DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Centers for Disease Control and Prevention
Yon Yu, Pharm. D.
Associate Director for Regulatory Affairs
Office of the Director
National Center for Emerging and Zoonotic Infectious Diseases
1600 Clifton Road, MS E-51
Atlanta, GA 30329-4027

August 9, 2017

Re: K172091
Trade/Device Names: CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/B Typing Kit, Influenza A Subtyping Kit (VER 2), Influenza B Lineage Genotyping Kit, and Influenza A/H5 Subtyping Kit (VER 3)
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: Class II
Product Code: OZE, OEP, NXD, OQW, NSU, OOI
Dated: July 10, 2017
Received: July 12, 2017

Dear Dr. Yu:

We have reviewed your Section 510(k) premarket notification of intent to market the devices referenced above and have determined the devices are 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 devices, 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 devices are classified (see above) into either class II (Special Controls) or class III (PMA), they may be subject to additional controls. Existing major regulations affecting your devices can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your devices 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 devices comply 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 devices on our labeling regulation (21 CFR Part 801), 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" (21CFR 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,

Uwe Scherf -S

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

Enclosure

Indications for Use

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

510(k) Number *(if known)*
K172091

Device Name
CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/B Typing Kit, Influenza A Subtyping Kit (VER 2), Influenza B Lineage Genotyping Kit, and Influenza A/H5 Subtyping Kit (VER 3)

Indications for Use *(Describe)*

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/B Typing Kit:

The Influenza A/B Typing Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this

device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A Subtyping Kit (VER 2):

The Influenza A Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For determination of the subtype of seasonal human influenza A viruses as seasonal A(H3), and/or A(H1)pdm09 from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza B Lineage Genotyping Kit:

The Influenza B Lineage Genotyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For the determination of the genetic lineage of human influenza B viruses as B/Victoria or B/Yamagata lineage from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza B lineage genotyping were established during a season when influenza B/Victoria and B/Yamagata lineages were found in approximately equal proportion.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/H5 Subtyping Kit (VER 3):

The Influenza A/H5 Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For the presumptive identification of virus in patients who may be infected with influenza A subtype A(H5) (Asian lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Testing with the influenza H5a and H5b primer and probe sets should not be performed unless the patient meets the most current U.S.Department of Health and Human Services (DHHS) clinical and epidemiologic criteria for testing suspect A(H5) specimens. The definitive identification of influenza A(H5) (Asian lineage) either directly from patient specimens or from virus cultures requires additional laboratory testing, along with clinical and epidemiological assessment in consultation with national influenza surveillance experts.

Negative results do not preclude influenza virus infection and should not be used as the sole basis

for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

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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8. 510(k) Summary

I. GENERAL INFORMATION

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Date Prepared: July 10, 2017

II. DEVICE INFORMATION

Proprietary Name:	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/B Typing Kit, Influenza A Subtyping Kit (VER 2), Influenza B Lineage Genotyping Kit, and Influenza A/H5 Subtyping Kit (VER 3)
Common Name:	Influenza A/B Typing Kit, Influenza A Subtyping Kit, Influenza B Lineage Genotyping Kit, and Influenza A/H5 Subtyping Kit
Regulation Section:	866.3980-Respiratory viral panel multiplex nucleic acid assay
Subsequent Regulation Sections:	866.3332-Reagents for detection of specific novel influenza A viruses 862.2570-Instrumentation for clinical multiplex systems
Device Classification:	Class II
Product Code:	OZE
Subsequent Product Codes:	NSU, OOI, NXD, OEP, OQW
Panel:	Microbiology

III. PREDICATE DEVICE

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/B Typing Kit (K133869), Influenza A Subtyping Kit (VER 2) (K161556), Influenza B Lineage Genotyping Kit (K140857), and Influenza A/H5 Subtyping Kit (VER 3) (K153148)

