July 30, 2018

Centers for Disease Control and Prevention (CDC)
Yon Yu, Pharm.D.
Associate Director for Regulatory Affairs
1600 Clifton Road
Ms E-51
Atlanta, GA 30329-4027

Re: K181736
Trade/Device Name: CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: 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, NSU, OOI
Dated: June 29, 2018
Received: July 2, 2018

Dear Yon Yu:

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

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

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

Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven R. Gitterman -S for

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K181736

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

Indications for Use *(Describe)*

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

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

Performance characteristics for influenza B lineage genotyping were established during a season when influenza B/ Victoria and B/Yamagata lineages were 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.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

8. 510(k) Summary

I. GENERAL INFORMATION

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

Contact Person:
CDR Yon Yu, Pharm. D.
Associate Director for Regulatory Affairs
Office of the Director
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton RD, MS E-51; Atlanta, GA 30329-4027 Phone: 404-639-3046
Fax: 404-498-1106
Email: fkb8@cdc.gov

Date Prepared: June 28, 2018

II. DEVICE INFORMATION

Proprietary Name:	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: Influenza B Lineage Genotyping Kit (VER 1.1) and Influenza B Lineage Genotyping Kit (VER 2)
Common Name:	Influenza B Lineage Genotyping Kit
Regulation Section:	866.3980-Respiratory viral panel multiplex nucleic acid assay
Subsequent Regulation Sections:	862.2570-Instrumentation for clinical multiplex systems
Device Classification:	Class II
Product Code:	OZE
Subsequent Product Codes:	NSU, OOI
Panel:	Microbiology

III. PREDICATE DEVICE

CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: Influenza B Lineage Genotyping Kit (K172091)

IV. DEVICE DESCRIPTION

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

V. INTENDED USE

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

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

Performance characteristics for influenza B lineage 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 modified CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel- Influenza B Lineage Genotyping Kit (VER 1.1. and VER 2) remain the same as the predicate device. Modifications were made primarily to address recent evolutionary changes in circulating influenza B viruses that may impact the reactivity of the current Influenza B Lineage Genotyping Kit. Two design approaches were evaluated that address specific genetic mutations in the targeted hemagglutinin (HA) gene of influenza B viruses.

CDC also evaluated the ZEN™ Double-Quenched Probe technology (manufactured by Integrated DNA Technologies) as an alternate fluorescent hydrolysis probe quencher chemistry for the InfB assay of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel.

VII. SUBSTANTIAL EQUIVALENCE COMPARISON

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza B Lineage Genotyping Kit (K172091), will serve as the predicate for the proposed change. See table 8-1 below for a detailed comparison of the modified device to the predicate.

Table 8-1: Device Comparison

	Predicate Device	Proposed Device
Item	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza B Lineage Genotyping Kit [K172091]**	**CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel, Influenza B Lineage Genotyping Kit (VER 1.1 and VER 2)**
Intended Use	The Influenza B Lineage Genotyping Kit contains reagents and controls of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel and is intended for use in real-time RT-PCR (rRT-PCR) assays on an Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR instrument in conjunction with clinical and epidemiological information: • For the determination of the genetic lineage of human influenza B viruses as B/Victoria or B/Yamagata lineage from viral RNA in upper respiratory tract clinical specimens (including nasopharyngeal swabs [NPS], nasal swabs [NS], throat swabs [TS], nasal aspirates [NA], nasal washes [NW] and dual nasopharyngeal/throat swabs [NPS/TS]) from human patients with signs and symptoms of respiratory infection and/or from viral culture; • To provide epidemiologic information for surveillance of circulating influenza viruses. Performance characteristics for influenza B lineage genotyping were established during a season when influenza B/Victoria and B/Yamagata lineages were found in approximately equal proportion. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Conversely, positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. All users, analysts, and any person reporting results from use of this device should be trained to perform and interpret the results from this procedure by a competent instructor prior to use. CDC Influenza Division will limit the distribution of this device to only those users who have successfully completed a training course provided by CDC instructors or designees.	Same
Organism Detected	Influenza B virus, lineages B/Victoria and B/Yamagata	Same
Specimen Types	Nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes and dual nasopharyngeal/throat swabs from human patients with signs and symptoms of respiratory infection and/or from viral culture	Same
Technological Characteristics	Real-time RT-PCR based assay	Same
Nucleic Acid Extraction	• QIAamp® DSP Viral RNA Mini Kit, QIAGEN • MagNA Pure Compact –Nucleic Acid Isolation Kit I, Roche • MagNA Pure Compact – RNA Isolation Kit, Roche • MagNA Pure LC – Total Nucleic Acid Kit, Roche • QIAcube – QIAamp® DSP Viral RNA Mini Kit, QIAGEN • NucliSENS® easyMAG®, bioMérieux • EZ1 Advanced XL – EZ1 DSP Virus Kit and EZ1 RNA Tissue Mini Kit, QIAGEN • MagNA Pure 96 - DNA and Viral NA Small Volume Kit, Roche	Same
Enzyme Master Mix	Invitrogen SuperScript™ III Platinum® One-Step Quantitative RT-PCR Kit (with or without ROX) **OR**	Same

