



September 30, 2026

Centers for Disease Control and Prevention
Melissa Ivey
Regulatory Affairs Specialist
1600 Clifton Rd.
Atlanta, Georgia 30329

Re: K263035

Trade/Device Name: CDC Human Influenza Virus Real-time RT-PCR Diagnostic Panel (includes Influenza A/B Typing Kit, Influenza A Subtyping Kit, Influenza A(H5) Subtyping Kit, and Influenza B Lineage Genotyping Kit)

Regulation Number: 21 CFR 866.3980

Regulation Name: Respiratory viral panel multiplex nucleic acid assay

Regulatory Class: Class II

Product Code: OZE

Dated: August 31, 2026

Received: August 31, 2026

Dear Melissa Ivey:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the Quality Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system>.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See

the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

JOSEPH BRIGGS -S

Joseph Briggs, Ph.D
Deputy Division Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K263035

Device Name

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: Influenza A/B Typing Kit (Ver 2), Influenza A Subtyping Kit (Ver 5), Influenza A(H5) Subtyping Kit (Ver 4), and Influenza B Lineage Genotyping Kit (Ver 1.1 & 2)

Indications for Use (Describe)

CDC Human Influenza Real-Time RT-PCR Diagnostic Panel: Influenza A/B Typing Kit (Ver 2)

The Influenza A/B Typing Kit contains reagents and controls of the Centers for Disease Control and Prevention (CDC) Human Influenza Virus Real-Time reverse transcription polymerase chain reaction (RT-PCR) Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an in vitro diagnostic real-time PCR instrument that has been U.S Food and Drug Administration (FDA)-cleared for use with this kit in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B viral ribonucleic acid (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 in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Black Box: 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 Real-Time RT-PCR Diagnostic Panel: Influenza A Subtyping Kit (Ver 5)

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 in vitro diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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.

Black Box: 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 Real-Time RT-PCR Diagnostic Panel: Influenza A(H5) Subtyping Kit (Ver 4)

The Influenza A/H5 Subtyping Kit contains reagents and controls of the Centers for Disease Control and Prevention (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 in vitro diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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, conjunctival swabs 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.

Black Box: 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 Real-time RT-PCR Diagnostic Panel: Influenza B Lineage Genotyping Kit (Ver 1.1 and 2)

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 in vitro diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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 in circulation.

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.

Black Box: 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)

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510(k) Summary

I. GENERAL INFORMATION

Submitter

Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30329

Contact Person

Dr. Marie Kirby, PhD
Lead, Genomics and Diagnostics Team
Virology, Surveillance and Diagnostic Branch, Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
mkirby@cdc.gov
(404)718-7689

Date Prepared: September 28, 2026

II. DEVICE INFORMATION

Proprietary Name:	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Influenza A/B Typing Kit (Ver 2) Influenza A Subtyping Kit (Ver 5) Influenza A(H5) Subtyping Kit (Ver 4) Influenza B Lineage Genotyping Kit (Ver 1.1 & 2)
Common Name:	CDC Flu rRT-PCR Dx Panel
Regulation Section:	866.3980-Respiratory viral panel multiplex nucleic acid assay
Device Classification:	Class II
Product Code:	OZE
Subsequent Product Codes:	NSU, NXD, OEP, OOI, OQW
Panel:	Microbiology

III. PREDICATE DEVICE

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (K243274)

IV. DEVICE DESCRIPTION

The CDC Human Influenza Real-Time RT-PCR Diagnostic Panel is used in real-time RT-PCR (rRT-PCR) assays on an in vitro diagnostic real-time PCR instrument that has been FDA-cleared for use with the CDC device. 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) or from viral culture. Oligonucleotide primers and probes for detection of influenza A, influenza B, and influenza A of 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 hemagglutinin (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.

The Influenza A/B Typing Kit consists of oligonucleotide primers and dual-labeled hydrolysis (TaqMan®) probes and controls, which may be used, in rRT-PCR assays for the in vitro qualitative detection and characterization of the human influenza virus RNA in respiratory specimens from patients presenting with influenza-like illness (ILI). The oligonucleotide primers and probes for detection of Influenza A and B viruses were selected from highly conserved regions of the matrix (M) and non-structural (NS) genes, respectively. Detection of viral RNA not only aids in the diagnosis of illness caused by seasonal, newly emerging, and novel influenza viruses in patients with ILI, but also provides epidemiological and surveillance information on influenza and aids in the presumptive laboratory identification of specific novel influenza A viruses.