IV. DEVICE DESCRIPTION

The CDC Human Influenza Real-Time RT-PCR Diagnostic Panel is used in real-time RT-PCR (rRT-PCR) assays on the Applied Biosystems® (ABI) 7500 Fast Dx Real-time PCR system. The panel is configured in four separate kits. Each kit consists of oligonucleotide primers, fluorescently labeled hydrolysis probes, and controls which are used in rRT-PCR assays for the *in vitro* qualitative detection and characterization of influenza virus RNA in respiratory specimens from patients presenting with influenza-like illness (ILI). Oligonucleotide primers and probes for detection of influenza A, influenza B, and 2009 influenza A (swine origin) were selected from highly conserved regions of the matrix (M), non-structural (NS), and nucleoprotein (NP) genes, respectively. Oligonucleotide primers and probes for characterization and differentiation of influenza A(H3) and A(H1)pdm09 viruses and genetic lineages of influenza B were selected from highly conserved regions of their HA genes. Oligonucleotide primers and probes to detect the human RNase P gene (RP) in control samples and clinical specimens is also included in the panel.

V. INTENDED USE

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/B Typing Kit:

The Influenza A/B Typing Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A Subtyping Kit (VER 2):

The Influenza A Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For determination of the subtype of seasonal human influenza A viruses as seasonal A(H3), and/or A(H1)pdm09 from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza B Lineage Genotyping Kit:

The Influenza B Lineage Genotyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For the determination of the genetic lineage of human influenza B viruses as B/Victoria or B/Yamagata lineage from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) from human patients with signs and symptoms of respiratory infection and/or from viral culture;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza B lineage genotyping were established during a season when influenza B/Victoria and B/Yamagata lineages were found in approximately equal proportion.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel - Influenza A/H5 Subtyping Kit (VER 3):

The Influenza A/H5 Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information:

- For the presumptive identification of virus in patients who may be infected with influenza A subtype A(H5) (Asian lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors;
- To provide epidemiologic information for surveillance of circulating influenza viruses.

Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses.

Testing with the influenza H5a and H5b primer and probe sets should not be performed unless the patient meets the most current U.S. Department of Health and Human Services (DHHS) clinical and epidemiologic criteria for testing suspect A(H5) specimens. The definitive identification of influenza A(H5) (Asian lineage) either directly from patient specimens or from virus cultures requires additional laboratory testing, along with clinical and epidemiological assessment in consultation with national influenza surveillance experts.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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.

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 unless a BSL 3E facility is available to receive and culture specimens.

All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.

VI. TECHNOLOGICAL CHARACTERISTICS

The technological characteristics of the modified CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel- Influenza A/B Typing Kit, Influenza A Subtyping Kit, Influenza B Lineage Genotyping Kit, and Influenza A/H5 Subtyping Kit remain the same as their respective predicate device. Additional options for viral RNA isolation are added to the CDC device to allow use of more recently available commercial nucleic acid isolation platforms and their accompanying chemistries.

VII. SUBSTANTIAL EQUIVALENCE COMPARISON

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza A/B Typing Kit (K133869), Influenza A Subtyping Kit (VER 2) (K161556), Influenza B Lineage Genotyping Kit (K140857), and Influenza A/H5 Subtyping Kit (VER 3) (K153148) will serve as the predicates for the proposed change to each of the bundled devices. See tables 8-1 through 8-4 below for a detailed comparison of each device to the corresponding predicate.

Table 8-1: Device Comparison

	Predicate Device	Proposed Device
Item	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A/B Typing Kit [K133869]**	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A/B Typing Kit**
Intended Use	The Influenza A/B Typing Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information: ▪ For qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture; ▪ To provide epidemiologic information for surveillance of circulating influenza viruses. Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses. Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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. 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 unless a BSL 3E facility is available to receive and culture specimens. All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.	Same
Organism Detected	Influenza A viruses (animal and human), influenza B viruses	Same

Specimen Types	Nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs, bronchoalveolar lavages, bronchial aspirates, bronchial washes, tracheal aspirates, sputum, and lung tissue from human patients with signs and symptoms of respiratory infection and/or from viral culture	Same
Technological Characteristics	Real-time RT-PCR based assay	Same
Nucleic Acid Extraction	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux • EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN • MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche
Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kit (with or without ROX) **OR** Quanta BioSciences qScript™ One-Step qRT-PCR Kit, Low ROX	Same
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software version 1.4	Same

