ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
Omni COVID-19 Assay by RT-PCR
(Omnipathology Solutions Medical Corporation)

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

(The Omni COVID-19 Assay by RT-PCR will be performed at Omnipathology Solutions Medical Corporation in Pasadena, California, certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a as per the laboratory procedures reviewed by the FDA under this EUA).

INTENDED USE

The Omni COVID-19 Assay by RT-PCR is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal swab, oropharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, nasopharyngeal wash/aspirate, nasal aspirate, and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to Omnipathology Solutions Medical Corporation in Pasadena, California, 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.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper and lower 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.

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

DEVICE DESCRIPTION AND TEST PRINCIPLE

The Omni COVID-19 Assay by RT-PCR is a real-time reverse transcription polymerase chain reaction (rRT -PCR) test. The primer and probe sets used in this test are identical to those described under the EUA for the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel and detect RNA from the SARS-CoV-2 virus in

nasopharyngeal swab, oropharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, nasopharyngeal wash/aspirate, nasal aspirate, and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider. This test differs from the CDC assay in that it uses an alternative automated nucleic acid extraction and amplification system (BD MAX System), and also the N1 and N2 primers and probes are multiplexed in a single reaction resulting in an additive FAM signal for detection of SARS-CoV-2.

For the Omni COVID-19 Assay by RT-PCR, 200 µL of the specimen (in UTM, VTM, or saline) is mixed with the BD MAX Sample Buffer Tube (containing 750 µL buffer) from the BDMAX ExK TNA-2 or 3 Kit. All necessary samples, components, and reagents are loaded onto the BD MAX System (with Software version 4.70). Using this system, all major processes from total nucleic acid extraction, to reverse transcription of RNA into cDNA, and through amplification and detection of assay targets with real-time PCR is automated on the system. The real-time PCR reaction exploits the 5' nuclease activity of the DNA polymerase to cleave a TaqMan probe during PCR. The TaqMan probe contains a reporter dye (FAM) at the 5' end of the probe and a quencher dye (BHQ1) at the 3' end of the probe. When the probe is intact, the proximity of the reporter dye to the quencher dye results in suppression of the reporter fluorescence. During real-time PCR, if the target of interest is present, the probe specifically anneals between the forward and reverse primer sites, and the 5'-3' nucleolytic activity of the DNA polymerase cleaves the probe between the reporter and the quencher. Cleavage results in increased fluorescence of the reporter. Accumulation of PCR products is detected directly by monitoring the increase in fluorescence of the reporter dye after each cycle.

INSTRUMENTS USED WITH THE TEST

The Omni COVID-19 Assay by RT-PCR test is to be used with the BD MAX System (Becton, Dickinson and Company 7 Loveton Circle Sparks, MD 21152 USA, Software version 4.70).

REAGENTS AND MATERIALS

Table 1: Reagents and materials required for use with the Omni COVID-19 Assay by RT-PCR

Component	Supplier	Catalog#	Description
BDMAX ExK TNA-3 Kit	Becton Dickinson and Company, 7 Loveton Circle, Sparks, MD 21152	442827	Extraction and specimen process control (SPC)
BDMAX ExK TNA-2 Kit	Becton Dickinson and Company, 7 Loveton Circle, Sparks, MD 21152	442825	Extraction and specimen process control (SPC)
BD MAX Microfluidic PCR Cartridge	Becton Dickinson and Company, 7 Loveton Circle, Sparks, MD 21152	437519	Amplification of nucleic acids

Table 1: Reagents and materials required for use with the Omni COVID-19 Assay by RT-PCR

Component	Supplier	Catalog#	Description
BD MAX TNA MMK (SPC)	Becton Dickinson and Company, 7 Loveton Circle, Sparks, MD 21152	442830	Primers and probes to detect the internal sample processing control (SPC)
2019-nCoV CDC EUA Kit	Integrated DNA Technologies, Inc. 1710 Commercial Park Coralville, Iowa 52241	10006606	Primers and probes to detect: 2019-nCoV_N1 2019-nCoV_N2
2019-nCoV_N Positive Control	Integrated DNA Technologies, Inc. 1710 Commercial Park Coralville, Iowa 52241	10006625	Plasmid DNA that contains portion of N gene to serve as positive control
Puritan UniTranz-RT transport system	Puritan Diagnostics LLC	UT-306	Universal transport medium for positive control diluent