The Influenza A Subtyping Kit consists of oligonucleotide primers and dual-labeled hydrolysis (TaqMan®) probes and controls, which may be used in rRT-PCR assays for the in vitro qualitative detection and characterization of the human influenza virus RNA in respiratory specimens from patients presenting with influenza-like illness (ILI). The oligonucleotide primers and probes for detection of Influenza A and 2009 Influenza A (swine origin) were selected from highly conserved regions of the matrix (M), and the nucleoprotein (NP), respectively. Oligonucleotide primers and probes for characterization and differentiation of seasonal influenza A(H3) and A(H1)pdm09 viruses were selected from highly conserved regions of their respective HA genes. Detection of viral RNA not only aids in the diagnosis of illness caused by seasonal, newly emerging, and novel influenza viruses in patients with ILI, but also provides epidemiological and surveillance information on influenza and aids in the presumptive laboratory identification of specific novel influenza A viruses.

The Influenza A/H5 Subtyping Kit consists of oligonucleotide primers and dual-labeled hydrolysis (TaqMan®) probes and controls which may be used in rRT-PCR assays for the in vitro qualitative detection and characterization of influenza virus RNA in respiratory specimens and conjunctival swabs from patients presenting with influenza-like illness (ILI) and/or symptoms associated with influenza A(H5) infection. The oligonucleotide primers and probes for detection of influenza A viruses were selected from highly conserved regions of the matrix (M) protein. Oligonucleotide primers and probes for characterization and differentiation of avian influenza A(H5) (Asian lineage) viruses were selected from highly conserved regions of the HA genes. Detection of viral RNA not only aids in the diagnosis of illness caused by seasonal, newly emerging, and novel influenza viruses in patients with ILI, but also provides epidemiological and surveillance information on influenza and aids in the presumptive laboratory identification of specific novel influenza A viruses.

The Influenza B Lineage Genotyping Kit consists of oligonucleotide primers and dual-labeled hydrolysis (TaqMan®) probes and controls which may be 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). The oligonucleotide primers and probes for detection of influenza B viruses were selected from highly conserved regions of the non-structural (NS) protein gene segment. Oligonucleotide primers and probes for characterization and differentiation of influenza B/Victoria and B/Yamagata viruses were selected from highly conserved regions of their HA genes. Detection of viral RNA not only aids in the diagnosis of illness caused by seasonal, newly emerging, and novel influenza viruses in patients with ILI, but also provides epidemiological and surveillance information on influenza and aids in the presumptive laboratory identification of specific novel influenza viruses.

V. INTENDED USE

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel includes:

Influenza A/B Typing Kit (Ver 2)

The Influenza A/B Typing Kit contains reagents and controls of the Centers for Disease Control and Prevention (CDC) Human Influenza Virus Real-Time reverse transcription polymerase chain reaction (RT-PCR) Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an *in vitro* diagnostic real-time PCR instrument that has been U.S Food and Drug Administration (FDA)-cleared for use with this kit in conjunction with clinical and epidemiological information:

- For qualitative detection of influenza virus type A or B viral ribonucleic acid (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 in these cases unless a BSL 3+ 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.

Influenza A Subtyping Kit (Ver 5)

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 *in vitro* diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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.

Influenza A(H5) Subtyping Kit (Ver 4)

The Influenza A/H5 Subtyping Kit contains reagents and controls of the Centers for Disease Control and Prevention (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 *in vitro* diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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, conjunctival swabs 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.

Influenza B Lineage Genotyping Kit (Ver 1.1)

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 *in vitro* diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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 in circulation.

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.

VI. TECHNOLOGICAL CHARACTERISTICS

The technological characteristics of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel remain the same as the predicate device. This 510k addressed a modification to the pdmH1 primer and probe sets for the Influenza A Subtyping kit in response to recent evolutionary changes in circulating influenza A viruses. No modifications were made to the other assays within the panel.

VII. SUBSTANTIAL EQUIVALENCE COMPARISON

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (K243274), will serve as the predicate for the proposed change.

