TCID50/mL	1.58E+01
Enterovirus C	Coxsackievirus A24. Strain DN-19	ATCC	TCID50/mL	4.99E+00
Enterovirus D	EV 70, species D, strain J670/71	ATCC	TCID50/mL	4.99E+01
Enterovirus D	Enterovirus D68. Strain US/MO/14-18947	ATCC	TCID50/mL	5.06E+02
HHV6	HHV-6A. (Strain: GS) Lysate	ZeptoMetrix	cp/mL	3.13E+04
HHV6	HHV-6B. (Strain: Z29)	ZeptoMetrix	cp/mL	7.29E+04
HPeV	Serotype 1. Strain Harris	ZeptoMetrix	TCID50/mL	1.07E+03
HPeV	Serotype 3	ZeptoMetrix	TCID50/mL	3.38E+01
VZV	Ellen	ZeptoMetrix	cp/mL	1.71E+02
VZV	Oka	ATCC	TCID50/mL	5.00E-02
Cryptococcus neoformans	Serotype D strain WM629, type VNIV	ATCC	CFU/mL	2.21E+03
Cryptococcus neoformans	C. neoformans H99	ATCC	CFU/mL	1.64E+02
Cryptococcus gattii	Serotype B strain R272, type VGIIb	ATCC	CFU/mL	1.32E+04
Cryptococcus gattii	A6MR38 [CBS 11545]	ATCC	CFU/mL	2.60E+03

Inclusivity (Analytical Reactivity)

The inclusivity (analytical reactivity) Study extended the list of pathogen strains tested during the QIAstat-Dx ME Limit of Detection (LoD) Study to confirm the reactivity of the detection

system in the presence of different strains of the same organisms at a concentration near the respective Limit of Detection.

A variety of clinically relevant strains of each target organism of the QIAstat-Dx ME Panel (Inclusivity Strains) representing organism sub-types, strains, and serotypes of different temporal and geographic diversity of each analyte were included in the study. Analytical Reactivity (Inclusivity) was performed in two steps:

- In vitro testing: analytical samples of every target included in the QIAstat-Dx ME Panel were tested to assess the reactivity of the assay. A collection of 179 samples representative of relevant strains, subtypes, serotypes, and genotypes for the different organisms (e.g. a range of different meningitis/encephalitis strains isolated from around the world and in different calendar years) were included in the study.
- In silico analysis: to make assay reactivity predictions of all primers-probe oligonucleotide sequences included in the panel against publicly available sequence databases to detect any possible cross-reaction or unexpected detection of any primer set, in silico analysis was performed. In addition, strains not available for in vitro testing were included in in silico analysis to confirm the predicted inclusivity of the different strains of the same organisms.

Table 10. Clinically relevant strains/subtypes detected per pathogen

Pathogen	Clinically relevant strains/subtypes detected
Neisseria meningitidis (encapsulated)	Encapsulated serotypes (A, B, C, D, E, H, I, K, L, NG, W, W135, X, Y, Z, 29E)
Cryptococcus gattii/ Cryptococcus neoformans	Serotype A (C. neoformans var neoformans), serotype D (C. neoformans var grubii), serotypes B and C (C. gattii including all VGI,VGII, VGIII, VGIV molecular types)

Table 10. Clinically relevant strains/subtypes detected per pathogen (continued)

Pathogen	Clinically relevant strains/subtypes detected
Human parechovirus	All human Parechovirus A strains with available 5'-UTR sequence (1, 2, 3, 4, 5, 6, 7, 8, 14, 16, 17, 18, and 19), including echovirus 22 (HPeV 1) and echovirus 23 (HPeV 2). Although there were polyprotein sequences for HPeV A strains 9, 10, 11, 12, 13 and 15, no 5'-UTR sequence were available
Listeria monocytogenes	Serotypes 1/2a,1/2b, 1/2c, 3a, 3b, 3c, 4a, 4b, 4c, 4d, 4e, 7
Human herpes virus 6	HHV6a and HHV6b
Haemophilus influenzae	All encapsulated serotypes (a, b, c, d, e, f) and unencapsulated strains (nontypeable, NTHi) including var. H. aegyptus
Enterovirus	Coxsackievirus A (CV-A1 through CV-A24), coxsackievirus B (CV-B1 through CV-B6), Echovirus (E-1 through E-33), Enterovirus A (EV-A71, EV-A76, EV-A89 through EV-A92, EV-A119, EV-A120), Enterovirus B (EV-B69, EV-B73 through EV-B75, EV-B79, EV-B80 through EV-B88, EV-B93, EV-B97, EV-B98, EV-B100, EV-B101, EV-B106, EV-B107, EV-B111), Enterovirus C (EV-C96, EV-C99, EV-C102, EV-C104, EV-C105, EV-C109, EV-C116 through EV-C118), Enterovirus D (EV-D68, EV-D70, EV-D94), Poliovirus (PV-1 through PV-3)
Escherichia coli K1	K1 strains

Table 11. Strains tested for inclusivity

Pathogen	Strain/Stereotype	Supplier
Escherichia coli K1	Strain C5 [Bort]; O18ac:K1:H7	ATCC
	NCTC 9001. Serovar O1:K1:H7	ATCC
	Strain Bi 7509/41; O7:K1:H-	NCTC
	NCDC Bi 7509-41 Serotype O7:K1(L):NM	ATCC
	NCDC F 11119-41	ATCC
	O-2, U9-41*	BEI Resources
	O-16, F1119-41*	BEI Resources
	Z136 CTX-M-15	ZeptoMetrix
	Sc15 02:K1:H6	NCTC
	Strain H61; O45:K1:H10	NCTC
Haemophilus influenzae	type b (cap)	ATCC
	Type e [strain AMC 36-A-7]	ATCC
	Non-typeable [strain Rd KW20]	ATCC
	Non-typeable [strain 180-a]	ATCC
	Type a [strain AMC 36-A-3]	ATCC
	Type b [strain Rab]	ATCC
	Type c [strain C 9007]	ATCC
	Type d [strain AMC 36-A-6]	ATCC
	Type f [strain GA-1264]	ATCC
	L-378	ATCC

