510(k) Summary

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K181443

1. Sponsor/Applicant Name and Address

Company Name:	Mesa Biotech, Inc.
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Date Summary Prepared:	05/25/2018

2. Device Name and Classification

Trade Name:	Accula RSV Test
Classification of Device:	21 CFR 866.3980, Respiratory viral panel multiplex nucleic acid assay
Product Code	OCC

3. Predicate Device

K161375, Alere i RSV Assay

4. Device Description

Operating Principle

The Accula RSV Test is a semi-automated, colorimetric, multiplex reverse-transcription polymerase chain reaction (RT-PCR) nucleic acid amplification test to qualitatively detect respiratory syncytial virus (RSV) viral RNA from unprocessed nasal swabs that have not undergone prior nucleic acid extraction. The system integrates nucleic acid extraction, reverse transcription, a novel Mesa Biotech PCR nucleic acid amplification technology named OscAR™, and hybridization-based visual detection into a completely self-contained and automated system. The Accula RSV system consists of a small reusable Dock to drive the automated testing process, and a single-use disposable test cassette that contains all the enzymes and reagents.

RSV Kit Contents

The Accula RSV Test Kit contains all the materials needed to run a test, except for the Accula Dock, which is provided separately. The Accula RSV Test Kit contains the following components.

- Puritan Rayon Swabs for nasal swab collection (25)
- Accula Nasal Swab Buffer (25)
- Accula Transfer Pipettes (25)
- Accula RSV Test Cassettes (25)
- RSV Positive Control Swab (1)
- Negative Control Swab (1)
- Instructions for Use
- Quick Reference Guide

5. Indications for Use

The Accula RSV Test performed on the Accula Dock is a molecular *in vitro* diagnostic test utilizing polymerase chain reaction (PCR) and lateral flow technologies for the qualitative, visual detection of respiratory syncytial virus (RSV) viral RNA. The Accula RSV Test uses a nasal swab specimen collected from patients with signs and symptoms of respiratory infection. The Accula RSV Test is intended as an aid in the diagnosis of RSV infection in children and adults in conjunction with clinical and epidemiological risk factors.

Negative results do not preclude RSV virus infection and should not be used as the sole basis for treatment or other patient management decisions.

6. Comparison to Predicate Device

The following table provides a comparison of the characteristics of the Accula RSV Test to the predicate device, the Alere i RSV assay.

Item	510(k) Device: Mesa Biotech Accula RSV Test	Predicate Device: Alere i RSV (K161375)
Indications for Use	The Accula RSV Test performed on the Accula Dock is a molecular *in vitro* diagnostic test utilizing polymerase chain reaction (PCR) and lateral flow technologies for the qualitative, visual detection of respiratory syncytial virus (RSV) viral RNA. The Accula RSV Test uses a nasal swab specimen collected from	The Alere i RSV assay performed on the Alere i Instrument is a rapid, molecular, in vitro diagnostic test utilizing an isothermal nucleic acid amplification technology for the qualitative detection of respiratory syncytial virus (RSV) viral RNA in direct nasopharyngeal swabs and nasopharyngeal swabs eluted in viral transport

	patients with signs and symptoms of respiratory infection. The Accula RSV Test is intended as an aid in the diagnosis of RSV infection in children and adults in conjunction with clinical and epidemiological risk factors. Negative results do not preclude RSV virus infection and should not be used as the sole basis for treatment or other patient management decisions.	media from patients with signs and symptoms of respiratory infection. It is intended for use as an aid in the diagnosis of RSV in children < 18 years and adults > 60 years in conjunction with clinical and epidemiological risk factors.
Assay Targets	Respiratory syncytial virus	Respiratory syncytial virus
Sample Type	Nasal swab	Nasopharyngeal swab
Assay Results	Qualitative	Qualitative
Intended Users and Use Locations	Clinical lab and point of care	Clinical lab and point of care
Nucleic Acid Purification	No	No
RSV Target	L viral polymerase gene	NS2 gene and nucleocapsid gene N
Internal Control	Yes	Yes
Positive and Negative Control Swabs	Yes	Yes
Assay Technology	PCR amplification and visual identification of amplification products by hybridization to a test strip.	Isothermal nucleic acid amplification and detection of specific amplification products using molecular beacon probes
Detection	Multiplex assay using dyed microparticle conjugates to specifically detect and identify amplification reaction products.	Multiplex assay using fluorescently-labeled molecular beacons to specifically identify amplified RNA targets.