Table 8-2: Device Comparison

	Predicate Device	**Proposed Device**
Item	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A Subtyping Kit (VER 2) [K161556]**	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A Subtyping Kit (VER 2)**
Intended Use	The Influenza A Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information: • For determination of the subtype of seasonal human influenza A viruses as seasonal A(H3), and/or A(H1)pdm09 from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) and lower respiratory tract specimens (including bronchoalveolar lavage [BAL], bronchial wash [BW], tracheal aspirate [TA], sputum, and lung tissue) from human patients with signs and symptoms of respiratory infection and/or from viral culture; • To provide epidemiologic information for surveillance of circulating influenza viruses. Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the	Same

	predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses. Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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. 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 unless a BSL 3E facility is available to receive and culture specimens. All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.	
Organism Detected	Influenza A viruses (animal and human), Swine-origin influenza A viruses, Influenza A subtypes: seasonal A(H3), A(H1)pdm09	Same
Specimen Types	Nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs, bronchoalveolar lavages, bronchial aspirates, bronchial washes, tracheal aspirates, sputum, and lung tissue from human patients with signs and symptoms of respiratory infection and/or from viral culture	Same
Technological Characteristics	Real-time RT-PCR based assay	Same
Nucleic Acid Extraction	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux • EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN • MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche
Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kit (with or without ROX) **OR** Quanta BioSciences qScript™ One-Step qRT-PCR Kit, Low ROX	Same
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software version 1.4	Same

Table 8-3: Device Comparison

	Predicate Device	**Proposed Device**
Item	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza B Lineage Genotyping Kit [K140857]**	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza B Lineage Genotyping Kit**
Intended Use	The Influenza B Lineage Genotyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information: • For the determination of the genetic lineage of human influenza B viruses as B/Victoria or B/Yamagata lineage from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) from human patients with signs and symptoms of respiratory infection and/or from viral culture; • To provide epidemiologic information for surveillance of circulating influenza viruses. Performance characteristics for influenza B lineage genbotyping were established during a season when influenza B/Victoria and B/Yamagata lineages were found in approximately equal proportion. Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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. All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.	Same
Organism Detected	Influenza B virus, lineages B/Victoria and B/Yamagata	Same
Specimen Types	Nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs from human patients with signs and symptoms of respiratory infection and/or from viral culture	Same
Technological Characteristics	Real-time RT-PCR based assay	Same
Nucleic Acid Extraction	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux • EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN • MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche

Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kit (with or without ROX) **OR** Quanta BioSciences qScript™ One-Step qRT-PCR Kit, Low ROX	Same
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software version 1.4	Same

Table 8-4: Device Comparison

	Predicate Device	**Proposed Device**
Item	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A/H5 Subtyping Kit (VER 3) [K153148]**	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Diagnostic Panel, Influenza A/H5 Subtyping Kit (VER 3)**
Intended Use	The Influenza A/H5 Subtyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information: • For the presumptive identification of virus in patients who may be infected with influenza A subtype A(H5) (Asian lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors; • To provide epidemiologic information for surveillance of circulating influenza viruses. Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and A(H3N2) were the predominant influenza A viruses in circulation and during a season when the A(H1N1)pdm09 influenza virus was the predominant influenza A virus in circulation. Performance characteristics may vary with other emerging influenza A viruses. Testing with the influenza H5a and H5b primer and probe sets should not be performed unless the patient meets the most current U.S. Department of Health and Human Services (DHHS) clinical and epidemiologic criteria for testing suspect A(H5) specimens. The definitive identification of influenza A(H5) (Asian lineage) either directly from patient specimens or from virus cultures requires additional laboratory testing, along with clinical and epidemiological assessment in consultation with national influenza surveillance experts. Negative results do not preclude influenza virus infection and should not be used as the sole basis for 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. 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	Same

	virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted unless a BSL 3E facility is available to receive and culture specimens. All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.	
Organism Detected	Influenza A viruses (animal and human), Influenza A subtype A(H5) (Asian lineage)	Same
Specimen Types	Human respiratory specimens and viral culture	Same
Technological Characteristics	Real-time RT-PCR based assay	Same
Nucleic Acid Extraction	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMerieux • EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN • MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche
Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kit (with or without ROX) **OR** Quanta BioSciences qScript™ One-Step qRT-PCR Kit, Low ROX	Same
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software version 1.4	Same