CONTROLS TO BE USED WITH THE OMNI COVID-19 ASSAY BY RT-PCR

- Negative Extraction/No Template Control: Universal Transport Media (from the Puritan UniTranz-RT Transport System – Universal Transport Medium Collection Tubes) will serve as the negative extraction and no template control. This control (one processed with each run) will monitor cross-contamination of reagents during the extraction process and RT-PCR.
- Positive Extraction/Internal Control: A Specimen Processing Control (SPC) is present within each BD MAX ExK TNA extraction tube and verifies the adequacy of the assay throughout the entire process to include processing of the sample, extraction and purification of the nucleic acids, and efficacy of the PCR reaction. This SPC is encapsulated synthetic RNA material and can be detected with the BD MAX TNA MMK (SPC) kit, which contains a real-time RT-PCR master mix including SPC-specific primers and probes.
- Positive Control: The positive control used for this assay is the same positive control material used in the 2019-nCoV CDC EUA Kit. This control is plasmid DNA containing a portion of the SARS-CoV-2 N gene, including both the N1 and N2 assay targets. The initial concentration of the positive control is 200,000 copies/µL. This is diluted using UTM to a working concentration of <5x LoD (< 6.2 copies/µL). Two positive controls are processed with each run.

INTERPRETATION OF RESULTS

All test controls should be examined prior to interpretation of patient results. If the controls are not valid, the patient results cannot be interpreted.

1) ***Omni COVID-19 Assay by RT-PCR Controls – Negative Control, Internal Control, and Positive Control***

A test result may be called NEG, POS, or UNR (Inconclusive) based on the amplification status of the target and of the Sample Processing Control (SPC). The IND (indeterminate) or INC (incomplete) results (reported as Specimen unsatisfactory) are due to BD MAX System failure. At least one of the two duplicate positive external controls must pass for a sample interpretation to be valid. The external positive control monitors for substantial reagent failure. The external negative control detects reagent or environmental contamination (i.e. carry-over) by target nucleic acids and must be negative for a valid assay run. The same cut-off criteria apply to control samples and patients' samples (See Tables 2 and 3).

Table 2: Interpretation of Control Sample Results. [a, b]

Control Type	N1/N2 Region Channel 475/520	Extraction / Internal Control (SPC) Channel 680/715	Result Interpretation	Consideration of Alternate Positive Control	Actions
Positive Control 1	POS	POS or NEG	Positive- presence of SARS-CoV-2	NA	Acceptable Run
	NEG	POS	Negative result indicates the absence of SARS-CoV-2	Pos Control 2 acceptable	Acceptable Run
				Pos Control 2 **not** acceptable	Reject Run and Repeat
	NEG	NEG	UNR	Pos Control 2 acceptable	Acceptable Run
				Pos Control 2 **not** acceptable	Reject Run and Repeat
Positive Control 2	POS	POS or NEG	Positive- presence of SARS-CoV-2	NA	Acceptable Run
	NEG	POS	Negative result indicates the absence of SARS-CoV-2	Pos Control 1 acceptable	Acceptable Run
				Pos Control 1 **not** acceptable	Reject Run and Repeat
	NEG	NEG	UNR	Pos Control 1 acceptable	Acceptable Run
				Pos Control 1 **not** acceptable	Reject Run and Repeat
Negative Control	NEG	POS	Negative result indicates the absence of SARS-CoV-2	NA	Acceptable Run

Table 2: Interpretation of Control Sample Results. [a, b]					
Control Type	**N1/N2 Region Channel 475/520**	**Extraction / Internal Control (SPC) Channel 680/715**	**Result Interpretation**	**Consideration of Alternate Positive Control**	**Actions**
	POS	POS or NEG	Positive-presence of SARS-CoV-2	NA	Reject Run and Repeat
	NEG	NEG	UNR	NA	Reject Run and Repeat

[a] All positive and extraction control samples should yield positive results at < 40 Ct for acceptance.
[b] NEG = negative, POS = positive, UNR = inconclusive

2) Examination and Interpretation of Patient Specimen Results:

Assessment of clinical specimen test results should be performed after the controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted. See Table 3 below for interpretation of patient specimen results.

