Compass Laboratory Services SARS-CoV2 Assay

ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
Compass Laboratory Services SARS-COV2 ASSAY
(Compass Laboratory Services, LLC)

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

(The Compass Laboratory Services SARS-Cov2 Assay will be performed in the Compass Laboratory Services, LLC's laboratory located at 1910 Nonconnah Blvd., Suite 108, Memphis TN 38132, which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity tests, per the laboratory procedures that were reviewed by the FDA under this EUA).

INTENDED USE

The Compass Laboratory Services SARS-CoV2 Assay 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, anterior nasal swabs, nasopharyngeal wash/aspirate or nasal aspirate) from individuals suspected of COVID-19 by their healthcare provider.

This test is also for use with nasal swab specimens that are self-collected at home or in a healthcare setting by individuals using an authorized home-collection kit specified in this EUA's authorized labeling when determined to be appropriate by a healthcare provider.

Testing is limited to Compass Laboratory Services, LLC's laboratory located at 1910 Nonconnah Blvd, Suite 108, Memphis TN 38132, 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 Compass Laboratory Services SARS-CoV2 Assay 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 Compass Laboratory Services SARS-CoV2 Assay 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 utilizes the Primerdesign Ltd Novel Coronavirus Strain 2019-nCoV (RUO) (Ref:Z-Path-2019-nCoV). The oligonucleotide primers and probe for the detection of SARS-CoV-2 were selected from the ORF 1ab genome region. This assay occurs in two wells. The first well assesses for the presence of SARS-CoV-2 with SARS-CoV-2 ORF 1ab specific oligos and probe labelled with the FAM fluorophore. The well also includes oligos and probe labelled with the VIC fluorophore specific to an internal RNA extraction control (which is from non-biologically relevant exogenous source). The second well assesses human endogenous RNA using a probe labelled with the FAM fluorophore. RNA extraction for all specimen types is performed using Life Technologies MagMax Viral Pathogen Kit automated on the MagMax Express 96 instrument. The input sample volume is 300 µL, the elution volume is 60 µL.

INSTRUMENTS USED WITH THE TEST

Instruments

The Compass Laboratory Services SARS-CoV2 Assay is to be used with the QuantStudio 12K Flex and QuantStudio 7 Flex Quantitative Real Time PCR Instruments. All results are interpreted using QuantStudio software version 12K Flex software v1.3 (QuantStudio 12K Flex) and QuantStudio RealTime PCR Software v1.3 (QuantStudio 7).

Collection Kits

This assay can be used with the Everlywell COVID-19 test home collection kit. Everlywell has granted Compass Laboratory Services a right of reference to the data supporting the use of this authorized home collection kit.

REAGENTS AND MATERIALS

Table 1. Reagents and materials required for use with Compass Laboratory Services SARS-CoV2 Assay

Material ID	Vendor	Catalog #
Novel Coronavirus Strain 2019-nCoV (RUO)	GENESIG Kits by Primerdesign Ltd	Z-Path-2019-NCoV
MagMax Viral and Pathogen Nucleic Acid Isolation kit	Applied Biosystems	A24352
Oasig 2X Lyophilized Master Mix	Primer Design	OASIG-Onestep-150

100% Ethanol	Koptec	V1005

LIMITATIONS

The performance of the Compass Laboratory Services SARS-CoV2 Assay was established using nasopharyngeal swabs. Upper respiratory specimens, such as oropharyngeal swabs and nasal swabs are considered acceptable specimen types for use with the Compass Laboratory Services SARS-CoV2 Assay but performance has not been established.

CONTROLS TO BE USED WITH THE Compass Laboratory Services SARS-CoV2 ASSAY

- Positive assay control is 2019-n-CoV Positive Control Template which is synthetic DNA representing the SARS-CoV-2 genomic region of interest. One positive assay control is analyzed for each batch of extractions. This control indicates that the primers and probes for detecting target SARS-CoV2 gene worked properly.

- Negative extraction control is molecular grade water (nuclease free). This control is carried through all experimental phases from extraction through analysis. One negative extraction control will be used for each batch of extractions.

- Internal extraction control is a synthetic, exogenous RNA that is co-purified with endogenous RNA. It indicates non-inhibition of PCR process from substances introduced during extraction process.

- Endogenous control is a human RNA that is detected in all samples that were adequately collected.

INTERPRETATION OF RESULTS

- **Positive control**: Positive control should generate a CT result of less than 40. If positive control does not pass, all samples that do not show the presence of SARS-CoV-2 RNA will be repeated.

- **Negative extraction control:** The result should be negative (CT > 40 or undetermined for SARS-CoV2 and >30 or undetermined for endogenous control) If negative control exhibits detection, all positive samples will be repeated.

- **Internal extraction control:** Internal extraction control should be detected at CT level ≤40. If internal extraction control is not detected, sample must be repeated from extraction.

Table 2. Interpretation of endogenous control and SARS-CoV-2 target

Endogenous Control	**SARS-CoV-2**	
	CT <40	**CT >40 or Undetermined**
CT ≤30	SARS-CoV-2 RNA Positive	SARS-CoV-2 RNA Negative
CT >30 or Undetermined	SARS-CoV-2 RNA Positive	Repeat sample or indeterminate*

*Sample analysis will be repeated once. If result is still inconclusive, report will show Indeterminate Result with recommendation to re-collect.