Substantial Equivalence Comparison

	Predicate Device	Proposed Device
Item	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel K243274 Influenza A/B Typing Kit (Ver 2) Influenza A Subtyping Kit (Ver 4) Influenza A(H5) Subtyping Kit (Ver 4) Influenza B Lineage Genotyping Kit (Ver 1.1 and 2)	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Influenza A/B Typing Kit (Ver 2) Influenza A Subtyping Kit (Ver 5) Influenza A(H5) Subtyping Kit (Ver 4) Influenza B Lineage Genotyping Kit (Ver 1.1 and 2)
Intended Use	<u>Influenza A/B Typing Kit</u> The Influenza A/B Typing Kit contains reagents and controls of the Centers for Disease Control and Prevention (CDC) Human Influenza Virus Real-Time reverse transcription polymerase chain reaction (RT-PCR) Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an <i>in vitro</i> diagnostic real-time PCR instrument that has been U.S Food and Drug Administration (FDA)-cleared for use with this kit in conjunction with clinical and epidemiological information:	Same

• For qualitative detection of influenza virus type A or B viral ribonucleic acid (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 in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Black Box: 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.

Influenza A Subtyping Kit

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 *in vitro* diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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. Black Box: 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. <u>Influenza A(H5) Subtyping Kit</u> The Influenza A/H5 Subtyping Kit contains reagents and controls of the Centers for Disease Control and Prevention (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 <i>in vitro</i> diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit 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, conjunctival swabs 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.	
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	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. Black Box: 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. <u>Influenza B Lineage Genotyping Kit</u> 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 <i>in vitro</i> diagnostic real-time PCR instrument that has been FDA-cleared for use with this kit in conjunction with clinical and epidemiological information:	
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	• 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 in circulation. 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. Black Box: 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 B viruses	Same
Specimen Types	Influenza A/B Typing Kit, and Influenza A Subtyping Kit- 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 Influenza B Lineage Genotyping Kit- Upper respiratory tract specimens from human patients with signs and symptoms of respiratory infection	Same

	Influenza A(H5) Subtyping Kit- Human respiratory specimens, conjunctival swabs, and viral culture in conjunction with clinical and epidemiological risk factors	
Technological Characteristics	Real-time RT-PCR	Same
Nucleic Acid Extraction	QIAamp® DSP Viral RNA Mini Kit, QIAGEN MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche Or RNA Isolation Kit, Roche MagNA Pure LC – Total Nucleic Acid Kit, Roche MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN NucliSENS® easyMAG®, bioMérieux EMAG®, bioMérieux EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN	QIAamp® DSP Viral RNA Mini Kit, QIAGEN MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN EMAG®, bioMérieux EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN *These platforms are the same as the predicate device. This change reflects the removal of three discontinued platforms (MagNA Pure Compact, Pure LC, Roche and the NucliSENS® easyMAG®, bioMérieux.
Enzyme Master Mix	Invitrogen SuperScript III Platinum One-Step Quantitative RT-PCR Kit (with or without ROX) Quanta BioSciences qScript One-Step qRT-PCR Kit, Low ROX	Same
Required Instrumentation	Applied Biosystem 7500 Fast Dx Real-time PCR system with SDS software version 1.4 Applied Biosystems QuantStudio Dx with version 1.0.3 software QIAGEN Rotor-Gene Q MDx with AssayManager 1.0.4.1 and Epsilon version 1.0.1 software	Same

VIII. Analytical Performance Evaluation

All studies outlined below were performed using the Qiagen EZ1 Advanced XL DSP Virus Kit, and the ABI™ 7500 Fast Dx following the instructions for use (IFU) for the CDC Flu RT-PCR Dx Panel, Influenza A Subtyping Kit. Further details or exceptions are provided in the following sections.

