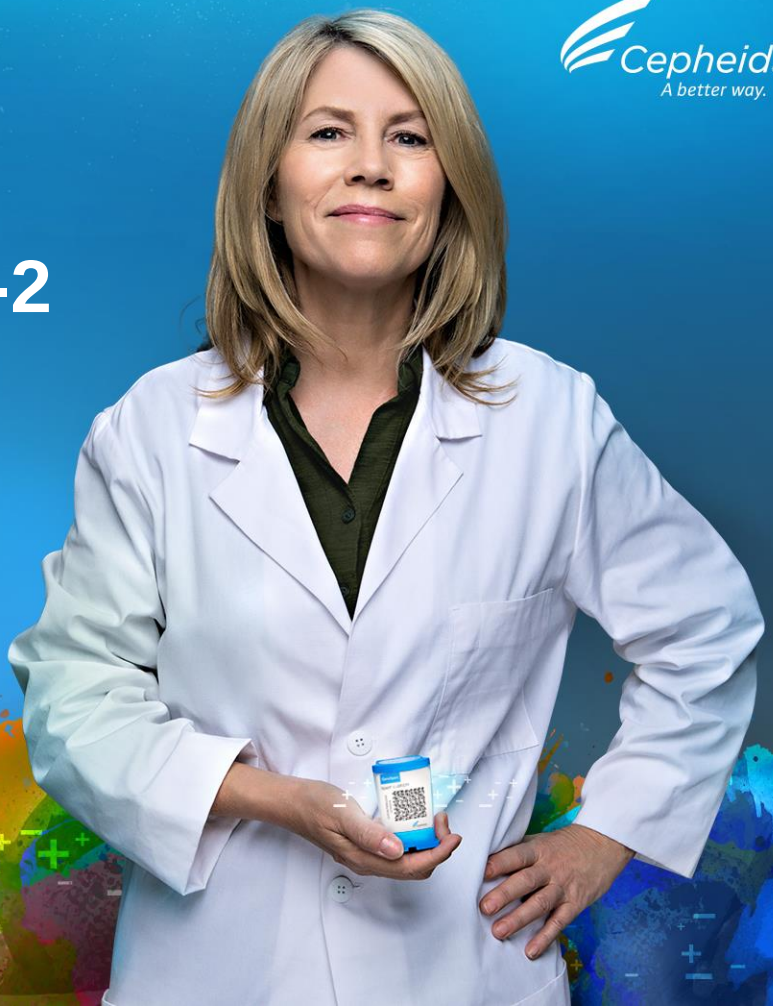
Assay Training:
Xpert® Xpress SARS-CoV-2

For Use Under an Emergency Use Authorization (EUA) Only



302-3759 Rev. A May 2020

Training Agenda

- **Xpert® Xpress SARS-CoV-2**
  - Reagents
  - Sample collection
  - Kit storage and handling
  - Preparing the cartridge
  - Quality Controls
  - Results analysis
- **Discussion**

Training Objectives

- **At the end of the training, users will be able to:**
  - Properly store and handle the Xpert® Xpress SARS-CoV-2 kit
  - Follow proper laboratory safety precautions
  - Collect and store appropriate specimen(s)
  - Prepare a cartridge and run the Xpert® Xpress SARS-CoV-2 test
  - Report the various software generated results
  - Understand the Xpert® Xpress SARS-CoV-2 control strategy

The Cepheid Solution

- Detection of SARS-CoV-2
- On-board internal controls for each sample
  - Probe Check Control (PCC)
  - Sample Processing Control (SPC)
- Closed cartridge system minimizes risk of contamination
- On-demand results
- Random access

Intended Use

- The Xpert Xpress SARS-CoV-2 test is a rapid, real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in either nasopharyngeal swab and/or nasal wash/ aspirate specimens collected from individuals suspected of COVID-19 by their healthcare provider.
- Testing of nasopharyngeal swab and nasal wash/aspirate specimens using the Xpert Xpress SARS-CoV-2 test run on the GeneXpert Dx and GeneXpert Infinity systems is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high and moderate complexity tests.
- Testing of nasopharyngeal swab specimens using the Xpert Xpress SARS-CoV-2 test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is authorized to be distributed and used in patient care settings outside of the clinical laboratory environment.

Intended Use (continued)

- Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in nasopharyngeal swab specimens and/or nasal wash/ aspirate specimens during the acute phase of infection. Positive results are indicative of active infection with SARS-CoV-2; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
- Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.
- Testing with the Xpert Xpress SARS-CoV-2 test is intended for use by trained operators who are proficient in performing tests using either GeneXpert Dx, GeneXpert Infinity and/or GeneXpert Xpress systems. The Xpert Xpress SARS-CoV-2 test is only for use under the Food and Drug Administration's Emergency Use Authorization.

