GenMark Dx

ePlex®
SARS-CoV-2 Test
Assay Manual

For Use Under the Emergency Use Aut[illegible]ization On[illegible]

EUA

For *in vitro* D[illegible]stic Use [illegible]y

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INTENDED USE

The ePlex SARS-CoV-2 Test is intended for the qualitative detection of SARS-CoV-2 nucleic acid in nasopharyngeal swab specimens (NPS) eluted in viral transport media (VTM) collected from individuals suspected of COVID-19 by their health care provider. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform moderate or high complexity tests.

Results are for the detection of SARS-CoV-2 RNA that are detectable in NPS specimens during 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 patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

Testing with the ePlex SARS-CoV-2 Test is intended for use by qualified and trained laboratory personnel who are have been trained and are proficient in performing testing on the ePlex system. The ePlex SARS-CoV-2 Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

SUMMARY AND EXPLANATION OF TEST

An outbreak of pneumonia caused by a novel coronavirus (SARS-CoV-2) in Wuhan City, Hubei Province, China was initially reported to the WHO on December 31, 2019. On January 31, 2020, Health and Human Services Secretary Alex M. Azar II declared a public health emergency for the United States to aid the nation's healthcare community in response to COVID-19. The emergence and rapid spread of SARS-CoV-2 to numerous areas throughout the world necessitates preparedness and response in public health laboratories, as well as healthcare facilities and other areas of society in general. The availability of specific and sensitive assays for the detection of the virus are essential for accurate diagnosis of cases, assessment of the extent of the outbreak, monitoring of intervention strategies, and surveillance studies.

The ePlex SARS-CoV-2 Test is an automated qualitative nucleic acid *in vitro* diagnostic test that aids in the detection of SARS-CoV-2 and diagnosis of COVID-19 using *The True Sample-to-Answer Solution*® instrument. The test is based on nucleic acid amplification technology and each test cartridge includes all reagents needed to extract, amplify and detect SARS-CoV-2 RNA in nasopharyngeal swab samples.

PRINCIPLES OF TECHNOLOGY

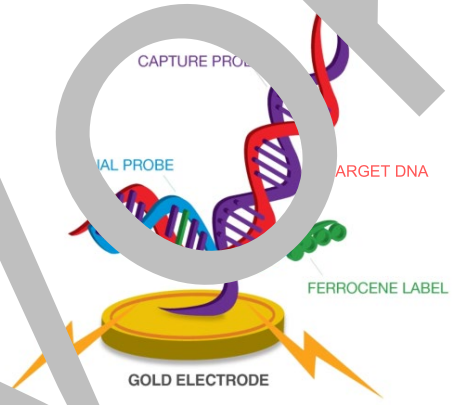
The True Sample-to-Answer Solution ePlex instrument automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and GenMark's eSensor® technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA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

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

A sample is loaded onto the ePlex cartridge and nucleic acids are extracted and purified from the specimen via magnetic solid phase extraction. A reverse transcription step is performed to generate complementary DNA from the viral RNA, followed by PCR to amplify the target. Exonuclease digestion creates single-stranded DNA in preparation for eSensor detection technology.

The target DNA is mixed with ferrocene-labeled signal probes that are complementary to the specific targets on the panel. Target DNA hybridizes to its complementary signal probe and capture probe which are bound to gold-plated electrodes, as shown below in **Figure 1**. The presence of each target is determined by voltammetry which generates specific electrical signals from the ferrocene-labeled signal probe.

Figure 1: Hybridization complex. Target-specific capture probes are bound to the gold electrodes in the eSensor microarray on the ePlex cartridge. The amplified target DNA hybridizes to the capture probe and to a complementary ferrocene-labeled signal probe. Electrochemical analysis determines the presence or absence of targets using voltammetry.



MATERIALS PROVIDED

Table 1: *The True Sample-to-Answer Solution*® ePlex SARS-CoV-2 Test Kit Contents

Product	Item number	Components (quantity)	Storage
ePlex SARS-CoV-2 Test	EA008222	ePlex SARS-CoV-2 Test Cartridge (12)	2–8 ºC
		Optional Sample Delivery Device – RP Panel (12)	2–8 ºC

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

REAGENT STORAGE, STABILITY, AND HANDLING

- Store the ePlex SARS-CoV-2 Test kit components at 2–8 ºC.
- Do not open a cartridge pouch until you are ready to perform testing.

