510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K201674

B Applicant

Merit Medical Systems, Inc.

C Proprietary and Established Names

Cultura Collection and Transport System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JSM, LIO	Class I, Reserved	21 CFR 866.2390 - Transport Culture Medium	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain substantial equivalence determination for Merit Medical Systems, Inc. Cultura Collection and Transport System for the collection, transport and storage of viral specimens for laboratory culture and downstream testing.

B Measurand:

Not applicable.

C Type of Test:

Non-propagating Transport Device with culture medium.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Merit Cultura™ Collection and Transport System is intended for collection and transport of clinical specimens to the laboratory for standard diagnostic/identification techniques. The Merit Cultura™ Collection and Transport System is a culture-based media that can be used for upper respiratory viral diagnostic assays including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Influenza A, Influenza B, Respiratory Syncytial Virus (RSV), and Rhinovirus.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The Cultura Collection and Transport System consists of Viral Transport Medium (VTM) and a sterile, nylon-flocked collection swab with a plastic shaft in a sterile pouch. The VTM contains antimicrobial agents to inhibit overgrowth of bacteria, fungi and yeasts; Hank's Balanced Salt Solution (HBSS) enriched with proteins and sugars for stabilization; a buffer system to maintain neutral pH; and, a pH indicator. The VTM is packaged in a quantity of 3 mL in a screw-cap tube. Table 1 shows the list of ingredients in purified water. The packaging also includes a biohazard specimen bag.

Table 1. Reagent Concentrations

Component	Concentration (g/L)
Hank's Balanced Salt Solution (HBSS)	10
Fetal Bovine Serum (FBS)	20
D-glucose	1
Phenol Red	< 1
Gentamicin sulfate	< 1
Amphotericin B	< 1

The VTM maintains cellular integrity and encourages preservation of viruses when properly stored. Prior to use, vials should be stored at either 2-8 or 23-25°C. After specimen collection, the transport tube containing the specimen can be stored for up to 120 hours at either 2-8 or 23-25°C, which provides convenience for transportation to the laboratory and storage. The medium has been evaluated for its ability to support transport of various respiratory viruses, including SARS-CoV-2 for viral recovery and other testing.

B Principle of Operation:

The Cultura Collection and Transport System is used to safely collect, transport and dispense pathogenic viruses. Intended for use by Health Care Professionals (HCPs), the transport system allows for the collection of the specimen via the sterile swab, maintenance via a buffered

salt/sugar/serum solution, prevention of microbial overgrowth via antimicrobial agents, as well as a pH indicator. The specimen can then be tested via PCR-based or other detection/identification methods for the presence of a target pathogen.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Puritan Universal Transport Medium (UTM-RT) Collection and Transport System

B Predicate 510(k) Number(s):
K113249

C Comparison with Predicate(s):

Device & Predicate Device(s):	K201674	K113249
Device Trade Name	Merit Cultura Collection and Transport System	Puritan Universal Transport Medium (UTM-RT) Collection and Transport System
Device Product Code and Classification	JSM, LIO, Class I	JSM, LIO, Class I
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Merit Cultura Collection and Transport System is intended for collection and transport of clinical specimens to the laboratory for standard diagnostic/identification techniques. The Merit Cultura Collection and Transport System is a culture-based media that can be used for upper respiratory viral diagnostic assays including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Influenza A, Influenza B, Respiratory Syncytial Virus (RSV), and Rhinovirus.	Puritan UTM-RT Collection and Transport System is intended for the collection and transport of clinical samples containing viruses, chlamydiae, mycoplasmas or ureaplasmas from the collection site to the testing laboratory. The specimen transported in the Puritan UTM-RT can be used in the laboratory to perform viral, chlamydial, mycoplasmal and ureaplasmal culture.
Storage Temperature	2-8 and 23-25°C	Same

List of Ingredients	Antimicrobial agents, Hanks Balanced Salt Solution enriched with proteins and sugars with a neutral pH and pH indicator.	Same
Tube Material	Plastic	Same
Single Use Device	Yes	Same
Sterile Device	Yes	Same
General Device Characteristic Differences		
List of Ingredients	• FBS as protein stabilizer • D-glucose as sugar	• BSA as protein stabilizer • Sucrose as sugar • Gelatin • Glutamic acid • HEPES
Swab Material	Flocked Nylon Fiber Tip with Breaking Point	• Flocked Nylon Fiber Tip with Breaking Point • Polyester tipped with breaking point
Samples Transported to Perform	Assays to detect viruses	Assays to detect viruses, chlamydiae, mycoplasmas, or ureaplasmas
Storage Time	Specimen should be processed within 120 hours	Specimen should be processed within 48 hours
Shelf Life	12 months	15 months
Validation	Molecular and culture	Culture

