510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K221802

B Applicant

Mawi DNA Technologies

C Proprietary and Established Names

iSWAB-Respiratory Tract Sample Collection Media-Extraction Less (iSWAB-RC-EL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QBD	Class II	21 CFR 866.2950 - Microbial Nucleic Acid Storage And Stabilization Device	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

The purpose of this submission is to obtain 510(k) substantial equivalence for the iSWAB-Respiratory Tract Sample Collection Media-Extraction Less (iSWAB-RC-EL) for the collection, transport and storage of unprocessed samples containing SARS-CoV-2.

B Measurand:

Nucleic acids from SARS-CoV-2

C Type of Test:

Microbial nucleic acid storage and stabilization device

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The iSWAB-Respiratory Tract Sample Collection Media-Extraction Less collection device is intended for the stabilization and inactivation of upper respiratory and saliva human specimens suspected of containing SARS-CoV-2. This device can be used for the collection, transport, and storage of specimens at ambient temperature. Specimens collected in the iSWAB-Respiratory Tract Sample Collection Media-Extraction Less collection device are suitable for use with legally marketed molecular diagnostic tests.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

N/A

IV Device/System Characteristics:

A Device Description:

The iSWAB-Respiratory Tract Sample Collection Media-Extraction Less (iSWAB-RC-EL) collection device consists of a collection tube that is pre-filled with 800 µL of the iSWAB-RC-EL non-toxic, stabilizing buffer and fitted with a proprietary insert. The insert is designed to optimize the release of specimens collected with swabs into the stabilizing buffer allowing for swab-free transport of specimens. The iSWAB-RC-EL collection device is designed to eliminate the RNA extraction step from diagnostic workflows. The media is designed to skip the solid phase extraction step of a traditional two step lysis and extraction of nucleic acids from specimens prior to amplification using traditional PCR techniques.

B Principle of Operation:

The iSWAB-RC-EL stabilizing buffer is intended to inactivate SARS CoV-2 by disrupting/lysing the capsid lipid membranes, denature proteins, inactivate enzymes, and stabilize SARS CoV-2 RNA. The iSWAB-RC-EL collection device is designed for storage of specimens between 15-30 °C for 28 days in nasal samples and 33 days in saliva samples. The stabilizing buffer contains the following components:

•Nontoxic inactivation agents
•Salts
•pH buffer
•Water

V Substantial Equivalence Information:

A Predicate Device Name(s):

DNA/RNA Shield Collection Tube

B Predicate 510(k) Number(s):

K202641

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K221802	Predicate: K202641
Device Trade Name	iSWAB-RC-EL	DNA/RNA Shield
General Device Characteristic Similarities		
Intended Use/Indications For Use	The iSWAB-Respiratory Tract Sample Collection Media-Extraction Less (iSWAB-RC-EL) collection device is intended for the stabilization and inactivation of upper respiratory and saliva human specimens suspected of containing SARS-CoV-2. This device can be used for the collection, transport, and storage of specimens at ambient temperature. Specimens collected in the iSWAB-Respiratory Tract Sample Collection Media-Extraction Less collection device are suitable for use with legally marketed molecular diagnostic tests.	The DNA/RNA Shield collection tube is intended for the stabilization and inactivation of upper and lower respiratory human specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at ambient temperatures (20- 25°C). Specimens collected and stored in a DNA/RNA Shield collection tube are suitable for use with legally marketed molecular diagnostic devices.
Viral Inactivation	SARS-CoV-2 inactivation	Same
Analyte	RNA from SARS-CoV-2	Same
General Device Characteristic Differences		
Specimen Storage	SARS-CoV-2 RNA: 28 days with nasal specimens and 33 days with saliva specimens at	SARS-CoV-2 RNA: 28 days at 20-25ºC

	15-30ºC	
Specimen type	Nasal and Saliva Specimens for SARS-CoV-2	Lower, Upper Respiratory and Saliva Specimens for SARS-CoV-2
Sample processing type	RNA extraction optional	Requires RNA extraction before use
Shelf Life	15 months	24 months

VI Standards/Guidance Documents Referenced:

Special controls that are applicable to regulation 21 CFR 866.2950.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility

   N/A

2. Linearity:

   N/A

3. Analytical Specificity/Interference:

   N/A

4. Assay Reportable Range:

   N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Shelf Life
   The shelf life for the iSWAB-RC-EL is 15 months after the date of manufacture. The stability of the iSWAB-RC-EL was performed using real time stability on a total of three lots. Stability studies assessed media appearance, pH, density, conductivity, and bacterial and fungal growth.

