

EMERGENCY USE AUTHORIZATION (EUA) SUMMARY

Clinical Enterprise SARS-CoV-2 RT-PCR Assay EUA210239

(Clinical Enterprise, Inc.)

For In vitro Diagnostic Use
For use under Emergency Use Authorization (EUA) only
For Prescription Only

(The Clinical Enterprise SARS-CoV-2 RT-PCR Assay will be performed at laboratories designated by Clinical Enterprise, Inc., which are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meet the requirements to perform high complexity tests, as described in the laboratory procedures reviewed by FDA under this EUA.)

INTENDED USE

The Clinical Enterprise (CE) SARS-CoV-2 RT-PCR Assay is a high-throughput real-time RT-PCR test intended for the qualitative detection of SARS-CoV-2 viral RNA in (1) nasopharyngeal swabs, mid turbinate swabs, anterior nasal swabs, nasopharyngeal wash, nasal wash, oropharyngeal (OP) swabs and bronchoalveolar lavage (BAL) from individuals suspected of COVID-19 by their healthcare provider (HCP); and (2) anterior nasal swab specimens collected from individuals without symptoms or other reasons to suspect COVID-19. Testing is limited to laboratories designated by Clinical Enterprise, Inc., which are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests.

The following indication is also authorized under the Pooling and Serial Testing Amendment (<https://www.fda.gov/media/147737/download>) for use in laboratories designated by Clinical Enterprise Inc., which are also certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meet the requirements to perform high complexity tests. The Clinical Enterprise (CE) SARS-CoV-2 RT-PCR Assay is intended for qualitative detection of RNA from SARS-CoV-2 in pooled samples containing up to 10 individual human anterior nasal swabs placed in a single vial after being collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals without symptoms or other reasons to suspect COVID-19, when tested as part of a serial testing program including testing at least once per week. This indication is authorized with the following validated protocol: 147251.127 CE SARS-CoV-2 RT-PCR Assay Swab Pooling Protocol. Negative results from pooled testing should not be treated as definitive. If a patient's clinical signs and symptoms are inconsistent with a negative result or results are necessary for patient management, then the patient should be considered for individual testing. Specimens included in pools with a positive or invalid result must be reported as presumptive positive or tested individually prior to reporting a result.

Results are for the identification of SARS-CoV-2 viral RNA. SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA. 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

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to report all test 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.

The CE SARS-CoV-2 RT-PCR Assay is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time RT-PCR assays and in vitro diagnostic procedures. The assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The CE SARS-CoV-2 RT-PCR Assay is a high-throughput, real-time reverse transcription polymerase chain reaction (rRT-PCR) test. The SARS-CoV-2 primer and probe set(s) are designed to detect SARS-CoV-2 viral RNA in respiratory specimens from patients as recommended for testing by public health authority guidelines.

Each primer/probe pair of the CE SARS-CoV-2 RT-PCR Assay (refer to the table below) is constructed with a unique fluorescent reporter dye (e.g., VIC). The assay targets two regions of the SARS-CoV-2 Nucleocapsid gene (N1 and N2, both FAM labeled) and the internal extraction standard MS2 (CY5) for all samples, and the human RNase P (VIC) for self-collected samples. The assay is performed in a single well with both N1 and N2 regions detected simultaneously using the FAM fluorophore. Presence of a target sequence in a sample causes the unique oligonucleotide probe to anneal to the target. During the extension phase of PCR, if a probe has annealed to the target sequence, cleavage of the probe occurs through the 5' nuclease activity of Taq polymerase. This reduces the effect of fluorescence resonance energy transfer (FRET) and increases the fluorescent signal. If the SARS-CoV-2 target sequences are present in a clinical sample, this signal will be detected by the instrument indicating whether a sample is positive or negative for SARS-CoV-2 RNA. Since both SARS-CoV-2 N1 and SARS-CoV-2 N2 assays use probes with the same fluorophore (FAM), a single SARS-CoV-2 Ct value is generated in each rRT-PCR reaction.

