510(k) SUMMARY

General Information

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Device Name

Trade Name: *artus*® Infl A/B RG RT-PCR Kit
Common Name: Influenza A/B Test
Classification Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay, (21 CFR 866.3980, Product Code OCC)

Predicate Device

Manufacturer	Product Name	510(k) No.
Gen-Probe Prodesse, Inc.	ProFlu+ Assay	K110968

Device Description

The *artus* Infl A/B RG RT-PCR Kit contains reagents and instructions for the detection and differentiation of Influenza A and Influenza B viral RNA in nasopharyngeal swabs of symptomatic patients.

The assay utilizes the EZ1 Advanced XL instrument with the EZ1 Advanced XL DSP Virus Card v. 1.0. and the EZ1 DSP Virus Kit (QIAGEN) for viral nucleic acid extraction. The Rotor-Gene Q MDx instrument with the *artus* Influenza Assay Software Package (QIAGEN) is used for amplification and detection.

Pathogen detection by the reverse transcription polymerase chain reaction (RT-PCR) is based on the reverse transcription of the RNA into complementary DNA (cDNA) and subsequent amplification of specific regions of the pathogen genome. In real-time PCR the amplified product is detected via fluorescent dyes. These are linked to

oligonucleotides that bind specifically to the amplified product. Monitoring the fluorescence intensities during the PCR run (i.e., in real time) allows the detection of the accumulating product without having to re-open the reaction tubes after the PCR run.

The Influenza A/B Master contains primers, probes, enzymes, and other reaction components (except Mg solution) needed for the specific amplification of a 141 bp region of the Influenza A virus genome and a 95 bp region of the influenza virus B genome, and for the direct detection of the specific amplicons in two fluorescence channels of the Rotor-Gene Q MDx instrument. The primers are complementary to highly conserved regions of the Matrix gene locus within the influenza A or influenza B virus genome. The probes are dual-labeled with a reporter dye attached to the 5'-end and a quencher dye attached to the 3'-end. Detection is performed on the Rotor-Gene Q MDx instrument at wavelengths listed in Table 5.1.

In addition, the Master contains a second heterologous primer/probe set to detect the Influenza A/B Internal Control (IC). The IC result identifies possible failure of RNA extraction or the presence of PCR inhibition. The Internal Control is detected in a third fluorescence channel.

Table 5.1. Target genes and detection channels

Component	Target	Target Gene	Detection Range (nm)
Influenza A/B Master	Influenza A Virus	Matrix	510 +/- 5
	Influenza B Virus	Matrix	710 +/- 5
	Internal Control	Synthetic sequence	610 +/- 5

An Influenza A Control and an Influenza B Control comprised of in vitro transcripts representing the amplified regions of the Influenza A virus genome and the Influenza B virus genome, respectively, are provided. PCR grade water is provided as a negative (no-template) control.

The procedure consists of four consecutive steps:

1. **Sample collection**: Collect nasopharyngeal swab specimens from symptomatic patients using a polyester, nylon, or rayon swab and place it into virus transport medium.

2. **Nucleic acid extraction**: Add the Influenza IC to the carrier RNA before starting the extraction procedure. Extract viral RNA using the EZ1 DSP Virus Kit in combination with the EZ1 Advanced XL instrument.

3. **Real-time RT-PCR**: Add the extracted RNA and positive and negative control material to Influenza A/B Master mix. Perform real-time RT-PCR using the Rotor-Gene Q MDx instrument.

4. **Result interpretation**: The Influenza Assay Package evaluates the results of the positive and negative controls to determine if the run is valid. If the run is valid, the internal control and target-specific results of each specimen are evaluated.

Intended Use

The *artus*® Infl A/B RG RT-PCR Kit is a multiplex real time PCR *in vitro* diagnostic test for the qualitative detection and identification of Influenza A and Influenza B virus RNA in nasopharyngeal swab specimens using the Rotor-Gene® Q MDx instrument. The test is intended for use as an aid in the differential diagnosis of Influenza A and Influenza B viral infections in patients symptomatic for respiratory tract infection in conjunction with clinical and epidemiological risk factors. It is not intended to detect Influenza C virus.

