EMERGENCY USE AUTHORIZATION (EUA) SUMMARY DxTerity SARS-CoV-2 RT-PCR Test (DxTerity Diagnostics Clinical Laboratory)

For in vitro diagnostic use
Rx only
For use under Emergency Use Authorization (EUA) Only

(The DxTerity SARS-CoV-2 RT-PCR Test will be performed in the DxTerity Diagnostics Clinical Laboratory, located at 19500 S. Rancho Way, Suite 116, Rancho Dominguez, CA 90220, that 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, as described in the Laboratory procedures that were reviewed by the FDA under this EUA).

INTENDED USE

The DxTerity SARS-CoV-2 RT-PCR Test is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in saliva specimens from individuals suspected of COVID-19 by their healthcare provider. Saliva specimens are collected in a healthcare setting under the supervision of a healthcare provider using the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device. Testing is limited to the DxTerity Diagnostics, Inc. laboratory located at 19500 S. Rancho Way, Suite 116, Rancho Dominquez, California 90220, which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42U.S.C. §263a, and meets 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 saliva 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 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. Negative results for SARS-CoV-2 RNA from saliva should be confirmed by testing of an alternative specimen type if clinically indicated.

Testing with the DxTerity SARS-CoV-2 RT-PCR Test is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and *in vitro* diagnostic procedures. DxTerity SARS-CoV-2 RT-PCR Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The DxTerity SARS-CoV-2 RT-PCR Test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test performed on saliva specimens using a MagMax 96 Magnetic Particle Processor (software BindIt 4.0) for RNA extraction and a Thermo Fisher Applied Biosystems ViiA 7 Real-Time PCR amplification system with the Applied Biosystems QuantStudio5 software v1.3 for data analysis. The assay uses primers and probes that were developed and validated under the Emergency Use Authorization (EUA) for the TaqPath COVID-19 Combo Kit and are designed to detect RNA from SARS-CoV-2 in respiratory specimens from patients as recommended for testing by public health authority guidelines.

Saliva specimens must be collected using the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device. Saliva specimens must be transported and stored at ambient temperature and tested within 48 hours of collection.

Please refer to FDA's FAQs on Diagnostic Testing for SARS-CoV-2 for additional information regarding the collection appropriate specimen types for the detection of SARS-CoV-2.

RNA extraction is performed using Sera-Mag SpeedBeads Carboxyl Magnetic Beads (GE Healthcare) using the Applied Biosystem MagMax 96 Magnetic Particle Processor. The input sample volume is 540 µL, the elution volume is 50 µL.

Reverse transcriptase-PCR (RT-PCR) is performed using the Thermo Fisher TaqPath COVID-19 Combo Kit with 10 µL of the extracted sample.

INSTRUMENTS USED WITH THE TEST

The DxTerity SARS-CoV-2 RT-PCR Test is to be used with the Applied Biosystem MagMax 96 Magnetic Particle Processor (software BindIt 4.0) for RNA extraction, the Thermo Fisher Applied Biosystems ViiA 7 Real-Time PCR System with the Applied Biosystems QuantStudio 5 software v1.3 for data analysis.

REAGENTS AND MATERIALS

Table 1. Reagents and materials required for use of the DxTerity SARS-CoV-2 RT-PCR Test

Reagent	Manufacturer	Catalogue #
DxPure Bead Mix	DxTerity Diagnostics	N/A - not commercially available
DxBind II	DxTerity Diagnostics	N/A - not commercially available
DxPure Wash Buffer	DxTerity Diagnostics	N/A - not commercially available
Sera-Mag Speedbeads	GE Life Sciences	24152105050250 or 24152105050350

Reagent	Manufacturer	Catalogue #
TaqPath COVID-19 Combo Kit	Thermo Fisher Scientific	A47815
COVID-19 Real Time PCR Assay Multiplex (Orf1ab, N gene, S gene)		
MS2 Phage Control		
TaqPath COVID-19 Control Kit	Thermo Fisher Scientific	A47816
TaqPath 1-Step Multiplex Master Mix (No ROX)	Thermo Fisher Scientific	A28523
MicroAmp Fast Optical 96-Well Reaction Plate, 0.1 mL	Thermo Fisher Scientific	4366932
MicroAmp Fast Optical Adhesive Film	Thermo Fisher Scientific	4311971
MicroAmp Adhesive Film Applicator	Thermo Fisher Scientific	4333183
Nuclease-free water	--	--
Ethanol (96-100%)	--	--

CONTROLS TO BE USED WITH THE DxTerity SARS-CoV-2 RT-PCR Test
The controls to be used with DxTerity SARS-CoV-2 RT-PCR Test are described in **Table 2**.

