EMERGENCY USE AUTHORIZATION (EUA) SUMMARY

LIFE SCIENCES TESTING CENTER COVID-19 TEST

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

For Use by Individuals 18 Years of Age or Older

(The Life Sciences Testing Center COVID-19 Test will be performed at the Life Sciences Testing Center, located at 147 S Bedford St., Burlington, MA 01803, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests as described in the Laboratory Standard Operation Procedures (SOPs) that were reviewed by the FDA under this EUA.)

INTENDED USE

The Life Sciences Testing Center COVID-19 Test is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in anterior nasal swab specimens that are self-collected (unsupervised) at home (which includes in a community-based setting) using the Life Sciences Testing Center COVID-19 Home Collection Kit, by individuals 18 years of age or older suspected of COVID-19 by their healthcare provider. Specimens collected using the Life Sciences Testing Center COVID-19 Home Collection Kit are transported at ambient temperature for testing at the authorized laboratory.

Testing is limited to the Life Sciences Testing Center, located at 147 S Bedford St., Burlington, MA, 01803, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high-complexity tests.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in anterior nasal swab 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.

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.

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

The Life Sciences Testing Center COVID-19 Test is intended for use by qualified laboratory personnel specifically instructed and trained in the techniques of real-time RT-PCR assays and in vitro diagnostic procedures. The Life Sciences Testing Center COVID-19 Test is intended for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

1) Life Sciences Testing Center COVID-19 Home Collection Kit:

The Life Sciences Testing Center COVID-19 Home Collection Kit consists of a sample label for the specific patient, anterior nasal swab, transport specimen vial (tube), instructions for use, return bag, small biohazard bag, help and contact number insert, and return labels if necessary.

Instructions included in the kit direct the user on how to open the nasal swab and collect the sample unobserved, and how to properly package the sample and return it to a predetermined drop box. Each Life Sciences Testing Center COVID-19 Home Collection Kit is intended to be returned on the same day the specimen/sample is collected, at ambient conditions in accordance with the standards as put forth by the CDC and WHO for transport of suspected COVID-19 samples.

Samples received at the clinical laboratory for testing will be inspected for proper sampling and swabbing prior to accessioning and acceptance for testing.

Testing will be performed at the Northeastern University Life Sciences Testing Center, a high complexity molecular diagnostic laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a.

Components manufactured by SteriPack USA and BD and supplied with the Life Sciences Testing Center COVID-19 Home Collection Kit include:

Name	Description	Qty/Kit	Material Supplier
3” Polyester Nasal Swab	Sterile Polyester Spun Swab	1	SteriPack USA
BD Vacutainer Plus Tube	13x75 mm 3 mL BD Vacutainer Plus tube. Clear BD Hemogard closure. Paper label. No additive.	1	BD

Life Sciences Testing Center COVID-19 Home Collection Kit contents include:

Patient specific barcode label
Anterior nasal swab
Transport specimen vial (tube)
Instructions for use with contact number
Return bag

Small biohazard bag

a) Home Collection Kit Ordering and Processing

Individuals will receive the Life Sciences Testing Center COVID-19 Home Collection Kit upon receiving a prescription from a physician. A physician will write the prescription based on his/her own professional judgement. As a prescription use device, the Life Sciences Testing Center COVID-19 Home Collection Kit is not to be dispensed at the community-based site to the patient before the prescription for the test is written.

Patients are instructed to unwrap the anterior nasal swab and to swab each nostril by rotating around the nares (contacting the nasal cavity) for 15 seconds per nostril and then place the anterior nasal swab with the swabbing side face down (towards bottom of the tube).

b) Shipping:

Self-collected anterior nasal swab samples will be transported under dry condition in a sterile collection container and dropped off in a designated drop box location either inside or outside a building located on a school campus. Samples will be retrieved from the drop box(es) and transported via certified medical courier to the Life Sciences Testing Center.

c) Specimen Accessioning:

Upon receipt into the laboratory samples will enter the accessioning area. Specimens will be opened by trained accessioning staff and inspected for the following prior to entering the lab workflow:

- All samples must be properly labeled. The label must include at least two patient identifiers and date/time of collection to ensure the specimen is received and processed within 56 hours of collection.
- Test Requisition/Manifest must match the samples received. Verify there are no missing samples or orders.
- The proper sample swab and tubes were used for collection.
- Containers and tubes are not compromised or broken.