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

Performance characteristics for Influenza A were established during the 2009/2010 and 2010/2011 flu seasons when Influenza A (H3N2) and Influenza A/2009 (H1N1) were the predominant Influenza A viruses in circulation. When other Influenza A viruses emerge, performance characteristics may vary.

If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Comparison of the *artus*® Infl A/B RG RT-PCR Kit and the Predicate Device

The *artus*® Infl A/B RG RT-PCR Kit is substantially equivalent to the predicate device:

- K110968: ProFlu+ Assay, Gen-Probe Prodesse, Inc.

Similarities and differences between the *artus*® Infl A/B RG RT-PCR Kit and the predicate device are shown in Table 5.2.

Table 5.2. Comparison of the *artus*® Infl A/B RG RT-PCR Kit with the predicate device.

Characteristic	Device	Predicate
Name	*artus*® Infl A/B RG RT-PCR Kit	ProFlu+™ Assay
510(k) No.	K113323	K110968
Regulation	866.3980	866.3980
Product Code	OCC	OCC
Device Class	II	II
Similarities		
Intended Use	The *artus*® Infl A/B RG RT-PCR Kit is a multiplex real time PCR *in vitro* diagnostic test for the qualitative detection and identification of influenza A and influenza B virus RNA in nasopharyngeal swab specimens using the Rotor-Gene® Q MDx instrument. The test is intended for use as an aid in the differential diagnosis of influenza A and influenza B virus infections in patients symptomatic for respiratory tract infection in conjunction with clinical and epidemiological risk factors. It is not intended to detect influenza C virus. Negative results do not preclude respiratory virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2009/2010 and 2010/2011 flu seasons when influenza A (H3N2) and influenza A/2009 (H1N1) were the predominant influenza A viruses in circulation. When other Influenza A viruses emerge, performance characteristics may	The ProFlu™+ Assay is a multiplex Real-Time PCR (RT-PCR) *in vitro* diagnostic test for the rapid and qualitative detection and discrimination of Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus (RSV) nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens obtained from symptomatic patients. This test is intended for use to aid in the differential diagnosis of Influenza A, Influenza B and RSV viral infections in humans and is not intended to detect Influenza C. Negative results do not preclude influenza or RSV virus infection and should not be used as the sole basis for treatment or other 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. Performance characteristics for Influenza **A** Virus were established when Influenza A/H3 and A/H1 were the predominant

Characteristic	Device	Predicate
	vary. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	Influenza A viruses in circulation (2006 - 2007 respiratory season). Performance characteristics for Influenza A were confirmed when Influenza A/Hl, Influenza A/H3, and Influenza A/2009 H1N1 were the predominant Influenza A viruses in circulation (2008 and 2009). When other Influenza A viruses are emerging, performance characteristics may vary. If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL **3+** facility is available to receive and culture specimens.
Specimen Type	Nasopharyngeal swab	Nasopharyngeal swab
Assay Targets	Influenza A, Influenza B	Influenza A, Influenza B, RSV
Amplification and Detection Technology	Multiplex real-time PCR	Multiplex real-time PCR
Assay Controls	Influenza A Control, Influenza B Control, Influenza A/B Internal Control, each prepared from *in vitro* transcripts.	Influenza A RNA Control, Influenza B RNA Control, RSV A RNA Control, RSV B RNA Control and Internal RNA Control, each prepared from *in vitro* transcripts.
Influenza A Virus Target	Matrix gene	Matrix gene
Differences		
Influenza B Virus Target	Matrix	Non-structural NS1 and NS2

Characteristic	Device	Predicate
Nucleic Acid Extraction	Automated extraction using the EZ1 DSP Virus Kit with the EZ1 Advanced XL instrument	Automated extraction using the Roche MagNA Pure LC System with the MagNA Pure Total Nucleic Acid Isolation Kit or the bioMerieux NucliSENS easyMAG System with the Automated Magnetic Extraction Reagents.
Amplification and Detection Instrument System	Rotor-Gene® Q MDx	Cepheid SmartCycler® II

Clinical Studies

Prospective clinical evaluation

The performance of the *artus* Infl A/B RG RT-PCR test was established during a prospective study at 3 clinical laboratories in the United States during the 2010–11 respiratory virus season. Nasopharyngeal (NP) swab specimens were collected for routine influenza testing by each site. In this prospective study the reference method was standard viral culture (shell vial) followed by direct fluorescent antibody (DFA) screening and identification. Demographic details for this patient population are summarized in Table .