Oligonucleotide Primers and Probes

Target	Primer/probe name	Sequence (5' – 3')	Position (GenBank NC 045512.2)	Final assay concentration
SARS CoV-2	SARS CoV-2 N1 F1	GCATTGGCATGGAAGTCACA	29229 – 29248	600 nM
	SARS CoV-2 N1 P1	[FAM]CGTGGTTGACCTACACAGGTGCCATCA[BHQ1]	29259 – 29285	150 nM
	SARS CoV-2 N1 R1	TTGATCTTTGAAATTTGGATCTTTGTC	28294 – 29320	600 nM
	SARS CoV-2 N2 F1	CAGTAGGGGAACTTCTCCTGCTAG	28876 – 28899	300 nM
	SARS CoV-2 N2 P1	[FAM]ATGGCTGGCAATGGCGGTGATG[BHQ1]	28901 – 28922	150 nM
	SARS CoV-2 N2 R1	CAAGCTGGTTCAATCTGTCAAGC	28942 – 28964	300 nM
MS2	MS2-3 F	CGTTCACAGGCTTACAAAGTAACC	1449 – 1472	100 nM
	MS2-3 P	[CY5]TCGTCAGAGCTCTGCGCAGAA TCG[BHQ2]	1481 – 1504	200 nM
	MS2-3 R	GCACCTCGACTTTGATGGTGT	1510 – 1530	100 nM
RNase P	RNase P Fwd	AGATTTGGACCTGCGAGCG	28-46	100 nM
	RNase P Probe	[VIC] – TTCTGACCTGAAGGCTCTGCGCG – [TAM]	49-71	100 nM
	RNase P Rev	GAGCGGCTGTCTCCACAAGT	73-92	100 nM

INSTRUMENTS USED WITH TEST

The CE SARS-CoV-2 RT-PCR Assay uses the ThermoFisher MagMax V2 Viral/Pathogen Nucleic Acid Isolation Kit and Hamilton STAR liquid handling system for high throughput automated nucleic acid extraction, and the Applied Biosystems QuantStudio5 384-Well Real-Time PCR System (Software V1.5.1) for nucleic acid amplification and detection.

REAGENTS AND MATERIALS

Item Name	Part Number	Manufacturer/Supplier
MagMAX™ Viral/Pathogen II Nucleic Acid Isolation Kit	A48383	ThermoFisher Scientific
Ethanol, 100% Molecular Biology Grade	A4094 or equivalent	Fisher Scientific or MLS
MS2 Phage Control	5728201701	Eurofins Abraxis
Nuclease Free Molecular Grade Water	AM9932	ThermoFisher Scientific or MLS
TaqPath™ 1-step RT-qPCR master mix, CG	A28523	ThermoFisher
Nuclease Free Molecular Grade Water	AM9932	ThermoFisher Scientific or MLS
SARS CoV-2 N1 F1	CUST-COV-N1F1	Eurofins Genomics
SARS CoV-2 N1 P1	CUST-COV-N1P1+	Eurofins Genomics
SARS CoV-2 N1 R1	CUST-COV-N1R1	Eurofins Genomics
SARS CoV-2 N2 F1	CUST-COV-N2F1	Eurofins Genomics
SARS CoV-2 N2 P1	CUST-COV-N2P1+	Eurofins Genomics
SARS CoV-2 N2 R1	CUST-COV-N2R1	Eurofins Genomics
MS2-3 F	CUST-COV-MS2-3F	Eurofins Genomics
MS2-3 P	CUST-COV-MS2-3PROBE	Eurofins Genomics
MS2-3 R	CUST-COV-MS2-3R	Eurofins Genomics
RNase P Forward primer	1330*	Eurofins Genomics
RNase P Probe	450003	ThermoFisher Scientific
RNase P Reverse primer	1330*	Eurofins Genomics
Synthetic positive control (N-gene) for SARS-CoV-2 RT-PCR Assays	5728201610	Eurofins Abraxis