VI Standards/Guidance Documents Referenced:

1. ASTM D4169-16 Standard Practice for Performance Testing of Shipping Containers and Systems
2. CLSI M40-A2:2014 Quality Control of Microbiological Transport Systems; Approved Standard – Second Edition
3. ISO 2233:2000 Complete, filled transport packages and unit loads – Conditioning for testing.
4. ISO 11137-2:2015 Sterilization of health care products – Radiation – Part 2: Establishing the radiation dose

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Not applicable.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Assay Reportable Range:

   Not applicable.

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

   Shelf life: The shelf life for the Merit Cultura Collection and Transport System was determined to be 12 months from the date of manufacture. The shelf life of the Merit Cultura Collection and Transport System was established using an accelerated stability study. Accelerated stability was assessed by storing components at 55°C ± 2°C with a relative humidity (RH) of 8.7 % ± 5% for 57 days to simulate storage at 22°C with an RH of 50% for 18 months.

   Results were elaborated by calculation of expected real time stability using the Arrhenius equation on a total of three lots. Shelf life stability was assessed using residual clinical specimens at the Wyoming Public Health Laboratory using the CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel. Extraction was performed on the Qiagen QIAcube using the QIAamp Viral RNA Mini Kit, and testing was performed on the Applied Biosystems 7500 Fast Dx PCR System with SDS v1.4 software, according to the CDC 2019-nCoV RT-PCR assay Instructions for Use. Lots subjected to accelerated stability testing were spiked with one positive specimen in triplicate, one negative specimen, and a control containing nuclease free water. Samples were held at 25°C (± 2°C) until hour 240 with aliquots taken at time 0, 120 and 240. All replicates at all timepoints gave a positive result (Ct < 40); the negative controls also performed as expected.

   Real-time stability testing was conducted concurrently and is continuing to verify shelf life and determine if it can be extended beyond the current labeled shelf life of 12 months.

   Sterilization: The Cultura Collection and Transport System VTM is provided to the end user as a sterile media per the Centers for Disease Control and Prevention's Standard Operating Procedure: "Preparation of Viral Transport Medium." [1] The manufacturing process includes sterilization by gamma radiation set at a dose of 25 KiloGray (KGy) in accordance with ISO

[1] Accessed at: https://www.cdc.gov/coronavirus/2019-ncov/downloads/Viral-Transport-Medium.pdf

11137-2:2015[2]. Sterility was confirmed using sterility checks in lots subjected to accelerated stability testing demonstrating no growth detected.

Transport: The stability of the Merit Cultura Collection and Transport System during transport was established using a simulated transport study. Extreme simulated transport testing was performed in accordance with ISO 2233:2000[3]: 9 hours at -35°C at ambient RH (Condition #2) followed by 9 hours at 20°C and 90% RH (Condition #6) followed by 9 hours at 55°C at 30% RH (Condition # 12), with 2 hours of ramp time between conditions and 24 hours of equilibrium time at ambient lab conditions at the end. Simulated distribution testing was performed in accordance with ASTM D4169-16[4], Distribution Cycle DC-13, Assurance Level II to include simulations of product handling, vehicle stacking, loose load vibration, and vehicle vibration.

Performance testing demonstrated that the candidate device provides adequate protection of the contents during normal handling, transit, and storage.

6. Detection Limit:

Viral Recovery:

Culture-Based Viral Recovery Studies: Performance of the Merit Cultura Collection and Transport System was evaluated for virus viability at different incubation times and temperatures.

Stock Preparation. Strains of Respiratory syncytial virus (RSV), influenza A (H1N1) virus, influenza B virus (IBV), and rhinovirus 14 were used for media validation. The following cell lines were obtained from ATCC and used for viral recovery: HEp-2 (for RSV), MDCK (for H1N1 and IBV), and H1-HeLa (for rhinovirus). Ten-fold serial dilutions were performed in cell culture medium (MEM with 10% FBS) and inoculated into the susceptible host cell line. Host cells were plated at a suitable density in cell culture medium in microwell plates 24 hours prior to inoculation. Virus-induced cytopathic effect (CPE) of each dilution was determined by microscopic observation.