VIII. ANALYTICAL PERFORMANCE EVALUATION

Analytical Sensitivity - Limit of Detection (LOD**)** Equivalency Study

The LOD performance equivalency between a cleared extraction method and either the Roche MagNA Pure 96 or the QIAGEN EZ1 Advanced XL instruments was demonstrated by testing 5-fold serial dilutions of a characterized influenza A(H3N2) virus, A/Hong Kong/4801/2014, of known infectious dose 50% titer. Virus dilutions were prepared using a suspension of beta-propiolactone (BPL) treated A549 cells in viral transport medium (VTM) as diluent. Triplicate samples of each dilution were extracted separately with the cleared Roche MagNA Pure Compact RNA Isolation Kit as well as the investigational instrument and method. The Roche MagNA Pure 96 was evaluated with the Roche DNA and Viral NA Small Volume Kit. The QIAGEN EZ1 Advanced XL was evaluated with the QIAGEN DSP Virus Kit and the QIAGEN RNA Tissue Mini Kit. Extracted RNA was tested with the InfA and H3 assays from the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel using Invitrogen SuperScript™ III Platinum® One-Step RT-PCR System (Invitrogen SuperScript™) and utilizing the Applied Biosystems 7500 Fast Dx (ABI 7500 Fast Dx) real-time PCR system. The acceptance criteria for LOD equivalence between the cleared and investigational methods was defined as a demonstration of 100% positivity (3 out of 3 replicates) at either the same endpoint concentration or within one 5-fold dilution. The results of the study are summarized in Tables 8-5 to 8-7. Each investigational instrument and method showed an equivalent endpoint concentration when compared to the cleared instrument and method.

Table 8-5. LOD Equivalency Determination - Roche MagNA Pure 96/ DNA and Viral NA Small Volume Kit

Titer (EID_{50}/mL)[1]	Roche MagNA Pure Compact- RNA Isolation Kit		Roche MagNA Pure 96 - DNA and Viral NA Small Volume Kit	
	InfA	H3	InfA	H3
$10^{3.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.3}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{0.4}$	1/3 (+)	0/3 (+)	2/3 (+)	2/3 (+)

[1]EID_{50} = Egg Infectious Dose 50%

Table 8-6. LOD Equivalency Determination – QIAGEN EZ1 Advanced XL/ DSP Virus Kit

Titer (EID_{50}/mL)	Roche MagNA Pure Compact- RNA Isolation Kit		QIAGEN EZ1 Advanced XL – DSP Virus Kit	
	InfA	H3	InfA	H3
$10^{3.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.3}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{0.4}$	1/3 (+)	0/3 (+)	1/3 (+)	0/3 (+)

Table 8-7. LOD Equivalency Determination – QIAGEN EZ1 Advanced XL/ RNA Tissue Mini Kit

Titer (EID_{50}/mL)	Roche MagNA Pure Compact- RNA Isolation Kit		QIAGEN EZ1 Advanced XL – RNA Tissue Mini Kit	
	InfA	H3	InfA	H3
$10^{3.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.3}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{0.4}$	1/3 (+)	0/3 (+)	2/3 (+)	2/3 (+)