	Visual interpretation of the presence or the absence of colored lines on a test strip.	Optical detection of fluorescence
Instrument	Amplification controlled by the Accula Dock. No detection by the instrument.	Amplification and detection performed on the Alere i instrument

7. Performance Summary

Expected Values

The prevalence of respiratory syncytial virus (RSV) varies from year to year, with outbreaks occurring during the fall and winter months. The RSV positivity rate is dependent upon many factors, including specimen collection, test method, and geographic location. Prevalence varies throughout the RSV season and from location to location.

The Accula RSV prospective clinical study was conducted during the 2017-2018 RSV season. The following table shows the prevalence of RSV observed in three subject age categories.

	Prospective Clinical Study during the 2017/2018 RSV Season		
Age Group	**Number of Nasal Swab Specimens**	**Number of RSV Positives**	**RSV Positivity Rate**
≤ 5 Years of Age	371	134	36.1%
6 to 18 Years of Age	134	9	6.7%
≥ 19 Years of Age	189	10	5.3%
Total	694	153	22.0%

Prospective Clinical Study: Accula™ RSV Test vs. a FDA-Cleared Molecular RSV Assay:

Clinical performance characteristics of the Accula RSV Test were evaluated in a multi-site prospective study during the 2017-2018 RSV seasons in the U.S. A total of ten investigational sites participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with RSV-like symptoms. Two nasal swabs were collected, one from each nostril, from each subject using standard collection methods. One nasal swab was eluted in 5 mL of Accula Nasal Swab Buffer and tested with the Accula RSV Test according to the product instructions. The other nasal swab was eluted with 3 mL universal transport media (UTM) and transported to a central reference laboratory for testing using the comparator method. All discrepant results were analyzed using an alternative FDA-cleared molecular assay at the reference laboratory.

A total of 749 subjects were enrolled in this study. Of those, 55 specimens are unevaluable (i.e. failed to meet inclusion/exclusion criteria, were not transported to the reference laboratory per the conditions required by the clinical protocol, had an invalid result for the comparative method, or had two invalid results on the Accula RSV Test. A total of 694 specimens were considered evaluable. The performance of the Accula RSV Test for RSV as compared to a FDA-cleared molecular comparator is presented in the table below.

Accula RSV Test Performance Compared to FDA-cleared Molecular Comparator

Accula RSV Test	Comparator		
	Positive	**Negative**	**Total**
Positive	129	24[a]	153
Negative	14[b]	527	541
Total	143	551	694
Sensitivity:	90.2% (95% CI: 84.2% - 94.1%)		
Specificity:	95.6% (95% CI: 93.6% - 97.1%)		

[a] RSV was detected in 22/24 False Positives specimens using an alternative FDA-cleared molecular RSV assay
[b] RSV was not detected in 12/14 False Negative specimens using an alternative FDA-cleared molecular RSV assay

Reproducibility Studies

The reproducibility study was performed to demonstrate the reproducibility of the Accula RSV Test with contrived nasal swabs at three CLIA-waived sites and one moderately complex site based in the United States. The objective of the study was to demonstrate reproducibility of the assay in the hands of multiple users at multiple sites over multiple non-consecutive days.

The test panel consisted of three samples at varying virus concentrations (i.e. RSV Negative, RSV Low Positive, and RSV Moderate Positive). Each positive sample was prepared by spiking the RSV-A2 strain into clinical matrix. The targeted concentration for the Moderate Positive sample was approximately 3X the LoD, and the targeted concentration for the Low Positive sample was approximately 1X the LoD (C95 concentration). The Negative sample contained no RSV virus.

Samples were provided to testing operators in panels of 3 samples (RSV Low Positive, RSV Moderate Positive, and Negative). Samples were blinded and randomized. Each operator tested one panel per day, testing a maximum of three samples at a time. Each sample was tested in triplicate (from separate swabs): 2 operators x 1 run x 3 swabs x 5 non-consecutive days = 30 observations for each site per sample type. Results are reported as percent agreement: actual result/expected result x 100. Agreement was 100% across all sites, operators, and days. There were no significant differences observed within run, between runs, between sites, or between operators. Agreement by site is shown in the table below.