6. Detection Limit:

   Nasal samples:
   The limit of detection (LoD) of SARS-CoV-2 for iSWAB-RC-EL was established using an EUA authorized assay to determine the lowest concentration of virus that can be repeatedly

recovered from the sample tube with an accuracy greater than 95%. Negative clinical nasal matrix was collected and pooled. 20 individual replicates of matrix were spiked with 25 cp/µL of ATCC VR-1986 and then added to the media. Samples were assessed using the BGI's "Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2" assay. 10 µL of sample in media was directly mixed with 20 µL of RT-PCR master mix targeting the ORF1ab region of SARS-CoV-2 genome (FAM channel) and the human housekeeping gene β-Actin (ACTB, VIC/HEX channel) as a sample control. At 25 cp/µL, 19/20 samples were positive indicating that the LoD for nasal clinical matrix is 25 cp/µL, The Ct values for each replicate and target are listed Table 1 below.

Table 1. LOD Studies in Nasal Matrix (25 cp/µL)

Replicate #	ORF1ab (average Ct)	SD	ACTB (average Ct)	SD
1	35.00	0.12	27.99	0.02
2	34.27	0.26	27.93	0.06
3	35.02	0.46	27.57	0.20
4	35.07	0.45	27.54	0.01
5	35.36	0.43	28.08	0.01
6	34.96	0.37	27.91	0.17
7	34.93	0.41	27.71	0.10
8	35.16	0.62	27.88	0.12
9	34.91	0.64	28.16	0.03
10	34.91	0.13	28.20	0.02
11	34.96	0.64	28.02	0.16
12	35.31	0.41	28.12	0.11
13	35.19	0.13	28.03	0.02
14	35.20	0.14	26.75	0.91
15	35.78	0.52	27.82	0.03
16	35.23	0.17	27.98	0.24
17	35.27	0.30	28.20	0.02
18	36.65	1.06	29.21	0.19
19	35.55	0.41	27.17	1.06
20	34.99	0.60	28.16	0.09

Saliva samples:

The limit of detection (LoD) of SARS-CoV-2 for iSWAB-RC-EL was established using an EUA authorized assay to determine the lowest concentration of virus that can be repeatedly recovered from the sample tube with an accuracy greater than 95%. Negative clinical saliva matrix was collected and pooled. 20 individual replicates of matrix were spiked with 30 cp/µL of ATCC VR-1986. Samples were assessed using the BGI's "Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2" assay. 10 µL of sample in media was directly mixed with 20 µL of RT- PCR master mix targeting the ORF1ab region of SARS-CoV-2 genome (FAM channel) and the human housekeeping gene β-Actin (ACTB, VIC/HEX channel) as a sample control. At 30 cp/µL, 20/20 samples were positive, however at 25 cp/µL only 13/20 samples

were positive, indicating that the LoD for nasal clinical matrix is 30 cp/µL The Ct values for each replicate and target are listed in Table 2 below.

Table 2. LOD studies in Saliva Matrix (30 cp/µL)

Replicate #	ORF1ab (average Ct)	SD	ACTB (average Ct)	SD
1	35.11	0.09	32.30	0.21
2	35.55	0.46	31.24	0.72
3	35.85	0.60	32.08	0.22
4	36.36	0.29	31.05	0.40
5	35.80	0.12	31.29	0.60
6	35.65	0.83	32.32	0.19
7	36.23	0.30	32.39	0.55
8	35.51	0.13	32.13	0.91
9	35.44	0.35	32.76	0.50
10	35.26	0.64	31.21	0.55
11	34.62	0.07	31.79	0.11
12	35.96	0.65	32.14	0.50
13	35.67	0.77	32.19	0.49
14	35.99	1.11	32.57	0.82
15	35.20	0.23	32.73	0.05
16	36.05	0.40	32.76	0.14
17	35.02	0.24	32.50	0.43
18	34.89	0.71	31.72	0.58
19	35.08	0.05	32.14	0.81
20	34.59	0.69	32.51	0.54

7. Specimen Stability

Nasal Matrix

The specimen stability of SARS-CoV-2 virus was determined in iSWAB-RC-EL media by spiking 110 cp/µL of ATCC VR-1986 in iSWAB-RC-EL media with negative clinical nasal matrix. 10 µL of sample was mixed directly without extraction with 20 µL of master mix from BGI Real Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2. A pre-defined acceptance criteria of ±3 Ct from time zero was used to establish stability after storage at

room temperature, 20-25ºC. The study results support that the transport media stabilizes SARS-CoV-2 RNA up to 28 days at 20-25ºC, as summarized in Table 3 below.

Table 3. Specimen Stability Results in Nasal Matrix

	Orf1ab average Ct	Delta Ct from baseline	ACTB average Ct	Delta Ct from baseline
Day 0	33.74	0.00	30.79	0.00
Day1	33.22	-0.52	31.84	1.05
Day 4	32.51	-1.23	28.62	-2.17
Day 7	32.77	-0.97	29.64	-1.15
Day 14	32.75	-0.99	28.59	-2.20
Day 21	33.20	-0.54	29.42	-1.37
Day 28	34.83	1.09	28.59	-2.20

Saliva Matrix

The specimen stability of SARS-CoV-2 virus was determined in iSWAB-RC-EL media by spiking 110 cp/µL of ATCC VR-1986 in iSWAB-RC-EL media with negative clinical saliva matrix. 10 µL of sample was mixed directly without an extraction step with 20 µL of master mix from BGI Real Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2. A pre-defined acceptance criteria of ±3 Ct from time zero was used to establish stability after storage at room temperature, 20-25ºC. The study results support that the transport media stabilizes SARS-CoV-2 RNA up to 33 days at 20-25ºC, as summarized in Table 4 below.