If any sample does not meet all the acceptance criteria stated above, contact the ordering physician to get a new sample or to get missing information. If a swab is missing, the test will be cancelled, and patient would be called to get recollected. Outcome and cancelled tests and/or recollection reasons will be documented in patient's chart.

If the sample or requisition does not meet the labs acceptability requirements, it will be set aside in a Quarantine Problem Sample box in the fridge, until all issues have been resolved.

2) <u>Life Sciences Testing Center COVID-19 Test:</u>

The Life Sciences Testing Center COVID-19 Test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test using the Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010) with a modified automated extraction method and TaqMan SARS-CoV-2 RNase P Assay Kit. The Life Sciences Testing Center COVID-19 Test is designed to detect RNA from the SARS-CoV-2 in anterior nasal swab specimens from patients suspected of COVID-19 by their healthcare providers.

SARS-CoV-2 nucleic acid from patient samples is extracted using the Thermo Fisher TaqPath COVID-19 Combo Kit with a modified automated extraction method (200-µl sample input volume), which uses the MagMAX Viral/Pathogen II Nucleic Acid Isolation Kit on the Agilent Bravo automated liquid handling platform instead of on the authorized Thermo KingFisher extraction system in EUA200010.

The SARS-CoV-2 primer and probe sets are designed to detect RNA from the SARS-CoV-2 N, ORF1ab and S genes with one additional primer and probe set used to detect an MS2 internal control in anterior nasal specimens. The RT-PCR test consists of three processes in a single tube: 1) reverse transcription of target RNA to cDNA, 2) PCR amplification of target and internal control, and 3) simultaneous detection of all three target amplicons using different fluorescent dye labeled probes. The RNase P control reaction uses one primer and probe set to detect human RNase P in a clinical sample and is run in a single plex format to ensure adequate sample collection.

During the amplification process, each probe anneals to a specific target sequence located between the forward and reverse primers. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades the bound probe, causing the reporter dye to separate from the quencher dye, generating a fluorescent signal. Fluorescence intensity is monitored at each PCR cycle by the Applied Biosystems™ (ABI) instruments. The data are analyzed, then interpreted by the ABI COVID-19 Interpretive Software.

Please refer to FDA EUA authorized Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010) IFU for more detailed information.

INSTRUMENTS USED WITH TEST

The Life Sciences Testing Center COVID-19 Test is performed using the following real-time fluorescence PCR instrument and associated software:

- Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software v1.4.1.

Automated RNA extraction is performed using the following:

- Agilent Bravo automated liquid handling platform

REAGENTS AND MATERIALS

- RNA Extraction kit: MagMAX Viral/Pathogen II Nucleic Acid Isolation Kit (Cat# A48383) with a specimen input volume of 200 µl.

- RT-PCR kit: Thermo Fisher TaqPath COVID-19 Combo Kit, 1,000 reactions (Cat# A47814) and TaqMan SARS-CoV-2 RNase P Assay, 1,000 reactions (Cat# A49564)

Component	Contents	Volume	Storage
TaqPath RT-PCR COVID-19 Kit, 1000 reactions	COVID-19 Real Time PCR Assay Multiplex (ORF1ab, N gene, S gene, MS2)	1,500 µl	-10 to -30˚C
	MS2 Page Control	10 x 1,000 µl	-10 to -30˚C
TaqPath COVID-19 Control Kit (1 x 10^4 copies/µl)		2 x 10 µl per kit; 5 kits included	≤-70˚C
Taqpath COVID-19 Control Dilution Buffer		2 x 250 µl per kit, 5 kits included	-10 to -30˚C
TaqMan SARS-CoV-2 RNase P Assay Kit		1 x 1,000 µl	-10 to -30˚C

CONTROLS TO BE USED WITH THE LIFE SCIENCES TESTING CENTER COVID-19 HOME COLLECTION KIT AND RT-PCR TEST

NTCs (No template controls):
A negative (no template) control is needed to assess the possibility of specimen contamination on the assay run and is used on every assay plate. This control is molecular grade, nuclease-free water and is included with each extraction and with each RT-PCR run.