Site to Site Reproducibility: Percent Agreement and Total Counts (Observed/Expected)

Sample Category	Site								Overall Percent Agreement and 95% CI
	ADP		GVP		LBC		NAZ		
	Percent Agreement	Count	Percent Agreement	Count	Percent Agreement	Count	Percent Agreement	Count	
Low Pos RSV	100%	30/30	100%	30/30	100%	30/30	100%	30/30	100% (120/120) (95.9%, 100%)
Mod Pos RSV	100%	30/30	100%	30/30	100%	31/31*	100%	30/30	100% (121/121) (96.0%, 100%)
True Neg	100%	30/30	100%	30/30	100%	29/29*	100%	30/30	100% (119/119) (95.9%, 100%)
* One negative swab was mistakenly spiked with MP RSV									

Limit of Detection

Multiple analyte levels were tested in 20 replicates until the LoD was determined (the level at which at least 19/20 results are positive). Two RSV A subtype strains and two RSV B subtype strains were tested in replicates of twenty (20) for each concentration. Virus was serially diluted into a pooled negative clinical matrix and spiked onto a swab to create the contrived samples for each technical replicate for LoD determination.

Results are summarized in the table below.

Limit of Detection: Observed Positives/Number of Replicates

Virus	LOD level	Observed Positives/ Replicates
RSV A2	300 TCID50/mL	20/20
RSV A Long	300 TCID50/mL	20/20
RSV B1	10 TCID50/mL	20/20
RSV B 18537	0.5 PFU/mL	19/20

Analytical Reactivity

Inclusivity verification was evaluated for the Accula RSV test at Mesa Biotech. The panel consisted of nine (9) RSV strains, representing both RSV-A and RSV-B subtypes. Each strain was tested in triplicate at a concentration of approximately 2X LoD. Virus was diluted in pooled clinical matrix and spiked onto a swab to create contrived swab samples. Test results are shown in the table below.

Inclusivity Results by RSV Strain: Target Concentrations and Test Results

Identification Code	Subtype	Test Level *	Percent Detection (# Positive / 3)
RSV 2012-10	RSV-B	1 PFU/mL	100% (3/3)
RSV 2012-11	RSV-B	1 PFU/mL	100% (3/3)
RSV A 12/2014	RSV-A	600 TCID50/mL	100% (3/3)
RSV A 3/2015	RSV-A	600 TCID50/mL	100% (3/3)

Identification Code	Subtype	Test Level *	Percent Detection (# Positive / 3)
RSV B 12/2014	RSV-B	20 TCID50/mL	100% (3/3)
RSV 2006 Isolate	RSV-A	600 TCID50/mL	100% (3/3)
RSV CH93(18)-18	RSV-B	20 TCID50/mL	100% (3/3)
RSV 9320	RSV-B	20 TCID50/mL	100% (3/3)
RSV B 3/2015	RSV-B	20 TCID50/mL	100% (3/3)
** Concentration of contrived sample after 10uL of virus dilution Spiked onto Swab and Swirled in 5mL pooled clinical matrix assuming 100% viral elution recovery.*			

Analytical Specificity (Cross-Reactivity)

Cross-reactivity was performed by testing 41 potentially cross-reacting organisms with the Accula RSV Test. Each organism was diluted in a clinical matrix and tested in triplicate. The organisms, concentrations, and test results are shown in the table below. All 41 organisms were negative at the concentrations tested.

Test Results of Possible Cross-Reactive Organisms			
Organism Key #	**Organism Name**	**Test Level**	**Test Results (# of RSV Pos / 3)**
1	Adenovirus Type 1	5.10E+05 TCID50/mL	0/3
2	Adenovirus Type 7	3.31E+04 TCID50/mL	0/3
3	Coronavirus	1.10E+04 TCID50/mL	0/3
4	Coronavirus	2.95E+05 TCID50/mL	0/3
5	Cytomegalovirus	1.10E+04 TCID50/mL	0/3
6	Cytomegalovirus	1.90E+04 TCID50/mL	0/3
7	Cytomegalovirus	2.52E+04 TCID50/mL	0/3
8	Echovirus	2.95E+05 TCID50/mL	0/3
9	Enterovirus	1.04E+04 TCID50/mL	0/3
10	Human Metapneumovirus	1.01E+04 TCID50/mL	0/3
11	Measles virus	2.95E+05 TCID50/mL	0/3
12	Mumps virus	9.75E+04 TCID50/mL	0/3
13	Parainfluenza Type 1	2.52E+04 TCID50/mL	0/3*
14	Parainfluenza Type 2	1.10E+04 TCID50/mL	0/3
15	Parainfluenza Type 3	1.18E+04 TCID50/mL	0/3
16	Rhinovirus	3.31E+04 TCID50/mL	0/3
17	Rhinovirus	3.31E+04 TCID50/mL	0/3
18	Rhinovirus	3.02E+04 TCID50/mL	0/3
19	Epstein-Barr virus	3.98E+07 cp/mL	0/3
20	*Bordetella pertussis*	4.22E+06 cfu/ml	0/3
21	*Candida albicans*	9.80E+05 cfu/ml	0/3
22	*Escherichia coli*	1.92E+07 cfu/ml	0/3
23	*Haemophilus influenzae*	1.20E+06 cfu/ml	0/3
24	*Klebsiella pneumoniae*	4.15E+07 cfu/ml	0/3
25	*Lactobacillus sp.*	3.00E+06 cfu/ml	0/3
26	*Legionella longbeachae*	9.65E+06 cfu/ml	0/3
27	*Moraxella catarrhalis*	1.99E+05 cfu/ml	0/3
28	*Mycobacterium tuberculosis*	3.62E+06 cfu/ml	0/3

