ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
Helix COVID-19 Test
(Helix OpCp LLC (dba Helix)

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

(The Helix COVID-19 Test will be performed in the Helix Laboratory located at 9875 Towne Centre Drive San Diego, CA 92121, which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity test, per the laboratory procedures that were reviewed by the FDA under this EUA).

INTENDED USE

The Helix COVID-19 Test is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (nasopharyngeal swabs, oropharyngeal (throat) swab, mid-turbinate nasal swabs and anterior nasal swabs) from individuals suspected of COVID-19 by their healthcare provider.

Testing is limited to the Helix Laboratory located at 9875 Towne Centre Dr San Diego, CA 92121, which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meets requirements to perform high-complexity tests.

Results are for the detection of SARS-CoV-2 RNA. The 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 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 Helix COVID-19 Test is intended for use by trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR assays and *in vitro* diagnostic procedures. The Helix COVID-19 Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The assay is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test. The SARS-CoV-2 primer and probe set(s) is designed to detect RNA from the SARS-CoV-2 in respiratory specimens from patients as recommended for testing by public health

authority guidelines. The assay simultaneously detects four targets: three SARS-CoV-2 viral targets, the Nucleocapsid gene (N gene), the ORF1ab gene and the Spike protein gene (S gene), and one primer/probe set detecting MS2 RNA spiked into the reaction as an extraction and process control.

Upper respiratory specimens (nasopharyngeal swabs, oropharyngeal (throat) swab, mid-turbinate nasal swabs and anterior nasal swabs) should be collected, transported and stored according to standard procedures. The acceptable transport media for these collected upper respiratory specimen types are VTM and iSwab Microbiome collection media (ISWAB-MD-1200, Mawi DNA Technologies). Anterior nasal swabs (502CS01, Copan FLOQSwabs) may also be self-collected under the supervision of a healthcare provider. The self-collected nasal swab specimens in iSwab Microbiome collection media (ISWAB-MD-1200, Mawi DNA Technologies) or VTM (ThermoFisher cat. #R125500 or equivalent) should be shipped and tested within 48 hours of collection. All specimens received at the clinical laboratory for testing will undergo review and accessioning prior to acceptance for testing.

RNA extraction for all specimen types is performed using the MagMax Viral/Pathogen II (MVP II) Nucleic Acid Isolation kit semi-automated on the Hamilton Microlab STAR liquid handler. The input sample volume for iSwab solution is 200ul, while the input sample volume for VTM is 400 µL, the elution volume is 50 µL in both cases.

Reverse-transcriptase-PCR (RT-PCR) is performed using the Applied Biosystems TaqPath COVID-19 Combo kit and plating of 384-well plates with STP Labtech Mosquito HV and used with the QuantStudio 7 Flex Quantitative Real Time PCR Instrument.

INSTRUMENTS USED WITH THE TEST

Instruments

The Helix COVID-19 Test is to be used with the QuantStudio 7 Flex Quantitative Real Time PCR Instrument. All results are interpreted using QuantStudio RealTime PCR Software v2.4.

The Helix COVID-19 Test can be used with the following liquid handling instruments:

- Hamilton Microlab STAR liquid handler with Software Venus 3 version 4.5.0.7797
- STP Labtech Mosquito HV with Software Mosquito Genomics V1.0.0.0

REAGENTS AND MATERIALS

Table 1. Reagents and materials required for use with the Helix COVID-19 Test

Material ID	Vendor	Catalog #
MagMax Viral/Pathogen II (MVP II) Nucleic Acid Isolation kit	Applied Biosystems	A48383
TaqPath COVID-19 Combo Kit	Applied Biosystems	A47814
TaqPath 1-Step Multiplex Master Mix	Applied Biosystems	A28523

CONTROLS TO BE USED WITH THE HELIX COVID-19 TEST

- **Internal Positive Control (IPC) –** MS2 phage control which is required as an extraction positive control. This is spiked into every well prior to extraction.

- **External positive control -** TaqPath COVID-19 Control contains the SARS-CoV-2 RNA genomic regions targeted by the kit. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions. One positive control will be included with each 384 well plate.

- **Negative Control -** molecular-grade, nuclease-free, non-DEPC-treated water used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents. One negative control will be included on each 384 well plate.

INTERPRETATION OF RESULTS

1) TaqPath SARS-CoV-2 RT-PCR Test Controls Interpretation:

All control wells must pass for the patient results to be considered valid and acceptable. A positive result for a target is defined as a Cq < 37 based on the TaqPath COVID-19 Combo Kit IFU. Refer to Table 2 for a summary of control results.

Table 2. Cq Values for Controls that Must Be Observed to Obtain Valid Results

	Cq Value			
	N gene	S gene	Orf 1ab	MS2 Phage
Negative Extraction Control	Undetermined >37	Undetermined >37	Undetermined >37	<37
Positive Control	<37	<37	<37	Undetermined[1] >37
NTC	Undetermined >37	Undetermined >37	Undetermined >37	Undetermined[1] >37
MS2 Internal Control	Any	Any	Any	<37

Undetermined/Negative (Cq > 37 or No Detectable Cq)
[1]MS2 Internal Control is not added to the Positive Control or No Template Control and no signal should be generated

2) ***Examination and Interpretation of Patient Specimen Results:***

The assay interpretation and reporting of results is shown in Table 3. Assessment of patient specimen test results should be performed after the positive, extraction and NTC controls have been examined and determined to be valid and acceptable.