* Custom oligo orders

CONTROLS TO BE USED WITH THE TEST

- RT-PCR SARS-CoV-2 amplification control (PC):** The PC is used to monitor the RT-PCR reaction, two amplification controls are used. The two controls consist of one “High” and one “Low” amplification control at concentrations of 50,000 copies/mL (200X LoD) and 500 copies/mL (2X LoD) respectively, and are used to ensure that the RT-PCR reaction is correctly detecting the SARS-CoV-2 targets. Ct results for the SARS-CoV-2 N-gene target is

tracked for each PCR plate. Material used for this control is a synthetic IVT with the regions of the SARS-CoV-2 N-Gene targeted by the test (Abraxis part# 5728201601).

- **MS2 Phage Control:** This control is used as an internal lysis, extraction, and amplification control (Abraxis #5728201701). It is added to each sample and control well at the beginning of the extraction and serves as a full process internal standard to monitor the extraction, reverse transcription, and amplification reagents and processes. The CE SARS-CoV-2 RT-PCR Assay oligonucleotides contain a primer/probe pair specific for this target. The expected Ct for the MS2 control is ≤ 35 . For samples with no Ct for the SARS-CoV-2 targets, and MS2 Ct ≤ 35 , it indicates proper nucleic acid extraction and RT-PCR.
- **RNase P Specimen Control:** This control assesses the quality of the clinical specimen. Oligonucleotide primers and probes for RNase P are included in the test to monitor the presence of sufficient quantity and quality of RNA. Each sample run for the CE SARS-CoV-2 RT-PCR Assay should exhibit a positive signal for the RNase P target with a Ct ≤ 35 .
- **Positive Extraction Control (PEC):** Two SARS-CoV-2 positive extraction controls (High and Low) are included in each extraction and are used to monitor the entire process and test reagents. The controls produce a specific N-gene and RNase P Ct range to ensure reproducibility of the test across the whole process on different days and instruments. Pooled positive clinical samples are used as the material for the PEC and are tested before use to establish the expected Ct range. The high positive extraction control has a mean SARS-CoV-2 N-Gene Ct of 23-28, and the low positive extraction control has a mean SARS-CoV-2 N-Gene Ct of 31-35.
- **Negative Extraction Control (NEC):** This control is included in each batch of extracted samples. The NEC is used to monitor for carryover and for contamination in the extraction reagents with amplifiable RNA. Phosphate buffered Saline (PBS) or TE buffer matrix is used in place of patient samples and goes through the entire extraction and RT-PCR process. MS2 Phage control is added to these samples. The eluted sample is then added to the RT-PCR plate to simulate a patient sample. The only target that should be present in this sample is MS2.
- **No Template Control/Negative Amplification Control (NTC):** The NTC is added to every RT-PCR plate to monitor for carryover and RT-PCR reagent contamination. The NTC includes DNase/RNase free water instead of extracted RNA along with the RT-PCR reagents.

INTERPRETATION OF RESULTS

1) Control Interpretation

All test controls must be examined prior to interpretation of patient results. If a given control or control group does not meet the expected criteria, it is investigated for a root cause. The entire run and/or extraction may require repeat and the results cannot be interpreted or reported. The table below describes the parameters used for control results and interpretation.

Interpretation of Control Results: Expected Results for Valid Controls

Control	Expected Result for Valid Controls		
	MS2 POS: $C_t \leq 35$ NEG: ND or >35	RNaseP POS: $C_t \leq 35$ NEG: ND or >35	SARS-CoV-2 N- Gene POS: $C_t < 38$ NEG: ND or ≥ 38
No template control (NTC)	NEG	NEG	NEG
“High” RT-PCR SARS-CoV-2 amplification control (PC_HI)	NEG	NEG	POS Ct within 2SD of current lot
“Low” RT-PCR SARS-CoV-2 amplification control (PC_LO)	NEG	NEG	POS ^a Ct within 2SD of current lot
“High” Positive extraction control (PEC_HI)	POS	POS ^a Ct within 2SD of current lot	POS ^a Ct within 2SD of current lot
“Low” Positive extraction control (PEC_LO)	POS	POS ^a Ct within 2SD of current lot	POS ^a Ct within 2SD of current lot
Negative extraction control	POS	NEG	NEG