Table 2. Controls utilized with the DxTerity SARS-CoV-2 RT-PCR Test

Control Type	Purpose	Frequency of Testing
Negative	To monitor for cross-contamination during RNA extraction and RT-PCR	Once per batch of specimens
Positive	To monitor the integrity of the RT-PCR reagents and process	Once per run of RT-PCR
Internal (MS2 Phage)	To monitor the integrity of nucleic acid extraction and RT-PCR for each specimen	Added to each specimen and the Negative Control prior to extraction

The Negative Control consists of water and the Positive Control is an RNA control that contains the genomic regions targeted for amplification by the assay. These elements are identical to those contained in the Thermo TaqPath COVID-19 control kit.

The results from the controls are interpreted according to the criteria shown in **Table 3**. If the results obtained with the Positive and Negative Controls do not meet the criteria shown, the results from the entire batch of samples are considered invalid and repeat testing must be performed.

Table 3. Ct values for controls that must be observed to obtain valid results

Control	Ct Value (Optical Channel)			
	N Gene (VIC)	S Gene (ABY)	ORF1a (FAM)	MS2 Phage (JUN)
Negative	>40	>40	>40	≤37
Positive	<37	<37	<37	Undetermined[1]

Internal (MS2)	Any	Any	Any	<37

[1] The MS2 Phage Internal Control is not added to the Positive Control and no signal should be obtained

INTERPRETATION OF RESULTS

The results from testing of patient samples are interpreted according to the criteria described in **Table 4**.

Table 4. Result interpretation for patient samples

Ct Value (Optical Channel)				Result Interpretation
N Gene (VIC)	**S Gene (ABY)**	**ORF1ab (FAM)**	**MS2 Phage (JUN)**	
Undetermined	Undetermined	Undetermined	<37	Negative
Two of three <37			Any Result[2]	Positive
One of three <37			Any Result[2]	Re-test[1]
Undetermined	Undetermined	Undetermined	Undetermined	Re-test[1]

[1] Re-test required from the residual extracted sample and by processing a new aliquot of the original sample if volume permits; if the re-test result is the same as the original then report result as "inconclusive"

[2] MS2 Phage signal is not required for a Positive Result

LIMITATIONS

Collection of saliva specimens is limited to patients with symptoms of COVID-19 and should be performed in a healthcare setting under the supervision of a trained healthcare provider using the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device. Negative results for SARS-CoV-2 RNA from saliva should be confirmed by testing of an alternative specimen type if clinically indicated.

Saliva specimens must be transported and stored at ambient temperature and tested within 48 hours of collection.

PERFORMANCE EVALUATION

1) Analytical Sensitivity

The LoD was determined using whole viral genomic RNA obtained from BEI Resources (Genomic RNA from SARS-Related Coronavirus 2, Item NR-52285) diluted in SARS-CoV-2 negative saliva samples collected into the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device. An initial estimate of the LoD was determined by testing three replicates at each of six different target levels: 500, 200, 150, 100, 50, and 20 copies/mL. The presumptive LoD was determined as the lowest level at which all three replicates were positive for all three SARS-CoV-2 targets as 100 copies/mL (**Table 5**). The estimated LoD was confirmed by testing an additional 20 replicates at the same target level (1X LOD) as well as 0.5X (50 copies/mL) and 2X (200 copies/mL) of the LOD (**Table 6**). 19/20 of the replicates at 0.5X LOD level generated positive results and the LoD as per the results interpretation algorithm was therefore confirmed to be 50 copies/mL.

Table 5. Summary of results from the Preliminary LOD study

Transcript Copies/mL	Replicate	Interpretation	Target (Optical Channel)			
			N Gene (VIC)	S Gene (ABY)	ORF1ab (FAM)	MS2 (JUN)
20	1	Negative	Undetermined	Undetermined	37.0	26.7
	2	Inconclusive	37.4	34.8	Undetermined	29.7
	3	Inconclusive	35.2	Undetermined	39.0	28.9
50	1	Positive	33.6	34.7	35.0	25.1
	2	Positive	35.2	34.5	34.1	25.4
	3	Inconclusive	37.4	34.9	37.1	30.1
100	1	Positive	34.0	32.8	33.8	26.8
	2	Positive	33.1	31.9	32.9	26.1
	3	Positive	34.5	32.9	33.1	27.0
150	1	Positive	33.6	31.7	33.4	27.6
	2	Positive	32.3	32.4	31.8	27.8
	3	Positive	27.63	29.67	28.15	26.10
200	1	Positive	33.0	30.7	32.4	27.6
	2	Positive	31.9	31.2	32.3	26.1
	3	Positive	32.5	31.9	33.3	26.4
500	1	Positive	31.8	30.6	32.1	28.1
	2	Positive	31.2	30.6	30.8	27.3
	3	Positive	32.4	30.5	32.0	28.1