- **Positive**- Indicates the presence of SARS-CoV-2 RNA above the level of detection.
- **Negative**- Indicates SARS-CoV-2 RNA was not detected above the level of detection and sufficient controls were detected to indicate proper sample collection. Negative results are possible during the early stages of infection when viral load is at its lowest.
- **Quantity not sufficient**- Indicates that the sample was not adequate for testing for the presence of SARS-CoV-2 RNA
  - Sample leaked out during transit or shipped under inadequate conditions
- **Indeterminate result**- Indicates that sample collection was not adequate for detection of SARS-CoV-2 RNA. Sample re-collection is recommended.

PERFORMANCE EVALUATION

I. Analytical Sensitivity

The LoD was determined using genomic SARS-CoV-2 RNA isolated from a patient specimen and quantified based on a standard curve generated using the plasmid control from Primerdesign to estimate the concentration. Nasopharyngeal samples were obtained from persons without symptoms of infection. RNA was spiked into the samples at appropriate concentrations.

An initial estimate of the LoD was obtained by testing six data points between 2.5 copies/µl and 50 copies/µl in triplicate run on the QuantStudio 12K Flex. At all analyte levels, all replicates were detected. Based on these results, two analyte concentration ranges (2.5 copies/µL and 5 copies/µl) were selected for confirmation: 12 replicates at 2.5 copies/µL and 20 replicates at 5 copies/µL. The 2.5 copies/ul concentration was only tested on the QuantStudio 12K Flex with 4/12 positive results. All 20 replicates at 5 copies/µL produced the expected results for the SARS-CoV-2 target on both the QuantStudio 7 Flex and QuantStudio 12K Flex; therefore, the LoD was confirmed to be 5 copies/µL.

Table 3: Summary of Analytical Sensitivity Results for Compass Laboratory Services SARS-CoV2 Assay

	QuantStudio 7 Flex	**QuantStudio 12K Flex**
5 copies/µL	20/20	20/20
2.5 copies/µL	ND	4/12

ND, Not determined

II. Analytical specificity

Inclusivity

The Compass Laboratory Services SARS-CoV2 Assay utilizes the identical oligonucleotide sequences for the ORF 1ab region as those used in the Primerdesign Ltd COVID-19 genesig Real-Time PCR assay. *In silico* testing was previously performed by Primerdesign Ltd as part of their EUA (EUA200019) and this information has been provided in the FDA authorized EUA granted to this manufacturer. Compass Laboratory Services, LLC obtained a right of reference from Primerdesign Ltd to use the *in silico* data.

Cross-reactivity

As stated previously, Compass Laboratory Services, LLC obtained a right of reference from Primerdesign Ltd to incorporate the *in silico* cross reactivity analysis findings. As part of Primerdesign's EUA, they performed an *in silico* analysis of potentially cross-reactive organisms and determined that there was low risk of non-specific amplification. Primerdesign Ltd also performed wet-testing in triplicate on 36 viruses and organisms and detected no cross-reactivity.

III. Clinical evaluation

A clinical study with contrived specimens was performed to evaluate the performance of the Compass Laboratory Services SARS-CoV2 Assay. 38 negative nasopharyngeal swab (NPS) specimens were spiked with genomic SARS-CoV-2 RNA isolated from a patient specimen, 28 at 1X LoD and 10 at 10X LoD. In addition, 39 negative NPS, obtained from persons without symptoms and without documented exposure to the virus were also tested. RNA was extracted using Life Technologies MagMax Viral Pathogen Kit automated on the MagMax Express 96 instrument. The results are shown in the Table 4.

Table 4. Contrived results of the Compass Laboratory Services SARS-CoV2 Assay

Fold of LoD	No. pos/No. tested	Performance (2-sided 95% CI)
Negative	39/39	100% (91.0% - 100.0%)
1X	27/28	96.4% (82.3% - 99.4%)
10X	10/10	100% (72.3% - 100.0%)

In addition, a total of 49 clinical nasopharyngeal swabs (NPS) specimens were tested with the Compass Laboratory Services SARS-CoV2 Assay and concordance was determined based on the FDA authorized CDC 2019-Novel Coronavirus (2019-nCoV) real time RT-PCR Diagnostic Panel. RNA was extracted using Life Technologies MagMax Viral Pathogen Kit automated on the MagMax Express 96 instrument. Of the 24 positive NPS patient samples, 24 (100%) were detected by the Compass Laboratory Services SARS-CoV2 assay and 24/25 (96%) negative NPS samples were confirmed negative with one false positive result. Results are summarized in Table 5.

Table 5. Evaluation with Clinical NPS Specimens

		CDC EUA assay	
		Positive	**Negative**
Compass Laboratory Services SARS CoV2 Assay	**Positive**	24	1
	Negative	0	24
	Total	24	25
Positive Agreement		24/24 = 100% (95% CI: 86.2% – 100%)	
Negative Agreement		24/25 = 96% (95% CI: 80.5% - 99.3%)	

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 SARS-CoV-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.