Analytical Sensitivity- Limit of Detection

Analytical sensitivity of the modified pdmH1 primers and probe were determined in LoD studies by comparing the modified pdmH1 (pdmH1_v4 with either ZEN or BHQ) primers and probes to the currently approved IVD pdmH1 (pdmH1_IVD) primers and probes. Serial dilutions of representative strains of influenza A/H1N1(pdm09) with and without the known mutations (Table 8-1) were tested in triplicate with the updated pdmH1_v4 and pdmH1_IVD primers and probes. The lowest concentration of virus positive for 3/3 replicates in the LoD comparison study using the pdmH1_v4 version was considered the preliminary LoD (Tables 8-3 and 8-4). LoD confirmation was performed by testing 20 replicates at the preliminary LoD and at one 3-fold dilution above and below on both representative strains. For all LoD studies, RNA was tested with two enzymes, the Invitrogen Superscript™ III Platinum and Quanta BioSciences

qScript™. The confirmed LoD of the modified pdmH1_v4 assay was confirmed to be equivalent to the predicate device (K243274) (Table 8-4).

Table 8-1: Viruses for LoD Studies

Virus	Type	Mutation
A/Rhode Island/06/2024	Influenza A/H1N1pdm09	Yes
A/Illinois/20/2018	Influenza A/H1N1pdm09	No

Table 8-2: LoD Comparison Study for A/Rhode Island/06/2024

Log (EID ₅₀ /mL)	SuperScript™ III			Quanta qScript		
	pdmH1_IVD	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)	pdmH1_IVD	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)
10 ^{2.65}	3/3	3/3	3/3	3/3	3/3	3/3
10 ^{2.17}	1/3	3/3	3/3	3/3	3/3	3/3
10 ^{1.69}	0/3	3/3	3/3	3/3	3/3	3/3
10 ^{1.22}	0/3	3/3	0/3	2/3	2/3	2/3
10 ^{0.74}	0/3	1/3	0/3	2/3	0/3	0/3

Table 8-3: LoD Comparison Study for A/Illinois/20/2018

Log (EID ₅₀ /mL)	SuperScript™ III			Quanta qScript		
	pdmH1_IVD	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)	pdmH1_IVD	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)
10 ^{1.63}	3/3	3/3	3/3	3/3	3/3	3/3
10 ^{1.16}	2/3	3/3	3/3	3/3	3/3	2/3
10 ^{0.68}	0/3	1/3	1/3	2/3	1/3	2/3

Table 8-4: LoD Confirmation Study

Strain	Enzyme	Confirmed LoD (ID ₅₀ /mL)		
		pdmH1_IVD	pdmH1_v4 ZEN	pdmH1_v4 BHQ
A/Rhode Island/06/2024	SuperScript™ III	4.1 x 10 ^{1.08}	4.1 x 10 ^{1.08}	4.1 x 10 ^{1.08}
	Quanta qScript	1.23x10 ^{2.08}	4.1 x 10 ^{1.08}	1.23x10 ^{2.08}
A/Illinois/20/2018	SuperScript™ III	4.1 x 10 ^{1.02}	1.37 x 10 ^{1.02}	1.37 x 10 ^{1.02}
	Quanta qScript	4.1 x 10 ^{1.02}	4.1 x 10 ^{1.02}	4.1 x 10 ^{1.02}

Analytical Sensitivity- Inclusivity

Inclusivity testing of the pdmH1_v4 was performed using the viruses listed in Table 8-5. RNA was extracted from a high titer dilution and a low titer dilution from each virus and tested in triplicate with the pdmH1_v4 (ZEN and BHQ) assay using both the Invitrogen Superscript™ III Platinum and the Quanta BioSciences qScript™. Inclusivity was not impacted by the modification to the pdmH1 primer and probe set as all strains were detected. The modified pdmH1_v4 assay performed equivalently to the predicate device (K243274). Results are summarized in Table 8-5.

Table 8-5 Inclusivity of the Modified Influenza A(pdmH1) Primers and Probes

Virus Designation	Log (ID ₅₀ /mL)	Enzyme	pdmH1_v4 ZEN	pdmH1_v4 BHQ
A/Brisbane/02/2018	10 ^{3.9}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.9}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Hawaii/17/2018	10 ^{3.5}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.5}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Michigan/45/2015	10 ^{3.3}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.3}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Connecticut/01/2021	10 ^{3.5}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.5}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Victoria/4897/2022	10 ^{3.32}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.32}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Wisconsin/67/2022	10 ^{3.67}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.67}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Utah/45/2025	10 ^{3.43}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.43}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Michigan/95/2024	10 ^{3.37}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{2.37}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/California/40/2025	10 ^{2.45}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{1.45}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
A/Guam/5964/2025	10 ^{2.66}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3
	10 ^{1.66}	SuperScript [™] III	3/3	3/3
		Quanta qScript	3/3	3/3