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Listeria monocytogenes	Type 1/2b	ZeptoMetrix
	Type 4b. Strain Li 2	ATCC
	Type 1/2a. Strain 2011L-2676	ATCC
	Type 1/2a. Strain Li 20	ATCC
	Type 4b	ZeptoMetrix
	serotype 4b. Strain 1071/53 [LMG 21264, NCTC 10527]	ATCC
	Li 23. Serotype 4a	ATCC
	FSL J2-064	BEI Resources
	Gibson	ATCC
	EGDe	ATCC
	PI 1428	ATCC
Mycoplasma pneumoniae	M129	ZeptoMetrix
	FH strain of Eaton Agent [NCTC 10119]	ATCC
	UTMB-10P	ATCC
	MAC	ATCC

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Neisseria meningitidis (encapsulated)	Serotype B. M2092 [CIP 104218, L. Cunningham]	ATCC
	Serotype Y. M-112 [BO-6]	ATCC
	Serogroup A, M1027 [NCTC10025]	ATCC
	Serogroup C, M1628	ATCC
	Serotype D. M158 [37A]	ATCC
	sequence with variant ctrA gene	IDT
	W135	ATCC
	MC58	ATCC
	79 Eur. Serogroup B	ATCC
	Serotype B. M997 [S-3250-L]	ATCC
Streptococcus agalactiae	Z019	ZeptoMetrix
	G19 group B	ATCC
	Serotype III. Typing strain D136C(3) [3 Cole 106, CIP 82.45]	ATCC
	type III-ST283	ATCC
	MNZ929	BEI Resources
	Typing strain H36B - type Ib	ATCC
	CDC SS700 [A909; 5541], type 1c	ATCC
	3139 [CNCTC 1/82] Serotype IV	ATCC
	Z023	ZeptoMetrix

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Streptococcus pneumoniae	19F	ZeptoMetrix
	Serotype 1. NCTC 7465	ATCC
	Serotype 4. TIGR4 [JNR.7/87]	ATCC
	Serotype 5. SPN1439-106 [Colombia 5-19]	ATCC
	Serotype 11A. Type 43	ATCC
	Serotype 14. VH14	ATCC
	Serotype 19A. Hungary 19A-6 [HUN663]	ATCC
	Z319; 12F	Zeptometrix
	Diplococcus pneumoniae; Type 3. Strain [CIP 104225]	ATCC
	DCC1476 [Sweden 15A-25]	ATCC
Streptococcus pyogenes	Z472; Serotype M1	ZeptoMetrix
	Bruno [CIP 104226]	ATCC
	Z018; Serotype M58	ZeptoMetrix
	Serotype M1. MGAS 5005	ATCC
	Lancefield's group A/C203 S	ATCC
	NCTC 8709 (Type 6 glossy)	ATCC
	Group a, type 12. Typing strain T12 [F. Griffith SF 42]	ATCC
	Group a, type 14	ATCC
	Group a, type 23	ATCC
	C203 -Type 3	ATCC

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Enterovirus A	Coxsackievirus A16	ZeptoMetrix
	A6, species A. Strain Gdula	ATCC
	A10. M.K. (Kowalik)	ATCC
	Enterovirus 71. Strain H	ATCC
	Species A, Serotype EV-A71 (2003 Isolate)	ZeptoMetrix
	Tainan/4643/1998	BEI Resources
	A2 Fl [Fleetwood]	ATCC
	A7 - 275/58	ATCC
	A12 - Texas 12	ATCC
	EV-A71. Strain BrCr	ATCC
Enterovirus B	Coxsackievirus B5	ZeptoMetrix
	Coxsackievirus A9, species B	ZeptoMetrix
	Species B, Serotype CV-B1, Strain Conn-5	ATCC
	Species B, Serotype CV-B2. Strain Ohio-1	ATCC
	Coxsackievirus B4	ZeptoMetrix
	Echovirus 6	ZeptoMetrix
	Echovirus 9	ZeptoMetrix
	Coxsackievirus B3	ZeptoMetrix
	Echovirus 18	NCPV
	Species B, Serotype E-11	ATCC

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Enterovirus C	Coxsackievirus A17, species C. Strain G-12	ATCC
	Coxsackievirus A24. Strain DN-19	ATCC
	Coxsackievirus A21. Strain Kuykendall [V-024-001-012]	ATCC
	A11 - Belgium-1	ATCC
	A13 - Flores	ATCC
Enterovirus C	A22 – Chulman	ATCC
	A20 - IH Pool 35	ATCC
	A18 - G-13	ATCC
	CV-A21. Strain H06452 472	NCTC
	CV-A21. Strain H06418 508	NCTC
Enterovirus D	EV 70, species D, strain J670/71	ATCC
	Enterovirus D68. Strain US/MO/14-18947	ATCC
	Enterovirus 68. 2007 Isolate	ZeptoMetrix
	Enterovirus D68. Strain US/IL/14-18952	ATCC
	D68. Strain F02-3607 Corn	ATCC
	Type 68 Major Group (09/2014 Isolate 2)	ZeptoMetrix
	Enterovirus D68. Strain US/KY/14-18953	ATCC
	Enterovirus D68. Strain Fermon	ATCC
	Enterovirus D68. US/MO/14-18949	BEI Resources
	Enterovirus D68. USA/2018-23089	BEI Resources

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Herpes Simplex Virus 1	HF	ATCC
	Macintyre	ZeptoMetrix
	F	ATCC
	KOS	ATCC
	ATCC-2011-1	ATCC
	ATCC-2011-9	ATCC
	17+	NCPV
	P5A	NCTC
	P6	NCTC
	Isolate 20	ZeptoMetrix
Herpes simplex virus 2	G	ATCC
	HSV-2. (Strain: MS)	ZeptoMetrix
	ATCC-2011-2	ATCC
	131596	NCPV
	HG52	NCPV
	Isolate 1	ZeptoMetrix
	132349 ACV-res	NCPV
	Isolate 11	Zeptometrix
	Isolate 15	Zeptometrix
	Isolate 20	Zeptometrix