MATERIALS REQUIRED BUT NOT PROVIDED

Equipment

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

Consumables

- Pipette tips, aerosol resistant, RNase/DNase-free
- Disposable, powder free gloves
- 10% bleach for decontamination of appropriate surfaces
- 70% ethanol or isopropyl alcohol

WARNINGS AND PRECAUTIONS

General

- For use under Emergency Use Authorization Only.
- For *in vitro* diagnostic use only.
- This test has not been FDA cleared or approved; this test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests.
- This test has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens.
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
- Positive results are indicative of SARS-CoV-2 RNA.
  Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions.
  Use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Any deviation from the procedures and guidelines may affect optimal test performance.
- Do not reuse ePlex SARS-CoV-2 Test kit components.
  Do not use a reagent that is damaged.
- Follow the procedure as described in this Assay Manual. Read all instructions before starting the test.

Safety

- Handle all specimens and waste materials as if they were capable of transmitting infectious agents in accordance with Universal Precautions. Refer to *Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS-CoV-2* https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html.
- Do not eat, smoke, drink, apply cosmetics, or handle contact lenses in areas where reagents or human specimens are handled.
- Observe safety guidelines such as wearing proper protective equipment including laboratory coats, gowns, gloves, eye protection, and a biological safety cabinet as outlined in *Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition* https://www.cdc.gov/labs/BMBL.html.
- Follow routine laboratory safety procedures for handling of reagents (*e.g.*, do not pipette by mouth, wear appropriate protective clothing and eye protection).
- Follow national biological safety recommendations for handling biological samples.
- If infection with SARS-CoV-2 is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent) prior to processing a specimen.
- Immediately clean up any spill containing potentially infectious material with a 0.5-1% (w/v) sodium hypochlorite (20% v/v bleach).
- Dispose materials used in this test, including reagents, specimens, and used vials, in accordance with all federal, state, and local regulations.
- Performance characteristics have been determined with nasopharyngeal swab samples from human patients with signs and symptoms of respiratory infection.
- Specimens should be processed in a Class II (or higher) biological safety cabinet.
- Do not stick fingers or other objects inside the ePlex instrument bays.
- Wash hands thoroughly with soap and water after handling reagents. Launder contaminated clothing prior to re-use.
- Do not puncture or pierce reagent blisters on the ePlex cartridge. Reagents may cause irritation to skin, eyes, and respiratory tract. Harmful if swallowed or inhaled. Contains oxidizing liquids.
- The ePlex SARS-CoV-2 Test cartridge contains chemicals that are classified as hazardous. Review the Safety Data Sheets (SDS) before use, and in cases of exposure, refer to the SDS for more information.
- To minimize the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.
- Contamination of the sample may occur if the sample is loaded in an area where PCR amplicons or respiratory pathogens are generated. Avoid loading sample in areas that are potentially contaminated with PCR amplicon.

SPECIMEN COLLECTION, HANDLING, AND STORAGE

Nasopharyngeal Swab Collection – Nasopharyngeal swab specimen collection should be performed according to standard technique and placed in viral transport media.

Minimum Sample Volume – 200 µL nasopharyngeal swab specimen in viral transport media is required for testing.

Transport and Storage – Clinical specimens can be stored at room temperature (15–30 ºC) for up to 12 hours or refrigerated at 2-8 ºC for up to 10 days after collection in transport media. Specimens can also be stored at -20 ºC or -80 ºC for 12 months with up to 2 freeze/thaw cycles.

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

Sample Collection

- Refer to the Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Patients Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19) https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html
- Follow manufacturer's instructions for proper use in specimen collection.

Transporting the Specimen

- Specimens must be packaged, shipped, and transported according to the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulations. Follow shipping regulations for UN 3373 Biological Substance, Category B when sending potential SARS-CoV-2 specimens.

PROCEDURE

The ePlex SARS-CoV-2 Test has been validated for two workflow options. Instructions for Workflow A, which requires the use of the Sample Delivery Device, and Workflow B, which does not use the Sample Delivery Device, are detailed below.

Procedural Notes

- All frozen samples should be thawed completely before testing.
- Samples should be nasopharyngeal swabs in viral transport media.
- Reagents and cartridge can be used immediately upon removal from 2-8 °C storage. There is no need to equilibrate to room temperature before use.
- Once cartridge is removed from foil pouch, it should be used within 2 hours. Do not open the cartridge pouch until the sample is ready to be tested.
- Once the sample is loaded in the ePlex SARS-CoV-2 Test cartridge, the sample should be tested as soon as possible.
- Do not re-use cartridges or Sample Delivery Devices.
- Do not use a Sample Delivery Device that is empty. Visually verify that the vial contains liquid prior to use by tapping it on the benchtop. Presence of liquid in the vial indicates that the vial can be used for testing. To prevent damage to the Sample Delivery Device, do not centrifuge the Sample Delivery Device.
- Use a new sterile pipette tip for loading each sample.
- If the sample is extremely viscous, avoid pipetting clumps or mucous.
  Do not insert a wet cartridge into the ePlex instrument. If the cartridge or sample has leaked, dispose of cartridge in accordance with all federal, state, and local regulations.
- Samples should be transferred into the ePlex SARS-CoV-2 Test cartridge in an amplicon-free, clean environment.
  Samples, consumables, and lab areas should be protected from aerosol or direct contamination with amplicon. Decontaminate laboratory areas and affected equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
- To mitigate the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.

