# SPECIAL 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY

## I Background Information:

### A 510(k) Number

K263035

### B Applicant

Centers for Disease Control and Prevention

### C Proprietary and Established Names

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)

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| OZE | Class II | 21 CFR 866.3980 | Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

The purpose of this submission is to address the modification of the Influenza A subtyping kit to update the influenza A H1N1pmd09 primers and probe sequences to maintain and improve the performance of the device with recently circulating influenza A H1N1 viruses. This regulatory pathway (Special 510(k)) has been utilized by the CDC for similar changes to the Influenza A subtyping kit to update influenza A H3 primers and probes.

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

### B Indication(s) for Use:

Influenza A/B Typing Kit (Ver 2)

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

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/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 (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.

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.

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.

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.

**C Special Conditions for Use Statement(s):**

Rx – For prescription use only

For In Vitro Diagnostic Use

**D Special Instrument Requirements:**

## IV Device/System Characteristics:

### 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.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):
CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: Influenza A/B Typing Kit (VER 2); Influenza A SubTyping Kit (VER 4); Influenza B Lineage Genotyping Kit (VER 1.1 and 2); and Influenza A/H5 Subtyping Kit (VER 4)

### B Predicate 510(k) Number(s):
K243274

### C Comparison with Predicate(s):

| Device & Predicate Device(s): | K263035 | K243274 |
|---|---|---|
| Device Trade Name | CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel<br>Influenza A/B Typing Kit (Ver 2)<br>Influenza A Subtyping Kit (Ver 5)<br>Influenza A(H5) Subtyping Kit (Ver 4)<br>Influenza B Lineage Genotyping Kit (Ver | CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel<br>Influenza A/B Typing Kit (Ver 2)<br>Influenza A Subtyping Kit (Ver 4)<br>Influenza A(H5) Subtyping Kit (Ver 4)<br>Influenza B Genotyping Kit (Ver 1.1 and 2) |

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| | 1.1 and 2) | |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | Same | <u>Influenza A/B Typing Kit</u><br>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:<br>• 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.<br>• To provide epidemiologic information for surveillance of circulating influenza viruses.<br>Performance characteristics for influenza were established |

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| | | 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.<br>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.<br>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.<br>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 |

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| | | only those users who have successfully completed a training course provided by CDC instructors or designees.<br><u>Influenza A Subtyping Kit</u><br>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:<br>• 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;<br>• To provide epidemiologic information for surveillance of circulating influenza viruses.<br>Performance characteristics for influenza were established during a season when seasonal influenza viruses A(H1N1) and |

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| | | 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.<br>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.<br>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.<br>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 |

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| | | CDC instructors or designees.<br>Influenza A(H5) Subtyping Kit<br>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:<br>• 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;<br>• To provide epidemiologic information for surveillance of circulating influenza viruses.<br>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.<br>Testing with the influenza H5a and H5b primer and probe sets should not be performed unless the patient meets the most |

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| | | 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.<br>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.<br>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.<br>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 |

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| | | 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.<br><u>Influenza B Genotyping Kit</u><br>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:<br>• 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;<br>• To provide epidemiologic information for surveillance of circulating influenza viruses.<br>Performance characteristics for influenza B lineage genotyping were established during a season when influenza B/Victoria and B/Yamagata lineages were in circulation.<br>Negative results do not preclude influenza virus infection and |

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| | | 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.<br>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. |
| Organisms Detected | Same | Influenza A viruses (animal and human)<br>Influenza B viruses |
| Specimen Types | Same | 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<br>Influenza B Lineage Genotyping Kit- Upper respiratory tract specimens from human patients with signs and symptoms of respiratory infection<br>Influenza A(H5) Subtyping Kit- Human respiratory specimens, |