SARS-CoV-2 Positive Control:
A positive template control is needed to verify that the assay run (ORF1ab, N gene, S gene of SARS-CoV-2) is performing as intended. TaqPath™ COVID-19 Control (1×10^4 copies/µL) diluted to a working stock of 25 copies/µL is used as the positive RNA

control.

Extraction Control:
An extraction control (MS2 phage) is used to verify the proper extraction of RNA from the samples.

Internal Control:
An internal human specimen control targeting RNase P is used to verify that nucleic acid is present in every sample and is used for every sample processed.

INTERPRETATION OF RESULTS

A minimum of two Negative Controls (one for the COVID-19 assay and one for the RNase P assay) and one Positive Control must be present for each run for the COVID-19 plus RNase P assay.

Additional Negative Control wells must be run for each extraction that is represented on a real-time RT-PCR plate. All control wells must pass for the real-time RT-PCR plate to be considered valid.

Validation of results is performed automatically by the Applied Biosystems COVID-19 Interpretive Software based on performance of the Positive and Negative Controls.

Table 1: COVID-19 Assay Ct cutoff values

Specimen	Target	Ct cutoff
Positive Control	MS2	Valid Ct values are >37
	Viral targets	Valid Ct values are ≤37
Negative Control	MS2	Valid Ct values are ≤32
	Viral targets	Valid Ct values are >37
Clinical Specimens	MS2	Valid Ct values are ≤32
	Viral targets	Valid Ct values are ≤37

Table 2: RNase P Assay Ct cutoff values

Specimen	Target	Ct cutoff
Negative Control	RNase P	Valid Ct values are >33
Clinical Specimens	RNase P	Valid Ct values are ≤33

Interpretation of Patient Results

ORF1ab	N gene	S gene	MS2	RNase P	Status	Result	Action
NEG	NEG	NEG	NEG	NEG	INVALID	NA	Repeat test by re-extracting the original sample and repeating the RT-PCR. If the repeat result remains invalid, consider collecting a new specimen.
NEG	NEG	NEG	NEG	POS	INVALID	NA	Repeat test by re-extracting the original sample and repeating the RT-PCR. If the repeat result remains invalid, consider collecting a new specimen.
NEG	NEG	NEG	POS	POS	VALID	SARS-CoV-2 Not Detected	Report results to the healthcare provider and appropriate public health authorities. Consider testing for other viruses.
NEG	NEG	NEG	POS	NEG	INVALID	NA	Repeat test by re-extracting the original sample and repeating the RT-PCR. If the repeat result remains invalid, consider collecting a new specimen.
Only one SARS-CoV-2 target = POS			POS or NEG		VALID	SARS-CoV-2 Inconclusive[1]	1. Repeat test by re-extracting the original sample and repeating the RT-PCR. 2. After retesting one time, report results to the healthcare provider and appropriate public health authorities. IMPORTANT! Samples with a result of SARS-CoV-2 Inconclusive shall be retested one time. If the repeat result remains inconclusive, the healthcare provider should conduct additional confirmation testing with a new specimen, if clinically indicated.
Two or more SARS-CoV-2 targets = POS			POS or NEG		VALID	Positive SARS-CoV-2	Report results to the healthcare provider and appropriate public health authorities.

[1] Samples with a result of SARS-CoV-2 Inconclusive shall be retested one time.

All results from the tests are reviewed by the clinical lab personnel and negative results are released to the patients via their patient portal. In the event of an inconclusive result the patients are contacted by the ordering physician or their designee and instructed to re-swab/retest. In the event a sample is positive the patient is contacted by the ordering physician or their designed and given appropriate medical instruction. Patients are emailed when their results are ready, and they then log into a secure server to obtain their results/lab report from the patient portal of our lab information management system.