Xpert® Xpress SARS-CoV-2 Requirements

GeneXpert® Systems

- GeneXpert® Dx software **version 4.7b** or higher
- Xpertise software **version 6.4b** or higher

Test Kits

- US-IVD: XPRSARS-COV2-10

Materials Required but not Provided

- 3mL viral transport media
- Nasopharyngeal swab or nasal aspirate/ wash
- Personal Protective Equipment (PPE)
- 1:10 Bleach
- 70% ethanol or denatured ethanol

Optional

- Uninterruptible Power Supply /Surge Protector
- Printer

Good Laboratory Practice

Personel Protective Equipment (PPE)	• Wear clean lab coats, safety glasses, and gloves • Change gloves between processing samples
Lab Bench area	• Clean work surfaces routinely with: ✓ 1:10 dilution of household bleach* ✓ 70% Ethanol Solution ** Final Active Chlorine concentration should be 0.5% regardless of the household bleach concentration in your country* • After cleaning, ensure work surfaces are dry
Specimens, Samples, and Kits Storage	• Store specimens and sample away from kit to prevent contamination
Equipment(s)	• Use filtered pipette tips when recommended • Follow the manufacturer's requirements for calibration and maintenance of equipment(s)

Kit Handling

Xpert® SARS-CoV-2 Kit Contents

Xpert® Xpress SARS-CoV-2	
Catalog Number	US-IVD: XPRSARS-COV2-10
Tests Per Kit	10
Kit CD	Assay Definition File (ADF)
	Assay Import Instructions
	Flyer- instructions to access on-line reference materials including Instructions For Use
Disposable Transfer Pipettes	12
Storage	2- 28 ˚C

Cartridges contain chemically hazardous substances-please see Instructions For Use and Safety Data Sheet for more detailed information.

Xpert® Xpress SARS-CoV-2 Kit Storage and Handling

- Store the Xpert® Xpress SARS-CoV-2 cartridges and reagents at 2–28°C
- Follow your institution's safety procedures for working with chemicals and handling biological samples
- Do not use collection devices that have not been validated by Cepheid

- Open the cartridge lid only when adding the sample, close the lid and proceed with processing
  - Start the test within 30 minutes of adding the sample to the cartridge.

Warnings and Precautions

- Do not shake the cartridge
- Do not use a cartridge… :
  - if it appears wet, has leaked, or if the lid seal appears to have been broken
  - if it appears damaged
  - that has been dropped after removing it from packaging
  - that has been dropped or shaken after you have added the sample
  - that has a damaged reaction tube
  - that has been used; each cartridge is single-use to process one test
  - that is expired
- Do not reuse pipettes

Dispose of cartridges and reagents according to your institution's and country's guidelines for disposal of hazardous materials.

Warnings and Precautions

- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents and require use of standard precautions.

- Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures.

- If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

Limitations

- Performance of the Xpert Xpress SARS-CoV-2 has only been established in nasopharyngeal swab and/or nasal wash/ aspirate specimens.
- A false negative result may occur if a specimen is improperly collected, transported or handled. False negative results may also occur if inadequate numbers of organisms are present in the specimen.
- As with any molecular test, mutations within the target regions of Xpert Xpress SARS-CoV-2 could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.

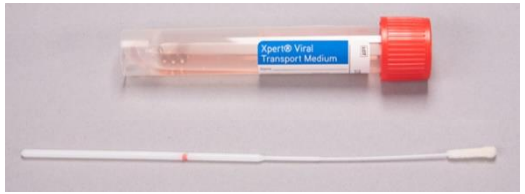
For detailed information, refer to the current Instructions For Use

Specimen Collection, Storage and Transport

Specimen Collection

Specimen Type:
nasopharyngeal swab
and/or
nasal wash/ aspirate specimens

Place into a viral transport tube containing 3mL transport medium
to preserve and transport respiratory virus specimens



Nasopharyngeal swab

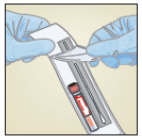
Refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19)
https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

Specimen Collection- Nasopharyngeal Swab

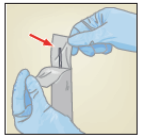
Nasopharyngeal Specimen Collection

For use with Xpert® Nasopharyngeal Sample Collection Kit - Catalog # SWAB/B-100

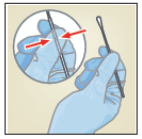
1 Open the package that contains the swab and transport medium tube. Set the tube aside before collecting the specimen.