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| | | conjunctival swabs, and viral culture in conjunction with clinical and epidemiological risk factors |
| Technological Characteristics | Same | Real-time RT-PCR |
| Enzyme Master Mix | Same | Invitrogen SuperScript III Platinum One-Step Quantiative RT-PCR Kit (with or without ROX)<br>Quanta BioSciences qScript One-Step qRT-PCR Kit, Low ROX |
| Required Instrument | Same | Applied Biosystem 7500 Fast Dx Real-time PCR system with SDS software version 1.4<br>Applied Biosystems QuantStudio Dx with version 1.0.3 software<br>QIAGEN Rotor-Gene Q MDx with AssayManager 1.0.4.1 and Epsilon version 1.0.1 software |
| Nucleic Acid Extraction | QIAamp DSP Viral RNA Mini Kit, QIAGEN<br>MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche<br>QIAcube – QIAamp DSP Viral RNA Mini Kit, QIAGEN<br>EMAG, bioMérieux<br>EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN<br>*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 | QIAamp DSP Viral RNA Mini Kit, QIAGEN<br>MagNA Pure Compact – Nucleic Acid Isolation Kit I, Roche<br>Or RNA Isolation Kit, Roche<br>MagNA Pure LC – Total Nucleic Acid Kit, Roche<br>MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche<br>QIAcube – QIAamp DSP Viral RNA Mini Kit, QIAGEN<br>NucliSENS easyMAG, bioMérieux<br>EMAG, bioMérieux<br>EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN |

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| | NucliSENS easyMAG, bioMérieux. | |
| **General Device Characteristic Differences** | | |
| Primer and Probe Sequence | Modified influenza A H1N1pdm09 forward and reverse primer sequences | Influenza A; Influenza B |

## VI Standards/Guidance Documents Referenced:

Not applicable

## VII Verification and Validation

### A Device Change(s)

Modification of the influenza A(H1) pdm09 primer and probe sequences was made to address recent evolutionary changes in circulating influenza A(H1) pdm09 viruses that may impact the reactivity of the current Influenza A Subtyping Kit. The modifications include changes to the existing influenza A(H1) pdm09 primers and probe sequences to improve or maintain sensitivity of the assays to circulating influenza A viruses.

### B Risks

A risk assessment process was conducted which identified the primary failures and risks associated with modifying oligonucleotides of the Influenza A Subtyping Kit, and labeling updates for the cease in distribution of the Influenza B Lineage Genotyping Kit within the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel were assessed. A summary of the risks identified is presented in **Table 1** below. Based on the risk analysis, appropriate verification and validation activities were required to ensure continued performance of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel after the modification. The CDC Influenza Division followed its established procedures for development, validation, and implementation of the modified assays. Analytical and clinical studies were conducted to demonstrate that the performance of the modified CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel successfully mitigates the identified potential risks to an acceptable level.

**Table 1**: Risks Associated and Control Measures

| Device Modification | Identified Risk | Hazardous Situation | Consequence | Risk Control Measure | Risk Acceptability Criteria | Verification Method | Summary Conclusion |
|---|---|---|---|---|---|---|---|
| Influenza A pdmH1 oligonucleotide | Modified oligonucleotides may demonstrate | Some influenza pdmH1 strains may | Humans infected with influenza A | Characterization of the performance of the | Updated assay will detect circulating | Analytical and clinical performance testing | Results demonstrated that the modified |