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Human herpes virus 6	HHV-6A. (Strain: GS)	ZeptoMetrix
	HHV-6B. (Strain: Z29)	ZeptoMetrix
	6B - strain SF	ATCC
	6B - strain HST	NCPV
	Human β-lymphotropic virus strain GS	ATCC
	6A – strain U1102	NCPV
Human parechovirus	Serotype 1. Strain Harris	ZeptoMetrix
	Serotype 3	ZeptoMetrix
	Serotype 2. Strain Williamson	ZeptoMetrix
	Serotype 4	ZeptoMetrix
	Serotype 5	ZeptoMetrix
	Serotype 6	ZeptoMetrix
	type 3. Strain US/MO-KC/2014/001	ATCC
	Parechovirus A3. Strain US/MO-KC/2012/006	ATCC

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Varicella-zoster virus	Ellen	ZeptoMetrix
	Oka	ATCC
	Isolate A	ZeptoMetrix
	Isolate B	ZeptoMetrix
	Strain 275	ZeptoMetrix
	Webster	ATCC
	Strain 82	ZeptoMetrix
	Isolate D	ZeptoMetrix
	Strain 9939	ZeptoMetrix
	Strain 1700	ZeptoMetrix
Cryptococcus neoformans	Serotype D strain WM629, type VNIV	ATCC
	H99	ATCC
	Strain, CBS 132	ATCC
	Serotype A strain WM148, type VNI	ATCC
	M2092	ATCC
	Serotype AD strain WM628, type VNIII	ATCC
	Serotype A	ZeptoMetrix
	NIH9hi90	BEI Resources
	NIH306	BEI Resources
	Var grubiiYL99α	BEI Resources

Table 11. Strains tested for inclusivity (continued)

Pathogen	Strain/Stereotype	Supplier
Cryptococcus gattii	Serotype B strain R272, type VGIIb	ATCC
	A6MR38	ATCC
	Serotype B strain WM179, type VGI	ATCC
	Serotype B strain WM161, type VGIII	ATCC
	Serotype C strain WM779, type VGIV	ATCC
	A1M R265	ATCC
	110 [CBS 883]	ATCC
	AIR265	BEI Resources
	Alg166	BEI Resources
	Alg254	BEI Resources

All inclusivity strains tested as part of the study were detected by the panel with the exception of five strains. These are detailed in Table 12.

Table 12. Inclusivity Strains Not Detected by the QIAstat-Dx ME Panel

Pathogen	Strain/Serotype
Escherichia coli K1	NCDC Bi 7509-41 Serotype O7:K1(L):NM
Escherichia coli K1	Z136 CTX-M-15
Enterovirus C	CV-A21. Strain H06452 472
Enterovirus C	CV-A21. Strain H06418 508
Streptococcus agalactiae	Serotype III. Typing strain D136C(3) [3 Cole 106, CIP 82.45]

Exclusivity

The analytical specificity study was carried out by in vitro testing and in silico analysis to assess the potential cross-reactivity and exclusivity of the QIAstat-Dx ME Panel. On-panel organisms were tested to assess the potential for intra-panel cross-reactivity and off-panel organisms were tested to evaluate cross-reactivity with organisms not covered by the panel content.

In silico testing results

The result of the in silico analysis performed for all primer/probe designs included in the QIAstat-Dx ME Panel pointed at 6 potential cross-reactions with off-panel targets (listed on Table 13)

Table 13. Potential cross reactions from in silico analysis

Off-panel organism	On-panel signal
*Streptococcus pseudopneumoniae**	*S. pneumoniae*
*Listeria innocua**	*L. monocytogenes*
Haemophilus haemolyticus	*H. influenzae*
Cryptococcus amylolentus	Cryptococcus neoformans/gatti
*Cryptococcus depauperatus**	
Cryptococcus wingfieldii	

*in silico cross-reactive risk was not confirmed by in vitro testing.

All the organisms on Table 13 were tested in the in vitro analytical specificity study.

In vitro testing results

To demonstrate analytical specificity performance of the QIAstat-Dx ME Panel for pathogens which might be present in the clinical sample but not covered by the panel content, a selection

of potential cross-reactive pathogens was tested (off-panel testing). In addition, the specificity and absence of cross-reactivity with pathogens that are part of the QIAstat-Dx ME Panel has been evaluated at high titers (on-panel testing).

Samples were prepared by spiking potential cross-reactive organisms into artificial CSF matrix at 10^5 $TCID_{50}$/mL for viral targets and 10^6 CFU/mL for bacterial targets and 10^5 CFU/mL for fungal targets, or the highest concentration possible based on the organism stock.

All strains tested for exclusivity are detailed on Table 14. For pathogens marked with * either quantitative synthetic DNA or inactivated material was used.

Table 14. Pathogens tested for exclusivity

Pathogen	Strain	Supplier	Catalog ID
Escherichia coli K1	Strain C5 [Bort]; O18ac:K1:H7	ATCC	700973
Haemophilus influenzae	Type e [strain AMC 36-A-7]	ATCC	8142
Listeria monocytogenes	Type 4b. Strain Li 2	ATCC	19115
Mycoplasma pneumoniae	M129	ZeptoMetrix	801579
Neisseria meningitidis	Serotype Y. M-112 [BO-6]	ATCC	35561
Streptococcus pneumoniae	19F	ZeptoMetrix	801439
Streptococcus agalactiae	Z019	Zeptometrix	801545
Streptococcus pyogenes	Z472; Serotype M1	Zeptometrix	804351
Enterovirus A	A6, species A. Strain Gdula	ATCC	VR-1801
Enterovirus B	Coxsackievirus B5	ZeptoMetrix	0810019CF
Enterovirus C	Coxsackievirus A17, species C. Strain G-12	ATCC	VR-1023
Enterovirus D	Enterovirus D68. Strain US/MO/14-18947	ATCC	VR-1823
Herpes simplex virus 1	Macintyre	ZeptoMetrix	0810005CF