2 Open the swab wrapper and remove the swab, taking care not to touch the tip of the swab to any surface.

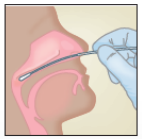


3 Hold the swab in your hand, pinching in the middle of the swab shaft on the scoreline.



4 Gently insert the swab into the nostril until you touch the posterior nasopharynx.

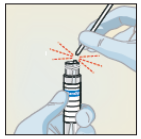
Rotate swab several times.



5 Remove the cap from the tube. Insert the swab into the transport medium.

6 Break the swab shaft against the side of the tube at the scoreline.

Avoid splashing contents on the skin. Wash with soap and water if exposed.



7 Replace the cap on the tube and close tightly.

For Xpert Xpress Flu and Xpert Xpress Flu/RSV:
Transport the specimen at 2-8°C.
Specimen may be stored for 24 hours at 15-30°C or up to 7 days at 2-8°C.

For Xpert Xpress SARS-CoV-2:
Specimen may be stored for 8 hours at 15-30°C or up to 7 days at 2-8°C.

* SWAB/B-100 contains Copan UTM 330C and Copan nylon swab 503CS01

In Vitro Diagnostic Use IVD

In Vitro Diagnostic Use CE IVD

301-6052, Rev. D March 2020

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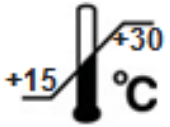
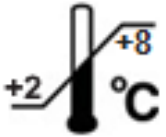
Specimen Collection- Nasal Wash/Aspirate

1. Transfer 600 µL of the sample into the 3 mL Viral Transport Medium tube.
2. Cap the tube.

Specimen Transport and Storage

Sample type	Transport and Storage Conditions
Viral Transport Medium containing nasopharyngeal swab	 Up to 8 hours  Up to 7 days

Cartridge Preparation

Proper Cartridge Handling Techniques

Correct

- Do not touch the reaction tube
- Keep the cartridge upright
- Do not tilt after sample is added

Incorrect

Cartridge Preparation

Xpert® Xpress SARS-CoV-2 Cartridge Preparation

Refer to the package insert for detailed instructions, precautions, and warnings.

For a copy of the SDS, visit
www.cepheid.com or
www.cepheidinternational.com

Contact information for all Cepheid Technical Support offices is available on our website:
www.cepheid.com/en/CustomerSupport.

Cepheid®
A better way.

1 Take one Xpert cartridge for each sample.

2 Rapidly invert the tube 5 times.

3 Open the cartridge lid.

4 Using a clean 300 µL pipette (supplied), transfer 300 µL (one draw), of the sample to the opening of the cartridge.

5 Close the cartridge lid.

6 Start the test within the timeframe specified in the package insert.

For use under the Emergency Use Authorization (EUA) only.

302-3755, Rev. A March 2020

Cepheid®

Run a Test

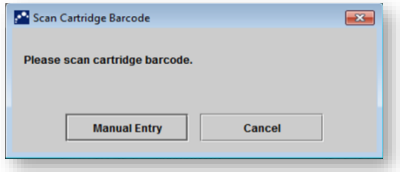
1 Create Test

GeneXpert

Start the test within 30 minutes after adding the sample to the cartridge

2 Scan barcode :

Cartridge/ Patient and/or Sample ID

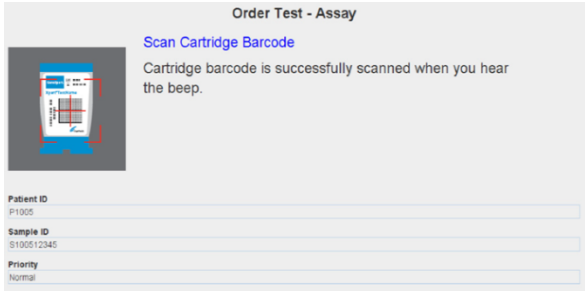


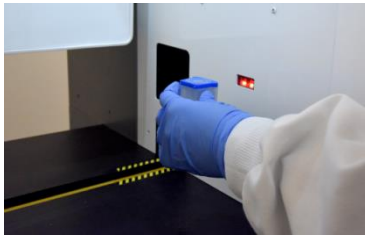
By default, do not click on **Manual Entry** or **Cancel**

3 Scan the cartridge

GeneXpert Infinity

Place the cartridge on the conveyor within 30 minutes of adding the sample.





"For complete details on how to run a test, refer to the Instructions For Use and the GeneXpert® Dx or Xpertise™ Operator Manuals.