Table 5.3 General Demographic Data for Prospectively Collected Specimens

Sex	Number of Subjects
Male	138 (54%)
Female	116 (46%)
Age (years)	
<5	90 (35.4%)
≥5 and ≤21	106 (41.7%)
≥22 and ≤59	51 (20.1%)
≥60	7 (2.8%)

A total of 254 NP swab specimens were evaluated. Of these, 60 specimens were positive by viral culture for influenza: 15 were positive for influenza A and 45 were positive for influenza B. The *artus* Infl A/B RG RT-PCR test identified all 15 influenza A specimens as positive for influenza A and all 45 influenza B specimens as positive for influenza B. There were no dual specimens identified by either the *artus* Infl A/B RG RT-PCR test or the reference test in the prospective study.

Table 5.4 Influenza A results from prospective clinical evaluation

		Reference method		
		+	–	Total
***artus* Infl A/B RG**	+	15	12[a]	27
RT-PCR test	–	0	227	227
Total		15	239	254
Sensitivity = 100% (95% confidence interval: 80–100%)				
Specificity = 95.0% (95% confidence interval: 91–97%)				

[a] The *artus* Infl A/B RG RT-PCR test also identified an additional 12 culture-negative specimens as positive for influenza A. Ten of these 12 specimens were confirmed by bidirectional sequencing

Table 5.5 Influenza B results from prospective clinical evaluation

		Reference method		
		+	–	Total
***artus* Infl A/B RG**	+	45	11[a]	56
RT-PCR test	–	0	198	198
Total		45	209	254
Sensitivity = 100% (95% confidence interval: 92–100%)				
Specificity = 94.7% (95% confidence interval: 91–97%)				

[a] An additional 11 culture-negative specimens were identified as positive for influenza B. Six of these 11 specimens could not be confirmed by bidirectional sequencing. However, 3 of these specimens were positive in a validated, independent, real-time PCR reference test for influenza B.

Retrospective clinical evaluation

A retrospective analyses was conducted. A total of 212 specimens from the 2009 and 2010 respiratory virus season were tested at 3 sites. After testing with the *artus* Infl A/B RG RT-PCR test, aliquots of all specimens were sent to a central reference laboratory for reference testing using an FDA cleared molecular test.

A total of 208 specimens were positive for influenza by the reference test: 175 were positive for influenza A and 33 were positive for influenza B. The *artus* Infl A/B RG RT-PCR test identified all 175 influenza A specimens as positive for influenza A and all 33 influenza B specimens as positive for influenza B.

Table 5.6 Influenza A results from retrospective clinical evaluation 1

		Reference method		
		+	–	Total
***artus* Infl A/B RG RT-PCR test**	+	175	2[a]	177
	–	0	35	35
Total		175	37	212
Positive agreement = 100% (95% confidence interval: 98–100%)				
Negative agreement = 94.6% (95% confidence interval: 82–99%)				

[a] The *artus* Infl A/B RG RT-PCR test also identified an additional 2 specimens as positive for influenza A that were called negative or "No Call" by the molecular test.

Table 5.7 Influenza B results from retrospective clinical evaluation 1

		Reference method		
		+	–	Total
***artus* Infl A/B RG RT-PCR test**	+	33	2[a]	35
	–	0	177	177
Total		33	179	212
Positive agreement = 100% (95% confidence interval: 90–100%)				
Negative agreement = 98.9% (95% confidence interval: 96–100%)				

[a] An additional 2 specimens were identified as positive for influenza B that were called negative by the molecular test .