Analytical Precision – Reproducibility

A study was performed to assess the reproducibility of the Roche MagNA Pure 96 and QIAGEN EZ1 Advanced XL instruments. The Roche MagNA Pure 96 was evaluated with the Roche DNA and Viral NA Small Volume Kit. The QIAGEN EZ1 Advanced XL was evaluated with the QIAGEN DSP Virus Kit and the QIAGEN RNA Tissue Mini Kit. A blinded panel of contrived samples containing a background of BPL treated A549 cells in VTM was assembled by adding a BPL treated influenza A(H3N2) virus, A/Hong Kong/4801/2014. The samples included a moderate positive sample, a low positive sample near the established assay LOD for the CDC Influenza A Subtyping Kit, and a negative sample consisting of background A549 cells and VTM. Three separate testing sites were selected for each extraction instrument platform. The sample panel was tested 5 times by two different analysts at each site over 5 different days. Analysts performed extractions with the investigational instrument and method and tested the extracted nucleic acids with the InfA, H3, and RP assays from the from the CDC Influenza A Subtyping Kit using Invitrogen SuperScript™ and utilizing the ABI 7500 Fast Dx real-time PCR system. The results for the reproducibility studies of each instrument and method are summarized in Tables 8-8 to 8-10. Each instrument and method showed good reproducibility with 100% agreement across different sites, analysts, and days.

Table 8-8. Reproducibility Summary -QIAGEN EZ1 Advanced XL, EZ1 DSP Virus Kit

Panel Sample	Primer / Probe Set	Site 1			Site 2			Site 3			Agreement Total	95%CI
		Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV		
A(H3) Moderate	InfA	10/10	25.46	2.36	10/10	26.45	2.80	10/10	28.46	4.12	30/30	100.0 (88.7-100.0)
	H3	10/10	27.15	2.92	10/10	28.22	3.25	10/10	28.61	4.40	30/30	100.0 (88.7-100.0)
	RP	10/10	22.45	1.44	10/10	23.47	2.42	10/10	24.50	5.68	30/30	100.0 (88.7-100.0)
A(H3) Low	InfA	10/10	28.96	3.41	10/10	30.35	1.87	10/10	32.21	2.55	30/30	100.0 (88.7-100.0)
	H3	10/10	30.56	2.60	10/10	31.70	1.96	10/10	32.63	3.18	30/30	100.0 (88.7-100.0)
	RP	10/10	22.26	1.08	10/10	23.53	1.12	10/10	24.58	4.63	30/30	100.0 (88.7-100.0)
Negative	InfA	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	H3	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	RP	10/10	24.80	1.49	10/10	25.35	3.91	10/10	26.93	4.83	30/30	100.0 (88.7-100.0)

n/a = not applicable

Table 8-9. Reproducibility Summary -QIAGEN EZ1 Advanced XL, EZ1 RNA Tissue Mini Kit

Panel Sample	Primer / Probe Set	Site 1			Site 2			Site 3			Agreement Total	95%CI
		Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV		
A(H3) Moderate	InfA	10/10	25.97	3.48	10/10	26.40	4.06	10/10	28.59	2.01	30/30	100.0 (88.7-100.0)
	H3	10/10	27.40	4.13	10/10	27.56	2.35	10/10	28.66	0.79	30/30	100.0 (88.7-100.0)
	RP	10/10	22.08	3.31	10/10	23.52	1.56	10/10	24.77	2.14	30/30	100.0 (88.7-100.0)
A(H3) Low	InfA	10/10	30.07	2.04	10/10	30.30	3.26	10/10	32.37	2.44	30/30	100.0 (88.7-100.0)
	H3	10/10	31.02	3.14	10/10	30.94	2.06	10/10	32.59	1.15	30/30	100.0 (88.7-100.0)
	RP	10/10	21.88	2.37	10/10	23.29	2.32	10/10	24.30	2.93	30/30	100.0 (88.7-100.0)
Negative	InfA	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	H3	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	RP	10/10	24.36	2.57	10/10	25.32	1.55	10/10	27.38	1.85	30/30	100.0 (88.7-100.0)

Table 8-10. Reproducibility Summary –Roche MagNA Pure 96, DNA and Viral NA Small Volume Kit

