February 18, 2020

Access Bio, Inc.
Jongrak Kim
Department General Manager, Regulatory Affairs
65 Clyde Road, Suite A.
Somerset, New Jersey 08873

Re: K191514
Trade/Device Name: CareStart Flu A&B Plus
Regulation Number: 21 CFR 866.3328
Regulation Name: Influenza Virus Antigen Detection Test System
Regulatory Class: Class II
Product Code: PSZ
Dated: Nov 20, 2019
Received: Nov 21, 2019

Dear Jongrak Kim:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven Gitterman, M.D., Ph.D.
Deputy Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
K191514

Device Name
CareStart™ Flu A&B Plus

Indications for Use *(Describe)*
The CareStart™ Flu A&B Plus is an in vitro rapid immunochromatographic assay for the qualitative detection of influenza virus type A and B nucleoprotein antigens directly from nasopharyngeal swab specimens of symptomatic patients.

The test is intended for use as an aid in the rapid differential diagnosis of acute influenza type A and B viral infections. This test is intended to distinguish between influenza type A and/or B virus in a single test. This test is not intended to detect influenza type C viral antigens. Negative test results are presumptive and should be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative results do not preclude influenza virus infections and should not be used as the basis for treatment or other patient management decisions.

Performance characteristics for influenza A and B were established during the 2018-2019 influenza season when influenza A/H3N2, A/H1N1pdm09, and B/Victoria were the predominant influenza viruses in circulation. When other influenza viruses are emerging, performance characteristics may vary.

If infection with a novel influenza 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 the state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to received and culture specimens.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5. 510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR 807.92.

The assigned 510(k) number is: **K191514**

5.1. Submitter

- Company Name: Access Bio Incorporate
- Address: 65 Clyde Road, Suite A, Somerset, NJ 08873
- Phone Number: 1-732-873-4040
- Fax Number: 1-732-873-4043
- FDA Registration Number: 3003966368

5.2. Contact Person

- Jongrak Kim / Manager, Regulatory Affairs Division
- Sang Joon Han / Manager, Research and Development Division

5.3. Device Information

- Trade Name: *CareStart*™ Flu A&B *Plus*
- Common Name: Influenza virus antigen detection test system
- Device Class: Class II under 21 CFR 866.3328
- Classification Name: Devices Detecting Influenza A and B Virus Antigens
- Product Code: PSZ

5.4. Predicate Device

- Device Name: BD Veritor™ System for Rapid Detection of Flu A + B CLIA waived Kit
- 510(k) Number: K180438
- Manufacturer: Becton, Dickinson and Company

65 Clyde Rd. Suite A. Somerset, NJ 08873 ‖ Tel: (732)-873-4040 ‖ Fax: (732)-873-4043 ‖ info@accessbio.net

5.5. Device Description

The *CareStart*™ Flu A&B *Plus* test is an immunochromatographic assay for detection of extracted influenza type A and B virus nucleoprotein antigens in nasopharyngeal specimens.

Nasopharyngeal swabs require a sample preparation step in which the sample is eluted and washed off into the extraction buffer solution. Extracted swab sample is added to the sample well of the test device to initiate the test. When the swab sample migrates in the test strip, influenza A or B viral antigens bind to anti-influenza antibodies conjugated to indicator particles in the test strip forming an immune complex. The immune complex is then captured by each test line and control line on the membrane as it migrates through the strip.

Test results are interpreted at 10 minutes. The presence of two colored lines, a purple-colored line in the control region “C” and a red-colored line in the influenza A test region “A”, indicates influenza A positive. The presence of two colored lines, a purple-colored line in the control region “C” and a blue-colored line in the influenza B test region “B”, indicates influenza B positive. The presence of three colored lines, a purple-colored line in the control region “C”, a red-colored line in the influenza A test region “A”, and a blue-colored line in the influenza B test region “B indicates, influenza A and B dual positive result. The absence of a line on both influenza A and B test regions with a purple-colored line in the control region “C” indicates negative. No appearance of purple-colored line in the control region “C” indicates invalid test.

5.6. Intended Use / Indications for Use

The *CareStart*™ Flu A&B *Plus* is an *in vitro* rapid immunochromatographic assay for the qualitative detection of influenza virus type A and B nucleoprotein antigens directly from nasopharyngeal swab specimens of symptomatic patients.

The test is intended for use as an aid in the rapid differential diagnosis of acute

influenza type A and B viral infections. This test is intended to distinguish between influenza type A and/or B virus in a single test. This test is not intended to detect influenza type C viral antigens. Negative test results are presumptive and should be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative results do not preclude influenza virus infections and should not be used as the basis for treatment or other patient management decisions.

Performance characteristics for influenza A and B were established during the 2018-2019 influenza season when influenza A/H3N2, A/H1N1pdm09, and B/Victoria were the predominant influenza viruses in circulation. When other influenza viruses are emerging, performance characteristics may vary.

If infection with a novel influenza 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 the state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to received and culture specimens.