Prospectively collected and archived clinical evaluation

A total of 462 well-characterized, de-identified, residual specimens were collected from August 2009 to May 2011 respiratory virus season. All specimens had been previously tested with FDA cleared molecular tests for routine patient management. These clinical results were used as the reference method. Demographic details for this patient population are summarized in Table 5.8

Table 5.8 General Demographic Data for Archived Specimens

Sex	Number of Subjects
Male	190 (41%)
Female	272 (59%)
Age (years)	
<5	7 (1.5%)
≥5 and ≤21	43 (9.3%)
≥22 and ≤59	327 (70.8%)
≥60	85 (18.4%)

A total of 110 specimens were positive for influenza by the reference method: 96 were positive for influenza A and 14 were positive for influenza B. The *artus* Infl A/B RG RT-

PCR test identified 94 of the 96 influenza A specimens as positive for influenza A and all 14 influenza B specimens as positive for influenza B.

Table 5.9 Influenza A results from retrospective clinical evaluation 2

		Reference method		
		+	–	Total
***artus* Infl A/B RG RT-PCR test**	+	94	19[a]	113
	–	2	347	349
Total		96	366	462
Positive agreement = 97.9% (95% confidence interval: 93–99%)				
Negative agreement = 94.8% (95% confidence interval: 92–97%)				

[a] The *artus* Infl A/B RG RT-PCR test also identified an additional 19 specimens as positive for influenza A that were reported as negative during routine clinical testing.

Table 5.10 Influenza B results from retrospective clinical evaluation 2

		Reference method		
		+	–	Total
***artus* Infl A/B RG RT-PCR test**	+	14	2[a]	16
	–	0	446	446
Total		14	448	462
Positive agreement = 100% (95% confidence interval: 79–100%)				
Negative agreement = 99.6% (95% confidence interval: 98–100%)				

[a] An additional 2 specimens were identified as positive for influenza B that were called negative during routine clinical testing.

Non-clinical Studies

Reproducibility

The reproducibility of the *artus* Infl A/B RG RT-PCR test was evaluated using 3 investigational sites. A panel of 10 simulated specimens was provided for testing. Five of the specimens contained influenza A and the other 5 specimens contained influenza B. Each half of the panel included duplicate low-positive specimens at approximately 2 times the limit of detection (Low Pos #1 and #2), duplicate moderately positive specimens at approximately 10 times the limit of detection (Mod Pos #1 and #2), and one specimen well below the limit of detection for each analyte (Neg). The 10-member panel plus 3 controls were tested by 2 different technologists each day for 6 days. Therefore, 10 samples plus 3 controls, times 2 technologists, for 6 days, at 3 sites equals 468. The overall percent agreement for the *artus* Infl A/B RG RT-PCR test was 99.4% (Table 5. , Table 5., Table 5. , Table 5.).

Table 5. 11 Reproducibility – site 1

Panel member	Agreement with expected result	Average C_T	CV%
Influenza A Neg	12/12	29.54	2.2
Influenza A Low Pos #1	12/12	31.38	0.9
Influenza A Low Pos #2	12/12	31.47	1.5
Influenza A Mod Pos #1	12/12	29.20	0.9
Influenza A Mod Pos #2	12/12	29.17	1.2
Influenza B Neg	12/12	29.55	2.2
Influenza B Low Pos #1	12/12	30.35	1.2
Influenza B Low Pos #2	12/12	30.42	1.1
Influenza B Mod Pos #1	12/12	28.21	1.1
Influenza B Mod Pos #2	12/12	28.27	1.1
Influenza A Control	12/12	34.35	2.2
Influenza B Control	12/12	30.85	1.9
Negative control	12/12	27.19	1.4

Table 5.3 Reproducibility – site 2

Panel member	Agreement with expected result	Average C_T	CV%
Influenza A Neg	11/12	29.89	2.5
Influenza A Low Pos #1	12/12	31.24	1.5
Influenza A Low Pos #2	12/12	31.35	1.2
Influenza A Mod Pos #1	12/12	29.17	1.4
Influenza A Mod Pos #2	12/12	29.16	1.4
Influenza B Neg	12/12	29.77	2.5
Influenza B Low Pos #1	12/12	30.39	1.2
Influenza B Low Pos #2	12/12	30.31	1.1
Influenza B Mod Pos #1	12/12	28.29	1.0
Influenza B Mod Pos #2	12/12	28.28	1.1
Influenza A Control	12/12	33.83	0.9
Influenza B Control	12/12	31.06	2.1
Negative control	12/12	27.48	2.1