^aC_t range may change for specific lot

2) Clinical Sample Interpretation

Clinical samples are assessed after the controls have been analyzed and determined to be valid and acceptable. For each patient on the plate, amplification curves are analyzed, along with other characteristics of the data such as AmpStatus and Ct confidence. Result interpretation is performed on all patient samples passing the data review. Data is interpreted according to the conditions are shown below.

Interpretation of Clinical Sample Results

MS2 POS: $C_t \leq 35$ NEG ^b : ND or >35	RNaseP POS: $C_t \leq 35$ NEG: ND or >35	N-Gene POS: $C_t < 38$ NEG: ND or ≥ 38	Status	Reported Result ^a	Action
POS ^c	POS ^c	POS ^c	Valid	Detected	Report results to healthcare provider and appropriate public health authorities
POS	POS	NEG	Valid	Not Detected	Report results to healthcare provider and appropriate public health authorities
NEG	NEG	NEG OR POS	Invalid	Repeat/ Inconclusive	Repeat test one time. If the result is valid, report results to healthcare provider

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NEG	POS				and appropriate public health authorities. If the result is Invalid again, report results to healthcare provider as Inconclusive. A new sample should be requested for retesting
POS	NEG				

^a Reported result is the result reported in the LIS. Only samples with valid status have results reported

^b ND=Not Detected or a false Ct. False Ct's have a signal above the threshold but no amplification curves.

^c RNase P and/or MS2 may be NEG *only* if SARS-CoV-2 Ct is very strong positive (Ct<23). For all other positive SARS-CoV-2 results, MS2 *and* RNase P must be POS.

The below table shows the specific parameters for reporting of results tested using 10-swab pooling. The results for the individual testing process are shown in the first column. All presumptive positive and inconclusive pooled results are reported to the program administrator.

MS2 POS: C _t ≤35 NEG ^b : ND or >35	RNaseP POS: C _t ≤35 NEG: ND or >35	N-Gene POS: C _t <38 NEG: ND or ≥38	Status	Reported Result^a	Action^f
POS ^c	POS ^c	POS ^c	Valid	Presumptive Positive^{d, e}	Report pooled result to program administrator with notification that subjects in the positive pool should isolate until receiving a negative result when re-tested individually. Individual should not be cohorted with other individuals who have received a positive or presumptive positive result. Individual samples from all subjects in the pool should be re-tested individually.
POS	POS	NEG	Valid	Negative^{d, g}	Report pooled result to program administrator and appropriate public health authorities
NEG	NEG	NEG OR POS	Invalid	Invalid	Repeat test on pooled sample one time.
NEG	POS				If the result is Negative, report pooled result to program administrator and appropriate public health authorities.
POS	NEG				If the result is Positive or Invalid, report the result as Presumed Positive to program administrator. A new sample from all subjects in the pool should be run and re-tested individually.

^a Reported result is the result reported in the LIS. Only samples with valid status have results reported

^b ND=Not Detected or a false Ct. False Ct's are those that have a signal above the threshold but that are noise/not actually amplification curves.

^c RNase P and/or MS2 may be NEG *only* if SARS-CoV-2 Ct is very strong positive (Ct<23). For all other positive SARS-CoV-2 results, MS2 *and* RNase P must be POS.

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^d“PresumptivePositive” and “Negative” are the specific result interpretations for samples tested as part of the 10-swab pooling procedure.

^eIndividuals included in a pool that returns a positive or invalid result should be treated as a presumptive positive unless or until they receive a negative result when re-tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, they should isolate until receiving a negative result when re-tested individually and should not be cohorted with other individuals who have received a positive or presumptive positive result. For serial testing programs, additional confirmatory testing for positive results may also be necessary, if there is a low likelihood of COVID-19, such as in individuals without known exposure to COVID-19 or residing in communities with low prevalence of infection.