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| reagents are updated to ensure reactivity of assays with current circulating influenza A(pdmH1) strains. | variable reactivity among different influenza A pdmH1 strains | not be detected in human specimens. | pdmH1 strains may not be identified in a timely manner. Reduced capability in influenza surveillance. | modified device with representative influenza A pdmH1 strains. | influenza A pdmH1 strains at equal or improved levels of sensitivity and specificity compared to the originally cleared device. | using established methods consistent with the methods used to establish performance with the originally cleared device. | device detects influenza A pdmH1 strains at equal or improved levels of reactivity to the original cleared device. Risk is mitigated to an acceptable level. |
| CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit package labeling and package inserts. | Differences exist between the package labeling of the currently cleared device and kits of the updated CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit. | Short term risk of confusing components of the currently cleared CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit. | End user confusing components from different versions could impact ability to accurately detect influenza A viruses. | A product update communication will be distributed instructing end users to transition to the updated kit. Currently distributed kits will expire, and older inventory will no longer be available to the end user. | CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit package labeling and package insert will provide part numbers of new components. | Appropriate package labeling and package insert instructions will be verified against product components by the end user upon receipt per CLIA requirements. | Risk of comminglin g and/or confusing components of currently cleared CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit is mitigated to an acceptable level. |
| CDC Human Influenza Real-Time RT-PCR Diagnostic Panel IFUs to reflect the pause in distribution | Distribution of the Influenza B Lineage Genotyping test is being stopped since the Influenza B Yamagata | There is a low possibility that the B Yamagata strain could reemerge and not be detected by state public | Identification of an emerged Influenza B Yamagata strain would be missed through testing with | NGS surveillance at CDC is constantly monitoring circulating influenza strains and would identify a | Impact to patient care in the event of reemergence is negligible. Acceptable monitoring of strains | Genotyping of Influenza B does not impact patient treatment as it is the same regardless of strain. | Risk is at an acceptable level. |

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| of the Influenza B Lineage Genotyping kit | strain has not been detected since 2020. Updated test algorithm is different from the currently cleared IFU. | health laboratories using the diagnostic | the RT-PCR panel. | reemergence of B Yamagata or another variant(s) that might emerge. As the Influenza B Lineage Genotyping kit is remaining on the cleared diagnostic panel the kit can be brought back to production quickly if needed. | for variants means low risk of missing reemergence of B Yamagata. | Therefore, patient care is not impacted as the AB Typing kit will still be used to diagnose influenza. Risk to patient care is low. NGS Influenza surveillance activities that look for variants will remain in place to monitor for the reemergence of the Yamagata strain. Risk to missing reemergence is negligible. | |

**C Verification/Validation Methods**

To demonstrate that there was no negative impact on the performance with the modifications listed above, the following studies were conducted using the modified and currently cleared versions of the influenza A(H1) pdm09 primer and probe sets from the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. All studies were performed using RNA extracted by the Qiagen EZ1 Advanced XL DSP Virus Kit, on the ABI 7500 Fast Dx using two enzymes: the Invitrogen Superscript III Platinum and Quanta BioSciences qScript. All analytical study samples were prepared in Viral Transport Medium with A549 cells to mimic respiratory specimens. This approach was utilized in a previous submission (K241110).

1. Limit of Detection

   Analytical sensitivity of the modified pdmH1 primers and probe were determined in Limit of Detection (LoD) studies by comparing the modified pdmH1 (pdmH1_v4) primers and probes

to the currently FDA-cleared versions of the pdmH1 (pdmH1_IVD) primers and probes in the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. Serial dilutions of representative strains of influenza A/H1N1(pdm09) with (A/Rhode Island/06/2024) and without (A/Illinois/20/2018) the known mutations were tested in triplicate with each assay. A comparison study of the updated versions versus the current versions was done by comparing the lowest concentration of virus positive for 3/3 replicates for each representative strain. The lowest concentration of virus positive for 3/3 replicates in the LoD comparison study using the FDA-cleared version (pdmH1_v4) was considered the new preliminary LoD. 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. Results for each strain of virus are shown in **Table 2, Table 3, and Table 4** below.

**Table 2**: LoD Comparison 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 3**: LoD Comparison 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 4**: LoD Confirmation Study Results