Estimated Limit of Detection (LoD). The LoD was determined. Virus was inoculated in 1, 10, and 100 particles in replicates of 3 into the susceptible host cell line. Host cells were plated at a suitable density in cell culture medium in microwell plates 1-2 days prior to testing. Virus-induced CPE of each dilution was determined in replicates of 4. The LoD is the minimum concentration of virus that can be reliably detected (CPE in ≥ 50% wells). The LoD was determined to be 1-9 virus particles for all viruses.

Viability Assay. Virus was inoculated to attain 2x LoD (~10 viral particles) in replicates of 4 into 3 lots of Merit VTM (600 µL in 2.4 mL). Tubes were stored refrigerated (2 to 8°C) or at ambient temperature (23 to 25°C) up to 5 days. Aliquots of each replicate were recovered at 0, 48, 72 or 120 hours, serially diluted, and inoculated in replicates of 4 into the susceptible host cell line. Host cells were plated at a suitable density in culture medium in microwell

[2] ISO 11137-2:2015 Sterilization of health care products – Radiation – Part 2: Establishing the radiation dose
[3] ISO 2233:2000 Complete, filled transport packages and unit loads – Conditioning for testing
[4] ASTM D4169-16 Standard Practice for Performance Testing of Shipping Containers and Systems

plates 1-2 days prior to testing. The following controls were run: a viability control containing no virus to ensure cell viability and no contamination; a virus control containing virus stock to ensure infectivity of virus; a cytotoxicity control containing Merit VTM to observe any CPE from the VTM; and, a recovery control containing virus in culture medium stored and tested under the same conditions as the test samples. Viability was determined by microscopic observation of virus induced CPE to determine the fifty-percent tissue culture infective dose ($TCID_{50}$). The Reed-Muench method was used: $TCID_{50}$= (% mortality above 50% - 50%)/(% mortality above 50% - % mortality below 50%) × log of the dilution factor. **Table 2** shows $TCID_{50}$ values of replicates for each virus tested at time 0 and viral recovery at storage times (T0 and T120 hours) and temperatures (2-8°C and 23-25°C).

Table 2. Test results ($TCID_{50}$) for viruses at T0 and T120 hours at 2-8°C and 23-25°C

Virus	Host cell	Virus recovered at T_0 ($TCID_{50}$)	T0		T120	
			2-8°C	23-25°C	2-8°C	23-25°C
RSV (ATCC VR-26)	HEp-2 (ATCC CCL-23)	$10^{1.5}$	Present	Present	Present	Present
Influenza A (ATCC VR-1496-TC)	MDCK (ATCC CCL-34)	10^{1}	Present	Present	Present	Present
Influenza B (ATCC VR-284)	MDCK (ATCC CCL-34)	$10^{1.5}$	Present	Present	Present	Present
Rhinovirus (ATCC VR-1535)	H1-HeLa (ATCC CRL-1958)	$10^{1.5}$	Present	Present	Present	Present

Merit VTM demonstrated virus viability of RSV, IAV and rhinovirus for all replicates in all lots, incubation times, and storage temperatures. For IBV, Merit VTM demonstrated virus viability of all undiluted samples (2x LoD), but at a 10^{-1} dilution (below LoD) some replicates demonstrated a loss of viability. The studies demonstrate that the Merit Cultura Collection and Transport System maintains the viability of all viruses tested out to 120 hours at refrigerated (2-8°C) and ambient (23-25°C) temperatures.

Amplification-Based Studies: Performance of the Merit Cultura Collection and Transport System was evaluated by amplification of SARS-CoV-2 nucleic acid.

Extraction and Downstream Amplification. Molecular testing was performed with 12 unique SARS-CoV-2 positive clinical specimens at the Wyoming Public Health Laboratory using the CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel, which detects SARS-CoV-2 (N1 and N2 nucleoprotein) markers. Extraction was performed on the Qiagen QIAcube using the QIAamp Viral RNA Mini Kit, and testing was performed on the Applied Biosystems 7500 Fast Dx PCR System with SDS v1.4 software, according to the CDC 2019-nCoV RT-PCR assay Instructions for Use.

Serial dilutions of specimens from the SereCare AccuPlex SARS-CoV-2 Verification Panel were spiked in the Merit Cultura Collection and Transport System at the LoD of the CDC 2019-nCoV RT-PCR assay to confirm that results are comparable to the LoD of the original authorization. The results confirmed that the LoD is at 1,000 copies/mL (20/20 positive, mean N1 Ct=35.13, mean N2 Ct=37.29).