Create a Test on GeneXpert® Dx Software

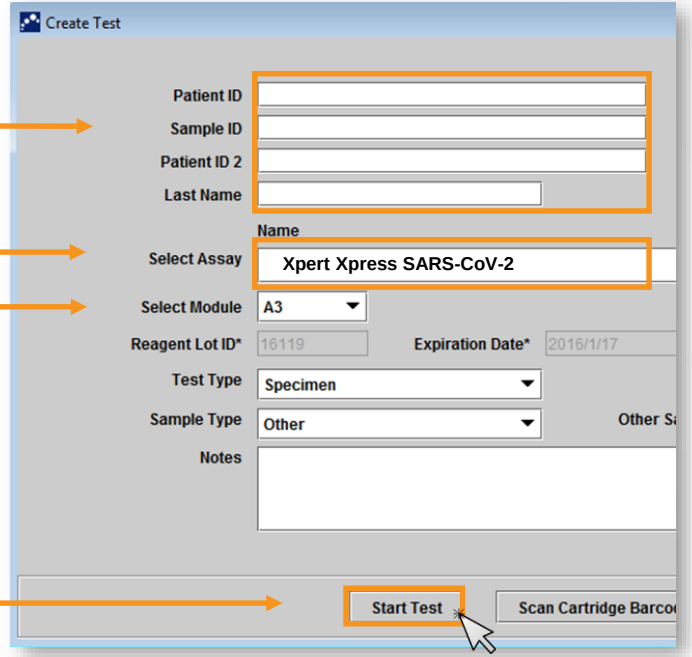
4 Complete the fields as required

5 The Assay Protocol is selected automatically

6 The module is selected automatically

7 Click on Start Test

8 A green light will flash on the module
Load the cartridge into module and close the door

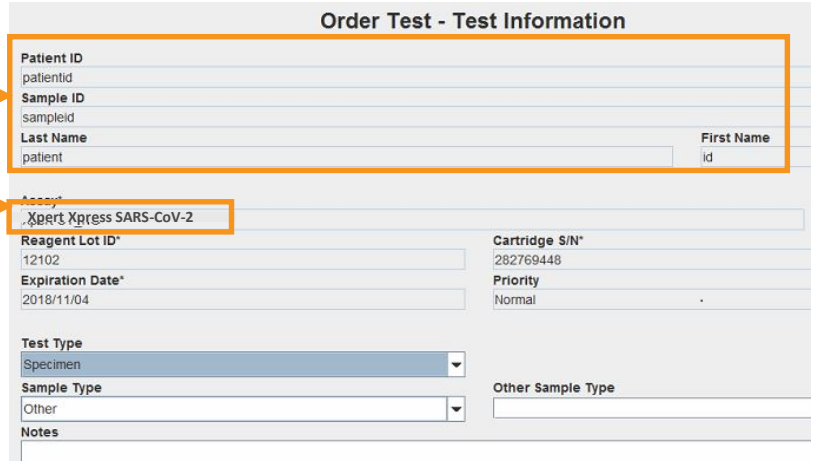


Create a Test on Xpertise™ Software

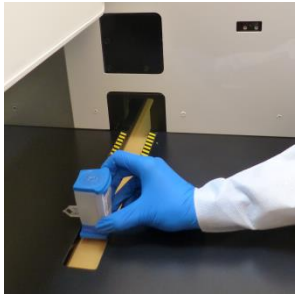
4 Complete the fields as required

5 The Assay Name Protocol is selected automatically

6 Click on SUBMIT



7 Place the cartridge into the conveyor belt



Automated Xpert® Protocol

1. Sample is added to the cartridge
2. The cartridge is loaded into the System
3. Nucleic acids are purified
4. Purified nucleic acids mix with the PCR reagents
5. Simultaneous amplification and detection occurs
6. Results are ready to view

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Quality Controls

Assay Control Strategy

CONTROL

- **Xpert® Xpress SARS-CoV-2 Quality Controls**
  - Each Xpert cartridge is a self-contained test device
  - Cepheid designed specific molecular methods to include internal controls that enable the system to detect specific failure modes within each cartridge
    - Sample Processing Control (SPC)
    - Probe Check Controls (PCC)

Refer to 301-4868 GeneXpert Quality Control Features for All Cepheid Xpert Assays

Internal Quality Controls

- **Probe Check Controls (PCC)**
  - Before the PCR step, fluorescence signal is measured on all probes and compared with default factory settings to monitor
    - reagent rehydration
    - PCR tube filling
    - probe integrity
    - dye stability

- **Sample Processing Controls (SPC)**
  - non-infectious spore in each cartridge
    - Verifies adequate sample processing
    - Verifies lysis, presence of the organism and detects PCR inhibition
    - Should be positive in a negative sample
    - Can be positive or negative in a positive sample

Commercially Available External Controls

Vendor	Description	Configuration	Storage
SeraCare **AccuPlex™ SARS-CoV-2 Reference Material Kit** Catalog # 0505-0126	Positive Control	1.5mL	2-8˚C or -20˚C
	Negative Control	1.5mL	2-8˚C or -20˚C

1. Open the cartridge lid.
2. Rapidly invert the external control tube 5 times.
3. Using a clean transfer pipette, transfer one draw of the external control sample into the large opening (Sample Chamber) in the cartridge.
4. Close cartridge lid.