Test Results of Possible Cross-Reactive Organisms			
Organism Key #	**Organism Name**	**Test Level**	**Test Results (# of RSV Pos / 3)**
29	*Neisseria gonorrhoeae*	6.30E+06 cfu/ml	0/3
30	*Neisseria meningitidis*	1.28E+06 cfu/ml	0/3
31	*Neisseria subflava*	7.30E+06 cfu/ml	0/3
32	*Proteus vulgaris*	2.07E+07 cfu/ml	0/3
33	*Pseudomonas aeruginosa*	6.05E+05 cfu/ml	0/3
34	*Staphylococcus aureus*	6.95E+07 cfu/ml	0/3
35	*Staphylococcus epidermidis*	3.24E+07 cfu/ml	0/3
36	*Streptococcus pneumonia*	2.09E+06 cfu/ml	0/3
37	*Streptococcus pyogenes*	2.72E+07 cfu/ml	0/3
38	*Streptococcus salivarius*	2.32E+06 cfu/ml	0/3
39	*Mycoplasma pneumoniae*	2.81E+05 CCU/ml	0/3
40	Influenza A/California/07/2009	2.15E+04 TCID50/mL	0/3
41	Influenza B/Massachusetts/2/2012	5.00E+05 TCID50/mL	0/3
**Replicate 3 of Organism # 13 Parainfluenza Type 1 was repeated due to an Invalid.*			

Interfering Substances

To assess substances with the potential to interfere with the performance of the Accula RSV Test, two (2) RSV strains were tested in replicates of three (3) with each interfering substance at the "worst case" concentration. For each sample, virus was diluted into a pooled negative clinical matrix to achieve a 1.5X LoD concentration. Each RSV strain was tested with an interferent concentration representing the highest concentration likely to be found in a respiratory sample. Additionally, each strain was tested without the interfering substance as a control. Potential interferents, their concentrations, samples tested, and test results are summarized in the table below. The Accula RSV Test performance is not negatively affected by the potentially interfering substances tested.

Interfering Substances - Agreement of Observed/Expected			
Potential Interferent	Interferent Concentration for Making Contrived Swab	Sample Tested	% Agreement with Expected Results
Controls	NA	Negative	100% (2/2)
	NA	RSV A2 at 450 TCID50/ml	100% (3/3)
	NA	RSV B1 at 15 TCID50/mL	100% (3/3)
Blood (Human)	1% (v/v)	Negative	100% (3/3)
	1% (v/v)	RSV A2 at 450 TCID50/ml	100% (3/3)
	1% (v/v)	RSV B1 at 15 TCID50/mL	100% (3/3)
Phenylephrine nasal spray	Neat	Negative	100% (3/3)
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3)
Oxymetazoline nasal spray	Neat	Negative	100% (3/3)
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)

