SoftCell Laboratories TaqPath COVID-19 Combo Assay EUA Summary

ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY FOR COVID-19 ASSAY
(SoftCell Laboratories)

For in vitro diagnostic use Rx only performed at SoftCell Laboratories, a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratory, per the Instructions for Use (IFU)
For use under Emergency Use Authorization (EUA) Only

The SoftCell Laboratories SARS-CoV-2 assay with saliva samples using the Spectrum Solutions SDNA-1000 collection kit with 7 days (168 hrs.) of sample stability.

A. PURPOSE FOR SUBMISSION

Emergency Use Authorization (EUA) request for use of a SARS-CoV-2 molecular diagnostic test to be performed for the in vitro qualitative detection of RNA from SARS-CoV-2 in respiratory samples from patients as recommended for testing by public health authority guidelines. The test will be performed in CLIA certified high-complexity laboratories. Additional testing and confirmation procedures should be performed in consultation with public health and/or other authorities to whom reporting is required.

Positive results should also be reported in accordance with local, state, and federal regulations.

B. MEASURAND

This test is a modification of the ThermoFisher TaqPath COVID-19 Combo Kit. The targeted genes are S gene, ORF1 ab, and N gene. In addition to the authorized sample types according to the IFU, the Spectrum Solutions, LLC SDNA-1000 Saliva Collection Device was tested for sample collection with stability for 7 days at ambient temperature.

C. LABORATORY/SPONSOR

Soft Cell L-form Laboratory, LLC, d.b.a, SoftCell Laboratories.
4616 Beehive Dr., Unit 4
Saint George, UT 84790
(435) 628-2215
Frank Spangler, COO
This will be the only location performing the testing.

D. REGULATORY INFORMATION

Approval/Clearance Status:

The SARS-CoV-2 assay test is not cleared, CLIA waived, approved, or subject to an approved investigational device exemption.

E. PROPOSED INTENDED USE

1) Intended Use:

The SARS-CoV-2 assay is a real-time RT-PCR test based on the ThermoFisher TaqPath COVID-19 Combo Kit which already has Emergency Use Authorization (EUA) intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in oropharyngeal (throat) swab, nasopharyngeal swab, anterior nasal swab, and mid-turbinate nasal swab from individuals suspected of COVID-19. In addition to the authorized sample types, saliva specimens are also added. Testing is limited to SoftCell Laboratories, LLC, Saint George, UT that is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratories.

Results are for the detection and identification 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 active infection with SARS-CoV-2 but 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 assay is intended for use by CLIA certified high-complexity laboratories with experience in developing molecular diagnostics and is only for use under the Food and Drug Administration's Emergency Use Authorization.

Collection of saliva specimens are performed 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 collected using the Spectrum Solutions SDNA-1000 kit according to manufacturer's protocol. Transportation and storage of saliva specimens are at ambient temperature and must be tested within 7 days (168 hrs) after collection.

2) Instruments Used with Test:

The TaqPath COVID-19 Combo Kit test is to be used with the AB 7500 Fast Dx with software 1.4.1, AB 7500 Fast with software v2.3, AB 7500 with software v2.3, AB

QuantStudio 5 (96-well 0.1 ml and 0.2 ml, and 384-well blocks) with software 1.3 according to the IFU. Extractions for SARS-CoV-2 RNA are performed on the KingFisher Flex according to the IFU.

F. DEVICE DESCRIPTION AND TEST PRINCIPLE

1) Product Overview/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 test uses the ThermoFisher TaqPath COVID-19 Combo Kit. This EUA submission is to add the Spectrum Solutions, LLC SDNA-1000 Saliva Collection Device to the sample types. Saliva specimens must be collected, transported, and stored at ambient temperature and tested within 168 hours (7 days) of collection. The TaqPath COVID-19 Combo Kit IFU is followed other than using 200 µL or 400 µL of the SDNA-1000 collected sample as the patient input volume.

Saliva specimens for SARS-CoV-2 testing have been shown to be as good as or better than nasopharyngeal samples. Rutgers Clinical Genomics Laboratory has already received an Emergency Use Authorization (EUA 200090) for the use of saliva specimens. Yale University has presented a preprint article also describing saliva samples as superior titled, "Saliva is more sensitive for SARS-CoV-2 in COVID-19 patients than nasopharyngeal swabs (https://doi.org/10.1101/2020.04.16.20067835). The Public Health Laboratory Services Branch in Hong Kong has also shown saliva to be a valid sample source for SARS-CoV-2 detection (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108139/#CIT0008).