- Dispose materials used in this test, including reagents, specimens, and used vials, in accordance with all regulations.

Detailed Procedure-Workflow A (With the Sample Delivery Device)

1. Decontaminate the clean area used for setting up the ePlex SARS-CoV-2 Test with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove SARS-CoV-2 Test cartridge pouch and Sample Delivery Device from kit packaging.
3. Open the SARS-CoV-2 Test cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the SARS-CoV-2 Test cartridge.
5. Write the accession ID or place a barcode label with accession ID on the Sample Delivery Device.
6. Vortex the sample for 3-5 seconds.
7. Gently tap the Sample Delivery Device on the counter or bench surface to collect liquid that may have adhered to the sides of the vial.
   NOTE: Contents of vial may adhere to side of vial and inside cap during transit. Visually verify presence of liquid inside vial after tapping vial.
8. Unscrew the purple cap from the Sample Delivery Device.
9. Use a calibrated pipette to aspirate 200 µL of sample and pipette into the Sample Delivery Device.
10. Replace purple cap on Sample Delivery Device. Ensure that cap is securely fastened on the Sample Delivery Device.
11. Vortex the Sample Delivery Device for 10 seconds.
    NOTE: This step should be done immediately before loading sample onto cartridge.
12. Remove the white cover from the top of the Sample Delivery Device cap.
13. Invert the Sample Delivery Device and dispense the entire volume by squeezing the vial and dispensing the drops into the sample loading port of the SARS-CoV-2 Test cartridge.
    NOTE: Minimize dispensing of bubbles into sample loading port.
14. Close the sample loading port by placing the cap over the port and firmly pushing down on the cap to securely seal the sample delivery port.
    NOTE: Bubbles can be present when cap is fully closed.
15. Scan the SARS-CoV-2 Test cartridge using the barcode reader provided with the ePlex instrument.
    NOTE: If an accession ID barcode label is not used, manually enter accession ID with the on-screen keyboard.
    NOTE: The barcode scanner will read both the accession ID barcode (if placed on the cartridge by the operator) and the 2D barcode printed on the cartridge label; however, the barcode scanner will only beep once to indicate that both barcodes have been read.
16. Insert the SARS-CoV-2 Test cartridge into any available bay, indicated by a flashing, white LED light. The test will begin automatically when the cartridge has been inserted into the bay and the pre-test check (cartridge initialization) is completed, indicated by a blue LED light.

Detailed Procedure-Workflow B (Without the Sample Delivery Device)

1. Decontaminate the clean area used for setting up the ePlex SARS-CoV-2 Test with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove SARS-CoV-2 Test cartridge pouch from kit packaging.
   Open the SARS-CoV-2 Test cartridge pouch.
3. Write the accession ID or place a barcode label with accession ID on the SARS-CoV-2 Test cartridge.
5. Vortex the sample for 3-5 seconds.
6. Use a calibrated pipette to aspirate 200 µL of sample and pipette into the sample loading port of the SARS-CoV-2 Test cartridge.

7. Close the sample loading port by sliding the cap over the port and firmly pushing down on the cap to securely seal the sample delivery port.
   NOTE: Bubbles can be present when closing the cap.
8. Scan the SARS-CoV-2 Test cartridge using the barcode reader provided with the ePlex instrument.
   NOTE: If an accession ID barcode label is not used, manually enter accession ID with th screen keyboard.
   NOTE: The barcode scanner will read both the accession ID barcode (if placed o e cartridge by the operator) and the 2D barcode printed on the cartridge label; however, th arcode scanner will only beep once to indicate that both barcodes have been read.
9. Insert the SARS-CoV-2 Test cartridge into any available bay, indicated by a flashin hite LED light. The test will begin automatically when the cartridge has been ins d into the and the pre-run check (cartridge initialization) is completed, indicated by a bl LED light.

QUALITY CONTROL

Internal Controls

Each cartridge includes internal controls that monitor performance f each step of th g process. A DNA control verifies extraction, amplification, and detec of DN argets, and RNA controls verify amplification and detection of RNA targets.