To minimize degradation of the control material, return any unused sample to the recommended storage conditions immediately after use.

- Many other vendors for quality control material are also available in addition to the one outlined above.
- External controls should be used in accordance with local, state accrediting organizations, as applicable

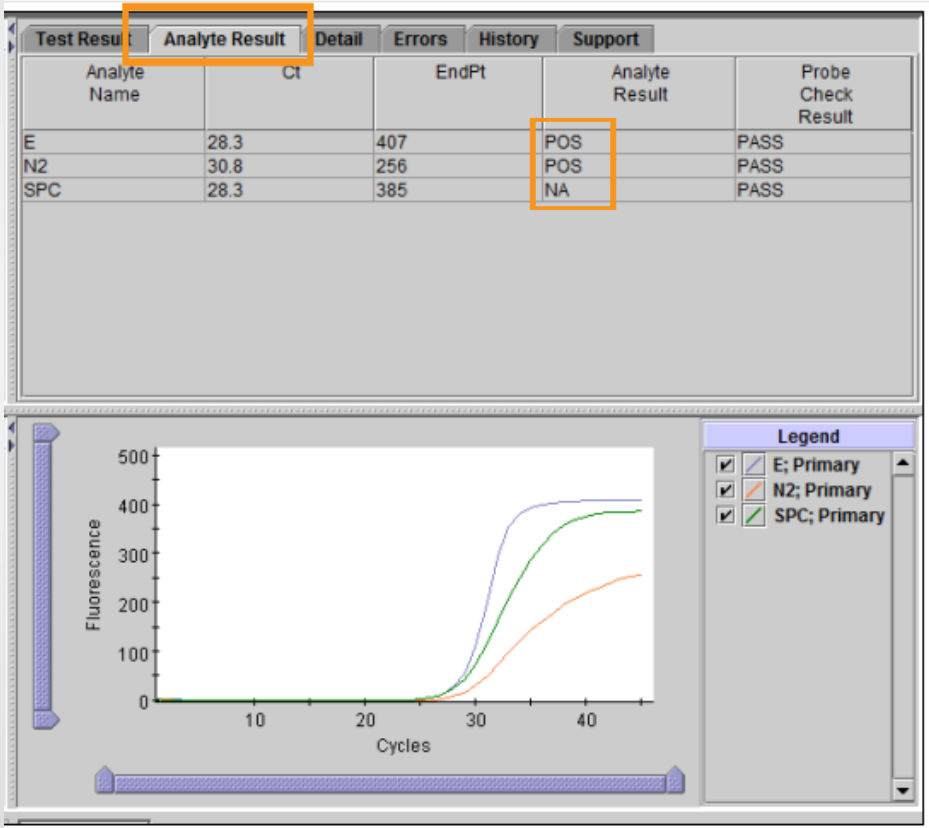
Result Interpretation

Results Summary

Result displayed	N2	E	SPC
SARS-CoV-2 POSITIVE	+	+	+/-
	+	-	
SARS-CoV-2 PRESUMPTIVE POSITIVE	-	+	+/-
SARS-CoV-2 NEGATIVE	-	-	+
INVALID	-	-	-
ERROR	NO RESULT	NO RESULT	NO RESULT
No Result	NO RESULT	NO RESULT	NO RESULT