Analytical Specificity- Exclusivity

Exclusivity testing of the pdmH1_v4 (ZEN and BHQ) primers and probes was performed using the viruses listed in Table 8-6. RNA was extracted from a high titer dilution from each virus and tested in triplicate with the pdmH1_v4 versions using a single enzyme, Invitrogen Superscript™ III Platinum enzyme. Cross-reactivity was seen in one strain, H1v/1A.3.3.3 strain A/Ohio/09/2015, however this cross-reactivity was established previously with the IVD primer and probe set. The modified pdmH1 primers and probes do not raise any new risk to exclusivity, as the assay performed equivalently to the predicate device (K243274). Results are summarized in Table 8-6.

Table 8-6- Exclusivity of Modified Influenza A(pdmH1) Primers and Probes

Subtype/Clade	Virus Designation	ID ₅₀ /mL	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)
H1v/1A.1.1	A/Ohio/24/2017	6.3	0/3	0/3
H1v/1A.2	A/Texas/14/2008	8.3	0/3	0/3
H1v/1A.3.3.3	A/Wisconsin/03/2021	6.07	0/3	0/3
H1v/1A.3.3.3	A/Ohio/09/2015	7.7	3/3	3/3
H1v/1B.2.1	A/Ohio/35/2017	6.9	0/3	0/3
H1v/1B.2	A/Brisbane/59/2007	9.2	0/3	0/3
H3v/2010.1	A/Ohio/13/2017	6.6	0/3	0/3
H3v/2010.1	A/Ohio/28/2016	10.2	0/3	0/3
H3v/1990.4	A/Michigan/84/2016	8.5	0/3	0/3
H3v/1990.4	A/Indiana/ 10/2011	10.2	0/3	0/3
H3v/1990.1	A/Hawaii/28/2020	8.2	0/3	0/3
H3N2	A/Darwin/09/2021	8.2	0/3	0/3
H3N2	A/Cambodia/e0826360/2020	8.2	0/3	0/3
H3N2	A/Hong Kong/2671/2019	8.5	0/3	0/3
H3N2	A/Hong Kong/4801/2014	8.94	0/3	0/3
H5N1	A/Texas/37/2024	9.25	0/3	0/3
H5N1	A/American Wigeon/South Carolina/22-000345-001/2021	10.2	0/3	0/3
H5N8	A/GYRFALCON/WASHINGTON/41088-6/2014 PR8-IDCDC-RG43A	8.9	0/3	0/3
H7N9	A/TAIWAN/1/2017	5.54	0/3	0/3
H9N2	A/BANGLADESH/0994/2011	10.5	0/3	0/3
H3N8	A/canine/Florida/43/2004	8.1	0/3	0/3
H3N8	A/equine/Ohio/01/2003	8.4	0/3	0/3
InfB/Yamagata	B/Phuket/3073/2013	9.9	0/3	0/3
InfB/Victoria	B/Sichuan-Jingyang/12048/2019	7.2	0/3	0/3
InfC	C/Minnesota/01/2016	NA ¹	0/3	0/3

¹Not Available

Analytical Specificity- Cross Reactivity

Cross-Reactivity testing of the pdmH1_v4 primers and probes was performed using high titer isolates (10^5 or 10^6 ID₅₀/ml or equivalent) of the pathogens in Tables 8-7 and 8-8 using the Invitrogen Superscript III Platinum enzyme to confirm exclusivity with bacteria and other respiratory viruses. The modified pdmH1 primers and probes do not raise any new risk, as the assay performed equivalent to the predicate device (K243274).