| Strain | Enzyme | Confirmed LoD ($ID_{50}$/mL) | | |
|---|---|---|---|---|
| | | pdmH1_IVD | pdmH1_v4 ZEN | pdmH1_v4 BHQ |
| A/Rhode Island/06/2024 | SuperScript III | $4.1 \times 10^{1.08}$ ($10^{1.69}$) (19/20) | $4.1 \times 10^{1.08}$ ($10^{1.69}$) (19/20) | $4.1 \times 10^{1.08}$ ($10^{1.69}$) (19/20) |
| | Quanta qScript | $1.23 \times 10^{2.08}$ ($10^{2.17}$) (20/20) | $4.1 \times 10^{1.08}$ ($10^{1.69}$) (20/20) | $1.23 \times 10^{2.08}$ ($10^{2.17}$) (20/20) |
| A/Illinois/20/2018 | SuperScript III | $4.1 \times 10^{1.02}$ ($10^{1.63}$) (20/20) | $1.37 \times 10^{1.02}$ ($10^{1.16}$) (19/20) | $1.37 \times 10^{1.02}$ ($10^{1.16}$) (19/20) |
| | Quanta qScript | $4.1 \times 10^{1.02}$ ($10^{1.63}$) (20/20) | $4.1 \times 10^{1.02}$ ($10^{1.63}$) (19/20) | $4.1 \times 10^{1.02}$ ($10^{1.63}$) (19/20) |

The confirmed LoD of the modified pdmH1 (pdmH1 v4) assay for both the ZEN and BHQ quenchers was found to be at or lower than the pdmH1 IVD assay.

2. Inclusivity

The inclusivity of the modified pdmH1 (pdmH1_v4) primers and probes was evaluated by testing viruses representing temporal, geographic, and genetic diversity within the subtype. Samples were prepared at low and high titer dilutions and tested in triplicate. The modified primers and probes were reactive with all pdmH1 strains tested. The inclusivity results are presented in **Table 5** below.

**Table 5**: Inclusivity of the Modified Influenza A(pdmH1) Primers and Probes

| Virus | Concentration (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 |

3. Exclusivity

The exclusivity of the modified H1N1pmd09 primers and probes was evaluated using 25 influenza viruses of different subtypes and lineages. Samples were prepared at high titer dilutions and tested in triplicate. Only one enzyme (Invitrogen Superscript III Platinum enzyme) was the only enzyme tested given the expected negative results. Of the 25 tested strains, 24 strains were not reactive with the updated primers and probes. Cross-reactivity was observed with H1v/1A.3.3.3 strain A/Ohio/09/2015, however this cross-reactivity was previously documented with the IVD primer and probe set. The exclusivity results are presented in **Table 6** below.

**Table 6**: Exclusivity Results for the Modified Influenza A(pdmH1) Primers and Probes

| Subtype/Clade | Virus Designation | ID50/mL | pdmH1_v4 (ZEN) | pdmH1_v 4 (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[a] | 0/3 | 0/3 |

[a] Not Available

4. Cross-Reactivity

Cross-reactivity of the influenza A H1N1pdm09 primers and probes was evaluated to verify the modification does not impact the specificity of the assay design. The pdmH1 v4 assay was tested with 42 strains of non-influenza human respiratory viruses, bacteria, and yeast commonly found in human respiratory samples. Each microorganism was tested in the absence of target virus and tested in triplicate at high concentrations ($10^5$ or $10^6$ $ID_{50}$/ml or equivalent) using one enzyme (Invitrogen Superscript III Platinum enzyme). No cross-reactivity was observed for any strains tested. Results from the cross-reactivity study are presented in **Table 7** below.