	Quanta BioSciences qScript™ One-Step qRT-PCR Kit, Low ROX	
Required Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDS software version 1.4	Same
Probe Quenching Molecule	Black Hole Quencher Probe® (BHQ-1) [InfB assay] Black Hole Quencher Plus (BHQ*Plus*) [VIC, YAM assays]	ZEN™ or BHQ-1 (InfB assay) BHQ*Plus* or BHQ-1 (VIC, YAM assays)

VIII. ANALYTICAL PERFORMANCE EVALUATION

Analytical Sensitivity - Influenza B Assay

A range finding study was performed to demonstrate LOD equivalency between the currently cleared InfB assay probe quenched with BHQ and the same probe quenched with ZEN. Two characterized influenza vaccine reference viruses of a known 50% egg infectious dose titer (EID_{50}/mL) were extracted using the Roche MagNA Pure Compact RNA Isolation Kit. The RNA was serially diluted and tested (n=3 replicates) in order to determine the apparent endpoint range using both enzymes cleared for use with the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. The acceptance criterion for LOD equivalency was defined as demonstrating 100% positivity (3 out of 3 replicates) at either the same endpoint LOD concentration or within a 5-fold dilution of each other. All assays demonstrated similar reactivity (Tables 8-2 and 8-3).

Table 8-2: Influenza B (InfB) Assay LOD Equivalency - B/Nevada/03/2011

Influenza B/Nevada/03/2011 Titer (EID_{50}/mL)	Invitrogen Superscript™		Quanta qScript™	
	InfB (BHQ) IVD	InfB (ZEN)	InfB (BHQ) IVD	InfB (ZEN)
$10^{4.2}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.1}$	1/3 (+)	1/3 (+)	0/3 (-)	0/3 (-)
$10^{1.4}$	2/3 (+)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.7}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.0}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

Table 8-3: Influenza B (InfB) Assay LOD Equivalency - B/Wisconsin/1/2010

Influenza B/Wisconsin/1/2010 Titer (EID_{50}/mL)	Invitrogen Superscript™		Quanta qScript™	
	InfB (BHQ) IVD	InfB (ZEN)	InfB (BHQ) IVD	InfB (ZEN)
$10^{4.2}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.8}$	1/3 (+)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{2.1}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{1.4}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.7}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.0}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

Analytical Sensitivity- Influenza B Lineage Genotyping Assay Update

A range finding study was performed with the currently cleared assays of the Influenza B Lineage Genotyping Kit and with modified VIC and YAM assays (VER 1.1) as well as newly designed VIC and YAM assays (VER 2). These studies were performed to demonstrate the LOD equivalency and improved reactivity of the VER 1.1 and VER 2 VIC and YAM assays with one historical benchmark strain and one current strain of both the B/Victoria and B/Yamagata lineages of influenza B virus. The test samples consisted of serially diluted RNA extracted with the Roche MagNA Pure Compact RNA Isolation Kit from characterized virus stocks of known 50% egg infectious dose titer (EID_{50}/mL). Three replicates per dilution were tested to determine the apparent endpoint range (Tables 8-4 to 8-7) using both enzymes cleared for use with the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. The acceptance criterion for LOD equivalency was defined as demonstrating 100% positivity (3 out of 3 replicates) at either the same endpoint LOD concentration or within a 5-fold dilution of each other. All assays demonstrated similar reactivity with apparent LOD endpoints within one 5-fold dilution of each other.