Table 3: Interpretation of Patient Specimen Results.[a, b]			
N1/N2 Region Channel 475/520	**Extraction / Internal Control (SPC) Channel 680/715**	**Result Interpretation**	**Actions**
POS	POS	Positive-presence of SARS-CoV-2	Report as Positive and send results to Provider and Local Health Authority
POS	NEG	Positive-presence of SARS-CoV-2	Report as Positive and send results to Provider and Local Health Authority
NEG	POS	Negative result indicates the absence of SARS-CoV-2	Report as Negative
NEG	NEG	UNR	Sample is repeated, if results remain unresolved, the result is reported as inconclusive.

[a] Positive in the table indicates a Ct value of <40 cycles. Negative in the table indicates a Ct value of ≥40 cycles.
[b] NEG = negative, POS = positive, UNR = inconclusive

PERFORMANCE EVALUATION

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

LoD Range Finding Study:

The RNA material selected for analytical validation is the AccuPlex SARS-CoV-2 Verification Panel (cat # 0505-0129), containing fully-extractable RNA with a real viral protein coat. This serves as a full-process reference material. Six serial dilutions (33.33, 11.11, 3.7, 1.23, 0.41, and 0.14 copies/µL) of this positive reference material were prepared in triplicate, spiked into clinical negative nasopharyngeal specimens, and individually extracted and tested on the BD MAX System. After running all 6 dilutions in triplicate, dilution #4 (1.23 copies/ µL) was selected as the preliminary LoD concentration. Results are shown in Table 4 LoD Range Finding Study below.

Table 4: LoD Range Finding Study

LoD Concentration (copies/µL)	Replicate	N1 and N2 (Ct 475/520)	SPC (Ct 680/715)	Result
Dilution # 1 (33.33)	1	30.4	28	POS
	2	30.4	27.9	POS
	3	30.2	27.8	POS
Dilution # 2 (11.11)	1	32.1	27.8	POS
	2	31.5	27.7	POS
	3	31.6	27.5	POS
Dilution # 3 (3.7)	1	33.1	27.7	POS
	2	33	27.9	POS
	3	32.7	27.7	POS
Dilution # 4 (1.23)	1	34.8	27.8	POS
	2	35.1	27.8	POS
	3	34.5	27.7	POS
Dilution # 5 (0.41)	1	40.4	29.8	NEG
	2	-1	27.6	NEG
	3	39	27.6	POS
Dilution # 6 (0.14)	1	-1	28.1	NEG
	2	-1	28.4	NEG
	3	40.6	27.8	NEG

LoD Confirmatory Study:

A clinical negative pool consisting of ten (10) negative nasopharyngeal respiratory samples in VTM were spiked with the AccuPlex RNA material. This pool was then split into twenty samples before extraction, then the twenty samples were extracted individually and tested on the BD MAX System according to the SOP.

The LoD was confirmed at 1.23 copies/µL after testing 20 independent extractions that resulted in 20/20 (100%) positive results (see Table 5 below).

Table 5: LoD Confirmation Study				
SAMPLE	**Sample**	**N1 and N2 (Ct 475/520)**	**SPC (Ct 680/715)**	**Result**
EXTERNAL NEGATIVE CONTROL	n/a	-1	27.4	NEG
EXTERNAL POSITIVE CONTROL	n/a	29.2	28	POS
EXTERNAL POSITIVE CONTROL	n/a	28.4	26.9	POS
LoD 4 (1.23 copies/ µL)	1	33.4	27.5	POS
LoD 4 (1.23 copies/ µL)	2	33.3	27.4	POS
LoD 4 (1.23 copies/ µL)	3	33.8	27.4	POS
LoD 4 (1.23 copies/ µL)	4	33.2	27.3	POS
LoD 4 (1.23 copies/ µL)	5	35.7	27.3	POS
LoD 4 (1.23 copies/ µL)	6	33.2	27.4	POS
LoD 4 (1.23 copies/ µL)	7	33.2	27.4	POS
LoD 4 (1.23 copies/ µL)	8	34.3	27.2	POS
LoD 4 (1.23 copies/ µL)	9	34.1	27.3	POS
LoD 4 (1.23 copies/ µL)	10	35.7	27.4	POS
LoD 4 (1.23 copies/ µL)	11	34.5	27.4	POS
LoD 4 (1.23 copies/ µL)	12	35.1	27.2	POS
LoD 4 (1.23 copies/ µL)	13	34.9	27.4	POS
LoD 4 (1.23 copies/ µL)	14	35.6	27.7	POS
LoD 4 (1.23 copies/ µL)	15	34.4	27.3	POS
LoD 4 (1.23 copies/ µL)	16	34.4	28	POS
LoD 4 (1.23 copies/ µL)	17	34.3	27.5	POS
LoD 4 (1.23 copies/ µL)	18	34.6	27.6	POS
LoD 4 (1.23 copies/ µL)	19	35.1	27.2	POS
LoD 4 (1.23 copies/ µL)	20	33.7	27	POS

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

The N1 and N2 primers/probe sequences were not changed compared to the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel EUA; as such *in silico* analyses of reactivity and cross-reactivity was not performed.