Table 5. 4 Reproducibility – site 3

Panel member	Agreement with expected result	Average C_T	CV%
Influenza A Neg	10/12	29.89	1.7
Influenza A Low Pos #1	12/12	31.45	0.8
Influenza A Low Pos #2	12/12	31.35	0.6
Influenza A Mod Pos #1	12/12	29.26	1.1
Influenza A Mod Pos #2	12/12	29.45	2.4
Influenza B Neg	12/12	30.02	1.4
Influenza B Low Pos #1	12/12	30.54	1.3
Influenza B Low Pos #2	12/12	30.52	1.3
Influenza B Mod Pos #1	12/12	28.46	1.8
Influenza B Mod Pos #2	12/12	28.40	1.3
Influenza A Control	12/12	34.58	2.6
Influenza B Control	12/12	31.53	2.4
Negative control	12/12	27.61	1.4

Table 5.5 Reproducibility – combined (sites 1 – 3)

Panel member	Agreement with expected result	Average C_T	CV%	95% confidence interval
Influenza A Neg	33/36	29.76	2.2	78–97%
Influenza A Low Pos #1	72/72	31.37	1.1	95–100%
Influenza A Mod Pos #1	72/72	29.23	1.5	95–100%
Influenza B Neg	36/36	29.78	2.1	90–100%
Influenza B Low Pos #1	72/72	30.42	1.2	95–100%
Influenza B Mod Pos #1	72/72	28.32	1.2	95–100%
Influenza A Control	36/36	34.25	2.2	90–100%
Influenza B Control	36/36	31.14	2.3	90–100%
Negative control	36/36	27.42	1.8	90–100%

Limit of Detection (LoD)

The limit of detection (LoD) of the *artus* Infl A/B RG RT-PCR Kit was determined and confirmed for six influenza A strains (two strains representing each of the influenza A subtypes of H1N1, H3N2, and 2009 H1N1) and two influenza B strains. Samples were prepared from cultured virus diluted in nasopharyngeal clinical matrix. The LoD of each strain was initially determined by limiting dilution testing of three replicates per dilution level. The result was confirmed by testing an additional 20 replicates at the LoD concentration. The LoD, defined as the level of virus that yields at least a 95% (19/20) detection rate with the *artus* Infl A/B RG RT-PCR Kit, ranged from 10e1.1 to 10e-0.1 $TCID_{50}$/ml (Table 5.).

Table 5.6 Limit of detection

Influenza strain	LoD concentration ($TCID_{50}$/ml*)
A/New Caledonia/20/1999 (H1N1)	10e0.5
A/Brisbane59/2007-like virus (H1N1)	10e1.1
A/Hong Kong/8/68 (TC-adapted) (H3N2)	10e0.2
A/Wisconsin/67/2005 (H3N2)	10e0.4
A/California/7/09-like virus (2009 H1N1)	10e0.9
A/Hamburg/05/09 (2009 H1N1)	10e0.4
B/Brisbane/60/2008-like virus	10e-0.1
B/Florida/4/2006-like virus	10e0.9

* Based on re-titered virus stock concentrations.

Reactivity

The analytical reactivity of the *artus* Infl A/B RG RT-PCR Kit was demonstrated by testing 18 strains of influenza A (including four strains originally identified in non-human species) and six strains of influenza B at concentrations near the limit of detection (LoD) of the test. Samples were prepared from cultured virus diluted in nasopharyngeal clinical matrix. Each viral strain was extracted and tested in triplicate. A "+" results indicates the concentration was detected positive in three of three replicates; a "–" result indicates a negative response in each of the replicates (Table 5.).