Table 6. Summary of overall results from LOD Confirmation

Transcript Copies/mL	Number Tested	Overall Percent Positive	Analysis	Target (Optical Channel)			
				N Gene (VIC)	S Gene (ABY)	ORF1ab (FAM)	MS2 (JUN)
50	20	95 (19/20)	Percent Positive	100 (20/20)	95 (19/20)	70 (14/20)	100 (20/20)
			Mean Ct (SD)	33.42 (0.77)	35.15 (1.22)	36.59 (1.91)	24.36 (0.30)
100	20	100 (20/20)	Percent Positive	100 (20/20)	100 (20/20)	100 (20/20)	100 (20/20)
			Mean Ct (SD)	31.86 (0.40)	33.20 (0.54)	34.08 (0.66)	24.40 (0.30)
200	20	100 (20/20)	Percent Positive	100 (20/20)	100 (20/20)	100 (20/20)	100 (20/20)
			Mean Ct (SD)	30.92 (0.43)	31.96 (0.38)	32.76 (0.50)	24.19 (0.28)

2) Inclusivity

The DxTerity SARS-CoV-2 RT-PCR Test is a modification of the previously authorized Thermo Fisher Applied Biosystems TaqPath COVID-19 Combo Kit. Inclusivity of target primer and probe sequences has already been evaluated by FDA under the EUA and therefore additional analysis is not required.

3) Analytical Specificity (Cross-reactivity)

Cross-reactivity

The DxTerity SARS-CoV-2 RT-PCR Test is a modification of the previously authorized ThermoFisher Applied Biosystems TaqPath COVID-19 Combo Kit. Cross-reactivity of target primer and probe sequences with other microorganisms has already been evaluated by FDA under the EUA and therefore additional analysis is not required.

4) Clinical Evaluation

Saliva Samples

Clinical evaluation was performed with true clinical samples to evaluate the use of saliva as a specimen type for detection of SARS-CoV-2 in individuals suspected of COVID-19 by their healthcare provider.

Paired NP swab and saliva collections were performed under an IRB approved protocol and informed consent and either purchased from The MT Group (Van Nuys, CA) with samples collected in California and Florida or obtained at testing clinics throughout the greater Los Angeles area and Phoenix, Arizona.

A total of 76 symptomatic subjects were evaluated as part of the study that included several individuals with a prior positive SARS-CoV-2 test result. Following collection of the nasopharyngeal swab, subjects self-collected a 2 mL saliva sample using the Spectrum Solutions SDNA-1000 Saliva Collection Device. A summary of the results of the study is presented in **Table 7** below.

There was 97.2% positive and 92.5% negative agreement between the results obtained from testing of saliva with the DxTerity SARS-CoV-2 RT-PCR Test and those obtained from nasopharyngeal swabs using the EUA authorized comparator. There were four discordant sample pairs with three of these testing positives by saliva and one testing positive by swab. Of the three false positive results, one had a previously positive SARS-CoV-2 test result approximately three weeks before the NP swab was collected for this study.

Overall mean Ct values were similar for saliva and nasopharyngeal swab specimens, there was no correlation between Ct values from different samples from the same patient. Nevertheless, the results support the use of saliva as a specimen type for use with the DxTerity SARS-CoV-2 RT-PCR Test

Table 7. Clinical Evaluation of the DxTerity SARS-CoV-2 RT-PCR Test

		Nasopharyngeal Swab		
		Positive	Negative	Total
Saliva	Positive	35	3*	38
	Negative	1¥	37	38
	Total	36	40	76
Positive Agreement		97.2% (35/36) [85.8%-99.5%]		

Negative Agreement	92.5% (37/40) [80.1%-97.4%]	
¥ The sole Negative discordant swab sample was Positive with the EUA authorized comparator assay, but Negative when evaluated with a different EUA authorized test. *2/3 false positive swab specimens were also evaluated with another EUA authorized test and determined to be Negative		

The sponsor has agreed to perform the following post-authorization studies: assessment of NPA by testing additional clinical samples and evaluation of sample stability in the saliva collection device (Conditions T and U of the Letter of Authorization).

WARNINGS

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by the DxTerity Diagnostics, Inc. laboratory located at 19500 S. Rancho Way, Suite 116, Rancho Dominquez, California 90220;
- This test has been authorized only for the detection of nucleic acid from SARSCoV-2, not for any other viruses or pathogens; and
- 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.