In order for a test to be valid, either the interna target must generate signal above the defined threshold in the amplification reaction. Inte al control re are in reted by the ePlex software and displayed on ePlex SARS-CoV-2 Test Re rts as Internal C rol with result of PASS, FAIL, N/A or INVALID. **Table 2** includes details on the terpretation of Inte al Control results.

able 2 nternal Contro esults

Internal Control Result	Explanation	Action
PASS	The inte trol or targe om the amplification reaction has enerated above threshold. he test was completed a nal controls were successful indicating valid results were generated.	All results are displayed on the SARS-CoV-2 Test Detection Report. Test is valid, report results.
FAIL	Neithe e internal control nor target in the amplification rea generated signal above the threshold. test was co eted but the internal control was not de ed, ind ng that results are not valid.	No results are displayed on the SARS-CoV-2 Test Report. Test is not valid, repeat the test using a new cartridge.
A	The inte al control did not generate signal above the threshold, but the target did generate signal above the hold. The test was completed and the internal control was not successful, however detection of signal above the threshold for the target indicates valid results were generated.	All results are displayed on the SARS-CoV-2 Test Detection Report. Test is valid, report results.
INVALID	An error has occurred during processing that prevents analysis of signal data. The test has not successfully completed and results for this test are not valid. This is often due to an instrument or software error.	No results are displayed on the SARS-CoV-2 Test Detection Report. Test is not valid, repeat the test using a new cartridge.

External Controls

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

RESULTS

Table 3: Interpretation of Results on the ePlex SARS-CoV-2 Te[illegible]Detection Report

Target Result	Explanation	[illegible]tion
Target Detected	The test was completed successfully, and the tar[illegible] has generated signal above its defined threshold and the Internal Control was reported as PASS.	A[illegible]ults[illegible] displayed on [illegible]he SAR[illegible]-2 Test Dete[illegible]n Report. Test is valid, [illegible]esults.
Target Not Detected	The test was completed successfully, a[illegible]e tar[illegible] did not generate signal above its defined th[illegible]o and the Internal Control was re[illegible]ted as PAS	All results are d[illegible]played on the [illegible]-CoV-2 Test Detection Report. Test is valid, report results.
Invalid	The test has not succe[illegible]ully completed, a[illegible] results for this test are not va[illegible]. This is often due [illegible]n instrument or softwar[illegible]rror or failure of an i[illegible]rnal control.	No results are displayed on the SARS-CoV-2 Test Detection Report. Test is not valid, repeat test.

TEST REPORTS

There are several differen[illegible]rts that a[illegible] available on the ePlex instrument. Results are provided in a printable forma[illegible]ay be viewed [illegible]tron[illegible]lly, or may be exported for additional analysis. Reports can be customiz[illegible] with account specific in[illegible]ion such as the address, logo, and institution specific footers on each r[illegible]ort. For mo[illegible] information on ePlex reports, refer to the ePlex Operator Manual.

Detectio[illegible]Re[illegible]t

[illegible]RS-Co[illegible] Test Det[illegible]on Report includes the results for each individual sample run on the ePlex instru[illegible]nt.

The [illegible]y section indicates the overall test result. The Results section includes a list of all targets on t[illegible] panel with a[illegible] individual result for each. Results for each target are reported as Detected, Not [illegible]etected, or Invalid (displayed as a red **x**); results for the Internal Control are reported as PASS, FAIL, [illegible]VALID, or N/A.

External Control Report

The SARS-CoV-2 Test External Control Report is generated for an external control that has been pre-defined in the ePlex RP Panel software. For more information on defining external controls on the ePlex SARS-CoV-2 Test, refer to the ePlex Operator Manual.

The Summary section indicates the overall result (Pass or Fail status) for that external control. The Results section includes a list of all panel targets with the result, expected result, and Pass or Fail status for each. Results are reported as Detected, Not Detected, or Invalid (displayed as a red **x**). Each target is reported as Pass if the actual result matches the expected result (as defined for that control). A target is reported as Fail if the actual result does not match the expected result. If the actual results for each target match the expected result for each target (all targets reported as Pass), the overall result for the external control is reported as Pass in the Summary section. If the actual result for any target does not match the expected result, the overall result for the external control is reported as Fail in the Summary section.

Summary Report

The Summary Report allows the operator to use defined searchable criteria to create customized reports, using specified targets, dates, range of dates, sample, external control, cartridge, or operator. For more information on creating Summary Reports, refer to the ePlex Operator Manual.