**Table 7**: Results for the Modified Influenza A(pdmH1) Primers and Probes

| Virus | Strain | $TCID_{50}$/ml | Nucleic Acid Conc. | pdmH1_v4 (ZEN) | pdmH1_v4 (BHQ) |
|---|---|---|---|---|---|
| Influenza C | C/Minnesota/1/2016 | NA[a] | NA[a] | 0/3 | 0/3 |
| Influenza C | C/Minnesota/4/2015 | NA[a] | NA[a] | 0/3 | 0/3 |
| Influenza C | C/Minnesota/29/2015 | NA[a] | NA[a] | 0/3 | 0/3 |
| MERS-CoV | NA | NA[a] | $5.3 \times 10^5$ copies/µL | 0/3 | 0/3 |
| Human Coronavirus | OC43 | $8.9 \times 10^6$ | NA[a] | 0/3 | 0/3 |
| SARS-CoV-2 | NA | NA[1] | NA[a] | 0/3 | 0/3 |
| Human Coronavirus | 229E | $2.8 \times 10^6$ | NA[a] | 0/3 | 0/3 |
| Human Coronavirus | NL63 | $1.6 \times 10^4$ | NA[a] | 0/3 | 0/3 |
| Human Coronavirus | HKU1 | NA[a] | $5.5 \times 10^5$ copies/µL | 0/3 | 0/3 |
| Enterovirus | Echo 6 | $10^{6.9}$ | NA[a] | 0/3 | 0/3 |
| Human Adenovirus, type 1 | Ad.71 | $10^{9.2}$ | NA[a] | 0/3 | 0/3 |
| Human Adenovirus, type 7a | S-1058 | $10^{7.1}$ | NA[a] | 0/3 | 0/3 |
| Human Rhinovirus A | 1A | $10^{5.8}$ | NA[a] | 0/3 | 0/3 |
| Human Parainfluenza 1 virus | | NA[a] | 3.0 ng/µL | 0/3 | 0/3 |
| Human Parainfluenza 2 virus | Greer | $10^{3.1}$ | NA[a] | 0/3 | 0/3 |
| Human Parainfluenza 3 virus | C-243 | $10^{7.9}$ | NA[a] | 0/3 | 0/3 |
| Respiratory Syncytial virus | CH93-18b | $10^{6.8}$ | NA[a] | 0/3 | 0/3 |
| Herpes Simplex Virus | KOS | $5 \times 10^{7.75}$ | NA[a] | 0/3 | 0/3 |
| Varicella-zoster Virus | AV92-3:H | $5 \times 10^{3.75}$ | NA[a] | 0/3 | 0/3 |
| Epstein Barr Virus | B95-8 | NA[1] | 1.7 ng/µL | 0/3 | 0/3 |
| Measles Virus | Edmonston | $5 \times 10^{4.5}$ | NA[a] | 0/3 | 0/3 |
| Mumps Virus | Enders | $5 \times 10^{6.5}$ | NA[a] | 0/3 | 0/3 |
| Cytomegalovirus | AD-169 | $5 \times 10^{6.25}$ | NA[a] | 0/3 | 0/3 |
| **Bacteria/Yeast** | **Strain** | **CFU/mL** | **Nucleic Acid Conc.** | **pdmH1_v4 (ZEN)** | **pdmH1_v4 (BHQ)** |
| *Bordetella pertussis* | Tohama I | $10^{10}$ | NA[a] | 0/3 | 0/3 |

| | | | | | |
|---|---|---|---|---|---|
| *Candida albicans* | 3147 | $10^{8.49}$ | NA[a] | 0/3 | 0/3 |
| *Chlamydia pneumoniae* | CM-1 | 40 IFU/mL | NA[a] | 0/3 | 0/3 |
| *Corynebacterium diphtheriae* | NCTC 13129 | NA[a] | 57.4 ng/uL | 0/3 | 0/3 |
| *Escherichia coli* | K12 | $10^{9.6}$ | NA[a] | 0/3 | 0/3 |
| *Streptococcus pyogenes* | MGAS 8232 | NA[a] | 41 ug/mL | 0/3 | 0/3 |
| *Haemphilus influenzae* | M15709 | $10^{6.4}$ | NA[a] | 0/3 | 0/3 |
| *Lactobacillus plantarum* | NA | $10^{8.8}$ | NA[a] | 0/3 | 0/3 |
| *Legionella pneumophila* | Philadelphia-1 | $10^{8.41}$ | NA[a] | 0/3 | 0/3 |
| *Moraxella catarrhalis* | M15757 | $10^{9.5}$ | NA[a] | 0/3 | 0/3 |
| *Mycobacterium tuberculosis* | H37Ra | 100 | NA[a] | 0/3 | 0/3 |
| *Mycoplasma pneumoniae* | PS 1428 | $10^{9}$ | NA[a] | 0/3 | 0/3 |
| *Neisseria elongata* | NA | 100 | NA[a] | 0/3 | 0/3 |
| *Neisseria meningitidis* | M2578 | $10^{7.9}$ | NA[a] | 0/3 | 0/3 |
| *Pseudomonas aeruginosa* | NA | $10^{10.5}$ | NA[a] | 0/3 | 0/3 |
| *Staphylococcus aureus* | NA | $10^{10.7}$ | NA[a] | 0/3 | 0/3 |
| *Staphylococcus epidermidis* | NA | $10^{10.5}$ | NA[a] | 0/3 | 0/3 |
| *Streptococcus pneumoniae* | 249-06[b] | $10^{6.6}$ | NA[a] | 0/3 | 0/3 |
| *Streptococcus salivarius* | DSM 13084 | NA[a] | 109 ng/uL | 0/3 | 0/3 |