Table 3. Result Interpretation for Patient Samples

Orf1ab gene	**N gene**	**S gene**	**MS2**	**Status**	**Result**	**Action**
NEG	NEG	NEG	NEG	Invalid	Invalid	Repeat test. If repeat test is also invalid, consider collecting a new sample
NEG	NEG	NEG	POS	Valid	SARS-CoV-2 not detected	Report results to healthcare provider. Consider testing for other viruses.
Only one SARS-CoV-2 target = POS			POS or NEG	Valid	SARS-Cov-2 Inconclusive	Repeat test. If repeat result is inconclusive, consider additional confirmation testing if clinically indicated.
Two or more SARS-CoV-2 targets = POS			POS or NEG	Valid	Positive for SARS-Cov-2	Report results to healthcare provider and appropriate public health authorities

NA, Not applicable

PERFORMANCE EVALUATION

I. Analytical Sensitivity

The LoD was performed by spiking in heat inactivated SARS-CoV-2 virus (ATCC, VR-1986HK) in negative anterior nares clinical matrix in VTM, and Mawi iSwab Microbiome Collection Media (Mawi) using a two-fold dilution series. Three extraction replicates were performed per concentration. The preliminary LoD was defined as the lowest concentration with 3 of 3 replicates that test positive which was 1000 GCE/mL (Table 4).

Table 4. Preliminary LoD Determination Results

Viral Concentration (GCE/ml)	Detection Rate (%) VTM	Detection Rate (%) Mawi
2000	3/3 (100%)	3/3 (100%)
1000	3/3 (100%)	3/3 (100%)
500	2/3 (66.7%)	3/3 (100%)

A LoD confirmation study was performed by spiking in heat inactivated SARS-CoV-2 virus (ATCC, VR-1986HK) in negative anterior nares clinical matrix in VTM and Mawi at the LoD previously determined. Twenty (20) extraction replicates were performed for each media type. The LoD was determined to be 1000 GCE/mL for VTM and Mawi (Table 5).

Table 5. Confirmatory LoD Study Results for Clinical Samples in Different Media Types

Preservation Solution	Viral Concentration (GCE/mL)	Detection Rate (%)
VTM	1000	20/20 (100%)
Mawi	1000	19/20 (95%)

II. Analytical specificity

Inclusivity

The Helix COVID-19 Test utilizes the identical oligonucleotide sequences for the spike (S), nucleocapsid (N) and ORF 1ab regions as those used in the TaqPath COVID-19 Combo Kit. *In silico* testing was previously performed by Thermo Fisher Scientific as part of their EUA (EUA200010) and this information has been provided in the FDA authorized EUA granted to this manufacturer. Helix Laboratory obtained a right of reference from Thermo Fisher Scientific to use the *in silico* data.

Cross-reactivity

As stated previously, Helix Laboratory obtained a right of reference from Thermo Fisher Scientific to incorporate the *in silico* cross reactivity analysis findings. As part of Thermo

Fisher Scientific's EUA, they performed an *in silico* analysis of potentially cross-reactive organisms and determined that there was low risk of non-specific amplification.

III. Clinical evaluation

A clinical study was performed to evaluate the performance of the Helix COVID-19 Test using sixty remnant positive upper respiratory clinical samples, and sixty negative upper respiratory clinical samples in two collection media types.

A total of 30 positive patient clinical samples (nasopharyngeal and oropharyngeal swabs) in Mawi iSwab Collection Media were previously tested using an EUA authorized comparator assay. RNA was extracted using MagMax Viral/Pathogen II (MVP II) Nucleic Acid Isolation kit and semi-automated workflow using the Hamilton Microlab STAR. Of the 30 positive patient samples, 30 (100.0%) were detected by the Helix COVD-19 test and 30/30 (100%) negative patient specimens were confirmed negative. Results are summarized in Table 6.

Table 6. Evaluation with Clinical Specimens in Mawi iSwab Collection Media

		EUA Authorized Comparator Assay		
		Positive	Negative	Total
Helix COVID-19 Test	Positive	30	0	30
	Negative	0	30	30
	Total	30	30	60
Positive Agreement		100.0% (30/30); 88.7% - 100.0%[1]		
Negative Agreement		100.0% (30/30); 88.7% - 100.0%		

[1]Two-sided 95% score confidence intervals

Additional 30 positive patient clinical samples (nasopharyngeal swabs, oropharyngeal swabs and anterior nasal swabs) in UTM were previously tested by an EUA authorized comparator assay. RNA was extracted using MagMax Viral/Pathogen II (MVP II) Nucleic Acid Isolation kit and semi-automated workflow using the Hamilton Microlab STAR. The results are summarized in Table 7, below. The positive agreement (29/30) was 96.7% and negative agreement (30/30) was 100.0%.

Table 7. Evaluation with Clinical Specimens in VTM

		EUA Authorized Comparator Assay		
		Positive	Negative	Total
Helix COVID-19 Test	Positive	29	0	29
	Negative	1*	30	31
	Total	30	30	60
Positive Agreement		96.7% (95% CI: 83.3% - 99.4%)		
Negative Agreement		100.0% (95% CI: 88.7% - 100.0%)		

*One result was invalid without enough clinical specimen for retesting

Helix COVID-19 Test

Warnings:

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by the authorized laboratory;
- 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.