Limitations

- This product can be used only with the GenMark ePlex instrument.
- The Sample Delivery Device should only be used with the ePlex SARS-CoV-2 Test.
- This test is a qualitative test and does not provide a quantitative value of detected organism present.
- The performance of the test was evaluated for use with human sample material only.
- This test has not been validated for testing samples other than nasopharyngeal swab samples in viral transport media. Please contact Technical Support for questions on other sample types.
- The performance of this test has not been established for immunocompromised individuals.
- The performance of this test has not been established for patients without signs and symptoms of respiratory infection.
- Results from this test must be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- Viral nucleic acids may persist in vivo, independent of viability. Detection of target(s) does not indicate the presence of infectious virus, or that the virus nucleic acid is the causative agent for clinical symptoms.
  The detection of viral nucleic acid is dependent upon proper specimen collection, handling, transportation, storage, and preparation. Failure to observe proper procedures in any one of these steps could lead to incorrect results. There is a risk of false positive or false negative values resulting from improperly collected, transported, or handled samples.
  There is a risk of false negative values due to the presence of sequence variants in the viral target of the test, the presence of inhibitors, technical error, or sample mix-up. Test results may be affected by concurrent antiviral therapy or levels of virus in the sample that are below the limit of detection for the test. A result of No Target Detected on the ePlex SARS-CoV-2 Test should not be used as the sole basis for diagnosis, treatment or other patient management decisions.
- There is a risk of false positive results due to contamination of the sample with target organisms, their nucleic acids, or amplicons. Particular attention should be given to the Laboratory precautions noted under the Warnings and Precautions section.

- There is a risk of false positive results due to non-specific amplification and cross-reactivity with organisms found in the respiratory tract. Erroneous results due to cross-reactivity with organisms that were not specifically evaluated or new variant sequences that emerge are possible.
- The performance of this test has not been established for monitoring treatment of infection with any of the panel organisms.
- At concentrations greater than 1% weight/volume in the sample, tobramycin was found [illegible] assay performance.
- Due to limited access to testing material, the LoD study was conducted with in vitro transcripts (IVT)s diluted in PBS buffer. Therefore, the LoD in clinical samples may be different than those determined in the LoD study.
- At high titers, cross-reactivity with SARS CoV-1 was observed with the ePlex SARS-CoV-2 Test.

Conditions of Authorization for the Laboratory

The ePlex SARS-CoV-2 Test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas.

However, to assist clinical laboratories using the ePlex SARS-CoV-2 Test, the relevant conditions of Authorization are listed below:

A. Authorized laboratories[1] using your product include the result reports of the ePlex SARS-CoV-2 Test, all authorized Fact Sheets. Under emergency circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

B. Authorized laboratories using the ePlex SARS-CoV-2 Test will use the ePlex SARS-CoV-2 Test as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized nucleic acid extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the ePlex SARS-CoV-2 Test are not permitted.

C. Authorized laboratories that receive the ePlex SARS-CoV-2 Test will notify the relevant public health authorities of their intent to run the ePlex SARS-CoV-2 Test prior to initiating testing.

D. Authorized laboratories using the ePlex SARS-CoV-2 Test will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

E. Authorized laboratories will collect information on the performance of the ePlex SARS-CoV-2 Test and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and GenMark Diagnostics, Inc. (via email: technicalsupport@genmarkdx.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the ePlex SARS-CoV-2 Test of which they become aware.

F. All laboratory personnel using the ePlex SARS-CoV-2 Test must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the ePlex SARS-CoV-2 Test in accordance with the authorized labeling.

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

PERFORMANCE CHARACTERISTICS

CLINICAL PERFORMANCE WITH WORKFLOW A

NPS specimens were collected from 65 symptomatic U.S. patients representative of the Intended Use population and tested with the ePlex SARS-CoV-2 Test using Workflow A (with the Sample D... Device). The samples were NPS in commercially-available VTM. The performance of the ...lex SARS-CoV-2 Test was compared to a SARS-CoV-2 Real-Time RT-PCR Diagnostic Panel auth...ed for EUA. The clinical samples were tested fresh with the comparator method and with the ePlex ...RS-CoV-2 Test. The performance is summarized in **Table 4**.

Table 4. ePlex SARS-CoV-2 Test Clinical Performance Estimates w... Workflo... A

ePlex SARS-CoV-2 Test	Comparator Result		
	Positive	Negative	Total
Positive	17	0	17
Negative	1*	...7	48
Total	18	...7	...5

*Initial ePlex SARS-CoV-2 Test was negative; repeat test was pos...ve.

Positive percent agreement = 94.4% (95% CI: 74.2% – 99...)
Negative percent agreement = 100% (95% CI: 92.4% – 100%

CLINICAL PERFORMANCE WIT... WORKFLOW ...

NPS specimens positive for SARS...CoV-2 ...y an FDA-cleared ...ARS-CoV-2 diagnostic test authorized for EUA) from 48 U.S. patients repres...tative ...he Intended U... population were tested with the ePlex SARS-CoV-2 Test using Workflow ... without ... of the S...ple Delivery Device). The samples were NPS in commercially-available VTM ...d included ... challenging clinical samples with Ct values of >30. Overall positive percent agreem...t between the ePlex SARS-CoV-2 Test and the comparator test method was observe...e 94% (45/4... The performance is summarized in **Table 5**.