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Herpes simplex virus 2	HSV-2. (Strain: MS)	ZeptoMetrix	0810006CF
Human herpes virus 6	HHV-6B. (Strain: Z29)	ZeptoMetrix	0810072CF
Human parechovirus	Serotype 3	ZeptoMetrix	0810147CF
Varicella-zoster virus	Ellen	ZeptoMetrix	0810171CF
Cryptococcus neoformans	WM629 [CBS 10079]	ATCC	MYA-4567
Cryptococcus gattii	Serotype B strain R272, type VGIIb	ATCC	MYA-4094
Adenovirus A12	Huie	ATCC	VR-863
Adenovirus C2	Adenoid 6 (NIAID 202-001-014)	ATCC	VR-846
Adenovirus D20	A.A	ATCC	VR-1090
Adenovirus E4	RI-67	ATCC	VR-1572
Adenovirus F41	Tak	ZeptoMetrix	0810085CF
BK polyoma virus	N/A	ATCC	VR-837
Coronavirus 229E	229E	ATCC	VR-740
Coronavirus NL63	NL63 (Amsterdam I)	BEI Resources	NR-470
Coronavirus OC43	OC43	ATCC	VR-1558
Dengue virus (Type 2)*	New Guinea C	ZeptoMetrix	0810089CFHI
Epstein-Barr Virus	B95-8	ZeptoMetrix	0810008CF
Hepatitis B virus (HBV)*	N/A	ZeptoMetrix	0810031C
Hepatitis C virus (HCV)*	N/A	ZeptoMetrix	0810032C
Human herpes virus 7	SB	ZeptoMetrix	0810071CF
Human herpes virus 8	N/A	ZeptoMetrix	0810104CF

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Human Immunodeficiency Virus*	Quantitative Synthetic Human immunodeficiency virus 1 (HIV-1) RNA	ATCC	VR-3245SD
Human Rhinovirus A1b	2060	ATCC	VR-1559
Human Rhinovirus A16	11757	ATCC	VR-283
Human Rhinovirus B3	FEB	ATCC	VR-483
Human Rhinovirus B83	Baylor 7 [V-190-001-021]	ATCC	VR-1193
JC polyoma virus	MAD-4	ATCC	VR-1583
Measles Virus	Edmonston	ATCC	VR-24
Mumps Virus	Jones	ATCC	VR-1438
West Nile Virus*	1986	ZeptoMetrix	VR-3274SD
Parainfluenza virus 2	Greer	ATCC	VR-92
Parainfluenza virus 4	N/A	ZeptoMetrix	0810060CF
Parvovirus B19	B19	ZeptoMetrix	0810064C
Respiratory Syncytial Virus	A2	ATCC	VR-1540
Rotavirus	RRV (Rhesus Rotavirus)	ZeptoMetrix	0810530CF
Rubella Virus	N/A	ZeptoMetrix	0810048CF
St. Louis Encephalitis Virus*	Parton	ZeptoMetrix	0810080CFHI
Candida glabrata	CBS 138	ATCC	2001
Candida krusei	N/A	ATCC	14243
Candida lusitaniae	Z010	ZeptoMetrix	801603
Candida metapsilosis	MCO429	ATCC	96143
Candida orthopsilosis	MCO471	ATCC	96140

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Candida viswanathii	PK 233 [NCYC 997, pK233]	ATCC	20336
Candida parapsilosis	CBS 604	ATCC	22019
Candida tropicalis	Vitek #8935	ATCC	750
Cryptococcus albidus	AmMS 228	ATCC	66030
Cryptococcus amylolentus	NRRY Y-7784	ATCC	56469
Cryptococcus laurentii	CBS 139	ATCC	18803
Cryptococcus uniguttulatus	AmMS 234	ATCC	66033
Cryptococcus adeliensis = Cryptococcus adeliae = Naganishia adeliensis	Cryptococcus adeliae	ATCC	201412
Cryptococcus flavescens = Papiliotrema flavescens	Cryptococcus laurentii var. flavescens (Saito) Lodder et Kreger-van Rij	ATCC	10668
Influenza A H1N1	A/Florida/3/2006	ATCC	VR-1893
Influenza A H1N1-2009	A/California/08/2009 (H1N1pdm)	ATCC	VR-1895
Influenza A H3N2	A/Port Chalmers/1/73	ATCC	VR-810
Influenza B	B/Virginia/ATCC4/2009	ATCC	VR-1784
Cryptococcus wingfieldii = Tsuchiyaea wingfieldii	OTU 26	Collection Belga	CBS 7118
Cryptococcus depauperatus = Aspergillus depauperatus = Filobasidiella depauperata	K [ARSEF 2058, CBS 7842]	ATCC	64866
Filobasidium capsuligenum	ML-186	ATCC	22179
*Naeglaria fowleri**	Genomic DNA from Naegleria fowleri	ATCC	30174D
Toxoplasma gondii	Haplogroup 2	ATCC	50611

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Aspergillus fumigatus	Z014	ZeptoMetrix	801716
Candida albicans	CBS 562	ATCC	18804
Candida dubliniensis	Z145	ZeptoMetrix	801915
Bacillus cereus	Z091	ZeptoMetrix	801823
Citrobacter freundii	[ATCC 13316, NCTC 9750]	ATCC	8090
Corynebacterium striatum	CDC F6683	ATCC	43751
Corynebacterium urealyticus	3 [Garcia strain]	ATCC	43044
Cronobacter (Enterobacter) sakazakii	CDC 4562-70	ATCC	29544
Enterobacter aerogenes	Z052	ZeptoMetrix	801518
Enterobacter cloacae	CDC 442-68	ATCC	13047
Escherichia coli (non-K1)	2003-3055	ATCC	BAA-2212
Escherichia fergusonii	Z302	ZeptoMetrix	804113
Escherichia hermannii	CDC 980-72	ZeptoMetrix	804068
Escherichia vulneris	CDC 875-72	ATCC	33821
Haemophilus ducreyi	CF101	ATCC	33940
Haemophilus haemolyticus	NCTC 10659	ATCC	33390
Haemophilus parahaemolyticus	536 [NCTC 8479]	ATCC	10014
Haemophilus parainfluenzae	NCTC 7857	ATCC	33392
Klebsiella pneumoniae	NCTC 9633 [NCDC 298-53, NCDC 410-68]	ATCC	13883
Listeria innocua	SLCC 3379	ATCC	33090
Listeria ivanovii	Li 1979	ATCC	19119