Table 8-4: B/Victoria Assay LOD Equivalency- VER 1.1 and VER 2 Designs - B/Nevada/03/2011

Influenza B/Nevada/03/2011 Titer (EID_{50}/mL)	Invitrogen Superscript™				Quanta qScript™			
	InfB IVD	VIC IVD	VIC VER 1.1	VIC VER 2	InfB IVD	VIC IVD	VIC VER 1.1	VIC VER 2
$10^{4.2}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.4}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	0/3 (+)	3/3 (+)	3/3 (+)
$10^{0.7}$	1/3 (+)	0/3 (-)	2/3 (+)	3/3 (+)	0/3 (-)	0/3 (+)	1/3 (+)	0/3 (-)
$10^{0.0}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{-0.7}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

Table 8-5: B/Victoria Assay LOD Equivalency- VER 1.1 and VER 2 Designs - B/Maryland/15/2016

Influenza B/Maryland/15/2016 Titer (EID_{50}/mL)	Invitrogen Superscript™				Quanta qScript™			
	InfB IVD	VIC IVD	VIC VER 1.1	VIC VER 2	InfB IVD	VIC IVD	VIC VER 1.1	VIC VER 2
$10^{4.5}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.4}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.7}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	2/3 (+)	3/3 (+)	3/3 (+)
$10^{1.0}$	3/3 (+)	0/3 (-)	3/3 (+)	3/3 (+)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.3}$	1/3 (+)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{-0.4}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

Table 8-6: B/Yamagata Assay LOD Equivalency- VER 1.1 and VER 2 Designs - B/Texas/06/2011

Influenza B/Texas/06/2011 Titer (EID_{50}/mL)	Invitrogen Superscript™				Quanta qScript™			
	InfB IVD	YAM IVD	YAM VER 1.1	YAM VER 2	InfB IVD	YAM IVD	YAM VER 1.1	YAM VER 2
$10^{4.9}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{4.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	2/3 (+)	3/3 (+)
$10^{2.8}$	3/3 (+)	3/3 (+)	0/3 (-)	3/3 (+)	3/3 (+)	2/3 (+)	0/3 (-)	3/3 (+)
$10^{2.1}$	2/3 (+)	1/3 (+)	1/3 (+)	1/3 (+)	0/3 (-)	2/3 (+)	0/3 (-)	2/3 (+)
$10^{1.4}$	2/3 (+)	0/3 (-)	0/3 (-)	1/3 (+)	0/3 (-)	1/3 (+)	0/3 (-)	2/3 (+)
$10^{0.7}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)
$10^{0.0}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

Table 8-7: B/Yamagata Assay LOD Equivalency- VER 1.1 and VER 2 Designs - B/Texas/81/2016

Influenza B/Texas/81/2016 Titer (EID_{50}/mL)	Invitrogen Superscript™				Quanta qScript™			
	InfB IVD	YAM IVD	YAM VER 1.1	YAM VER 2	InfB IVD	YAM IVD	YAM VER 1.1	YAM VER 2
$10^{4.3}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{3.6}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{2.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
$10^{1.5}$	3/3 (+)	2/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)	1/3 (+)	2/3 (+)
$10^{0.8}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	1/3 (+)	0/3 (-)	0/3 (-)
$10^{0.1}$	1/3 (+)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	2/3 (+)	0/3 (-)	0/3 (-)
$10^{-0.6}$	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)	0/3 (-)

*Indicates number of positive replicates out of three total.

A confirmation of the LOD for each modified or new assay was performed using a current strain of the corresponding influenza B/Victoria or B/Yamagata lineage. The VER 1.1 and VER 2 VIC and YAM primer and probe sets were tested alongside the currently cleared InfB assay as required for interpretation by the routine testing algorithm. The confirmatory LOD testing for each primer and probe set was performed on extraction replicates (n=20) of each dilution. The lowest virus concentration where InfB and VIC or InfB and YAM primer and probes sets demonstrated ≥ 95% detection is reported as the LOD for each virus (Table 8-8).

Table 8-8: LOD Confirmation Summary

Influenza B Lineage	Influenza Strain Designation	Assay Design	LOD (EID_{50}/mL)	
			Invitrogen SuperScript™	Quanta qScript™
Victoria	B/Maryland/15/2016	VER 1.1	$10^{1.7}$	$10^{1.7}$
		VER 2	$10^{1.7}$	$10^{1.7}$
Yamagata	B/Texas/81/2016	VER 1.1	$10^{2.2}$	$10^{1.5}$
		VER 2	$10^{2.2}$	$10^{1.5}$

Analytical Sensitivity – Inclusivity

Inclusivity testing was performed to demonstrate the capability of the modified VER 1.1 and VER 2 VIC and YAM primer and probe sets to detect strains of the corresponding influenza B lineage at or near the established LOD. Ten influenza B viruses of each lineage and representative of different geographic locations and phylogenetic clades were selected. Characterized stocks were serially diluted to concentrations near the LOD of the assays and extracted using the Roche MagNA Pure Compact RNA Isolation Kit. Samples were tested in triplicate with the VER 1.1 and VER 2 VIC and YAM assays with both enzyme systems cleared for use with the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. The inclusivity results are summarized in Tables 8-9 and 8-10.