Panel Sample	Primer / Probe Set	Site 1			Site 2			Site 3			Agreement Total	95%CI
		Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV	Agreement	Ave. Ct	%CV		
A(H3) Moderate	InfA	10/10	31.29	3.97	10/10	30.05	3.37	10/10	27.61	3.93	30/30	100.0 (88.7-100.0)
	H3	10/10	32.00	3.36	10/10	31.92	3.32	10/10	28.44	4.05	30/30	100.0 (88.7-100.0)
	RP	10/10	27.16	4.07	10/10	24.25	1.66	10/10	23.35	3.48	30/30	100.0 (88.7-100.0)
A(H3) Low	InfA	10/10	34.91	2.97	10/10	33.49	2.86	10/10	31.40	3.07	30/30	100.0 (88.7-100.0)
	H3	10/10	35.45	2.54	10/10	35.35	2.75	10/10	32.37	3.30	30/30	100.0 (88.7-100.0)
	RP	10/10	26.97	3.85	10/10	24.22	0.98	10/10	23.11	2.70	30/30	100.0 (88.7-100.0)
Negative	InfA	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	H3	10/10	0.00	n/a	10/10	0.00	n/a	10/10	0.00	n/a	30/30	100.0 (88.7-100.0)
	RP	10/10	29.40	3.66	10/10	26.64	1.36	10/10	25.58	2.91	30/30	100.0 (88.7-100.0)

n/a = not applicable

IX. CLINICAL PERFORMANCE EVALUATION

The clinical performance of the Roche MagNA Pure 96 and QIAGEN EZ1 Advanced XL instruments was evaluated to demonstrate equivalency to a method currently cleared with the CDC Human Influenza Real-Time Diagnostic Panel. The Roche MagNA Pure 96 was evaluated using the Roche DNA and Viral NA Small Volume Kit. The QIAGEN EZ1 Advanced XL was evaluated using the QIAGEN DSP Virus Kit and the QIAGEN RNA Tissue Mini Kit. The comparator was the Roche MagNA Pure Compact instrument using the RNA Isolation Kit. The study was performed internally using retrospective clinical specimens collected during the 2011-2012 and 2013-2014 influenza seasons. A total of thirty specimens that were previously determined to be positive for influenza A(H3) virus and thirty negative specimens were evaluated with the InfA, H3, and RP assays from the CDC Human Influenza Real-Time Diagnostic Panel. Testing was performed using Invitrogen SuperScript™ and utilizing the ABI 7500 Fast Dx real-time PCR system. The results are summarized in the Tables 8-11 to 8-13. Each method demonstrated 100% agreement with the comparator.

Table 8-11. Retrospective Clinical Results- Roche MagNA Pure 96, DNA and Viral NA Small Volume Kit

	Roche MagNA Pure Compact- RNA Isolation Kit				
Roche MagNA Pure 96 - DNA and Viral NA Small Volume Kit	Positive	Negative	Total	Percent Agreement	95% CI
Positive	30	0	30	100	88.7-100.0
Negative	0	30	30	100	88.7-100.0
Total	30	30	60		

Table 8-12. Retrospective Clinical Results- QIAGEN EZ1 Advanced XL, EZ1 DSP Virus Kit

	Roche MagNA Pure Compact- RNA Isolation Kit				
QIAGEN EZ1 Advanced XL – EZ1 DSP Virus Kit	Positive	Negative	Total	Percent Agreement	95% CI
Positive	30	0	30	100	88.7-100.0
Negative	0	30	30	100	88.7-100.0
Total	30	30	60		

Table 8-13. Retrospective Clinical Results- QIAGEN EZ1 Advanced XL, EZ1 RNA Tissue Mini Kit

	Roche MagNA Pure Compact- RNA Isolation Kit				
QIAGEN EZ1 Advanced XL – EZ1 RNA Tissue Mini Kit	Positive	Negative	Total	Percent Agreement	95% CI
Positive	30	0	30	100	88.7-100.0
Negative	0	30	30	100	88.7-100.0
Total	30	30	60		

X. CONCLUSION

Performance studies were conducted to evaluate the modification of the CDC Human Influenza Virus rRT-PCR Diagnostic Panel to add nucleic acid isolation options. Evaluation of the LOD equivalency, reproducibility, and clinical performance demonstrated that the modified device is substantially equivalent to the predicate. The change raises no new issues of safety and effectiveness and the indications for use remain the same.