^fResults of follow-up testing are reported to the program administrator and appropriate public health authorities.

^gSpecimens with low viral loads may not be detected with pooled testing due to decreased sensitivity or increased interference from pooled testing. For serial testing programs, additional confirmatory testing for negative results may be necessary, if there is a high likelihood of COVID-19, such as an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection.

PERFORMANCE EVALUATION

The CE SARS-CoV-2 RT-PCR Assay is identical in reagents and processing steps with the CE SARS-CoV-2 RT-PCR Assay DTC. Unless otherwise indicated, the performance data for the CE SARS-CoV-2 RT-PCR Assay are identical to the ones described for CE SARS-CoV-2 RT-PCR Assay DTC.

1) Limit of Detection (LoD) -Analytical Sensitivity

LoD experiments were performed using a residual patient sample quantified with an EUA authorized test using IVT standards. The stock material had an initial concentration of 1.0E+06 copies/mL. To determine the preliminary LoD, the positive sample was spiked into pooled nasopharyngeal swab matrix in VTM from specimens that tested negative for SARS-CoV2 using an EUA authorized assay. The preliminary LoD was the lowest concentration where 100% of replicates are positive (valid Ct <38). Results from the range-finding experiments are shown below and indicate a preliminary LoD of 250 copies/mL.

Preliminary LoD Study in NP Swab Matrix

Target Level (Copies/mL)	Valid tested replicates	MS2			N-Gene			RNaseP			Overall detection
		Mean Ct	SD	CV%	Mean Ct	SD	CV%	Mean Ct	SD	CV%	
500	3	28.02	0.28	1.0%	35.89	1.14	3.2%	27.08	0.37	1.4%	100% (3/3)
250	3	27.92	0.43	1.6%	36.46	1.04	2.9%	27.22	0.07	0.3%	100% (3/3)
125	3	27.72	0.38	1.4%	36.82	0.43	1.2%	26.96	0.19	0.7%	66.6% (2/3)
62.5	3	28.02	0.26	0.9%	ND	--	--	27.13	0.11	0.4%	0% (0/3)

Confirmation of the LoD was performed by testing 20 individual extraction/amplification replicates at the preliminary LoD value generated as described above. Results are shown below and demonstrate detection rates of $\geq 95\%$ at 250 copies/mL in nasopharyngeal swab matrix. All replicates tested were valid based upon the results for the specimen control RNase P and extraction control MS2.

Confirmatory LoD Study in NP Swab Matrix

Target Level (Copies/mL)	Valid tested replicates	MS2			N-Gene			RNaseP			Overall detection
		Mean Ct	SD	CV%	Mean Ct	SD	CV%	Mean Ct	SD	CV%	
250	20	28.30	0.34	1.21%	36.32	1.12	3.09%	25.01	1.03	4.10%	95% (19/20)

To confirm equivalent performance of the test in nasal swab samples, the same material used for the original LoD study described above was spiked into pooled, known SARS-CoV-2 negative nasal swab samples collected in 0.9% buffered saline. A confirmatory LoD study was performed

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with 20 individually processed replicates. Results show $\geq 95\%$ detection at 250 copies/mL which agrees with the LoD in NP matrix.

Confirmatory LoD Study in Nasal Swab Matrix

Target Level (Copies/mL)	Valid tested replicates	MS2			N-Gene			RNaseP			Overall detection
		Mean Ct	SD	CV%	Mean Ct	SD	CV%	Mean Ct	SD	CV%	
250	20	28.31	0.25	0.87%	36.00	0.88	2.44%	27.68	0.55	1.98%	95% (19/20)

The final claimed LoD is 250 copies/mL.