Table 4. Specimen Stability Results in Saliva Matrix

	Orf1ab average Ct	Delta Ct from baseline	ACTB average Ct	Delta Ct from baseline
Day 0	33.62	0.00	31.34	0.00
Day1	35.00	1.38	29.00	-2.33
Day 8	35.56	1.94	29.02	-2.31
Day 19	32.65	-0.97	29.89	-1.45
Day 26	34.25	0.63	30.80	-0.54
Day 33	34.90	1.29	31.48	0.14

8. Inactivation:

Media cytopathic effect

Cell lines were spiked with iSWAB-RC-EL media without dilution and no cytopathic effect was observed over 2 hours. This supported the addition of media without dilution

to cell culture monolayers for less than 2 hours for the viral inactivation phase of the inactivation study.

Inactivation time

The viral inactivation phase of the study was conducted to assess the time the virus needs to be exposed to the media to render the virus inactive. The iSWAB-RC-EL was spiked with known concentrations of SARS-CoV-2 virus and negative nasal matrix (Table 5) or saliva matrix (Table 6), and incubated at room temperature for 30 minutes, 2 hours and 6 hours. At each time point 100 µL of the iSWAB-RC-EL spiked with respective matrix and SARS-CoV-2 virus was inoculated onto MDCK II cell culture. The cultures were incubated for up to 48 hours post infection and observed by inverted light microscopy for cytopathic effect (CPE). The Reed and Muench method was used to determine the 50% tissue culture infectious dose per mL (TCID50/mL). In cases where sample showed no sign of detectable virus, statistical analysis based on the Poisson distribution was carried out to ascertain the theoretical maximum potential titer. Cells spiked with virus without incubation in iSWAB-RC-EL media showed CPE within 10 minutes.

Table 5. Inactivation Study Results in Nasal Clinical Matrix

Volume (mL)	Replicate	Input Viral Load ($Log_{10}TCID_{50}$)	Output Viral Load (Log10TCID50)	Reduction (Log10TCID50)
30 minutes	1	5.93 ± 0.28	1.48 ± 0.18	4.45 ± 0.34
	2		1.35 ± 0.16	4.58 ± 0.33
	3		1.35 ± 0.16	4.58 ± 0.33
	Average		1.39 ± 0.17	4.54 ± 0.33
2 hours	1	5.81 ± 0.27	0.60 ± 0.19	5.21 ± 0.33
	2		0.48 ± 0.18	5.33 ± 0.32
	3		0.23 ± 0.12	5.58 ± 0.29
	Average		0.44 ± 0.16	5.37 ± 0.31
6 hours	1	5.81 ± 0.30	0.06 ± 0.02	5.75 ± 0.35
	2		0.05 ± 0.03	5.76 ± 0.35
	3		0.05 ± 0.02	5.76 ± 0.32
	Average		0.18 ± 0.02	5.76 ± 0.34

Table 6. Inactivation Study Results in Saliva Clinical Matrix

Volume (mL)	Replicate	Input Viral Load (Log10TCID50)	Output Viral Load (Log10TCID50)	Reduction (Log10TCID50)
30 minutes	1	5.93 ± 0.28	1.35 ± 0.16	4.58 ± 0.33
	2		1.35 ± 0.16	4.58 ± 0.33
	3		1.60 ± 0.19	4.33 ± 0.34
	Average		1.43 ± 0.17	4.50 ± 0.33

2 hours	1	5.81 ± 0.27	0.10 ± 0.17	5.71 ± 0.32
	2		0.23 ± 0.12	5.58 ± 0.29
	3		0.35 ± 0.16	5.46 ± 0.31
	Average		0.23 ± 0.15	5.58 ± 0.31
6 hours	1	5.81 ± 0.30	0.05 ± 0.01	5.80 ± 0.34
	2		0.07 ± 0.03	5.80 ± 0.35
	3		0.04 ± 0.03	5.81 ± 0.35
	Average		0.05 ± 0.02	5.80 ± 0.35

The results support that the iSWAB-RC-EL media requires a minimum of 6 hours to inactivate SARS-CoV-2 at room temperature as shown by a >5 log reduction in TCID50/mL values when used with nasal or saliva matrix.

9. Assay Cut-Off:

N/A

B Comparison Studies:

1. Method Comparison with Predicate Device:

N/A

2. Matrix Comparison:

N/A

C Clinical Studies:

1. Clinical Sensitivity:

N/A

2. Clinical Specificity:

N/A

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

N/A

D Clinical Cut-Off:

N/A

E Expected Values/Reference Range:

N/A

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.