[a] Not Available
[b] Blood from Thailand

5. Clinical Testing

Retrospective Study

The clinical performance of the pdmH1_v4 assay was evaluated using residual human upper respiratory specimens (nasopharyngeal swabs (NPS), throat swabs (TS), and nasal swabs (ANS)) in Viral Transport Media (VTM) collected during previous influenza seasons in the United States that were previously sequenced through the Influenza Division surveillance program. The modified assay was tested against a set of positive and negative specimen panels. Due to the potential decrease in sensitivity for strains containing the mutation with the cleared pdmH1_IVD primers and probe, Next Generation Sequencing (NGS) was used to confirm the identity of positive and negative specimens.

The positive specimen panel consisted of 61 influenza A(H1)pdm09 specimens, 58 confirmed by NGS to contain the current mutations and 3 confirmed not to contain the mutations. The negative specimen panel consisted of 60 specimens from symptomatic patients known to be positive for influenza H3N2. RNA was extracted using the Qiagen EZ1 instrument, and 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 calculating positive percent agreement (PPA) and negative percent agreement (NPA) for both assay versions and can be found in **Table 8** and **Table 9**. Both PPA and NPA were found to perform better or equal to the FDA-cleared assay.

**Table 8**: Modified pdmH1 Primers and Probe Retrospective Clinical Evaluation- Positive Agreement

| Primer/Probe Set | Invitrogen Superscript III | | Quanta qScript | |
|---|---|---|---|---|
| | # of Positives[a] | % Positive Agreement (95% CI) | # of Positives[a] | % Positive Agreement (95% CI) |
| pdmH1_v4 (ZEN) | 61/61 | 100% (94.1%-100%) | 61/61 | 100% (94.1%-100%) |
| pdmH1_v4 (BHQ) | 61/61 | 100% (94.1%-100%) | 61/61 | 100% (94.1%-100%) |
| pdmH1_IVD | 60/61 | 98.4% (91.3%-99.7%) | 60/61 | 98.4% (91.3%-99.7%) |

[a] Proportion of positive specimens correctly identified versus the comparator (NGS)

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

| Primer/Probe Set | Invitrogen Superscript III | | Quanta qScript | |
|---|---|---|---|---|
| | # of Negatives[a] | % Negative Agreement (95% CI) | # of Negatives[a] | % Negative Agreement (95% CI) |
| pdmH1_v4 (ZEN) | 60/60 | 100% (94.0%-100%) | 60/60 | 100% (94.0%-100%) |
| pdmH1_v4 (BHQ) | 60/60 | 100% (94.0%-100%) | 60/60 | 100% (94.0%-100%) |
| pdmH1_IVD | 60/60 | 100% (94.0%-100%) | 60/60 | 100% (94.0%-100%) |

[a] Proportion of positive specimens correctly identified versus the comparator (NGS)

## D Acceptance Criteria

Analytical and clinical data demonstrate that the performance of the device to detect influenza A H1N1 pdm09 viruses is accomplished with high positive and negative percent agreement (100%) in a manner substantially equivalent to the predicate. The changes rise no new issues of safety and effectiveness and the indications for use remain the same.

