DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Silver Spring, MD 20993-0002

Alere Scarborough, Inc.
Angela Drysdale
Vice President Regulatory Affairs
10 Southgate Road
Scarborough, ME 04074

August 18, 2016

Re: K161375
Trade/Device Name: Alere i RSV
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid System
Regulatory Class: II
Product Code: OCC, OOI
Dated: May 19, 2016
Received: May 20, 2016

Dear Ms. Drysdale:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Tamara V. Feldblyum -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
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and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161375

Device Name
Alere™ i RSV

Indications for Use *(Describe)*
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 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

This summary of 510(k) 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: K161375

SUBMITTER

Alere Scarborough, Inc.
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Establishment Registration Number: 1221359

PRIMARY CONTACT PERSON

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DATE PREPARED

August 15, 2016

TRADE NAME

Alere™ i RSV

COMMON NAME

Alere™ i RSV, Alere™ i

CLASSIFICATION NAME

Respiratory Viral Panel Multiplex Nucleic Acid System (per 21 CFR 866.3980)
Instrumentation for Clinical Multiplex Test Systems (per 21 CFR 862.2570)

CLASSIFICATION

Class II

PRODUCT CODE

OCC, OOI

PANEL

Microbiology (83)

PREDICATE DEVICE

Quidel Molecular RSV + hMPV Assay (Lyra) K131813

DEVICE DESCRIPTION

The Alere™ i RSV is a rapid, instrument-based test for the qualitative detection and differentiation of respiratory syncytial virus (RSV) viral RNA from direct nasopharyngeal swab (NPS) and NPS eluted in viral transport media from patients with signs and symptoms of respiratory infection. The Alere™ i RSV System utilizes isothermal nucleic acid amplification technology and is comprised of:

- Sample Receiver – single use, disposable containing the elution buffer
- Test Base – single use, disposable comprising two sealed reaction tubes, each containing a lyophilized pellet
- Transfer Cartridge – Single use, disposable for transfer of the eluted sample to the Test Base, and
- Alere™ i Instrument – repeat use reader

The reaction tubes in the Test Base contain the reagents required for amplification of the target nucleic acid and an internal control. Alere™ i RSV utilizes a pair of templates (similar to primers) for the specific amplification of RNA from RSV A and B, which occur in two separate reaction tubes. Each reaction tube contains a fluorescently labeled molecular beacon designed to specifically identify the amplified RNA targets. Alere™ i RSV is performed within the confinement of the Test Base, and no other part of the Alere™ i Instrument has contact with the sample during the amplification process. This minimizes the risk of instrument contamination and sample carry-over between measurements.

To perform the assay, the Sample Receiver and Test Base are inserted into the Alere™ i Instrument and the elution buffer is automatically heated by the instrument. The sample is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, re-suspending the lyophilized pellets contained within the Test Base and initiating target amplification. Heating, mixing and detection by fluorescence are provided by the instrument, with results automatically reported.

Results are displayed by the Alere™ i Instrument and are also stored in an on-board archive and are assigned to a sample ID that has been entered into the Alere™ i Instrument by the operator, and the date/time the test was performed. Data can be retrieved and downloaded by the operator at any time after testing. An external Alere™ Universal Printer can be attached via USB to the Alere™ i Instrument to print test results.

INTENDED USE

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 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.

TECHNICAL CHARACTERISTICS

Alere™ i RSV and the predicate device, Quidel Molecular RSV + hMPV Assay, have the same intended use, indications for use, and utilize similar basic principles of operation. They are both molecular tests for the qualitative detection of RSV viral RNA.

DEVICE COMPARISON

Alere™ i RSV was compared to the legally marketed predicate device, the Quidel Molecular RSV + hMPV Assay.

Parameter	Alere™ i RSV	Quidel Molecular RSV + hMPV Assay (Lyra) (K122189, K131813)
FDA Product Code	OCC, OOI	OEM, OCC
Assay Target	RSV	RSV + hMPV
Intended Use	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 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.	The Quidel Molecular RSV + hMPV Assay is a multiplex Real-Time PCR (RT-PCR) assay for the qualitative detection and identification of respiratory syncytial virus (RSV) and human metapneumovirus (hMPV) ribonucleic acid (RNA) extracted from nasal and nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. This *in vitro* diagnostic test is intended to aid in the differential diagnosis of RSV and hMPV infection in humans in conjunction with clinical and epidemiological risk factors. This test is not intended to differentiate the two subtypes of RSV or the four genetic sub-lineages of hMPV. Negative results do not preclude RSV infection and/or hMPV infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Conversely, 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. The use of additional laboratory testing and clinical presentation must be considered in order to obtain the final diagnosis of respiratory viral infection. The Quidel Molecular RSV + hMPV Assay can be performed using the Life Technologies QuantStudio™ Dx RT-PCR Instrument, the Applied Biosystems® 7500 Fast Dx RT-PCR Instrument, or the Cepheid SmartCycler® II System.