Table 5.7 Analytical reactivity

Influenza strain	Concentration	Influenza A	Influenza B
A/Virginia/ATCC2/2009 (2009 H1N1)	1 x 10^2 $TCID_{50}$/ml	+	–
A/PR/8/34 (H1N1)	1 x 10^1 $TCID_{50}$/ml	+	–
A/FM/1/47 (H1N1)	1 x 10^1 $CEID_{50}$/ml	+	–
A/Solomon Islands/3/2006 like virus (H1N1)	1 x 10^1 $TCID_{50}$/ml	+	–
A/Mal/302/54 (H1N1)	1 x 10^1 $CEID_{50}$/ml	+	–
A/New Jersey/8/76 (H1N1)	1 x 10^1 $CEID_{50}$/ml	+	–
A/NWS/33 (H1N1)	1 x 10^2 $CEID_{50}$/ml	+	–
A1/Denver/1/57 (H1N1)	1 x 10^3 $CEID_{50}$/ml	+	–
A/Weiss/43 (H1N1)	1 x 10^4 $CEID_{50}$/ml	+	–
A/Victoria x187 (H3N2)	1 x 10^1 $TCID_{50}$/ml	+	–
A2/Aichi2/68 (H3N2)	1 x 10^1 $CEID_{50}$/ml	+	–

Influenza strain	Concentration	Influenza A	Influenza B
A/Victoria/3/75 (H3N2)	1 x 10^1 $CEID_{50}$/ml	+	–
A/Alice (H3N2)	1 x 10^2 EID_{50}/ml	+	–
A/MRC2 (H3N2)	1 x 10^2 $CEID_{50}$/ml	+	–
A/Turkey/Germany 176/95 - like (H9N2)	1 x 10^0 $TCID_{50}$/ml	+	–
A/Duck/Potsdam 2243/84-like (H5N6)	1 x 10^0 $TCID_{50}$/ml	+	–
A/Swine/Iowa/15/30 (H1N1)	1 x 10^2 $CEID_{50}$/ml	+	–
A/Equine/2/Miami/63-like (H3N8)	1 x 10^4 $CEID_{50}$/ml	+	–
B/Lee/40	1 x 10^1 $TCID_{50}$/ml	–	+
B/Allen/45	1 x 10^1 $CEID_{50}$/ml	–	+
B/Taiwan/2/62	1 x 10^1 $CEID_{50}$/ml	–	+
B/Hong Kong/5/72	1 x 10^1 $CEID_{50}$/ml	–	+
B/Maryland/1/59	1 x 10^1 $CEID_{50}$/ml	–	+
B/Malaysia/2506/2004	1 x 10^1 $TCID_{50}$/ml	–	+

Interfering Substances

The potential for blood or medications that might be present in a nasopharyngeal swab specimen to interfere with the detection of low levels of influenza A or influenza B by the *artus* Infl A/B RG RT-PCR test was evaluated. Human blood and substances representing the active ingredient in over-the-counter or prescription medications were tested. Each potentially interfering substance was evaluated in triplicate with each of two reference influenza strains, one influenza A strain and one influenza B strain. The reference influenza strains were successfully detected in all samples except for one aliquot containing the reference influenza B strain and Mupirocin at 10 mg/ml. The reference influenza B strain was successfully detected in three of three aliquots with Mupirocin at 2 mg/ml. (Mupirocin is an antibiotic ointment used to treat skin infections. The product tested contains Mupirocin at 20mg/g.). Substances tested are shown in Table 5..

Table 5.8 Potentially interfering substances

Source	Description / Active Ingredient	Concentration
Blood (human)	Blood (human)†	5% v/v
Visadron	Phenylephrine	10% v/v (125 µg/ml)

Source	Description / Active Ingredient	Concentration
Beclomet Nasal Aqua (nasal spray)	Beclomethasone dipropionate	61.73 µg/ml
Luffa opperculata	Luffa opperculata	4.5 mg/ml
Galphimia glauca	Galphimia glauca	4.5 mg/ml
Menthol	Menthol	5 mg/ml
Relenza	Zanamivir	3 mg/ml
Infectopyoderm (ointment)	Mupirocin	10 mg/ml, 2mg/ml
Tobramaxin	Tobramycin	0.3 mg/ml

† The human blood sample was stored frozen before testing.

Analytical Specificity

The analytical specificity of the *artus* Infl A/B RG RT-PCR Kit was evaluated by testing a panel of respiratory pathogens consisting of 21 non-target respiratory viruses and 18 bacterial strains. The pathogens were tested at medically relevant levels. Samples were prepared by diluting the cultured virus or bacteria in Universal Transport Medium. Each strain was extracted once and tested in triplicate. There were no false positive or invalid results among the 21 non-target respiratory viruses tested. Of the 18 bacterial strains evaluated, 16 were negative for influenza A and influenza B; two strains, *Bordetella pertussis* (at 10^3 cfu/ml) and *Streptococcus pneumoniae* (at 2 x 10^5 cfu/ml), were invalid in three of three replicates. Each strain was prepared at a one-log lower concentration, extracted once, and tested in triplicate. At the lower concentration each strain generated valid negative results for influenza A and influenza B in three of three replicates (Table 5.).