Table 8-9: B/Victoria Assay Inclusivity VER 1.1 and VER 2 Designs

Influenza Virus Strain Designation	EID_{50}/mL or $TCID_{50}$/mL	Invitrogen SuperScript™		Quanta qScript™	
		VIC VER 1.1	VIC VER 2	VIC VER 1.1	VIC VER 2
B/Hong Kong/259/2010	$10^{1.2}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Bolivia/1526/2010	$10^{2.4}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Laos/89/2011	$10^{1.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Michigan/09/2011	$10^{1.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/New Jersey/01/2012	$10^{1.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Montana/05/2012	$10^{2.4}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Texas/02/2013	$10^{2.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Florida/103/2016	$10^{0.3}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Florida/76/2016	$10^{1.5}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Hong Kong/269/2017	$10^{-0.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)

*Indicates number of positive replicates out of three total.

Table 8-10: B/Yamagata Assay Inclusivity VER 1.1 and VER 2 Designs

Influenza Virus Strain Designation	EID_{50} /mL or $TCID_{50}$/mL	Invitrogen SuperScript™		Quanta qScript™	
		YAM VER 1.1	YAM VER 2	YAM VER 1.1	YAM VER 2
B/Brisbane/03/2007	$10^{2.4}$	3/3* (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Pennsylvania/07/2007	$10^{2.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Hubei-Wujiagang/158/2009	$10^{2.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Wisconsin/01/2010	$10^{2.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Finland/39/2010	$10^{2.1}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Estonia/55669/2011	$10^{2.8}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Taiwan/1242/2011	$10^{3.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Massachusetts/02/2012	$10^{2.2}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Phuket/3073/2013	$10^{2.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)
B/Guangdong-Liwan/1133/2014	$10^{3.9}$	3/3 (+)	3/3 (+)	3/3 (+)	3/3 (+)

*Indicates number of positive replicates out of three total.

Analytical Specificity – Cross-Reactivity

Cross-reactivity of the modified VER 1.1 and VER 2 VIC and YAM primer and probe sets was evaluated by testing each set with influenza B viruses of the opposite lineage and from diverse geographic locations. Samples were extracted from high titer preparations of viruses ($\geq 10^6$ EID_{50} or $TCID_{50}$/mL) using the Roche MagNA Pure Compact RNA Isolation Kit. Cross-reactivity was evaluated with both enzyme systems cleared for use with the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel. No cross-reactivity was detected with either primer and probe set design (Tables 8-11 and 8-12).

Table 8-11: B/Victoria Assay Cross-Reactivity VER 1.1 and VER 2 Designs

Influenza Virus Strain Designation B/Yamagata Lineage	EID_{50}/mL or $TCID_{50}$/mL	Invitrogen SuperScript™		Quanta qScript™	
		VIC VER 1.1	VIC VER 2	VIC VER 1.1	VIC VER 2
B/Brisbane/03/2007	$10^{8.2}$	-	-	-	-
B/Pennsylvania/07/2007	$10^{8.4}$	-	-	-	-
B/Hubei-Wujiagang/158/2009	$10^{6.2}$	-	-	-	-
B/Wisconsin/01/2010	$10^{8.5}$	-	-	-	-
B/Finland/39/2010	$10^{8.9}$	-	-	-	-
B/Estonia/55669/2011	$10^{8.4}$	-	-	-	-
B/Taiwan/1242/2011	$10^{9.1}$	-	-	-	-
B/Massachusetts/02/2012	$10^{6.3}$	-	-	-	-
B/Phuket/3073/2013	$10^{6.5}$	-	-	-	-
B/Guangdong-Liwan/1133/2014	$10^{4.2}$	-	-	-	-

Table 8-12: B/Yamagata Assay Cross-Reactivity VER 1.1 and VER 2 Designs

Influenza Virus Strain Designation B/Victoria Lineage	EID_{50}/mL or $TCID_{50}$/mL	Invitrogen SuperScript™		Quanta qScript™	
		YAM VER 1.1	YAM VER 2	YAM VER 1.1	YAM VER 2
B/Hong Kong/259/2010	$10^{8.4}$	-	-	-	-
B/Bolivia/1526/2010	$10^{8.2}$	-	-	-	-
B/Laos/89/2011	$10^{8.2}$	-	-	-	-
B/Michigan/09/2011	$10^{8.9}$	-	-	-	-
B/New Jersey/01/2012	$10^{8.1}$	-	-	-	-
B/Montana/05/2012	$10^{7.8}$	-	-	-	-
B/Texas/02/2013	$10^{9.9}$	-	-	-	-
B/Florida/103/2016	$10^{9.2}$	-	-	-	-
B/Florida/76/2016	$10^{9.9}$	-	-	-	-
B/Hong Kong/269/2017	$10^{9.9}$	-	-	-	-