Table 8-7 Cross-Reactivity of Non-influenza Respiratory Viruses

Virus	Strain	TCID₅₀/ml	Nucleic Acid Conc.	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)
Influenza C	C/Minnesota/1/2016	NA ¹	NA ¹	0/3	0/3
Influenza C	C/Minnesota/4/2015	NA ¹	NA ¹	0/3	0/3
Influenza C	C/Minnesota/29/2015	NA ¹	NA ¹	0/3	0/3
MERS-CoV	NA	NA ¹	5.3×10^5 copies/ μ L	0/3	0/3
Human Coronavirus	OC43	8.9×10^6	NA ¹	0/3	0/3
SARS-CoV-2	NA	NA ¹	NA ¹	0/3	0/3
Human Coronavirus	229E	2.8×10^6	NA ¹	0/3	0/3
Human Coronavirus	NL63	1.6×10^4	NA ¹	0/3	0/3
Human Coronavirus	HKU1	NA ¹	5.5×10^5 copies/ μ L	0/3	0/3
Enterovirus	Echo 6	$10^{6.9}$	NA ¹	0/3	0/3
Human Adenovirus, type 1	Ad.71	$10^{9.2}$	NA ¹	0/3	0/3
Human Adenovirus, type 7a	S-1058	$10^{7.1}$	NA ¹	0/3	0/3
Human Rhinovirus A	1A	$10^{5.8}$	NA ¹	0/3	0/3
Human Parainfluenza 1 virus		NA ¹	3.0 ng/ μ L	0/3	0/3
Human Parainfluenza 2 virus	Greer	$10^{3.1}$	NA ¹	0/3	0/3
Human Parainfluenza 3 virus	C-243	$10^{7.9}$	NA ¹	0/3	0/3
Respiratory Syncytial virus	CH93-18b	$10^{6.8}$	NA ¹	0/3	0/3
Herpes Simplex Virus	KOS	$5 \times 10^{7.75}$	NA ¹	0/3	0/3
Varicella-zoster Virus	AV92-3:H	$5 \times 10^{3.75}$	NA ¹	0/3	0/3
Epstein Barr Virus	B95-8	NA ¹	1.7 ng/ μ L	0/3	0/3
Measles Virus	Edmonston	$5 \times 10^{4.5}$	NA ¹	0/3	0/3
Mumps Virus	Enders	$5 \times 10^{6.5}$	NA ¹	0/3	0/3
Cytomegalovirus	AD-169	$5 \times 10^{6.25}$	NA ¹	0/3	0/3

¹NA= not available

Table 8-8 Cross-Reactivity of Bacteria and Yeast

Bacteria/Yeast	Strain	CFU/mL	Nucleic Acid Conc.	pdmH1_v4 (ZEN)	pdmH1_v4 (BHQ)
<i>Bordetella pertussis</i>	Tohama I	10 ¹⁰	NA ¹	0/3	0/3
<i>Candida albicans</i>	3147	10 ^{8.49}	NA ¹	0/3	0/3
<i>Chlamydia pneumoniae</i>	CM-1	40 IFU/mL	NA ¹	0/3	0/3
<i>Corynebacterium diphtheriae</i>	NCTC 13129	NA ¹	57.4 ng/uL	0/3	0/3
<i>Escherichia coli</i>	K12	10 ^{9.6}	NA ¹	0/3	0/3
<i>Streptococcus pyogenes</i>	MGAS 8232	NA ¹	41 ug/mL	0/3	0/3
<i>Haemophilus influenzae</i>	M15709	10 ^{6.4}	NA ¹	0/3	0/3
<i>Lactobacillus plantarum</i>	NA	10 ^{8.8}	NA ¹	0/3	0/3
<i>Legionella pneumophila</i>	Philadelphia-1	10 ^{8.41}	NA ¹	0/3	0/3
<i>Moraxella catarrhalis</i>	M15757	10 ^{9.5}	NA ¹	0/3	0/3
<i>Mycobacterium tuberculosis</i>	H37Ra	100	NA ¹	0/3	0/3
<i>Mycoplasma pneumoniae</i>	PS 1428	10 ⁹	NA ¹	0/3	0/3
<i>Neisseria elongata</i>	NA	100	NA ¹	0/3	0/3
<i>Neisseria meningitidis</i>	M2578	10 ^{7.9}	NA ¹	0/3	0/3
<i>Pseudomonas aeruginosa</i>	NA	10 ^{10.5}	NA ¹	0/3	0/3
<i>Staphylococcus aureus</i>	NA	10 ^{10.7}	NA ¹	0/3	0/3
<i>Staphylococcus epidermidis</i>	NA	10 ^{10.5}	NA ¹	0/3	0/3
<i>Streptococcus pneumoniae</i>	249-06 ²	10 ^{6.6}	NA ¹	0/3	0/3
<i>Streptococcus salivarius</i>	DSM 13084	NA ¹	109 ng/uL	0/3	0/3