SARS-CoV-2 POSITIVE

Test Result | SARS-CoV-2 POSITIVE

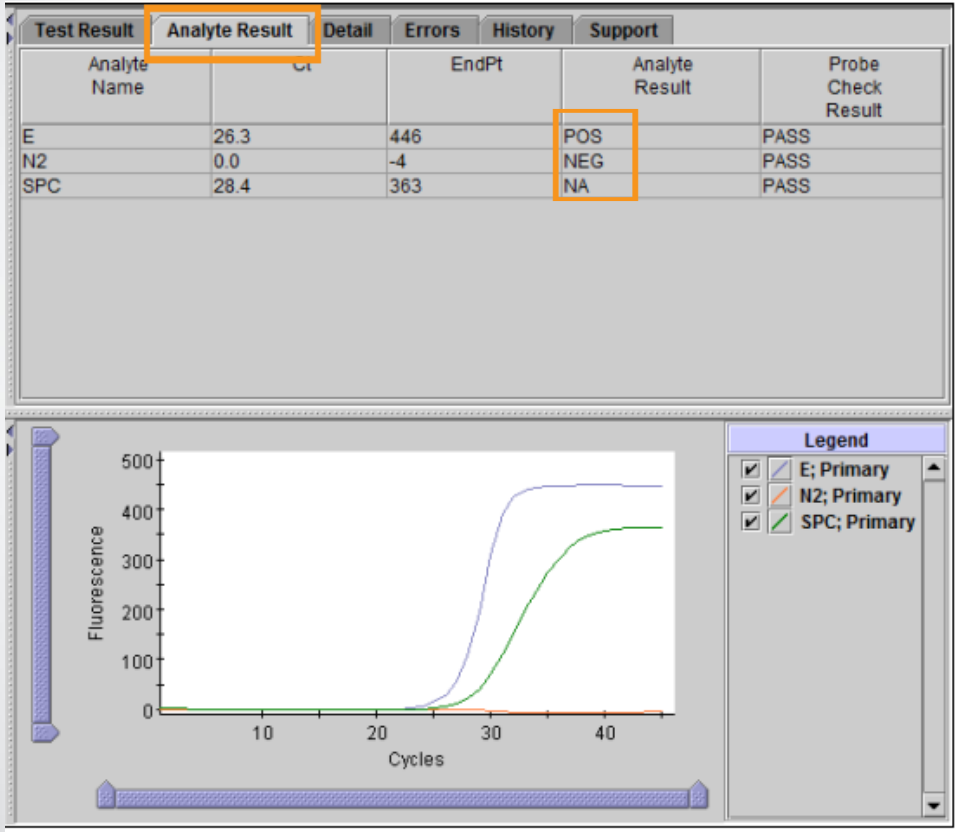


The 2019 novel coronavirus (SARS-CoV-2) target nucleic acids are detected.

- The SARS-CoV-2 signal for the N2 nucleic acid target or signals for both nucleic acid targets (N2 and E) have a Ct within the valid range and endpoint above the minimum setting
- SPC: NA; SPC is ignored because coronavirus target amplification occurred
- Probe Check: PASS; all probe check results pass

SARS-CoV-2 PRESUMPTIVE POS

Test Result	SARS-CoV-2 PRESUMPTIVE POS

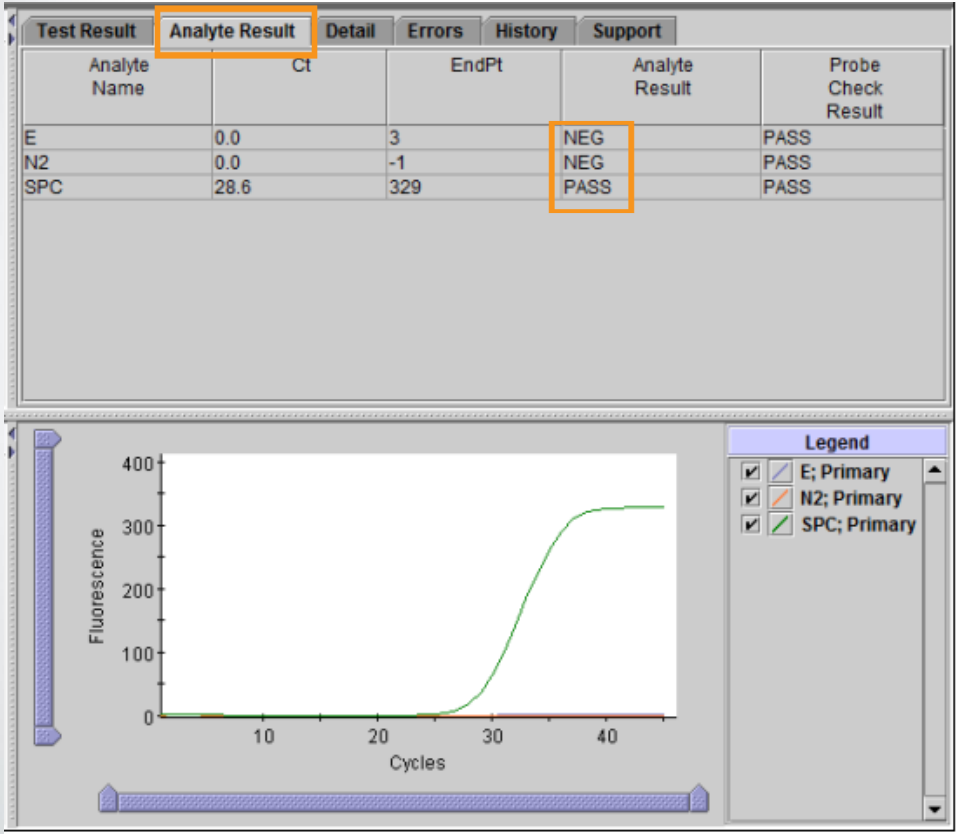


The 2019 novel coronavirus (SARS-CoV-2) nucleic acids may be present.
Sample should be retested. For samples with a repeated Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.