Analytical Specificity – Exclusivity

Exclusivity with Influenza A Viruses

Exclusivity of the VER 1.1 and VER 2 VIC and YAM assays was examined with influenza A viruses of various subtypes that circulate in humans and from animal origin that infect humans (Table 8-13 and 8-14). Samples were prepared from characterized, high titer stocks ($\geq 10^6$ TCID50 or EID50/mL) by extracting RNA using the Roche MagNA Pure Compact RNA Isolation Kit. Testing was performed using both of the currently cleared enzyme systems.

Table 8-13: Exclusivity with Influenza A Viruses- VER 1.1 and VER 2 -Invitrogen SuperScript™

Influenza Virus Strain Designation	Origin	Subtype	EID_{50}/mL or $TCID_{50}$/mL	Invitrogen SuperScript™			
				VIC VER 1.1	VIC VER 2	YAM VER 1.1	YAM VER 2
A/Michigan/45/2015	Human	A(H1N1) pdm09	$10^{8.3}$	-	-	-	-
A/Hong Kong/4801/2014	Human	A(H3N2)	$10^{7.9}$	-	-	-	-
A/Ohio/35/2017	Swine	A(H1N2)v	$10^{6.9}$	-	-	-	-
A/Ohio/13/2017	Swine	A(H3N2)v	$10^{6.9}$	-	-	-	-
A/gyrfalcon/ Washington/ 41088-6/2014	Avian	A(H5N8)	$10^{9.75}$	-	-	-	-
A/Northern pintail/Washington/ 40964/2014	Avian	A(H5N2)	$10^{9.4}$	-	-	-	-
A/Bangladesh/ 0994/2011	Avian	A(H9N2)	$10^{10.5}$	-	-	-	-
A/Anhui/01/2013	Avian	A(H7N9)	$10^{10.9}$	-	-	-	-

Table 8-14: Exclusivity with Influenza A Viruses- VER 1.1 and VER 2 -Quanta qScript™

Influenza Virus Strain Designation	Origin	Subtype	EID_{50}/mL or $TCID_{50}$/mL	Quanta qScript™			
				VIC VER 1.1	VIC VER 2	YAM VER 1.1	YAM VER 2
A/Michigan/45/ 2015	Human	A(H1N1) pdm09	$10^{8.3}$	-	-	-	-
A/Hong Kong/4801/2014	Human	A(H3N2)	$10^{7.9}$	-	-	-	-
A/Ohio/35/2017	Swine	A(H1N2)v	$10^{6.9}$	-	-	-	-
A/Ohio/13/2017	Swine	A(H3N2)v	$10^{6.9}$	-	-	-	-
A/gyrfalcon/ Washington/ 41088-6/2014	Avian	A(H5N8)	$10^{9.75}$	-	-	-	-
A/Northern pintail/Washington/ 40964/2014	Avian	A(H5N2)	$10^{9.4}$	-	-	-	-
A/Bangladesh/ 0994/2011	Avian	A(H9N2)	$10^{10.5}$	-	-	-	-
A/Anhui/01/2013	Avian	A(H7N9)	$10^{10.9}$	-	-	-	-

Exclusivity with Non-Influenza Respiratory Pathogens

Exclusivity of the VER 2 VIC and YAM assays was examined with non-influenza human respiratory viruses, bacteria, and yeast (Table 8-15). Nucleic acids were extracted using the Roche MagNA Pure Compact RNA Isolation Kit from 36 organisms (16 viruses, 19 bacteria, and 1 yeast) representing common respiratory pathogens or flora commonly present in specimens collected from the nasopharynx region. All bacteria, yeast, and non-influenza viruses were from CDC repositories or acquired from American Type Culture Collection (ATCC, Manassas, VA) and tested at high titers, typically $\geq 10^6$ $TCID_{50}$ or EID_{50}/mL, $\geq 10^6$ CFU/mL, or as high as culture allowed. Testing was performed using both of the currently cleared enzyme systems.