## E Summary of Results

| Device Modification | Identified Risk | Hazardous Situation | Consequence | Risk Control Measure | Risk Acceptability Criteria | Verification Method | Summary Conclusion |
|---|---|---|---|---|---|---|---|
| Influenza A pdmH1 oligonucleotide reagents are updated to | Modified oligonucleotides may demonstrate variable | Some influenza pdmH1 strains may not be detected in | Humans infected with influenza A pdmH1 strains may not be | Characterization of the performance of the modified | Updated assay will detect circulating influenza A pdmH1 strains | Analytical and clinical performance testing using established | Results demonstrated that the modified device detects |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ensure reactivity of assays with current circulating influenza A(pdmH1) strains. | reactivity among different influenza A pdmH1 strains | human specimens. | identified in a timely manner. Reduced capability in influenza surveillance. | device with representative influenza A pdmH1 strains. | at equal or improved levels of sensitivity and specificity compared to the originally cleared device. | methods consistent with the methods used to establish performance with the originally cleared device. | influenza A pdmH1 strains at equal or improved levels of reactivity to the original cleared device. Risk is mitigated to an acceptable level. |
| CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit package labeling and package inserts. | Differences exist between the package labeling of the currently cleared device and kits of the updated CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit. | Short term risk of confusing components of the currently cleared CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit. | End user confusing components from different versions could impact ability to accurately detect influenza A viruses. | A product update communication will be distributed instructing end users to transition to the updated kit. Currently distributed kits will expire, and older inventory will no longer be available to the end user. | CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit package labeling and package insert will provide part numbers of new components. | Appropriate package labeling and package insert instructions will be verified against product components by the end user upon receipt per CLIA requirements. | Risk of commingling and/or confusing components of currently cleared CDC Human Influenza Real-Time RT-PCR Diagnostic Panel, Influenza A Subtyping Kit is mitigated to an acceptable level. |
| CDC Human Influenza Real-Time RT-PCR Diagnostic Panel IFUs to reflect the pause in distribution of the Influenza B Lineage Genotyping kit | Distribution of the Influenza B Lineage Genotyping test is being stopped since the Influenza B Yamagata strain has not been detected since 2020. Updated test algorithm is different from the currently cleared IFU. | There is a low possibility that the B Yamagata strain could reemerge and not be detected by state public health laboratories using the diagnostic | Identification of an emerged Influenza B Yamagata strain would be missed through testing with the RT-PCR panel. | NGS surveillance at CDC is constantly monitoring circulating influenza strains and would identify a reemergence of B Yamagata or another variant(s) that might emerge. As the Influenza B Lineage Genotyping kit is remaining on the cleared diagnostic panel the kit can be brought back to production | Impact to patient care in the event of reemergence is negligible. Acceptable monitoring of strains for variants means low risk of missing reemergence of B Yamagata. | Genotyping of Influenza B does not impact patient treatment as it is the same regardless of strain. Therefore, patient care is not impacted as the AB Typing kit will still be used to diagnose influenza. Risk to patient care is low. NGS Influenza surveillance activities that look for variants will remain in place to | Risk is at an acceptable level. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | quickly if needed. | | monitor for the reemergence of the Yamagata strain. Risk to missing reemergence is negligible. | |

**VIII Proposed Labeling:**

The labeling supports the finding of substantial equivalence for this device.

**IX Review Summary:**

This 510(k) submission contains information/data on modifications made to the submitter's own CLASS II device requiring 510(k). The following items are present and acceptable.

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.

2. Submitter's statement that the **INDICATIONS FOR USE/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed. This change was for updates to the influenza A H1N1 pdm09 virus primer and probe sequences that address evolutionary changes in the current circulating influenza strains.**

4. Comparison Information (i.e., similarities and differences) to the submitter's legally marketed predicate device including, labeling, intended use, and physical characteristics.

5. A Design Control Activities Summary which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied.

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as

specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.