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Morganella morganii	AM-15	ATCC	25830
Streptococcus salivarius	C699	ATCC	13419
Streptococcus sanguinis	DSS-10	ATCC	10556
Streptococcus pseudopneumoniae	CDC-SS-1757	ATCC	BAA-960
Mycoplasma genitalium	M30	ATCC	49895
Neisseria lactamica	NCDC A7515	ATCC	23970
Neisseria mucosa	AmMS 138	ATCC	49233
Neisseria sicca	AMC 14-D-1	ATCC	9913
Neisseria gonorrhoeae	Z017	ZeptoMetrix	801482
Pantoea agglomerans	*Enterobacter agglomerans*	ATCC	27155
Proprionibacterium acnes	NCTC 737	ATCC	6919
Proteus mirabilis	LRA 08 01 73 [API SA, DSM 6674]	ATCC	7002
Pseudomonas aeruginosa	PRD-10 [CIP 103467, NCIB 10421, PCI 812]	ATCC	15442
Saccharomyces cerevisiae	NRRL Y-567	ATCC	9763
Salmonella bongori	CIP 82.33	ATCC	43975
Salmonella enterica	CDC K-1891 [ATCC 25928]	ATCC	13076
Serratia marcescens	PCI 1107	ATCC	14756
Shigella boydii	CDC C-123	ATCC	12033
Shigella flexneri	Z046	ZeptoMetrix	801757
Shigella sonnei	AMC 43-GG9	ATCC	9290
Staphylococcus aureus	FDA 209	ATCC	CRM6538

Table 14. Pathogens tested for exclusivity (continued)

Pathogen	Strain	Supplier	Catalog ID
Staphylococcus capitis	PRA 360 677	ATCC	35661
Staphylococcus epidermidis	FDA strain PCI 1200	ATCC	12228
Staphylococcus haemolyticus	SM 131	ATCC	29970
Staphylococcus hominis	Z031	ZeptoMetrix	801727
Staphylococcus lugdunensis	LRA 260.05.79	ATCC	49576
Staphylococcus saprophyticus	NCTC 7292	ATCC	15305
Streptococcus anginosus	NCTC 10713	ATCC	33397
Streptococcus bovis	Z167	ZeptoMetrix	804015
Streptococcus dysgalactiae	Grouping strain C74	ATCC	12388
Streptococcus intermedius	Z126	ZeptoMetrix	801895
Streptococcus oralis	Z307	ZeptoMetrix	804293
Streptococcus mitis (tigurinus)	Clinical Isolate	ZeptoMetrix	801695
Streptococcus mutans	LRA 28 02 81	ATCC	35668

All tested organisms/viruses showed negative results in all three replicates tested (no unexpected positive signals detected), except for the pathogens shown in the table below. Pathogens exhibiting cross-reactivity with the panel, and the lowest concentration where cross reactivity is detected are listed in Table 15.

Table 15. Samples showing cross-reactivity with the panel

Table 15. Samples showing cross-reactivity with the panel

QIAstat-Dx ME Target	Potential cross-reactive organism†	Claimed cross reactive concentration in the IFU
Mycoplasma pneumoniae	Propionibacterium acnes*	≥1.00E+04 CFU/mL

Table 15. Samples showing cross-reactivity with the panel (continued)

QIAstat-Dx ME Target	Potential cross-reactive organism†	Claimed cross reactive concentration in the IFU
Mycoplasma pneumoniae	Mycoplasma genitalium	≥1.00E+06 CCU/mL
Haemophilus influenzae	Haemophilus haemolyticus	≥1.00E+03 CFU/mL
Cryptococcus neoformans/gattii	Cryptococcus wingfieldii = Tsuchiyaea wingfieldii	≥1.00E+01 CFU/mL
Cryptococcus neoformans/gattii	Cryptococcus flavescens = Papiliotrema flavescens	≥4.00E+03 CFU/mL
Cryptococcus neoformans/gattii	Cryptococcus amylolentus	≥1.00E+01 CFU/mL

* *Propionibacterium acnes* was not predicted to cross-react with the Mycoplasma pneumoniae.

†The in silico predicted cross-reactivity for Listeria innocua with the Listeria monocytogenes assay and Cryptococcus depauperatus with Cryptococcus neoformans/gattii assay were not confirmed in vitro

Co-infections

Combined samples containing a mixture of two different targets spiked at low and high concentrations into artificial CSF were tested. Bacterial, viral and yeast targets were included, and organisms detected in the same reaction chamber were chosen for sample preparation and testing. Selection and combinations of targets tested was based on clinical relevance. Three replicates were tested per sample.

A summary of the final co-infection mixes whereby the High Percentage Analyte (HPA) does not inhibit the Low Percentage Analyte (LPA) is shown in Table 16.

Table 16. Co-infection Mixes where concentration of the HPA does not inhibit the LPA

LPA			HPA		
Pathogen	**Concentration**	**Units**	**Pathogen**	**Concentration**	**Units**
Escherichia coli K1	3.30E+02	CFU/mL	*Haemophilus influenzae*	1.00E+06	CFU/mL

Table 16. Co-infection Mixes where concentration of the HPA does not inhibit the LPA (continued)

LPA			HPA		
Pathogen	**Concentration**	**Units**	**Pathogen**	**Concentration**	**Units**
Haemophilus influenzae	9.48E+02	CFU/mL	*Escherichia coli K1*	1.00E+06	CFU/mL
Mycoplasma pneumoniae	2.84E+02	CFU/mL	HSV1	1.00E+05	$TCID_{50}$/mL
HSV1	2.67E+02	$TCID_{50}$/mL	*Mycoplasma pneumoniae*	1.00E+03	CFU/mL
Haemophilus influenzae	9.48E+02	CFU/mL	HSV2	1.00E+02	$TCID_{50}$/mL
HSV2	3.78E+01	$TCID_{50}$/mL	*Haemophilus influenzae*	1.00E+06	CFU/mL
HHV6	9.39E+04	CFU/mL	*Listeria monocytogenes*	1.00E+06	CFU/mL
Listeria monocytogenes	5.58E+03	CFU/mL	HHV6	1.00E+05	cp/mL
HSV1†	2.67E+02	$TCID_{50}$/mL	*Streptococcus pneumoniae*	1.00E+02	CFU/mL
Streptococcus pneumoniae	6.78E+02	CFU/mL	HSV1	1.00E+05	$TCID_{50}$/mL
Haemophilus influenzae	9.48E+02	CFU/mL	*Streptococcus pneumoniae*	1.00E+06	CFU/mL
Streptococcus pneumoniae	6.78E+02	CFU/mL	*Haemophilus influenzae*	1.00E+06	CFU/mL
Listeria monocytogenes	5.58E+03	CFU/mL	*Streptococcus pneumoniae*	1.00E+06	CFU/mL
Streptococcus pneumoniae	6.78E+02	CFU/mL	*Listeria monocytogenes*	1.00E+06	CFU/mL