2) Description of Test Steps:

The testing procedure is briefly as follows:

1. Patient samples are collected in the SDNA-1000 collection kit according to manufacturer's protocol and sent to the lab.
2. Samples are extracted using either 200 µL or 400 µL of the patient specimen on the KingFisher FLEX 96 DW extraction robot using either the ThermoFisher MVP I or MVP II extraction reagents according to the IFU.
3. The real-time RT-PCR master mix and the extracted sample are amplified on one of the above listed thermal cyclers according to the IFU.
4. Sample calls are made with the Interpretive Software according to the IFU.

3) Control Material(s) to be Used:

The controls supplied with the ThermoFisher TaqPath COVID- 19 Combo Kit are described in Table 1.

Table 1. Controls supplied with the Applied Biosystems TaqPath COVID-19 Combo Kit

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

4) Assay results and interpretation

Interpretation of the results is performed by the Applied Biosystems COVID-19 Interpretive Software according to IFU.
Quality control and validity of results:
One Negative Control and one Positive Control are processed with each run.
Validation of results is performed automatically by the Applied Biosystems COVID-19 Interpretive Software based on performance of the Positive and Negative Controls (see Table 2).

Table 2. Result interpretation for patient samples

ORF1ab	N gene	S gene	MS2	Status	Result	Action
NEG	NEG	NEG	NEG	INVALID	NA	Repeat test. If the repeat result remains invalid, consider collecting a new specimen.
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[1]	Repeat test. If the repeat result remains inconclusive, additional confirmation testing should be conducted if clinically indicated.
Two or more SARS-CoV-2 targets = POS			POS or NEG	VALID	Positive SARS- CoV-2	Report results to healthcare provider and appropriate public health authorities.

[1] Samples with a result of SARS-CoV-2 Inconclusive shall be retested one time. Retesting must happen from the original sample.

G. PRODUCT MANUFACTURING

Please note that Under the Emergency Use Authorization (EUA) most of the 21 CFR 820 Quality System Regulation (QSR) requirements can be waived for the duration of the EUA. FDA expects that the high-complexity laboratories performing these tests follow comparable practices as much as possible and may consider previous compliance history when determining whether or not to waive certain QSR requirements for a specific product. Please note adverse events, as per 21 CFR Part 803, have to be reported for authorized devices.

H. PERFORMANCE EVALUATION

The following validation studies should be performed during your assay development:

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

The LoD was determined using SARS-CoV-2 heat inactivated virus from bei RESOURCES (beiresources.org). SDNA-1000 negative samples were spiked with virus at 1,000 copies/mL, 500 copies/mL, 250 copies/mL, and 125 copies/mL. These spiked samples were run in triplicate on an AB 7500 Fast instrument using the ThermoFisher COVID-19 TaqPath Combo Kit. 250 copies/mL was the lowest level in which all replicates were detected as positive. 20 replicates were then tested at 250 copies/mL, and all were detected as positive confirming the LoD.

2) Inclusivity (analytical sensitivity):

The test uses the ThermoFisher COVID-19 Combo Kit. All inclusivity data is referred to the IFU for the kit.

3) ***Cross-reactivity (Analytical Specificity)***

Recommended List of Organisms to be analyzed *in silico* or by Wet Testing*

Other high priority pathogens from the same genetic family	High priority organisms likely in circulating areas
Human coronavirus 229E	**Adenovirus (e.g. C1 Ad. 71)**
Human coronavirus OC43	**Human Metapneumovirus (hMPV)**
Human coronavirus HKU1	**Parainfluenza virus 1-4**
Human coronavirus NL63	**Influenza A & B**
SARS-coronavirus	**Enterovirus (e.g. EV68)**
MERS-coronavirus	**Respiratory syncytial virus**
	Rhinovirus
	Chlamydia pneumoniae
	Haemophilus influenzae
	Legionella pneumophila
	Mycobacterium tuberculosis
	Streptococcus pneumoniae
	Streptococcus pyogenes
	Bordetella pertussis
	Mycoplasma pneumoniae
	***Pneumocystis jirovecii* (PJP)**
	Pooled human nasal wash – *to represent diverse microbial flora in the human respiratory tract*
	Candida albicans
	Pseudomonas aeruginosa
	Staphylococcus epidermis
	Staphylococcus salivarius

* For wet testing, concentrations of 10^6 CFU/ml or higher for bacteria and 10^5 pfu/ml or higher for viruses is recommended.].

The test uses the ThermoFisher COVID-19 Combo Kit. All cross-reactivity data is referred to the IFU for the kit.