- The SARS-CoV-2 signal for only the E nucleic acid target has a Ct within the valid range and endpoint above the minimum setting
- SPC: NA; SPC is ignored because a target amplification has occurred.
- Probe Check: PASS; all probe check results pass

SARS-CoV-2 NEGATIVE

Test Result | SARS-CoV-2 NEGATIVE



The 2019 novel coronavirus (SARS-CoV-2) target nucleic acids are not detected.

- The SARS-CoV-2 signals for two nucleic acid targets (N2 and E) do not have a Ct within the valid range and endpoint above the minimum setting
- SPC: PASS; SPC has a Ct within the valid range and endpoint above the minimum setting
- Probe Check: PASS; all probe check results pass

Troubleshooting

Factors That Negatively Affect Results

- Improper specimen collection
  - The performance of this assay with other specimen types or samples has not been evaluated.
- Inadequate numbers of organisms are present in the specimen.
- Improper transport or storage of collected specimen
  - Storage and transport conditions are specimen specific
  - Refer to the Package Insert for the appropriate handling instructions
- Improper testing procedure
  - Modification to the testing procedures may alter the performance of the test
  - Careful compliance with the package insert is necessary to avoid erroneous results

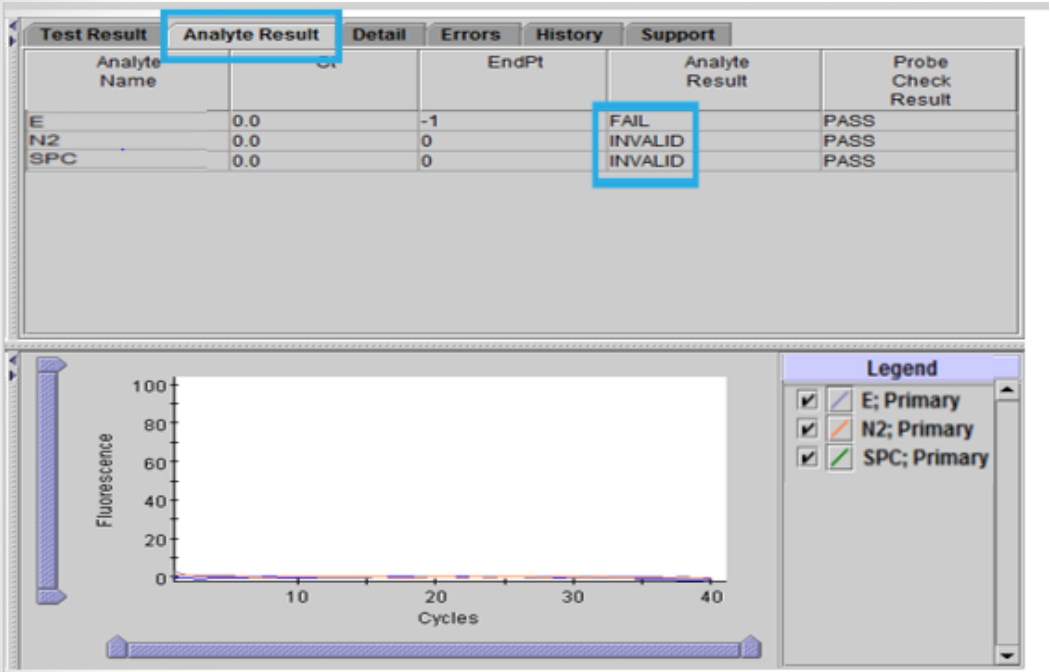
Reasons to Repeat the Assay

- A **PRESUMPTIVE POSITIVE** indicates the 2019 novel coronavirus (SARS-CoV-2) nucleic acids may be present.
- An **INVALID** result indicates that the control SPC failed. The sample was not properly processed, PCR is inhibited, or the sample was not properly collected.
- An **ERROR** result could be due to, but not limited to, Probe Check Control failure, system component failure, or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, cartridge failed integrity test, the operator stopped a test that was in progress, or a power failure occurred.

If an External Control fails to perform as expected, repeat external control test and/or contact Cepheid for assistance.

INVALID Result

INVALID



SPC does not meet acceptance criteria. Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined.