Table 16. Co-infection Mixes where concentration of the HPA does not inhibit the LPA (continued)

LPA			HPA		
Pathogen	**Concentration**	**Units**	**Pathogen**	**Concentration**	**Units**
Cryptococcus neoformans	6.63E+03	CFU/mL	*Streptococcus pneumoniae*	1.00E+06	CFU/mL
Streptococcus pneumoniae	6.78E+02	CFU/mL	*Cryptococcus neoformans*	1.00E+05	CFU/mL
Neisseria meningitidis	3.99E+01	CFU/mL	*Haemophilus influenzae*	1.00E+06	CFU/mL
Haemophilus influenzae	9.48E+02	CFU/mL	*Neisseria meningitidis*	1.00E+06	CFU/mL
VZV	1.62E+02	CFU/mL	*Neisseria meningitidis*	1.00E+06	CFU/mL
Neisseria meningitidis	3.99E+01	CFU/mL	VZV	1.00E+05	CFU/mL
Enterovirus	4.80E+02	$TCID_{50}$/mL	*Streptococcus pyogenes*	1.00E+06	CFU/mL
Streptococcus pyogenes	1.71E+03	CFU/mL	Enterovirus	1.00E+05	$TCID_{50}$/mL
Parechovirus	1.01E+02	CFU/mL	Enterovirus	1.00E+05	$TCID_{50}$/mL
Enterovirus	4.80E+02	CFU/mL	Parechovirus	1.00E+05	CFU/mL
HHV6	9.39E+04	cp/mL	HSV1	1.00E+05	$TCID_{50}$/mL
HSV1	2.67E+02	$TCID_{50}$/mL	HHV6	1.00E+05	cp/mL

Table 16. Co-infection Mixes where concentration of the HPA does not inhibit the LPA (continued)

LPA			HPA		
Pathogen	**Concentration**	**Units**	**Pathogen**	**Concentration**	**Units**
Streptococcus agalactiae	5.25E+03	CFU/mL	HSV2	1.00E+05	$TCID_{50}$/mL

* Lowest concentration that does not inhibit the LPA

† The HPA concentration (S. pneumoniae) that does not inhibit the LPA (HSV1) was identified as 1.00E+02 CFU/mL. However, this concentration is below the determined assay LoD for S. pneumoniae (7.14E+02 CFU/mL) and a drop-out of the HPA was observed. (Note: comparable detection was demonstrated when S. pneumoniae was tested at 6.78E+02 CFU/mL and HSV1 was tested at 1.00E+05 $TCID_{50}$/mL. As such it appears that high concentrations of HSV1 do not interfere with S. pneumoniae detection, but S. pneumoniae does interfere with HSV1 detection).

Interfering Substances

The effect of potentially interfering substances on the detectability of the QIAstat-Dx ME Panel organisms was evaluated. The substances tested in the study (31) included endogenous as well as exogenous substances that are commonly found and/or introduced into CSF specimens during specimen collection.

All QIAstat-Dx ME Panel target organisms were tested at 3x LoD in artificial CSF matrix and testing was performed in triplicates. Potential interfering substances were spiked into the samples at a level predicted to be above the concentration of the substance likely to be found in CSF sample.

Table 17. Summary of interfering substances

Name	Concentration Tested	Interference
Endogenous substances		
Human Blood	10% (v/v)	No
gDNA	20 µg/mL	Yes
gDNA	2 µg/mL	No

Table 17. Summary of interfering substances (continued)

Name	Concentration Tested	Interference
D(+)Glucose	10 mg/mL	No
L-lactate (Na)	2.2 mg/mL	No
Immunoglobulin G (human)	20 mg/mL	No
Albumin (human)	30 mg/mL	No
Peripheral blood mononuclear cells	10,000 cells/uL	No
Exogenous substances		
Chlorhexidine	0.4% (w/v)	No
Ethanol	7% (v/v)	No
Bleach	1% (v/v)	Yes
Bleach	0.1% (v/v)	Yes
Bleach	0.01% (v/v)	No
Acyclovir	69 µg/mL	No
Amphotericin B	5.1 µg/mL	No
Ampicillin	210 µg/mL	No
Ceftriaxone (aCSF)	840 µg/mL	No
Ceftriaxone (PBS)	840 µg/mL	No
Cefotaxime	645 µg/mL	No
Ganciclovir	25 µg/mL	No
Gentamicin	30 µg/mL	No
Meropenem	339 µg/mL	No
Vancomycin	180 µg/mL	No
Voriconazole	11 µg/mL	No

Table 17. Summary of interfering substances (continued)

Name	Concentration Tested	Interference
Oseltamivir	0.399 µg/mL	No
Non-target microorganisms		
Epstein-Barr virus	1E+05 cp/mL	No
Influenza A H1N1-2009	1E+05 CEID50/mL	No
Cutibacterium acnes	1E+06 CFU/mL	No
Staphylococcus epidermidis	1E+06 CFU/mL	No
Escherichia coli (non-K1)	1E+06 CFU/mL	No
Staphylococcus aureus	1E+06 CFU/mL	No
Measles Virus	1E+05 TCID50/mL	No

Note: Any solvents or buffers used in the preparation of interfering substances were also tested for possible interference, none was found.

All potentially interfering endogenous and exogenous substances have been evaluated and have been confirmed not to interfere with any of the panel target assays at concentrations potentially found in clinical samples. This is except for Bleach and gDNA, where interference was observed and as such the lowest concentration of the substance causing interference has been determined.

Carryover

A carryover study was performed to evaluate the potential occurrence of cross-contamination between consecutive runs when using the QIAstat-Dx ME Panel on the QIAstat-Dx Analyzer 1.0. Pathogenic CSF samples with alternating high-positive (10^5-10^6 organism/mL) and negative samples, were conducted on two QIAstat-Dx Analyzer 1.0 instruments. No carryover between samples was observed in the QIAstat-Dx ME panel, demonstrating that the system design and recommended sample handling and testing practices are effective in preventing unexpected results due to carryover or cross-contamination between samples.