4) ***Clinical Evaluation:***

SDNA-1000 Saliva Kit
The use of a saliva collection kit is desirable in the current SARS-CoV-2 pandemic. It is less invasive, requires less healthcare provider interaction with a patient, and could relieve some of the strain on nasopharyngeal swab collection kits and PPE use during the pandemic. A total of 40 contrived positive and negative samples were tested at 2x LoD

(500 copies/mL). There was one false negative sample in the study. We interpreted this to the fact that we are operating next to the LoD. The results are shown in Table 3.

Table 3. Summary of contrived positive and negative samples with SDNA-1000 kit.

		Contrived Specimen Type		
		Positive	**Negative**	**Total**
TaqPath COVID-19 Results	**Positive**	39	0	39
	Negative	1	40	41
	Total	40	40	80
Sensitivity	**Specificity**	**PPV**	**NPV**	
97.50%	100.00%	100.00%	97.56%	

SDNA-1000 Saliva Kit Sample Stability at Ambient Temperature
A study has already been conducted and has received an EUA for the testing of SARS-CoV-19 using Spectrum Solutions, LLC SDNA-1000 Saliva collection kit (Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay EUA 200090). This study shows that equivalent results can be obtained using the extraction system detailed in the manufacturer's IFU, and that 7 days of sample stability can be achieved at ambient temperature.

A total of 10 samples were created at 2x LoD (500 copies/mL) and immediately ran through the test protocol. Samples were then incubated at ambient temperature for 7 days (168 hours) and ran through the test protocol again. Table 4 lists the beginning and the final Ct values for the 10 samples.

Table 4. Ct values for starting (Day Zero) and ending (Day Seven) time points.

	Day Zero Ct	Day Seven Ct
S01-POS	35.53	35.09
S02-POS	33.31	34.23
S03-POS	34.74	33.26
S04-POS	35.13	32.91
S05-POS	34.88	36.11
S06-POS	34.67	34.46
S07-POS	34.39	35.10
S08-POS	33.68	35.73
S09-POS	33.36	34.42
S10-POS	34.82	33.96
Average	34.45	34.53
STDEV	0.72	0.96

Using the Crossing Threshold (Ct) values for Day Zero and for Day Seven samples, a paired t-Test for two samples means was performed for the before and after effect of seven days incubation at ambient temperature. The t Stat value is -0.17 and the t Critical value is 2.26 (see Table 5). Since the t Stat absolute value is less than the t Critical value, this shows that there is no statistical difference between the Day Zero samples and the

Day Seven samples indicating that no detectable sample degradation took place in the viral RNA. We have set our saliva specimen stability at seven days at ambient temperature using the SDNA-1000 collection kit.

Table 5.

7 Days		
t-Test: Paired Two Sample for Means		
	Variable 1	*Variable 2*
Mean	34.45	34.53
Variance	0.57	1.03
Observations	10.00	10.00
Pearson Correlation	-0.13	
Hypothesized Mean Difference	0.00	
df	9.00	
t Stat	-0.17	
P(T<=t) one-tail	0.43	
t Critical one-tail	1.83	
P(T<=t) two-tail	0.87	
t Critical two-tail	2.26	

I. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

J. APPROVED/CLEARED ALTERNATIVE PRODUCTS

Currently no methods for the detection of the SARS-CoV-2 have been approved/ cleared by FDA.

K. BENEFITS AND RISKS:

This section will be completed by FDA.

L. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

Fact Sheets for Patients – Patient Fact Sheet SCBR Covid-19.pdf
Fact Sheets for Healthcare Providers – Provider Fact Sheet SCBR Covid-19.pdf

M. INSTRUCTIONS FOR USE/ PROPOSED LABELING/PACKAGE INSERT:

ThermoFisher
TaqPathTM COVID-19 Combo Kit INSTRUCTIONS FOR USE (IFU)
Multiplex real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2
Catalog Number A47814 Publication Number MAN0019181 Revision C.0

N. RECORD KEEPING AND REPORTING INFORMATION TO FDA:

The laboratory will track adverse events and report to FDA under 21 CFR Part 803. A website is available to report on adverse events, and this website is referenced in the Fact Sheet for Health Care providers. The laboratory will maintain information on the performance of the test, and report to FDA any suspected change in performance of which they become aware. The laboratory will maintain records associated with this EUA and ensure these records are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

O. FDA ADMINISTRATIVE INFORMATION:

This section will be finalized by the FDA Reviewer upon completion of the review process. This will document any interactions of communications with the laboratory. the interactive review of this submission and any conclusions resulting from the interactive review.

Product Code:
QJR