Table 8-15: Assay Exclusivity with Respiratory Viruses, Bacteria, and Yeast- VER 2 Design

Organism Tested			SuperScript		qScript	
Bacteria and Yeast	Strain	cfu / mL	VIC VER2	YAM VER2	VIC VER2	YAM VER2
Bordetella pertussis	A639	$10^{8.3}$	-	-	-	-
Candida albicans	2001-21-196	$10^{8.8}$	-	-	-	-
Chlamydia pneumoniae[1]	TW183	40 IFU/mL	-	-	-	-
Corynebacterium diphtheriae	NA[2]	10^{10}	-	-	-	-
Escherichia coli	K12	$10^{9.6}$	-	-	-	-
Haemophilus influenzae	M15709	$10^{6.4}$	-	-	-	-
Lactobacillus plantarum	NA	$10^{8.8}$	-	-	-	-
Legionella pneumophila	NA	$10^{10.3}$	-	-	-	-
Moraxella catarrhalis	M15757	$10^{9.5}$	-	-	-	-
Mycobacterium tuberculosis[3]	H37Rv	95 ng/ µL	-	-	-	-
Mycoplasma pneumoniae	MI-29	$10^{7.7}$	-	-	-	-
Neisseria elongata	NA	$10^{8.6}$	-	-	-	-
Neisseria meningitidis	M2578	$10^{7.9}$	-	-	-	-
Pseudomonas aeruginosa	NA	$10^{10.5}$	-	-	-	-
Staphylococcus epidermidis	NA	$10^{10.5}$	-	-	-	-
Staphylococcus aureus	NA	$10^{10.7}$	-	-	-	-
Streptococcus pneumoniae	249-06 (Thailand)	$10^{6.6}$	-	-	-	-
Streptococcus pyogenes	7790-06	$10^{7.5}$	-	-	-	-
Streptococcus salivarius	SS1672	$10^{8.4}$	-	-	-	-
Viruses	Strain	EID_{50} /mL or $TCID_{50}$/mL	VIC VER2	YAM VER2	VIC VER2	YAM VER2
Enterovirus	Echo 6	$10^{6.9}$	-	-	-	-
Human Adenovirus, type 1	Ad.71	$10^{9.2}$	-	-	-	-
Human Adenovirus, type 7a	S-1058	$10^{7.1}$	-	-	-	-
Human Coronavirus virus[3]	OC43	50.4 ng /µL	-	-	-	-
Human Coronavirus virus[3]	299E	31.6 ng /µL	-	-	-	-
Human Rhinovirus A	1A	$10^{5.8}$	-	-	-	-
Human Parainfluenza 1 virus[3]	NA	3.0 ng/ µL	-	-	-	-
Human Parainfluenza 2 virus	Greer	$10^{3.1}$	-	-	-	-
Human Parainfluenza 3 virus	C-243	$10^{7.9}$	-	-	-	-
Respiratory Syncytial virus	CH93-18b	$10^{6.8}$	-	-	-	-
Herpes Simplex Virus	KOS	$10^{8.4}$	-	-	-	-
Varicella-zoster Virus	AV92-3	$10^{4.4}$	-	-	-	-
Epstein Barr Virus[3]	B95-8	1.7 ng/µL	-	-	-	-
Measles Virus	Edmonston	$10^{5.2}$	-	-	-	-
Mumps Virus	Enders	$10^{7.2}$	-	-	-	-
Cytomegalovirus	AD-169	$10^{6.9}$	-	-	-	-

[1] Organism quantified by Infectious Forming Units (IFU)

[2] NA = not applicable

[3] Organism quantified by spectrophotometry (ng/µL)

IX. CLINICAL PERFORMANCE EVALUATION

Influenza B Assay –Retrospective Study

The clinical performance of the InfB oligonucleotide probe quenched with ZEN was evaluated using retrospective clinical samples collected during the 2011-2012 influenza season that were previously determined to be positive or negative for influenza B virus. A total of 30 positive and 50 negative upper respiratory tract samples were evaluated with the cleared InfB assay using either the existing oligonucleotide probe quenched with BHQ or the investigational probe quenched with ZEN. Testing was performed with both enzymes cleared for use with the CDC Human Influenza Real-Time RT-PCR Diagnostic Panel and one of the currently cleared extraction methods. Result interpretation followed the instructions of the Package Insert for the cleared Influenza B Lineage Genotyping Kit. The InfB assay containing the investigational probe quenched with ZEN demonstrated 100% positive and negative agreement with the cleared oligonucleotide probe quenched with BHQ (Tables 8-16 and 8-17).