Parameter	Alere™ i RSV	Quidel Molecular RSV + hMPV Assay (Lyra) (K122189, K131813)
Intended Environment for Use	Professional use, in a medical laboratory or point-of-care	Professional use, in a medical laboratory
Instrumentation	Alere™ i Instrument	Cepheid SmartCycler® II System, the Applied Biosystems® 7500 Fast Dx RT-PCR Instrument, or the Life Technologies QuantStudio™ Dx RT-PCR Instrument
Assay Information		
Sample Type	Nasopharyngeal Swab, Nasopharyngeal Swab eluted in Viral Transport Media	Nasopharyngeal swab and nasal swab
RSV Target	NS2 gene and nucleocapsid gene N	NS2 genes, L viral polymerase
Technology	Isothermal nucleic acid amplification for detecting the presence/absence of viral RNA in clinical specimens.	RT-PCR-based system for detecting the presence or absence of viral RNA in clinical specimens
Internal Control	Yes	Yes
Results Interpretation	Automated	Same
Assay Result	Qualitative	Same
Time to Result	<15 minutes	< 70 minutes

PERFORMANCE SUMMARY

CLINICAL STUDY

The clinical performance of Alere™ i RSV was established in a multi-center, prospective clinical study conducted at nine US trial sites during the 2015-2016 respiratory season.

A total of 497 evaluable nasopharyngeal swab and 501 evaluable nasopharyngeal swab specimens eluted in Viral Transport Media (VTM) collected from children <18 years and adults ≥60 years presenting with symptoms of respiratory infection, were evaluated with Alere™ i RSV, and compared to PCR. 46.6% of the population tested was female and 53.4% was male.

In this study, two nasopharyngeal swabs were collected from each Subject. One swab was tested directly with Alere™ i RSV, according to product instructions for testing swabs. The other swab was eluted in VTM, and a sample of the VTM eluate was tested with Alere™ i RSV.

Alere™ i RSV performance, including 95% confidence intervals, versus FDA-cleared PCR test, is provided below for nasopharyngeal swab direct specimens and nasopharyngeal swab eluted in VTM specimens.

Nasopharyngeal Swab Direct

	PCR +	PCR -	
Alere™ i +	137	7	144
Alere™ i -	2	351	353
	139	358	497

Sensitivity: 137/139 = 98.6%
(95% CI: 94.9%, 99.6%)

Specificity: 351/358 = 98.0%
(95% CI: 96.0%, 99.1%)

Nasopharyngeal Swab Eluted in VTM

	PCR +	PCR -	
Alere™ i +	138	8	146
Alere™ i -	2	353	355
	140	361	501

Sensitivity: 138/140 = 98.6
(95% CI: 94.9%, 99.6%)

Sensitivity: 353/361 = 97.8%
(95% CI: 95.7%, 98.9%)

During the prospective clinical study, the initial invalid rate for direct nasopharyngeal swab samples (before repeat testing per the product instructions) was 4.1% (21/506) (95% CI: 2.7% to 6.3%). After repeat testing per the product instructions, the invalid rate was 0.8% (4/506) (95% CI: 0.3% to 2.0%).

The initial invalid rate for nasopharyngeal swabs eluted in viral transport media was 2.2% (11/506) (95% CI: 1.2% to 3.9%). After repeat testing per the product instructions, the invalid rate was 0% (0/506) (95% CI: 0.0% to 0.8%).

ANALYTICAL STUDIES

ANALYTICAL SENSITIVITY

Alere™ i RSV limit of detection (LOD or C_{95}), defined as the concentration of RSV that produces positive Alere™ i RSV results approximately 95% of the time, was identified by evaluating one RSV A strain and one RSV B strain for both direct swab and swab eluted in VTM testing in Alere™ i RSV. The concentrations identified as the LOD (or C_{95}) levels for each strain and testing method are listed below.

Testing Method	Strain	Concentration $TCID_{50}$/mL	Concentration Genome Equivalents/mL
Swab Direct	RSV A/2	5.82×10^2	7.78×10^4
	RSV B/9320	6.0×10^1	5.43×10^3
VTM	RSV A/2	9.15×10^3	1.06×10^6
	RSV B/9320	9.64×10^2	1.48×10^5

ANALYTICAL REACTIVITY (INCLUSIVITY)

The following RSV strains were tested and produced positive reactions at or near the stated assay limit of detection of the Alere™ i RSV test: RSV A Long, RSV B1 and RSV B 18537.

ANALYTICAL SPECIFICITY (CROSS-REACTIVITY)

To determine the analytical specificity of Alere™ i RSV, 40 commensal and pathogenic microorganisms (21 bacteria, 18 viruses and 1 yeast) that may be present in the nasal cavity or nasopharynx were tested. All of the following microorganisms were negative when tested at concentrations ranging from 10^3 to 10^{10} cells/mL or CFU/mL (bacteria), 10^4 to 10^8 $TCID_{50}$/mL, and 10^8 cells/mL (yeast).