Interfering Substances - Agreement of Observed/Expected			
Potential Interferent	Interferent Concentration for Making Contrived Swab	Sample Tested	% Agreement with Expected Results
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3)
Ocean Saline Nasal Spray	Neat	Negative	100% (3/3)
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3)
Chloraseptic Max	Neat	Negative	100% (3/3)
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3)
Nasacort (Triamcinolone, nasal corticosteroid)	Neat	Negative	100% (3/3)
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3)
Zicam (Nasal gel, homeopathic allergy relief medicine)	Neat	Negative	100% (3/3) *
	Neat	RSV A2 at 450 TCID50/ml	100% (3/3)
	Neat	RSV B1 at 15 TCID50/mL	100% (3/3) **
Cepacol (throat lozenge)	1 lozenge/5mL	Negative	100% (3/3)
	1 lozenge/5mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	1 lozenge/5mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Mucin, Type II	5 mg/mL	Negative	100% (3/3)
	5 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	5 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Beclomethasone	1.6 mg/mL	Negative	100% (3/3)
	1.6 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	1.6 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Budesonide	3.2 mg/mL	Negative	100% (3/3)
	3.2 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	3.2 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Dexamethasone	30 mg/mL	Negative	100% (3/3)
	30 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	30 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3) *
Flunisolide	1.6 mg/mL	Negative	100% (3/3)
	1.6 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	1.6 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Fluticasone Propionate	0.25 mg/mL	Negative	100% (3/3)
	0.25 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	0.25 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Mometasone furoate	1 mg/mL	Negative	100% (3/3)
	1 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	1 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Mupirocin (antibiotic)	20 mg/mL	Negative	100% (3/3)
	20 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)

Interfering Substances - Agreement of Observed/Expected			
Potential Interferent	Interferent Concentration for Making Contrived Swab	Sample Tested	% Agreement with Expected Results
	20 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Tobramycin (antibacterial)	75 mg/mL	Negative	100% (3/3)
	75 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	75 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Triamcinolone	0.05 mg/mL	Negative	100% (3/3)
	0.05 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3) *
	0.05 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
Zanamivir (anti-viral drug)	50 mg/mL	Negative	100% (3/3) *
	50 mg/mL	RSV A2 at 450 TCID50/ml	100% (3/3)
	50 mg/mL	RSV B1 at 15 TCID50/mL	100% (3/3)
One replicate was repeated due to an invalid result* * Two replicates were repeated due to invalid results*			

CLIA Waiver Studies

The performance of the Accula RSV Test was evaluated at ten intended use sites by non-laboratory personnel in a prospective clinical study during the 2017-2018 RSV season in the U.S. Nasal swabs were collected from patients with RSV-like symptoms and were tested with the Accula RSV Test and the comparator method, a FDA-cleared molecular RSV assay. All specimens generating discrepant results were investigated by testing with an alternative FDA-cleared molecular assay. The performance of the Accula RSV test compared with the comparator method is presented in the table below.

Accula RSV Test Performance Compared to FDA-cleared Molecular Comparator

Accula RSV Test	Comparator		
	Positive	**Negative**	**Total**
Positive	129	24[a]	153
Negative	14[b]	527	541
Total	143	551	694
Sensitivity:	90.2% (95% CI: 84.2% - 94.1%)		
Specificity:	95.6% (95% CI: 93.6% - 97.1%)		

[a] RSV was detected in 22/24 False Positives specimens using an alternative FDA-cleared molecular RSV assay
[b] RSV was not detected in 12/14 False Negative specimens using an alternative FDA-cleared molecular RSV assay

Performance Near the Cut-off

Three CLIA-waived sites that participated in the prospective clinical study also participated in the Near-Cutoff study. The testing was performed by three (3) untrained intended operators at each of the sites. This study was conducted to demonstrate that untrained intended users could

perform the Accula RSV Test and consistently detect Low Positive samples at the Limit of Detection (LoD).

The test panel consisted of two contrived samples: RSV Low Positive and a True Negative. The Low Positive sample was prepared using the RSV-A2 strain spiked into negative clinical matrix at a concentration of approximately 1X LoD (C95 concentration). The Negative sample was prepared from negative clinical matrix with no RSV virus. Samples were applied to swabs, coded and blinded to the testing operators. Swab specimens were presented to the intended use operators throughout the course of a normal working day and were masked as subject samples. Testing took place during the course of two weeks on non-consecutive days, while the clinical study was in progress. Each site ultimately tested a panel of 60 samples: 30 replicates of each sample.

Test results are shown in the table below. The study demonstrates that untrained intended use operators are able to accurately perform and interpret the Accula RSV Test at the level of the LoD.

Near-Cutoff Study Test Results: Agreement of Observed/Expected

Site	Sample Type	
	RSV Positive	RSV Negative
ADP	30/30	30/30
GVP	30/30	30/30
LBC	30/30	30/30
Total	90/90	90/90

8. Conclusion

The information presented in this Premarket Notification demonstrates that the performance of the Accula RSV Test is substantially equivalent in intended use, technological characteristics, and performance to the predicate device.