3) ***Clinical Evaluation:***

A total of 60 leftover clinical nasopharyngeal negative specimens in VTM were divided into two groups of 30 each. One group of 30 specimens were individually spiked with the AccuPlex SARS-CoV-2 RNA material (AccuPlex SARS-CoV-2 Verification Panel, cat. # 505-0129) at a final concentration of 1.23 copies/µl (n=10), 2.46 copies/µl (n=10), or 3.69 copies/µl (n=10) and individually extracted and tested on the BD MAX System. The second group of 30 specimens were retained as

negatives, and RNA was extracted from each individual sample. These samples were processed over the course of three separate runs spanning two separate days. The summary results for the 30 positive contrived samples and the 30 clinical negatives are shown in the Summary Results Table below. An acceptance criterion of 19/20 (95%) was met.

Table 6: Summary of Contrived Clinical Validation Results			
Sample Count	**Results**	**N1/N2**	**Concordance 95 % at 1x-2x LoD**
10	Positive (1x LoD =1.23 copies/µl)	9 out of 10 Positive	90 %
10	Positive (2x LoD =2.46 copies/ µl)	10 out of 10 Positive	100%
10	Positive (3x LoD =3.69 copies/µl)	10 out of 10 Positive	100%
30	Negative	30 out of 30 Negative	100%

Positive Percent Agreement: 29/30 = 96.7% (CI: 88.3-99.4%)
Negative Percent Agreement: 30/30 = 100% (CI: 88.7-100%)

Clinical validation data for each sample is shown in the Individual Results Table below.

Table 7: Individual Contrived Sample Clinical Evaluation Results				
LoD Spiking Range	**Case number**	**N1 and N2 (Ct 475/520)**	**SPC (Ct 680/715)**	**Result**
POS CONTROL 1	n/a	29.3	27.4	POS
POS CONTROL 2	n/a	29.2	27.2	POS
NEG CONTROL	n/a	-1	27.4	NEG
No spike	1	-1	28	NEG
1x LoD (1.23 copies/µl)	2	34.2	27.6	POS
No spike	3	-1	27.2	NEG
1x LoD (1.23 copies/µl)	4	33.9	27.4	POS
No spike	5	-1	27.7	NEG
1x LoD (1.23 copies/µl)	6	33.9	27.2	POS
No spike	7	-1	28	NEG
1x LoD (1.23 copies/µl)	8	37.7	28.6	POS
No spike	9	-1	27.1	NEG

Table 7: Individual Contrived Sample Clinical Evaluation Results				
LoD Spiking Range	**Case number**	**N1 and N2 (Ct 475/520)**	**SPC (Ct 680/715)**	**Result**
1x LoD (1.23 copies/µl)	10	33.9	27	POS
No spike	11	-1	27.1	NEG
1x LoD (1.23 copies/µl)	12	-1	27.8	NEG
No spike	13	-1	27.5	NEG
1x LoD (1.23 copies/µl)	14	33.9	27.4	POS
No spike	15	-1	26.8	NEG
1x LoD (1.23 copies/µl)	16	33.5	26.7	POS
No spike	17	-1	28.2	NEG
1x LoD (1.23 copies/µl)	18	34.4	28.1	POS
No spike	19	-1	27.2	NEG
1x LoD (1.23 copies/µl)	20	33.5	27.1	POS
POS CONTROL 1	n/a	29.1	27.3	POS
POS CONTROL 2	n/a	28.9	27.1	POS
NEG CONTROL	n/a	-1	27.2	NEG
No spike	21	-1	27.1	NEG
2x LoD (2.46 copies/ µl)	22	32	26.6	POS
No spike	23	-1	27.5	NEG
2x LoD (2.46 copies/ µl)	24	32.5	27.2	POS
No spike	25	-1	30.3	NEG
2x LoD (2.46 copies/ µl)	26	34.9	33.2	POS
No spike	27	-1	27.5	NEG
2x LoD (2.46 copies/ µl)	28	33.4	27.6	POS
No spike	29	-1	29	NEG
2x LoD (2.46 copies/ µl)	30	34.2	29.4	POS
No spike	31	-1	29	NEG
2x LoD (2.46 copies/ µl)	32	33.7	29.6	POS
No spike	33	-1	30.7	NEG
2x LoD (2.46 copies/ µl)	34	34.7	30.2	POS