Bacteria	**Viruses**	**Yeast**
Bordetella pertussis	Adenovirus Type 1	*Candida albicans*
Corynebacterium diptheriae	Adenovirus type 7	
*Escherichia coli**	Coxsackievirus B4	
Haemophilus influenzae	Enterovirus Type 70	
Klebsiella pneumoniae	Epstein Barr virus	
Lactobacillus plantarum	Human Coronavirus OC43	
Legionella pneumophila	Human Coronavirus 229E	
*Moraxella/Branhamella catarrhalis**	Human Cytomegalovirus (CMV) (Herpes V)	
Mycobacterium tuberculosis	Human Echovirus 7, Strain Wallace	
Mycoplasma pneumoniae	Human metapneumovirus	
Neisseria gonorrhoeae	Influenza A	
Neisseria meningitidis	Influenza B	
Neisseria sicca	Measles virus, strain Edmonston	
Neisseria subflava	Mumps virus, strain Enders	
*Proteus vulgaris**	Parainfluenza virus 1	
Pseudomonas aeruginosa	Parainfluenza virus 2	
Staphylococcus aureus	Parainfluenza virus 3	
Staphylococcus epidermidis	Rhinovirus Type 1A	
Streptococcus Group A		
Streptococcus pneumoniae		
Streptococcus salivarius		

* Some cross-reactivity was observed for *E. coli* at concentrations greater than 2.75 x10^9, *Moraxella catarrhalis* at concentrations greater than 1.50 x10^9, and *Proteus vulgaris* at concentrations greater than 4.69 x 10^8.

In addition, *in silico* analysis was performed to determine whether there is any significant overlap between Alere™ i RSV target nucleic acid sequence and the genomes of the following upper respiratory tract microorganism. None of the organisms maintained genomic sequence that was significantly similar to the Alere™ i RSV target sequences.

Bacteria	**Viruses**
Bordetella bronchiseptica	Adenovirus 2
Chlamydia pneumonia	Adenovirus 3
Chlamydia trachomatis	Adenovirus 4
Neisseria mucosa	Adenovirus 5

Proteus mirabilis	Adenovirus 11 Adenovirus 14 Adenovirus 31 Coronavirus NL63 Coxsackievirus B35 Echovirus 6 Echovirus 9 Echovirus 11 Enterovirus 71

INTERFERING SUBSTANCES

The following substances, naturally present or artificially introduced into the nasal cavity/nasopharynx were evaluated with Alere™ i RSV at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Mucin	0.0625%
Whole Blood	1%
NeoSynephrine Cold & Sinus Extra Strength Spray	20%
Afrin Pump Mist Original	20%
Ocean Saline	20%
Chloroseptic Max	20%
Zicam Allergy Relief	20%
Beclomethasone	0.068 mg/mL
Dexamethasone	0.48 mg/mL
Flunisolide	0.04 mg/mL
Triamcinolone	0.04 mg/mL
Budesonide	0.051 mg/mL
Mometasone furoate	0.04 mg/mL
Fluticasone propionate	0.04 mg/mL
Zanamivir (Relenza)	0.284 mg/mL
Mupirocin	4.3 mg/mL
Tobramycin	1.44 mg/mL

INHIBITION BY OTHER MICROORGANISMS

Alere™ i RSV test performance in the presence of non-RSV respiratory pathogens was evaluated. Vendor provided stocks of RSV A and B strains were diluted in UTM to approximately 3 times the limit of detection. Contrived RSV A and B positive swab specimens were prepared by coating 10 microliters of virus dilution onto each swab. The following panel of non-RSV viruses was tested at the concentration provided in the table below and was found not to affect test performance.

Virus Panel	Concentration ($TCID_{50}$/ml)
Adenovirus Type 1	1.58×10^7
Rhinovirus Type 1A	1.58×10^7
Influenza A	5.00×10^7
Influenza B	1.00×10^8

CARRY-OVER CONTAMINATION

An analytical carry-over study was performed to demonstrate that when recommended laboratory practices are followed, there is little risk of false positive results caused by carryover or cross-contamination in the Alere™ i RSV test. Vendor provided stocks of RSV A and B strains were diluted in UTM to approximately 30 times the limit of detection. Contrived RSV A and B positive swab specimens were prepared by coating 10 microliters of virus dilution onto each swab. Testing of the contrived positive swabs was alternated with testing of a negative swab sample for a total of 15 rounds. In addition, testing of contrived positive VTM samples was alternated with negative VTM samples following the test procedure for Nasopharyngeal Swab Eluted in Viral Transport Media for a total of 15 rounds. No false positive results were observed in this study.

REPRODUCIBILITY

A reproducibility study of Alere™ i RSV was conducted by operators from 3 sites using panels of blind coded specimens containing negative, low positive (at the limit of detection), and moderate positive (above the limit of detection) RSV A and B samples. Participants tested each sample multiple times on 5 different days. The percent agreement with expected results for the RSV A moderate positive and low positive samples were 100% (89/89) and 98.9% (89/90), respectively. The percent agreement with expected results for the RSV B moderate positive and low positive samples were 98.9% (89/90) and 100% (90/90), respectively. All of the negative samples (90) generated negative test results. There were no significant differences within run (replicates tested by one operator), between run (5 different days), between sites (3 sites), or between operators (9 operators).

The results of the analytical and clinical studies performed with Alere™ i RSV support the determination of substantial equivalence in accordance with the stated intended use and device labeling.