Table 5.9 Analytical specificity

Strain	Concentration	Influenza A	Influenza B
RSVA VR-26	10e5.0 $TCID_{50}$/ml	–	–
RSVB VR-1400	10e4.45 $TCID_{50}$/ml	–	–
PIV1 VR-94	10e3.45 $TCID_{50}$/ml	–	–
PIV2 VR-92	10e5.0 $TCID_{50}$/ml	–	–
PIV3 VR-93	10e5.0 $TCID_{50}$/ml	–	–
PIV4a VR-1378	10e3.95 $TCID_{50}$/ml	–	–
ADVE 4 VR-1572	10e5.0 $TCID_{50}$/ml	–	–

Strain	Concentration	Influenza A	Influenza B
ADVB 3 VR-3	10e5.0 $TCID_{50}$/ml	–	–
ADVC 5 VR-5	10e5.0 $TCID_{50}$/ml	–	–
Echovirus 11 VR-41	10e5.0 $TCID_{50}$/ml	–	–
Rhinovirus 1a VR-1559	10e5.0 $TCID_{50}$/ml	–	–
Rhinovirus 39 VR-340	10e5.0 $TCID_{50}$/ml	–	–
Coxsackie B1 VR-28	10e5.0 $TCID_{50}$/ml	–	–
229E VR-740	10e4.2 $TCID_{50}$/ml	–	–
OC43 VR-1558	10e4.45 $TCID_{50}$/ml	–	–
CMV VR-538	10e4.95 $TCID_{50}$/ml	–	–
HSV VR-260	10e5.0 $TCID_{50}$/ml	–	–
Varicella-zoster virus VR-1367	10e3.95 $TCID_{50}$/ml	–	–
EBV VR-603	10e3.0 cfu/ml	–	–
Measels VR-24	10e3.2 $TCID_{50}$/ml	–	–
Mumps virus VR-106	10e5.0 $TCID_{50}$/ml	–	–
Bordetella pertussis	10e3.0 cfu/ml	Invalid*	Invalid*
Bordetella pertussis	10e2.0 cfu/ml	–	–
Chlamydophila pneumoniae	10e5.0 $TCID_{50}$/ml	–	–
Corynebacterium sp.	10e3.0 cfu/ml	–	–
Escherichia coli	10e6.0 cfu/ml	–	–
Hemophilus influenzae	10e6.0 cfu/ml	–	–
Lactobacillus sp.	10e3.0 cfu/ml	–	–
Legionella spp.	9 x 10e5.0 bacteria/ml	–	–
Moraxella catarrhalis	10e3.0 cfu/ml	–	–
Mycobacterium tuberculosis avirulent	10e2.0 cfu/ml	–	–
Mycoplasma pneumoniae	10e3.0 cfu/ml	–	–
Neisseria ssp. #14685	10e2.0 cfu/ml	–	–

Strain	Concentration	Influenza A	Influenza B
Neisseria meningitis	10e6.0 bacteria/ml	–	–
Pseudomonas aeruginosa	10e6.0 cfu/ml	–	–
Staphylococcus aureus Protein A producer	10e6.0 bacteria/ml	–	–
Staphylococcus epidermidis	10e6.0 bacteria/ml	–	–
Streptococcus pneumoniae	2 x 10e5.0 cfu/ml	Invalid*	Invalid*
Streptococcus pneumoniae	2 x 10e4 cfu/ml	–	–
Streptococcus pyogenes	10e3.0 cfu/ml	–	–
Streptococcus salivarius	10e6.0 cfu/ml	–	–

* Samples were invalid because influenza A and influenza B results were negative and the C_T of the IC was outside of the acceptance range for specimen validity. A second concentration was tested successfully and is presented below the "invalid" sample.