Table 5. ...lex S...RS-CoV-2 Test Clinical Performance Estimates wi...kflow B (Known Positive Samples)

Sample	Comparat...r Ct Va...	ePlex SARS-CoV-2 Result	Sample	Comparator Ct Value	ePlex SARS-CoV-2 Result
1	1...	Detected	25	28.7	Detected
2	...4.8	Detected	26	28.7	Detected
...	14.8	Detected	27	29.3	Detected
4	...	Detected	28	29.7	Detected
5	18.7	Detected	29	30.0	Not Detected*
...	...8.9	Detected	30	30.4	Detected
7	19.3	Detected	31	31.7	Detected
8	20.5	Detected	32	31.9	Detected
...	21.3	Detected	33	32.0	Detected
10	21.8	Detected	34	32.0	Detected
11	23.1	Detected	35	32.3	Detected
12	23.3	Detected	36	32.3	Detected

Sample	Comparator Ct Value	ePlex SARS-CoV-2 Result
13	23.5	Detected
14	24.0	Detected
15	24.7	Detected
16	25.0	Detected
17	25.1	Detected
18	25.2	Detected
19	25.3	Detected
20	26.2	Detected
21	27.1	Detected
22	27.5	Detected
23	27.6	Detected
24	28.4	Detected

Sample	Comparator Ct Value	ePlex SARS-CoV-2 Result
37	32.6	Detected
38	33.1	Detected
39	33.2	Detected
40	33.3	Detected
41	33.7	Detected
42	34.5	Detected
43	35.2	Detected
44	35.2	Not Detected
45	[illegible]	Detected
46	35.9	Detected
47	[illegible]	Not Detected
48	37.0	Detected

* The run was repeated and SARS-CoV-2 was detected by the ePlex SARS-CoV-2 Test.

Thirty previously frozen samples presumed negative for SARS-CoV-2 (due to collection prior to 2017) were tested on the ePlex SARS-CoV-2 Test. Overall negative percent agreement between the ePlex SARS-CoV-2 Test and the expected result was observed to be [illegible]% (30/30).

ANALYTICAL PERFORMANCE

Limit of Detection

The limit of detection (LoD), or analytical sensitivity, was identified and verified for SARS-CoV-2 using quantified reference material and tested using Workflow A (with the Sample Delivery Device) and Workflow B (without the Sample Delivery Device). A minimum of twenty replicates per concentration were tested in the study. The limit of detection was defined as the lowest concentration at which SARS-CoV-2 was detected in at least 95% of the tests. The confirmed LoD for SARS-CoV-2 with Workflow A is shown in **Table 6** and the LoD for the ePlex SARS-CoV-2 Test using Workflow B is shown in **Table 7.**

Table 6: ePlex SARS-CoV-2 LoD Results Summary with Workflow A

Target	Source	LoD Concentration
SARS-CoV-2	WA1 viral RNA	1 x 10^3 copies/mL

Table 7: ePlex SARS-CoV-2 LoD Results Summary with Workflow B

Target	Source	LoD Concentration
SARS-CoV-2	USA-WA1/2020	3 x 10^{-2} $TCID_{50}$/mL[a]

[a] The LoD concentration for detection of SARS-CoV-2 was determined to be 0.03 $TCID_{50}$/mL, which corresponds to 750 genomic copies per milliliter, as determined by digital droplet PCR.

Analytical Reactivity (Inclusivity)

Inclusivity of viral targets on the ePlex SARS-CoV-2 Test was evaluated at high concentration using bench testing of organisms in the same genetic family. Due to the limited availability of testing material, RNA for SARS-CoV-2 (WA1) was tested at 1 x 10^7 copies/mL. SARS-CoV-2 (Wuhan-Hu-1) *in vitro* transcript was tested at 1 x 10^6 copies/mL. As expected, all replicates were detected by the ePlex SARS-CoV-2 Test as shown in **Table 8**.

Table 8: Analytical Reactivity (Inclusivity) Results

Target	Strain	Concentration	Result
SARS-CoV-2	WA1 viral RNA	1 x 10^7 copies/mL	Detected
SARS-CoV-2	Wuhan-Hu-1 *in vitro* transcript	1 x 10^6 copies/mL	Detected

Analytical Specificity (Cross-Reactivity and Exclusivity)

Cross-reactivity of viruses, bacteria, and fungi that are not targets of the ePlex SARS-CoV-2 Test was evaluated using *in silico* analysis and bench testing of organisms in the same genetic family, organisms commonly found in respiratory specimens, and other respiratory organisms in circulation. Viral, bacterial, and fungal cultures at high titers were used for testing; for organisms where no high titer material was available (Coronavirus HKU1, Middle East Respiratory Syndrome (MERS) coronavirus, and SARS-CoV-2-Wuhan-Hu-1) synthetic constructs were used for testing. Testing was done at high concentrations (1 x 10^4 to 1 x 10^6 $TCID_{50}$/mL, 1 x 10^8 CFU/mL for bacterial and fungal isolates, or 1 x 10^6 copies/mL for synthetic constructs) of quantified strains/isolates as shown in **Table 9**.