For verification and evaluation of acceptable specimen transport time and temperature, 12 clinical specimens were spiked in triplicate at a dilution of 1:10 (300 µL in 3mL) into each of

3 lots of Merit VTM at time (T) 0, 72 hours, 120 hours, and 216 hours. Samples were selected to span the range of Ct values (low, mid-range and high). Samples were stored at 2 different temperatures: 2-8°C and 23-25°C. The tables below show mean Ct values obtained from testing of 9 replicates (3 replicates × 3 lots) for each sample at each timepoint and the difference in Ct (Δ Ct) between time 0 and the specimen stability claim of 120 hours. Results are presented according to storage temperature (**Tables 3 and 4**).

Table 3. Test results (Ct, Δ Ct) for samples at storage times (hours) and temperature of 2-8°C

	Storage Time (T, hours) and Detected Markers (N1, N2)								Δ Ct	
	T_0		T_{72}		T_{120}		T_{216}		T_0 vs. T_{120}	
Sample	N1	N2	N1	N2	N1	N2	N1	N2	N1	N2
A	18.56	18.39	18.83	18.48	18.36	18.33	18.14	18.73	-0.20	-0.06
B	18.45	18.55	18.36	18.98	18.47	18.64	18.86	19.13	0.02	0.09
C	25.22	24.66	24.36	24.85	25.57	25.05	24.74	24.34	0.36	0.39
D	31.20	31.40	31.02	30.98	30.51	31.40	30.64	31.56	-0.69	0.00
E	25.72	24.65	24.95	24.79	25.02	24.57	24.99	25.08	-0.69	-0.09
F	38.01	38.58	38.04	39.19	37.95	38.08	38.91	38.60	-0.06	-0.50
G	37.51	37.21	38.13	37.82	38.54	37.90	37.77	38.64	1.03	0.70
H	33.85	34.45	33.81	34.58	33.75	33.86	33.84	34.29	-0.10	-0.59
I	22.05	22.91	22.74	22.98	23.15	23.52	21.91	21.82	1.11	0.61
J	32.40	31.78	31.09	31.32	31.70	31.16	31.19	31.63	-0.70	-0.61
K	20.00	19.38	20.95	19.87	19.68	20.12	19.88	19.63	-0.32	0.74
L	32.08	32.71	32.12	32.70	32.60	32.15	33.75	32.28	0.52	-0.57

Table 4. Test results (Ct, Δ Ct) for samples at storage times (hours) and temperature of 23-25°C

	Storage Time (T, hours) Detected Markers (N1, N2)								Δ Ct	
	T_0		T_{72}		T_{120}		T_{216}		T_0 vs. T_{120}	
Sample	N1	N2	N1	N2	N1	N2	N1	N2	N1	N2
A	18.40	18.50	18.57	18.67	17.94	18.84	18.00	18.27	-0.46	0.34
B	18.73	18.59	18.49	18.52	19.10	18.21	18.07	18.41	0.37	-0.38
C	24.80	24.88	24.89	24.58	24.91	25.17	25.10	25.82	0.11	0.29
D	31.29	30.10	30.85	30.21	30.76	30.45	30.81	30.87	-0.53	0.35
E	25.43	25.53	24.34	24.79	24.98	24.84	24.88	25.00	-0.45	-0.69
F	38.03	39.08	38.82	38.06	38.13	38.86	37.92	39.66	0.10	-0.22
G	37.91	38.29	37.81	38.13	38.93	38.33	37.57	38.01	1.02	0.04
H	34.51	33.89	34.41	33.36	33.59	34.82	33.74	33.70	-0.92	0.93
I	21.82	23.18	22.43	22.75	21.88	22.61	22.76	23.00	0.06	-0.57
J	31.71	31.70	31.03	31.36	31.86	31.01	31.61	31.58	0.15	-0.69
K	20.14	19.61	19.95	19.86	19.92	19.34	20.64	19.75	-0.23	-0.28
L	33.04	32.15	32.40	33.10	32.46	32.16	32.28	32.70	-0.58	0.01

The results show 100% concordance of the qualitative result (Ct < 40 is a positive result). No notable differences in Ct values were observed in the samples according to lot number, incubation time, or storage condition. The studies demonstrate that the Merit Cultura Collection and Transport System maintains the stability of the target nucleic acid to 120 hours at refrigerated and ambient temperatures in a reproducible manner.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable.

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

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

   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

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.