PERFORMANCE EVALUATION

1) *Limit of Detection (LoD) - Analytical Sensitivity:*

The LoD of the Life Sciences Testing Center COVID-19 Test was determined using quantified inactivated SARS-CoV-2 virus (ATCC VR-1986HK). All swabs used were swabbed in human nasals. Swabs with natural clinical matrix in 3 mL of VTM in replicates of 5 were spiked with inactivated SARS-CoV-2 virus at concentrations of 41.67 copies/reaction, 50 copies/reaction, 62.5 copies/reaction, 71.4 copies/reaction, 83.3 copies/reaction and 90.9 copies/reaction. The preliminary LoD determination of the Life Sciences Testing Center COVID-19 Home Collection Kit and RT-PCR Test was 71.4 copies/reaction.

Table 3. Preliminary LoD Determination Results

Concentration (copies/reaction)	Positive	Not Detected
41.67	4/5	1/5
50	4/5	1/5
62.5	4/5	1/5
71.4	5/5	0/5
83.3	5/5	0/5
90.9	5/5	0/5

The preliminary LoD was confirmed by testing additional 20 spiked nasal swab replicates at 71.4 copies/reaction. All tested replicates (20/20) produced the expected results. The LoD for the Life Sciences Testing Center COVID-19 Test was therefore confirmed to be 71.4 copies/reaction.

2) *Analytical Specificity (Inclusivity and Cross-Reactivity):*

Thermo Fisher Scientific, Inc. has granted Life Sciences Testing Center a right of reference to leverage the performance data from the Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010). The details of the performance of the Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010) can be found here: https://www.fda.gov/media/136112/download.

3) *Clinical Evaluation:*

Thermo Fisher Scientific, Inc. has granted Life Sciences Testing Center a right of reference to leverage the Clinical Evaluation data from the Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010). The details of the performance of the Thermo Fisher TaqPath COVID-19 Combo Kit (EUA200010) can be found here:

https://www.fda.gov/media/136112/download.

4) ***Specimen Stability Studies***

a) Specimen Stability:

Specimen stability of dry spun polyester swabs has been demonstrated by Quantigen Biosciences with support from The Gates Foundation and United Health Group. The Quantigen study demonstrated up to 56-hour stability for dry anterior nasal spun polyester swabs when subjected to both summer and winter thermal excursions.

Quantigen Biosciences has granted a right of reference to the stability data to any sponsor, such as Life Sciences Testing Center, pursing an EUA for which a claimed specimen type is dry spun polyester swabs. Therefore, the stability of anterior nasal samples collected using dry spun polyester swabs were not evaluated in a separate sample stability study.

Briefly, to simulate summer shipping conditions, dry anterior nasal swabs were prepared by spiking with one of two concentrations (2X LoD and 10X LoD) of pooled SARS-CoV-2 positive patient samples. Swabs were then incubated at 40°C for 12 hours, followed by 32°C for 42 hours. Samples were hold at room temperature for 2 hours and were then tested using an EUA authorized assay at time 0 and 56 hours post-incubation (Table 4).

To simulate winter shipping conditions, dry anterior nasal swabs were prepared by spiking with the pooled SARS-CoV-2 positive patient samples at the concentration of 10X LoD. Swabs were then subject to three freeze-thaw cycles altering between -20°C for 18-20 hours and room temperature (25-27°C) for 4 hours. Samples were tested using an EUA authorized assay at time 0 and 72 hours post-incubation (Table 4).

Table 4. Summary of the simulated shipping study

Profile	Swab	Time Point	N	MS2	N Gene	ORF1ab	S Gene
Summer	**2xLoD Dry poly swab**	0h	5	23.2	32.1	29.6	31.7
	10xLoD Dry poly swab	0h	5	23.2	29.1	26.6	27.9
	2xLoD Dry poly swab	56h	20	23.8	31.5	29.0	33.0
	10xLoD Dry poly swab	56h	10	23.7	29.4	27.8	30.1
Winter	**10xLoD Dry poly swab**	0h	10	-	29.4	29.4	30.4
	10xLoD Dry poly swab	72h	10	-	29.9	30.0	31.8

All tested dry swab samples produced the expected results and the average Ct values for the N gene, ORF1ab gene and S gene did not change more than 3Ct.

b) Dry Swab Resuspension:

The Life Sciences Testing Center COVID-19 Home Collection Kit leverages dry transport of the nasal swab specimen, as validated by Quantigen. Therefore, the swab must be rehydrated in advance of performing SARS-CoV-2 and RNase P testing using the following swab rehydration process:

1. Add 3 mL of Viral Transport Medium (VTM) to each sample tube containing the dry swab
2. Mixed for 5 minutes by a shaker at 1000 RPM

To demonstrate that dry spun polyester swabs were an acceptable specimen type for testing with the Life Sciences Testing Center COVID-19 Test, performance of the assay was evaluated using dry swabs resuspended using the process described above.