¹NA= not available²Blood from Thailand

IX. Clinical Performance Evaluation

The clinical performance of the pdmH1_v4 assay was evaluated using residual human respiratory specimens collected during previous influenza seasons in the United States that were previously sequenced through the Influenza Division surveillance program. Given the potential decrease in sensitivity for strains containing the mutation with the IVD pdmH1 assay, Next Generation Sequencing (NGS) was used as the comparator assay for performance evaluation to confirm the identity of positive specimens.

Retrospective Study

Positive and negative upper respiratory specimens (including nasopharyngeal swabs, throat swabs, and nasal swabs), archived at CDC in previous influenza seasons were used in this evaluation. All specimens were collected in VTM using minitip flocked swabs. A total of 61 positive influenza A(H1)pdm09 specimens were evaluated in this study. In total, 58 specimens were confirmed to contain the current mutations with NGS and 3 specimens were confirmed to not contain the current mutations with NGS. A panel of 60 negative specimens for pdmH1 were also included. Negative specimens were taken from symptomatic patients known to be positive for influenza H3N2.

RNA was extracted using the Qiagen EZ1 instrument with the EZ1 Advanced XL DSP Virus Kit. Testing was conducted using both the pdmH1_IVD and pdmH1_v4 assays with both

Invitrogen Superscript™ III Platinum and Quanta BioSciences qScript™ enzymes on the ABI™ 7500 Fast Dx instrument. Performance was evaluated by positive percent agreement (PPA) for the pdmH1_v4 and the pdmH1_IVD versions when compared to NGS data for all 61 positive specimens. Negative percent agreement (NPA) was also calculated for both assays across all 60 negative specimens. Results are in Tables 9-1 and 9-2. The clinical evaluation showed a PPA of 100% (94.08-100) for the pdmH1_v4 assay when compared to NGS while the pdmH1_IVD assay showed a PPA of 98.36% (91.28-99.71). Both versions of the assay showed a NPA of 100% (93.98-100). Clinical performance of the modified pdmH1 assay was equivalent to the predicate device (K243274).

Table 9-1: Modified pdmH1 Primers and Probe Retrospective Clinical Evaluation- Positive Agreement

Primer/Probe Set	Invitrogen Superscript™ III		Quanta qScript™	
	# of Positives ¹	% Positive Agreement (95% CI) ²	# of Positives ¹	% Positive Agreement (95% CI) ²
pdmH1_v4 (ZEN)	61/61	100 (94.08-100)	61/61	100 (94.08-100)
pdmH1_v4 (BHQ)	61/61	100 (94.08-100)	61/61	100 (94.08-100)
pdmH1_IVD	60/61	98.36 (91.28-99.71)	60/61	98.36 (91.28-99.71)

¹Proportion of positive specimens correctly identified versus the comparator (NGS)

²Confidence Interval calculated by Wilson method

Table 9-2: Modified pdmH1 Primers and Probe Retrospective Clinical Evaluation – Negative Agreement

Primer/Probe Set	Invitrogen Superscript™ III		Quanta qScript™	
	# of Negatives ¹	% Negative Agreement (95% CI) ²	# of Negatives ¹	% Negative Agreement (95% CI) ²
pdmH1_v4 (ZEN)	60/60	100 (93.98-100)	60/60	100 (93.98-100)
pdmH1_v4 (BHQ)	60/60	100 (93.98-100)	60/60	100 (93.98-100)
pdmH1_IVD	60/60	100 (93.98-100)	60/60	100 (93.98-100)

¹Proportion of negative specimens correctly identified versus the comparator (NGS)

²Confidence Interval calculated by Wilson method

X. Conclusion

The modification of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, specifically the pdmH1 primer and probe set in the Influenza A Subtyping Kit, does not substantially change the device. Analytical and clinical data demonstrate that the performance of the device to detect currently circulating viruses is accomplished with high positive and negative agreement in a manner substantially equivalent to the predicate. The change raises no new issues of safety and effectiveness and the indications for use remain the same.