2) Inclusivity (Analytical Sensitivity)

The CE SARS-CoV-2 RT-PCR Assay utilizes the same primer and probes as in the Viracor SARS-CoV-2 Assay. The inclusivity of the Viracor SARS-CoV-2 Assay has been demonstrated by Viracor Eurofins Clinical Diagnostics, Inc. in the EUA submission authorized on 02/26/2021. Details of the performance can be found here:

<https://www.fda.gov/media/143069/download>. Viracor Eurofins Clinical Diagnostics, Inc. granted Right of Reference for the authorized Viracor SARS-CoV-2 Assay.

FDA internal analysis of the recently emerging variants indicates no significant risk of false negative results.

3) Cross-reactivity (Analytical Specificity)

The CE SARS-CoV-2 RT-PCR Assay utilizes the same primer and probes as in the Viracor SARS-CoV-2 Assay. The cross-reactivity of the Viracor SARS-CoV-2 Assay has been demonstrated by Viracor Eurofins Clinical Diagnostics, Inc. in the EUA submission authorized on 02/26/2021. Details of the performance can be found here:

<https://www.fda.gov/media/143069/download>. Viracor Eurofins Clinical Diagnostics, Inc. granted Right of Reference for the authorized Viracor SARS-CoV-2 Assay.

4) Clinical Evaluation

a) Study #1 - Evaluation of retrospective NP and nasal swab specimens

To evaluate clinical performance, 35 positive and 35 negative natural clinical NP specimens as determined by a highly sensitive EUA authorized comparator test were tested using the CE SARS-CoV-2 RT-PCR Assay. 4 of the 35 positive samples are low positive (11%)(within 3 Cts of the average Ct at LoD concentration with the comparator method).

In addition, to demonstrate performance in low positive samples as defined by being within 3 Cts of the average Ct at LoD concentration with the comparator method, 20 low positive clinical nasal specimens previously tested with an EUA authorized test were compared to the result using the CE SARS-CoV-2 RT-PCR Assay. The percent positive and negative agreements between the EUA authorized comparator method and the CE SARS-CoV-2 RT-PCR Assay was then evaluated.

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Results demonstrate 100% (35/35) positive agreement and 100% (35/35) negative agreement for NP swabs, and 100% (20/20) positive agreement for Nasal swabs. Combined performance of the upper respiratory specimens is shown below. For all comparator negative samples, there was no SARS-CoV-2 target signal using the CE SARS-CoV-2 RT-PCR Assay. All samples had MS2 and RNaseP Ct values meeting the expected QC criteria.

Summary of Clinical Study #1

Retrospective Upper respiratory Specimens (NP and Nasal Swabs)		FDA Authorized SARS-CoV-2 RT-PCR Test		
		Positive	Negative	Total
CE SARS-CoV-2 RT-PCR Assay	Positive	55	0	55
	Negative	0	35	35
	Total	55	35	
Positive Percent Agreement (95% CI ¹)		100% (55/55), 95%CI: (93.5-100%)		
Negative Percent Agreement (95% CI ¹)		100% (35/35), 95%CI: (90.1-100%)		

¹Two-sided 95% confidence interval by a score method

b) Study #2 - Evaluation of a Boca Biolistics SARS-CoV-2 Reference Panel (retrospective NP Samples)

Clinical performance was also demonstrated using a Boca Biolistics SARS-CoV-2 Validation panel containing 60 fully characterized NP specimens that had been collected in April of 2020. All samples were originally tested using an EUA authorized test and stored at -80C. A summary of results is shown below, which demonstrates 100% (30/30) positive agreement and 96.7% (29/30) negative agreement between the EUA authorized comparator test and the CE SARS-CoV-2 RT-PCR Assay.

Summary of Clinical Study #2

Retrospective NP specimens		FDA authorized SARS-CoV-2 test		
		Positive	Negative	Total
CE SARS-CoV-2 RT-PCR Assay	Positive	30	1 ²	31
	Negative	0	29	29
	Total	30	30	
Positive Percent Agreement (95% CI ¹)		100% (30/30), 95%CI: (88.7%-100%)		
Negative Percent Agreement (95% CI ¹)		96.7% (29/30), 95%CI: (83.3%-99.4%)		

¹Two-sided 95% confidence interval by a score method

²Ct with the candidate test is 34.64; N-Gene Ct with a third independent assay is 32.96, indicative of a low positive sample

c) Study #3 – Evaluation of performance in asymptomatic individuals

The validation data provided below is in support of adding population screening of individuals without symptoms or other reasons to suspect COVID-19.