Competitive Inhibition

Competitive inhibition of the *artus* Infl A/B RG RT-PCR test was evaluated by testing samples containing reference strains A/California/7/09-like virus or B/Florida/4/2006-like virus at the limit of detection (LoD) concentration of 10e1 $TCID_{50}$/ml. Samples containing the influenza A reference strain also contained high levels of one of three competing influenza B strains while samples containing the influenza B reference strain also contained high levels of one of seven competing influenza A strains. Samples were extracted once and tested in triplicate with the *artus* Infl A/B RG RT-PCR Kit.
Detection of the reference influenza A strain was inhibited when the competing influenza B strains B/Florida/4/2006-like virus or B/Brisbane/60/2008-like virus was present at 10e5 $TCID_{50}$/ml; no inhibition was observed when the same competing virus strains were present at 10e4 $TCID_{50}$/ml. No inhibition was observed with the competing influenza B strain B/Malaysia/2506/2004. The reference influenza B strain was successfully detected in the presence of each of the seven competing Influenza A strains present at 10e5 $TCID_{50}$/ml (Table 5.).

Table 5.10 Competitive inhibition

Competing virus strain	Concentration ($TCID_{50}$/ml)	Positive replicates/total replicates	
		Influenza A reference strain	Influenza B reference strain
A/California/7/09-like virus	10e5	n/a*	3/3
A/Hong Kong/8/68 (TC adapted)	10e5	n/a	3/3
A/PR/8/34	10e5	n/a	3/3
A2/Wisconsin/67/2005	10e5	n/a	3/3
A/Solomon Islands/3/2006 (H1N1)-like virus	10e5	n/a	3/3
A/Duck/Potsdam 2243/84	10e5	n/a	3/3
A/Brisbane/59/2007 (H1N1)-like virus	10e5	n/a	3/3
B/Florida/4/2006-like virus	10e5	1/3	n/a
B/Florida/4/2006-like virus	10e4	3/3	n/a
B/Brisbane/60/2008-like virus	10e5	2/3	n/a
B/Brisbane/60/2008-like virus	10e4	3/3	n/a
B/Malaysia/2506/2004	10e5	3/3	n/a

Carryover / Cross Contamination

The *artus* Infl A/B RG RT-PCR test (including extraction using the EZ1 DSP Virus Kit with the EZ1 Advanced XL) showed no evidence of carryover or cross-contamination when 5 runs of a panel of 6 members of mock samples containing influenza A at a concentration just below the limit of detection of the assay were extracted and tested in alternating order with a panel of 6 members of mock samples of the same strain present at a high concentration.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

FEB - 6 2012

Qiagen GmbH
c/o Hina Patel
Associate Director, Regulatory and Clinical Affairs
1201 Clopper Road
Gaithersburg, MD 20878

Re: k113323
Trade/Device Name: *artus*® Infl A/B RG RT-PCR Kit
Regulation Number: 21 CFR§ 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC, OOI, JJH
Dated: October 24, 2011
Received: November 10, 2011

Dear Ms. Patel:

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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket

notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k113323

Device Name: *artus*® Infl A/B RG RT-PCR Kit

Indications for Use:

The *artus*® Infl A/B RG RT-PCR Kit is a multiplex real time PCR *in vitro* diagnostic test for the qualitative detection and identification of Influenza A and Influenza B virus RNA in nasopharyngeal swab specimens using the Rotor-Gene® Q MDx instrument. The test is intended for use as an aid in the differential diagnosis of Influenza A and Influenza B viral infections in patients symptomatic for respiratory tract infection in conjunction with clinical and epidemiological risk factors. It is not intended to detect Influenza C virus.

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

Performance characteristics for Influenza A were established during the 2009/2010 and 2010/2011 flu seasons when Influenza A (H3N2) and Influenza A/2009 (H1N1) were the predominant Influenza A viruses in circulation. When other Influenza A viruses emerge, performance characteristics may vary.

If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Prescription Use ☒ (21 CFR 801 Subpart D) And/Or Over-The-Counter Use ☐ (21 CFR 807 Subpart C)

(Do Not Write Below This Line – Continue on Another Page if Needed)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Tamara V. Feldblyum

Division Sign-Off
Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K113323

10/24/2011