- SPC: FAIL; SPC and SARS-CoV-2 signals do not have a Ct within valid range and endpoint below minimum setting
- Probe Check – PASS; all probe check results pass

Possible Causes

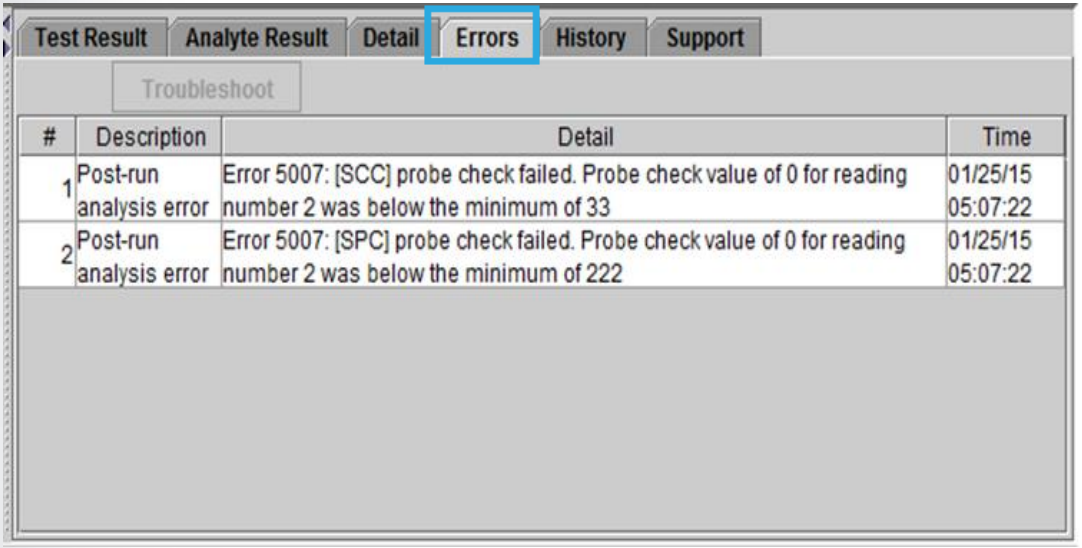
- Improper sample collection or preparation
- Presence of interfering substances in the sample

Solution

- Repeat the test with a new cartridge

ERROR Result

ERROR



Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure in IFU (Section 17.2).

- SARS-CoV-2: NO RESULT
- SPC: NO RESULT
- Probe Check: FAIL; all or one of the probe check results fail

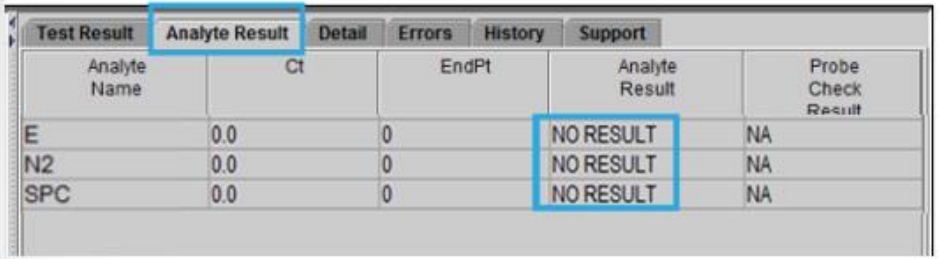
If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.

Solution

- Repeat the test with a new cartridge.

NO RESULT

Test Result | NO RESULT



Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress.

- SARS-CoV-2: NO RESULT
- SPC: NO RESULT
- Probe Check: NA (not applicable)

Possible Causes

A NO RESULT indicates that insufficient data were collected.

- Test was stopped with stop test button
- Electrical failure

Solution

- Secure the power
- Repeat the test with a new cartridge.

Retest Procedure

1

Discard used cartridge

Follow your institution's safety guidelines for disposal of cartridges

2

Obtain the residual specimen, mix according to Package Insert

If the leftover specimen volume is insufficient, or the retest continues to return an INSTRUMENT ERROR or NO RESULT, collect a new specimen.

3

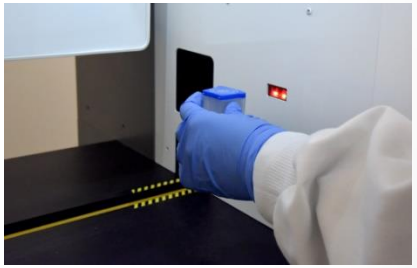
Obtain a new cartridge

Label appropriately as retest on the new cartridge

Process the specimen per the Package Insert

4

Run the test on the System



Technical Assistance

- Before contacting Cepheid Technical Support, collect the following information:
  - Product name
  - Lot number
  - Serial number of the System
  - Error messages (if any)
  - Software version and, if applicable, Computer Service Tag number

- Log your complaint online using the following link ***http://www.cepheid.com/us/support*** **:**

Create a Support Case


Thank You.
www.Cepheid.com
GeneXpert
Xpert
Cepheid
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