Table 8-16: InfB Assay-Retrospective Positive Clinical Study Results

	Invitrogen SuperScript™		Quanta qScript™	
Specimen Type	# of Positives[1]	% Positive Agreement (95% CI)	# of Positives[1]	% Positive Agreement (95% CI)
NPS, NS	18/18	100.0 (82.4-100.0)	18/18	100.0 (82.4-100.0)
NPS/TS	11/11	100.0 (74.1-100.0)	11/11	100.0 (74.1-100.0)
NW	1/1	100.0 (20.7-100.0)	1/1	100.0 (20.7-100.0)
Total	30/30	100.0 (88.7-100.0)	30/30	100.0 (88.7-100.0)

[1]Proportion of positive samples correctly identified versus the comparator.

Table 8-17: InfB Assay-Retrospective Negative Clinical Study Results

	Invitrogen SuperScript™		Quanta qScript™	
Specimen Type	# of Negatives[1]	% Negative Agreement (95% CI)	# of Negatives[1]	% Negative Agreement (95% CI)
NPS, NS	48/48	100.0 (92.6-100.0)	48/48	100.0 (92.6-100.0)
TS	2/2	100.0 (34.2-100.0)	2/2	100.0 (34.2-100.0)
Total	50/50	100.0 (92.9-100.0)	50/50	100.0 (92.9-100.0)

[1]Proportion of negative samples correctly identified versus the comparator.

Influenza B Lineage Genotyping Kit (VER 2) – Prospective Study

A prospective clinical investigation was conducted at 3 U.S. public health laboratories using upper respiratory tract specimens collected during the 2016-2017 influenza season. Samples were taken from specimens collected for routine influenza testing at each site from individuals symptomatic for influenza-like illness. The range of patient ages and specimen types for the total of 592 samples collected are represented in Table 8-18. A total of 13 were excluded for reasons of unspecified specimen type, inconclusive result of the comparator, or technician testing error. A total of 579 upper respiratory tract specimens were included in the data analysis.

Table 8-18: Specimen Information

Patient Age	Totals
0-16	149
17-54	192
≥55	249
Not Reported	2
Specimen Type[1]	Totals
NPS	374
NPS/TS	44
NA	12
NW	34
TS	13
NS	114
Not Reported	1

[1] NPS=nasopharyngeal swab, NPS/TS=dual nasopharyngeal and throat swab, NA=nasal aspirate, NW=nasal wash, TS=throat swab, NS=nasal swab

Specimens were tested with assays from the FDA-cleared CDC Human Influenza Real-Time RT-PCR Diagnostic Panel and the investigational Influenza B Lineage Genotyping Kit (VER 2). The performance is summarized in Tables 8-19 and 8-20. Due to the low prevalence of influenza B/Victoria lineage viruses in specimens collected during the prospective study, the performance of the Influenza B Lineage Genotyping Kit (VER 2) was also evaluated in a retrospective study.

Table 8-19: B/Victoria Assay - VER 2 Design- Prospective Study Results

Specimen Type[1]	# of Positives[2]	% Sensitivity (95% CI)	# of Negatives[3]	% Specificity (95% CI)
NPS, NS	5/5	100.0 (56.6 – 100.0)	472/472	100.0 (99.2 - 100.0)
NPS/TS	0/0	NA[4]	44/44	100.0 (92.0 - 100.0)
TS	0/0	NA	13/13	100.0 (77.2 – 100.0)
NA, NW	0/0	NA	45/45	100.0 (92.1 – 100.0)
Total[5]	5/5	100.0 (56.6 – 100.0)	574/574	100.0 (99.3 – 100.0)

[1] NPS=nasopharyngeal swab, NPS/TS=dual nasopharyngeal and throat swab, NA=nasal aspirate, NW=nasal wash, TS=throat swab, NS=nasal swab
[2]Proportion of positive samples correctly identified versus the comparator.
[3]Proportion of negative samples correctly identified versus the comparator.
[4]NA=not applicable

Table 8-20: B/Yamagata Assay - VER 2 Design - Prospective Study Results

Specimen Type[1]	# of Positives[2]	% Sensitivity (95% CI)	# of Negatives[3]	% Specificity (95% CI)
NPS, NS	31/31	100.0 (89.0 – 100.0)	446/446	100.0 (99.1 - 100.0)
NPS/TS	2/2	100.0 (34.2 – 100.0)	42/42	100.0 (91.6 - 100.0)
TS	0/0	NA[4]	13/13	100.0 (77.2 – 100.0)
NA, NW	5/5	100.0 (56.6 – 100.0)	39/40	97.5 (87.1 – 99.6)
Total[5]	38/38	100.0 (90.8 – 100.0)	540/541	99.8 (99.0 – 100.0)