The samples used for this performance study were nasal swabs in 0.9% sterile saline collected from asymptomatic individuals during community screening events. A total of 321 samples were collected and tested initially using an EUA authorized high sensitivity test. Of the total, 22 consecutively collected positives and 110 consecutively collected negatives were re-tested with the same EUA authorized test and the results from this retesting were considered as the comparator results in this performance study. The samples were then shipped to CE on dry ice, stored at -70°C, and tested using the CE SARS-CoV-2 RT-PCR Assay. A results summary is shown in the table below. Two of the 22 comparator positive samples are low positive as determined by the comparator (within 3 Cts of the average Ct at LoD concentration with the comparator method).

Summary of Clinical Study #3 (Asymptomatic Individuals)

Retrospective Nasal specimens		FDA authorized SARS-CoV-2 test		
		Positive	Negative	Total
CE SARS-CoV-2 RT-PCR test	Positive	22	1 ¹	23
	Negative	0	109	109
	Total	22	110	132

¹ Ct 34.783 with investigational device; original result at the sample collection site using the comparator was N-Gene Ct 34.20

Performance of CE SARS-CoV-2 RT-PCR Assay is presented below:

Performance Estimates for Asymptomatic Individuals

	Performance Estimate	95%CI
PPA	100% (22/22)	(85.1%; 100%)
NPA	99.1% (109/110)	(95.0%; 99.8%)

WARNINGS:

- For in vitro diagnostic use.
- For use under Emergency Use Authorization (EUA) only.
- Rx only.
- This product has not been FDA cleared or approved, but has been authorized by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and,
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for

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detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

- Samples and controls should always be treated as if infectious and/or biohazardous in accordance with safe laboratory procedures.
- Follow necessary precautions when handling specimens. Use personal protective equipment (PPE) consistent with current guidelines for the handling of potentially infectious samples.
- Always use pipette tips with aerosol barriers. Tips that are used must be free from DNases and RNases.
- Do not eat, drink, smoke, or apply cosmetic products in the work areas.
- Modifications to assay reagents, assay protocol, or instrumentation are not permitted, and are in violation of the product Emergency Use Authorization.
- Reagents must be stored and handled as specified and must not be used beyond their expiration date.
- Do not use the kit after the indicated expiry date.
- Dispose of waste in compliance with local, state, and federal regulations.
- Safety Data Sheets are available upon request.
- Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
- Positive Results are indicative of the presence of SARS-CoV-2 RNA

TEST LIMITATIONS:

- The performance of the CE SARS-CoV-2 RT-PCR Assay was established using nasopharyngeal swabs and nasal swabs only.
- Positive results are indicative of active infection with SARS-CoV-2 but 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.
- The impacts of vaccines, antiviral therapeutics, antibiotics, chemotherapeutic or immunosuppressant drugs have not been evaluated. The Clinical Enterprise SARS-CoV-2 RT-PCR test cannot rule out diseases caused by other bacterial or viral pathogens.
- The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- **False Negative Results** may arise from:
 1. Degradation of the SARS-CoV-2 RNA during shipping/storage
 2. Improper sample collection

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3. Specimen collection after SARS-CoV-2 RNA can no longer be found in the specimen matrix
 4. Using unauthorized extraction or assay reagents
 5. The presence of RT-PCR inhibitors
 6. Mutation in the SARS-CoV-2 virus
 7. Failure to follow the standard operating procedure
- **False-Positive Results** may arise from:
 1. Cross contamination during wet bench processing
 2. Cross contamination between patient samples
 3. Specimen mix-up
 4. RNA contamination during product handling