Twenty contrived positive specimens at 2X LoD were prepared by spiking inactivated SARS-CoV-2 virus (ATCC VR-1986HK) into VTM followed by spiking the solution directly onto the spun polyester swabs with natural clinical matrix (the swabs used have been swabbed in human nasals). The spiked swab was dried overnight (~24 hour) in an BD Vacutainer Plus tube (dry swab) and then rehydrated following the swab rehydration process described above. This has been done side by side with samples prepared using VTM spiked with the same virus material at the same concentration (VTM swab). Twenty individual replicates of each sample type were tested. Results are summarized in the table below. The detection is similar in both dry swab and VTM swab sample types (95% agreement, similar Ct values).

Table 3. Dry Swab Rehydration Study Data

Swab Type	Sample Type (N)	Concentration	Number of Positives	Mean Ct				
				N Gene	S Gene	ORF1ab	MS2	RNase P
Spun Polyester	Dry swab (20)	2X LoD (142 copies /reaction)	19/20	30.9	32.7	30.8	24.0	25.1
	VTM swab (20)		20/20	31.1	34.6	31.3	24.3	26.9

5) Human Usability Study

Clinical Research Sequencing Platform, LLC at the Broad Institute has granted Life Sciences Testing Center a right of reference to leverage the Human Usability data from the CRSP Self Swab kit EUA submission (EUA200147/S002).

Additional Requirement as a Post-Authorization Condition:

Life Sciences Testing Center will submit a report to the FDA (within 30 days of implementation) summarizing any testing performed with the Life Sciences Testing Center COVID-19 Test including how many Life Sciences Testing Center COVID-19 Home Collection Kit were requested and sent for home collection. Life Sciences Testing Center will also document the number of kits that were disseminated and returned to the laboratory according to the instructions, how many specimens were rejected during accessioning and the reasons for rejection, and the positivity rate of the first Life Sciences

Testing Center COVID-19 Home Collection Kit lot using the Life Sciences Testing Center COVID-19 Test.

Limitations:

• The use of this assay as an in vitro diagnostic under the FDA Emergency Use Authorization (EUA) is limited to Life Sciences Testing Center, located at 147 S Bedford St., Burlington, MA 01803, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, and meets requirements to perform high complexity tests. Use of this assay is limited to personnel who are trained in the procedure. Failure to follow these instructions may result in erroneous results.

• A false negative result may occur if a specimen is improperly collected, transported or handled. False negative results may also occur if amplification inhibitors are present in the specimen or if inadequate numbers of organisms are present in the specimen.

• This test cannot rule out diseases caused by other bacterial or viral pathogens.

• Samples must be collected, transported, and stored using appropriate procedures and conditions. Improper collection, transport, or storage of specimens may hinder the ability of the assay to detect the target sequences.

• Results from the Life Sciences Testing Center COVID-19 Test should be used as an adjunct to clinical observations and other information available to the physician. The result is only for clinical reference, and the clinical management of patients should be considered in combination with their symptoms/signs, history, other laboratory tests and treatment responses.

• Although the detected target sequences of this kit are in conserved regions of the SARS-CoV-2 genome, rare mutations may lead to negative results.

• 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. Optimum specimen types and timing for peak viral levels during infections caused by SARS-CoV-2 have not been determined.

• Specimens that are collected at home will not be tested with an internal control to confirm that the specimen was properly collected. Specimens collected at home from SARS-CoV-2 positive individuals may yield negative results if the specimen was not collected properly.

• 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.

Warnings:

- This product has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by the authorized laboratory.
- 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 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.