Table 9: Cross-reactivity with Organisms Not Detected by the ePlex SARS-CoV-2 Test (Exclusivity)

Target	Strain	Concentration	Cross-Reactivity Results
Coronavirus[a]	SARS CoV-1	1 x 10^6 copies/µL	Cross-reactive
Coronavirus[a]	MERS	1 x 10^4 copies/µL	Not observed
Human coronavirus	229E	1 x 10^4 $TCID_{50}$/mL	Not observed
Human coronavirus	OC43	1 x 10^6 $TCID_{50}$/mL	Not observed
Human coronavirus[a]	HKU1	5 x 10^4 $TCID_{50}$/mL	Not observed
Human coronavirus	NL63	1 x 10^4 $TCID_{50}$/mL	Not observed
Adenovirus C	1	1 x 10^4 $TCID_{50}$/mL	Not observed
Echovirus	30	1 x 10^5 $TCID_{50}$/mL	Not observed
Enterovirus	68	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza A	H1N1/NY01/2009	1 x 10^5 $TCID_{50}$/mL	Not observed
Influenza B	Yamagata	1 x 10^5 $TCID_{50}$/mL	Not observed
hMPV	B2 Peru1-2002	1 x 10^5 $TCID_{50}$/mL	Not observed
RSV	B14	1 x 10^5 $TCID_{50}$/mL	Not observed
PIV	1	1 x 10^5 $TCID_{50}$/mL	Not observed
PIV	2	1 x 10^5 $TCID_{50}$/mL	Not observed
PIV	3	1 x 10^5 $TCID_{50}$/mL	Not observed
PIV	4a	1 x 10^5 $TCID_{50}$/mL	Not observed
RSV A	2006	1 x 10^5 $TCID_{50}$/mL	Not observed
Bordetella pertussis	ATCC53894	1 x 10^8 CFU/mL	Not observed

Target	Strain	Concentration	Cross-Reactivity Results
Candida albicans	ATCC24433	1 x 10^8 CFU/mL	Not observed
Corynebacterium diphtheriae	ATCC53281	1 x 10^8 CFU/mL	Not observed
Haemophilus influenzae	ATCC43065	1 x 10^8 CFU/mL	Not observed
Legionella pneumophila	ATCC35096	1 x 10^8 CFU/mL	Not observed
Mycobacterium tuberculosis	H37Rv	1 x 10^8 CFU/mL	Not obser
Moraxella catarrhalis	ATCC23246	1 x 10^8 CFU/mL	Not ob ed
Neisseria meningitidis	NCTC10026	1 x 10^8 CFU/mL	Not obse
Pseudomonas aeruginosa	ATCC BAA-1744	1 x 10^8 CFU/mL	observed
Staphylococcus aureus	ATCC25923	1 x 10^8 CFU/mL	Not observed
Staphylococcus epidermidis	ATCC700567	1 x 10^8 CFU/m	Not obs ed
Staphylococcus salivarius	ATCC25975	1 x 10^8 CFU	Not erved
Streptococcus pneumoniae	ATCC49136	1 x 10^8 FU/mL	observed
Streptococcus pyogenes	ATCC49399	1 x 10 FU/mL	ot observed
Pooled Nasal Swabs[b]	N/A	N/A	bse

[a] in vitro transcript

[b] human clinical sample

In Silico Analysis – Cross Reactivity

In silico analysis was performed for the gen gions ta d by t Plex SARS-CoV-2 Test to evaluate cross-reactivity. GenMark conducted a pr er BLAST sea of the I database against all bacteria, negative-stranded RNA viruses (negarna riota), picornaviru , adenoviruses, common human coronaviruses, MERS, *Candida albicans*, nd Pneumocysitis. he BLAST searches did not identify any cross-reactivity with the exceptio SAR oronavirus, whic s in the same subgenus (Sarbecovirus) as SARS-CoV-2.

TROUBLESHOO G

ble 0: Troubleshooting Table

For a comp list of all ePlex error me es and a description of the messages, please refer to the ePlex Op tor Manua

Error	Erro essages	Description	Re-test Recommendations
Test did not	idge failure rtridge in zation test faile Cartridg present Bay heater failure own error Bay main / fluid motor failure EEPROM failure Bay over pressured Bay temperature out of range The system was unable to read the cartridge	An error that occurs during pre-run checks (cartridge initialization) of the cartridge upon insertion into the bay. Cartridge initialization occurs when the cartridge is first inserted into the bay and takes approximately 90 seconds. Upon completion of cartridge initialization, the cartridge cannot be restarted, but prior to this point, the cartridge can be restarted. To verify cartridge initialization has completed, examine the cartridge label upon removal	1. Remove cartridge from bay. a. Reset bay to clear the error b. Restart cartridge in any available bay 2. If the cartridge is not able to be run on the second try and again generates an error during cartridge initialization, this indicates an issue with the cartridge. This cartridge should be discarded following laboratory procedures and the sample should be repeated using a new cartridge. Bay(s) should be reset to clear the errors. Please contact MAS or GenMark Technical Support to alert them of the issue.