Repeatability and Reproducibility

For the reproducibility assessment, a multi-site scheme was followed by testing both negative and positive samples at two different study sites with varying workflow variables, such as sites, days, instruments, operators and cartridge lots that could have an impact on the precision of the system. Negative samples consisted of artificial CSF. Positive combined samples consisted of artificial CSF spiked with a representative panel of pathogens covering all types targeted by the QIAstat-Dx ME Panel (i.e. DNA virus, RNA virus, gram (+) bacteria, gram (-) bacteria and yeast) at the limit of detection (1x LoD) and at 3x LoD. For each site, testing was performed across 5 non-consecutive days per mix with 9 replicates per day per mix (leading to a total of 45 replicates per target, concentration, and site), a minimum of 9 different QIAstat-Dx Analyzers per site, and at least 3 operators on each testing day.

Reproducibility testing was designed to evaluate the critical variables that may impact the performance of the QIAstat-Dx ME Panel in the context of its routine and intended use.

For the repeatability study, the same sample panel was tested following a single-site scheme. Repeatability testing was designed to evaluate the precision of a QIAstat-Dx ME Panel cartridge under similar (*intra* laboratory) conditions. Repeatability study was assessed with the same samples used for Reproducibility testing using Site 1.

Table 18. Proportion of Correct Repeatability Results

Grouping Variable(s)		Proportion		Two-Sided 95% Confidence Limit	
Cryptococcus neoformans/gattii	1x LoD	60/60	100.00%	94.04%	100.00%
	3x LoD	61/61	100.00%	94.13%	100.00%
Enterovirus	1x LoD	60/60	100.00%	94.04%	100.00%
	3x LoD	61/61	100.00%	94.13%	100.00%

Table 18. Proportion of Correct Repeatability Results (continued)

Grouping Variable(s)		Proportion		Two-Sided 95% Confidence Limit	
Listeria monocytogenes	1x LoD	60/60	100.00%	94.04%	100.00%
	3x LoD	61/61	100.00%	94.13%	100.00%
Mycoplasma pneumoniae	1x LoD	60/60	100.00%	94.04%	100.00%
	3x LoD	61/61	100.00%	94.13%	100.00%
Negative	Negative	60/60	100.00%	94.04%	100.00%
Streptococcus agalactiae	1x LoD	60/60	100.00%	94.04%	100.00%
	3x LoD	61/61	100.00%	94.13%	100.00%
Varicella Zoster Virus	1x LoD	51/60	85.00%	73.43%	92.90%
	3x LoD	60/61	98.36%	91.20%	99.96%

Table 19. Proportion of Correct Reproducibility Results

Grouping variable(s)			Proportion		Two-sided 95% Confidence Limit	
Target	Concentration	Site	Fraction	Percentage	Lower	Upper
Cryptococcus neoformans/ gattii	1xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
	3xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%

Table 19. Proportion of Correct Reproducibility Results (continued)

Grouping variable(s)			Proportion		Two-sided 95% Confidence Limit	
Target	**Concentration**	**Site**	**Fraction**	**Percentage**	**Lower**	**Upper**
Enterovirus	1xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
	3xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
Listeria monocytogenes	1xLoD	1	45/45	100.00%	92.13%	100.00%
		2	44/45	97.78%	88.23%	99.94%
		All	89/90	98.89%	93.96%	99.97%
	3xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
Mycoplasma pneumoniae	1xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
	3xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
Negative	Negative	1	44/44	100.00%	91.96%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	89/89	100.00%	95.94%	100.00%

Table 19. Proportion of Correct Reproducibility Results (continued)

Grouping variable(s)			Proportion		Two-sided 95% Confidence Limit	
Target	**Concentration**	**Site**	**Fraction**	**Percentage**	**Lower**	**Upper**
Streptococcus agalactiae	1xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
	3xLoD	1	45/45	100.00%	92.13%	100.00%
		2	45/45	100.00%	92.13%	100.00%
		All	90/90	100.00%	95.98%	100.00%
Varicella Zoster Virus	1xLoD	1	39/45	86.67%	73.21%	94.95%
		2	38/45	84.44%	70.54%	93.51%
		All	77/90	85.56%	76.57%	92.08%
	3xLoD	1	44/45	97.78%	88.23%	99.94%
		2	45/45	100.00%	92.13%	100.00%
		All	89/90	98.89%	93.96%	99.97%

In conclusion, reproducibility and repeatability of the tests performed with QIAstat-Dx Meningitis Panel have been met.

Appendices

Appendix A: Installing the Assay Definition File

The Assay Definition File of the QIAstat-Dx ME Panel must be installed on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 prior to testing with QIAstat-Dx ME Panel Cartridges.

Note: Whenever a new version of the QIAstat-Dx ME Panel assay is released, the new QIAstat-Dx ME 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 file type) must be saved onto a USB Drive prior to installation on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0. This USB Drive must be formatted with a FAT32 file system.

To import assays to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, proceed with the following steps:

1. Insert the USB storage device containing the Assay Definition File into one of the USB ports on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0.
2. Press the Options button and then select Assay Management. The Assay Management screen appears in the Content area of the display (Figure 25).

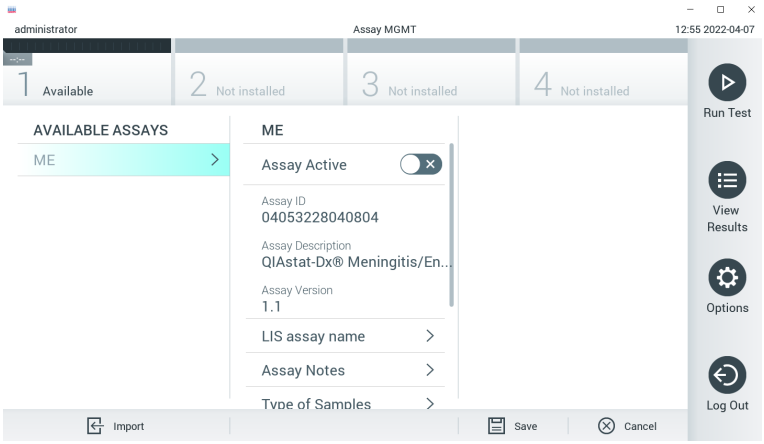


Figure 26. Assay Management screen.