[1] NPS=nasopharyngeal swab, NPS/TS=dual nasopharyngeal and throat swab, NA=nasal aspirate, NW=nasal wash, TS=throat swab, NS=nasal swab
[2]Proportion of positive samples correctly identified versus the comparator.
[3]Proportion of negative samples correctly identified versus the comparator.
[4]NA=not applicable

Influenza B Lineage Genotyping Kit VER 1.1 and VER 2 - Retrospective Study Results

A retrospective study was performed using the VER 1.1 and VER 2 VIC and YAM assays to evaluate their clinical performance. Upper respiratory tract clinical samples were collected during the 2016-2017 and 2017-2018 influenza seasons and determined to be positive or negative for influenza B/Victoria or B/Yamagata viruses using the FDA-cleared Influenza B Lineage Genotyping Kit. In the current study, specimens were tested using the cleared InfB assay and the investigative VER 1.1 and VER 2 VIC and YAM assays. A total of 126 specimens positive for either influenza B/Victoria or influenza B/Yamagata viruses and 61 specimens negative for influenza B viruses were tested. Four lung tissue specimens were included in the testing, but were used for informational purposes only and not included in calculations of assay performance (Tables 8-21 to 8-24). Result interpretation followed the instructions of the Package Insert for the cleared Influenza B Lineage Genotyping Kit.

Table 8-21: VIC VER 1.1 Design-Retrospective Study Results

Specimen Type	# of Positives[1]	% Positive Agreement (95% CI)	# of Negatives[2]	% Negative Agreement (95% CI)
NPS, NS	29/29	100.0 (88.3 – 100.0)	156/156	100.0 (97.6 – 100.0)
TS	1/1	100.0 (20.7 - 100.0)	1/1	100.0 (20.7 - 100.0)
Total	30/30	100.0 (88.7 – 100.0)	157/157	100.0 (97.6 – 100.0)

[1]Proportion of positive samples correctly identified versus the comparator.
[2]Proportion of negative samples correctly identified versus the comparator.

Table 8-22: YAM VER 1.1 Design-Retrospective Study Results

Specimen Type	# of Positives[1]	% Positive Agreement (95% CI)	# of Negatives[2]	% Negative Agreement (95% CI)
NPS, NS	95/95	100.0 (96.1 – 100.0)	90/90	100.0 (95.9 – 100.0)
TS	1/1	100.0 (20.7 - 100.0)	1/1	100.0 (20.7 - 100.0)
Total	96/96	100.0 (96.2 - 100.0)	91/91	100.0 (96.0 – 100.0)

[1]Proportion of positive samples correctly identified versus the comparator.
[2]Proportion of negative samples correctly identified versus the comparator.

Table 8-23: VIC VER 2 Design-Retrospective Study Results

Specimen Type	# of Positives[1]	% Positive Agreement (95% CI)	# of Negatives[2]	% Negative Agreement (95% CI)
NPS, NS	29/29	100.0 (88.3 – 100.0)	156/156	100.0 (97.6 – 100.0)
TS	1/1	100.0 (20.7 - 100.0)	1/1	100.0 (20.7 - 100.0)
Total	30/30	100.0 (88.7 – 100.0)	157/157	100.0 (97.6 – 100.0)

[1]Proportion of positive samples correctly identified versus the comparator.
[2]Proportion of negative samples correctly identified versus the comparator.

Table 8-24: YAM VER 2 Design-Retrospective Study Results

Specimen Type	# of Positives[1]	% Positive Agreement (95% CI)	# of Negatives[2]	% Negative Agreement (95% CI)
NPS, NS	95/95	100.0 (96.1 – 100.0)	90/90	100.0 (95.9 – 100.0)
TS	1/1	100.0 (20.7 - 100.0)	1/1	100.0 (20.7 - 100.0)
Total	96/96	100.0 (96.2 - 100.0)	91/91	100.0 (96.0 – 100.0)

[1]Proportion of positive samples correctly identified versus the comparator.
[2]Proportion of negative samples correctly identified versus the comparator.

X. CONCLUSION

The modification of the Influenza B Lineage Genotyping Kit of the CDC Human Influenza Virus rRT-PCR Diagnostic Panel to ensure comprehensive detection of influenza B viruses does not

change the fundamental scientific technology of the device. Analytical and clinical data demonstrate that the performance of the modified device to detect and characterize influenza B viruses is accomplished with high positive and negative percent agreement in a manner substantially equivalent to the predicate. The indications for use remain the same.