Error	Error Messages	Description	Re-test Recommendations
	Cartridge inserted doesn't match the serial number of the cartridge scanned The system is not ready to accept the cartridge The system was unable to enable cartridge insertion for the bay The system failed to prepare the cartridge for processing	from the bay. If the cartridge label has been pierced, the test has already started and cartridge cannot be reused. If the label has not been pierced, follow the recommendation as stated.	If the bay remains in an error state (flashing red) after the cartridge has been removed, then the bay must be reset through the Bay Configuration menu before it can be used to cartridges.
Test did not finish	Bay heater failure Bay main / fluid motor failure Bay voltage failure Bay sub-system communication timeout Cartridge failure Bay over pressured Bay auto-calibration failure Bay temperature out of range The system was unable to eject the cartridge from the bay	This type of error occurs during the run, after pre-run checks (cartridge initialization) have finished, and prevents the cartridge from being processed to completion.	Reagents e been consu and the ca ge cannot be reuse Co GenMark Technical Sup a roceed with r t testing of ple using a r cartridge. If the r ins in an error (flashin after the cartri has been rem then the b must be reset throug Bay figuration menu before it sed to run cartridges.
Invalid		This is an error that resu o valid generat A t eport will be erated, targets and the i al ontrol will be invalid.	Reagents have been consumed and the cartridge cannot be reused. Contact GenMark Technical Support nd proceed with repeat testing of the ample using a new cartridge.

Technical Support

GenMark Technical support is availa e 24 hour days a week to provide the highest level of customer support and satisfaction.

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Email: t nicalsu t@genmarkdx.com

GLO SARY O SYM OLS

S	Description	Symbol	Description
LOT	Batch Code		Date of Manufacture YYYY-MM-DD
⚠	Caution	SN	Serial number

Symbol	Description	Symbol	Description
	Contains sufficient for <n> tests		Catalog number
	Consult instructions for use		Biological risks
	Temperature range		Upper limit of [illegible]mperatu
	Lower limit of temperature		Cart[illegible]e Lot
	Manufacturer		Irrita[illegible]erma[illegible]nsitizer, acut[illegible] toxicity ([illegible]ul), narcotic e[illegible]s, respiratory [illegible]t irritation
	Oxidizers		Carcinogen, R[illegible]irat[illegible] Sensitizer, Reproductive To[illegible], Target Organ [illegible]oxicity, Mutagenicity, Aspiration [illegible]
	For Use Under the Emergency Use Authorization Only		

TRADEMARKS

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PATENT IN[illegible]ORMATION

ePlex® [illegible]RS-CoV-2 [illegible]t and/or use thereof features technology claimed in one or more of the following United S[illegible]s and [illegible]opean patents owned or licensed by GenMark Diagnostics Inc. or its subsidiaries, with multipl[illegible]onal foreign [illegible] domestic patents pending: U.S. Patent Nos. 6,753,143, 7,172,897, [illegible]087, 7,5[illegible]331, 7,820[illegible]1, 8,486,247, 9,222,623, 9,410,663, 9,453,613, 9,498,778, 9,500,663, 9,598[illegible]2; 9,874,[illegible] 9.[illegible],553, 10,001,476, 10,391,489, 10,495,656, 10,352,983, 10,564,211, D8814[illegible] Internation[illegible]tent Nos. 1218541, 1246699, 60125713.8, 2220102, 602008031596.7, 1249[illegible]9, 2278757, 60125713.8, 3548159, 9874542, 60017809.9, 1350568, 3548159, 2965817, 2[illegible]9415, 32[illegible], 005250651-00001; and other international counterparts.

[illegible]less otherwise agreed to in writing, by using a cartridge, Recipient acknowledges that Recipient has re[illegible]accepts and agrees to be bound by and comply with the General Terms and Conditions of Sale availa[illegible]e on GenMark's website which can be amended from time to time by GenMark without consent. If Recipient does not accept and agree to be bound by the General Terms and Conditions of Sale, Recipient will immediately cease any further use of the cartridge.

This product is subject to a limited license to use the product in the field of human *in vitro* diagnostics and research reasonably related thereto. Users are prohibited from using this product for other applications, including in the field of forensics (including human identification testing).

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