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. If a previous version of the QIAstat-Dx ME Panel was installed, a dialog will appear to override the current version by the new one. Press Yes to override.
7. The assay becomes active by selecting Assay Active (Figure 26).

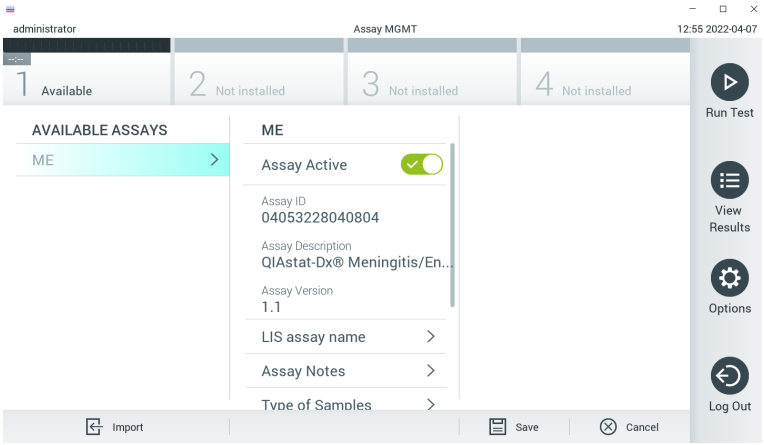


Figure 27. Activating the assay.

8. Assign the active assay to the user by pressing the Options button and then the User Management button. Select the user who should be allowed to run the assay. Next, select Assign Assays from the User Options. Enable the assay and press the Save button (Figure 27).

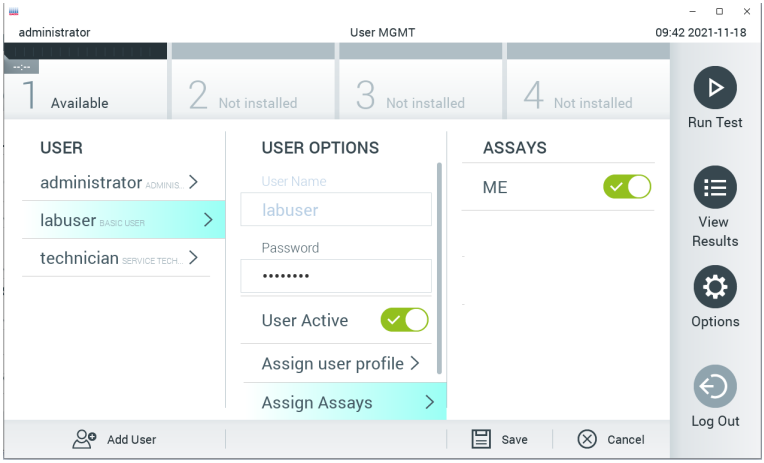


Figure 28. Assigning the active assay.

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 or the QIAstat-Dx Analyzer 2.0 hardware module, in charge of executing tests on QIAstat-Dx ME 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 or the QIAstat-Dx Analyzer 2.0 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 or the QIAstat- Dx Analyzer 2.0. The Analytical Module contains the hardware and software for sample testing and analysis.

- QIAstat-Dx Analyzer 2.0: The QIAstat-Dx Analyzer 2.0 consists of an Operational Module PRO and an Analytical Module. The Operational Module PRO includes elements that provide connectivity to the Analytical Module and enables user interaction with the QIAstat-Dx Analyzer 2.0. The Analytical Module contains the hardware and software for sample testing and analysis.
- QIAstat-Dx ME 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 meningitis/encephalitis pathogens.
- IFU: Instructions For Use.
- Main port: In the QIAstat-Dx ME 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).
- Operational Module PRO (OM PRO): The dedicated QIAstat-Dx Analyzer 2.0 hardware that provides the user interface for 1-4 Analytical Modules (AM).
- PCR: Polymerase Chain Reaction.
- RT: Reverse Transcription.
- User: A person who operates the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0/QIAstat-Dx ME 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 ME Panel Cartridge, QIAGEN ASSUMES NO LIABILITY WHATSOEVER AND

DISCLAIMS ANY EXPRESS OR IMPLIED WARRANTY RELATING TO THE USE OF THE QIAstat-Dx ME 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.

References

1. Meningitis and Encephalitis Fact Sheet. **https://www.ninds.nih.gov/disorders/patient-caregiver-education/fact-sheets/meningitis-and-encephalitis-fact-sheet**

2. Meningitis. **https://www.cdc.gov/meningitis/index.html**

Symbols

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

	Contains reagents sufficient for <N> reactions
	Use by
	In vitro diagnostic medical device
	CE marking for European Conformity
	Catalog number
	Lot number
	Material number (i.e., component labeling)
Rn	R is for revision of the Handbook and n is the revision number
	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
	Flammable, risk of fire
	Corrosive, risk of chemical burn
	Health hazard, risk of sensitization, carcinogenicity
	Risk of harm

Revision History

Date	Changes
Revision 2 April 2022	• Updated images to reflect ADF SW Version 1.1 • Update to the Clinical Performance section.
Revision 3 September 2022	• Correction in Table 9
Revision 4 January 2024	• Corrections in Table 6, Table 7 (Correction of Clinical sample number and deletion of pathogen table in contrived sample subgroup), Table 9 (Correction to include VZV Oka strain), Table 11 (Correction of pathogen for strains Li 23 Serotype 4a, FSL J2-064, Gibson and EGDe to L. monocytogenes) and Table 12 (Removal of HSV1 ATCC-2011-1) • Correction of concentration of Fungal targets in Exclusivity in-vitro testing • Update to clarify contamination precautions in Laboratory precautions section • Inclusion of QIAstat-Dx Analyzer 2.0 and Operational Module PRO • Update of Reagent Storage Handling header to Cartridge Storage handling for clarification • Addition of statement "For handling of damaged cartridge refer to chapter Safety Information" to the following chapters:, Cartridge storage and handling and Laboratory Precautions. • Addition of clarification in the Clinical Performance section to add: Out of the 585 eligible clinical specimens, 579 produced an evaluable result, 6 samples which were considered in the analysis that had a positive with warning result.

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