Table 7: Individual Contrived Sample Clinical Evaluation Results				
LoD Spiking Range	**Case number**	**N1 and N2 (Ct 475/520)**	**SPC (Ct 680/715)**	**Result**
No spike	35	-1	27.8	NEG
2x LoD (2.46 copies/ µl)	36	33.5	28.5	POS
No spike	37	-1	28	NEG
2x LoD (2.46 copies/ µl)	38	33.4	28.2	POS
No spike	39	-1	28.2	NEG
2x LoD (2.46 copies/ µl)	40	33.4	28.8	POS
POS CONTROL 1	n/a	29.1	26.9	POS
POS CONTROL 2	n/a	29.7	27.5	POS
NEG CONTROL	n/a	-1	27.4	NEG
No spike	41	-1	27.5	NEG
3x LoD (3.69 copies/µl)	42	31.5	27.3	POS
No spike	43	-1	27.5	NEG
3x LoD (3.69 copies/µl)	44	31.6	27.7	POS
No spike	45	-1	27.6	NEG
3x LoD (3.69 copies/µl)	46	31.9	27.5	POS
No spike	47	-1	27.4	NEG
3x LoD (3.69 copies/µl)	48	31.6	27	POS
No spike	49	-1	27.4	NEG
3x LoD (3.69 copies/µl)	50	32	27.5	POS
No spike	51	-1	27.5	NEG
3x LoD (3.69 copies/µl)	52	32.1	27.4	POS
No spike	53	-1	27	NEG
3x LoD (3.69 copies/µl)	54	31.8	27	POS
No spike	55	-1	27.5	NEG
3x LoD (3.69 copies/µl)	56	32.5	27.5	POS
No spike	57	-1	27	NEG
3x LoD (3.69 copies/µl)	58	32.6	27.1	POS
No spike	59	-1	27.8	NEG

Table 7: Individual Contrived Sample Clinical Evaluation Results				
LoD Spiking Range	**Case number**	**N1 and N2 (Ct 475/520)**	**SPC (Ct 680/715)**	**Result**
3x LoD (3.69 copies/µl)	60	32.2	27.2	POS

Clinical Confirmation with EUA test

The first 7 positive and the first 5 negative nasopharyngeal specimens as determined by the Omni COVID-19 Assay by RT-PCR were sent to a high complexity CLIA laboratory using an authorized SARS-CoV-2 real-time RT-PCR assay. There was 100% (7/7) positive and 100% (5/5) negative agreement for the specimens tested. The results are acceptable and support use of the Omni COVID-19 Assay by RT-PCR for testing clinical specimens.

LIMITATIONS

The performance of the Omni COVID-19 Assay by RT-PCR was established using nasopharyngeal swab specimens in VTM. Oropharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, nasopharyngeal wash/aspirate, nasal aspirate, and bronchoalveolar lavage specimens are also considered acceptable specimen types for use with the Omni COVID-19 Assay by RT-PCR, but the performance has not been established with these specimens.

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

FDA SARS-CoV-2 Reference Panel Testing

The evaluation of sensitivity and MERS-CoV cross-reactivity was performed using reference material (T1), blinded samples and a standard protocol provided by the FDA. The study included a range finding study and a confirmatory study for LoD. Blinded sample testing was used to establish specificity and to confirm the LoD. The extraction method and instrument used were BDMAX ExK TNA-3 Kit and the BD MAX System. The results are summarized in the following Table.

Table 8: Summary of LoD Confirmation Result using the FDA SARS-CoV-2 Reference Pane l

Reference Materials Provide d by FDA	Spe cimen Type	Product LoD	Cross-Reactivity
SARS-CoV-2	Nasopharyngeal Swab	$1.8x10^5$ NDU/mL	N/A
MERS-CoV		N/A	ND

NDU/mL = RNA NAAT detectable units/mL
N/A: Not applicable
ND: Not Detected