5.7. Product Contents

Contents Name	Quantity (in a kit)	Description
Test device	20 each	Foil pouched test device containing one test strip which is encased on plastic device cassette.
Extraction vial / cap	20 vials and caps	The extraction vial contains 400 µL extraction buffer solution.
Nasopharyngeal swab	20 each	Swab for nasopharyngeal specimen collection.
Influenza A positive control swab	1 each	Influenza A positive and influenza B negative external control swab. Inactivated influenza A antigen is dried on the tip of the swab.
Influenza B positive control swab	1 each	Influenza A negative and influenza B positive external control swab. Inactivated influenza B antigen is dried on the tip of the swab.

Influenza Negative control swab	1 each	Influenza A negative and influenza B negative external control swab. Inactivated Group A, *Streptococcus* is dried on the tip of the swab.
Package insert	1 each	Instructions for use
Quick Reference Instructions (QRI)	1 each	Quick reference instructions

The following materials are needed but not provided:

- Pair of gloves
- Timer / Pen
- Biohazard or sharps container

5.8. Comparison of Technological Characteristics with the Predicate Device

Contents	Predicate Device	Proposed Device
	BD Veritor™ System for Rapid Detection of Flu A+B	*CareStart*™ Flu A&B *Plus*
510(k) Number	K180438	K191514
Regulation Number	21 CFR 866.3328	Same
Regulation Name	Influenza virus antigen detection test system	Same
Regulatory Class	Class II	Same
Product Code	PSZ	Same
Assay Target	Influenza A and B nucleoprotein antigens	Same

Contents	Predicate Device	Proposed Device
	BD Veritor™ System for Rapid Detection of Flu A+B	*CareStart*™ Flu A&B *Plus*
Intended Use	The BD Veritor™ System for Rapid Detection of Flu A+B CLIA waived assay is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasal and nasopharyngeal swabs of symptomatic patients. The BD Veritor™ System for Rapid Detection of Flu A+B (also referred to as the BD Veritor™ System and BD Veritor™ System Flu A+B) is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Outside the U.S., a negative test is presumptive and it is recommended that these results be confirmed by viral culture or a molecular assay cleared for diagnostic use in the country of use. FDA has not cleared this device for use outside of the U.S. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to detect influenza C antigens. Performance characteristics for influenza A and B were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage,	The *CareStart*™ Flu A&B *Plus* is an *in vitro* rapid immunochromatographic assay for the qualitative detection of influenza virus type A and B nucleoprotein antigens directly from nasopharyngeal swab specimens of symptomatic patients. The test is intended for use as an aid in the rapid differential diagnosis of acute influenza type A and B viral infections. This test is intended to distinguish between influenza type A and/or B virus in a single test. This test is not intended to detect influenza type C viral antigens. Negative test results are presumptive and should be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative results do not preclude influenza virus infections and should not be used as the basis for treatment or other patient management decisions. Performance characteristics for influenza A and B were established during the 2018-2019 influenza season when influenza A/H3N2, A/H1N1pdm09, and B/Victoria were the predominant influenza viruses in circulation. When other influenza viruses are emerging, performance characteristics may vary. If infection with a novel influenza 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

Contents	Predicate Device	Proposed Device
	BD Veritor™ System for Rapid Detection of Flu A+B	*CareStart*™ Flu A&B *Plus*
	and B/Yamagata lineage were the predominant influenza viruses in circulation according to the Morbidity and Mortality Weekly Report from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses. If infection with a novel influenza 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 the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	novel virulent influenza viruses and sent to the state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to received and culture specimens.
Specimens Type	Nasopharyngeal and nasal swabs	Nasopharyngeal swabs
Assay Result	Qualitative	Same
Technology	Immunochromatographic assay	Same
Instrumentation	BD Veritor™ System Reader	None

Contents	Predicate Device	Proposed Device
	BD Veritor™ System for Rapid Detection of Flu A+B	*CareStart*™ Flu A&B *Plus*
Detection Format	An optoelectronic instrument evaluates the line signal intensities at each of the spatially defined test and control line positions, interprets the results using a scoring algorithm, and reports a positive, negative, or invalid result on the LCD screen based on pre-set thresholds.	Visual determination of presence or absence of colored line indicators for the test line and control line on the test strip indicate the presence of influenza A and/or B antigen.
Time to Result	10 minutes	Same
Intended environment for use	Prescription use and CLIA waived	Prescription use
Storage Condition	2–30 °C	1–30 °C
Controls	Kit Flu A+/B- dry swab procedural control Kit Flu B+/A- dry swab procedural control Internal positive control Internal negative control	Influenza A positive control swab Influenza B positive control swab Influenza negative control swab Internal positive control

5.9. Summary of Performance

To verify and validate the device performance and characteristics, the following studies were conducted.

5.9.1. Analytical Sensitivity: Limit of Detection (LoD)

To determine the Limit of Detection (LoD) of *CareStart*™ Flu A&B *Plus*, four influenza A virus with two common currently or recently circulating influenza A subtypes (i.e.,

H3N2, H1N1 pdm09) and four influenza B virus with two genetic lineages (i.e., Victoria lineage and Yamagata lineage) were tested in this study.

In this study, each influenza virus strain of the panel was serially diluted to the concentration at which at least one negative result was obtained from replicate testing. The estimated LoD for each virus strain was confirmed by testing twenty replicates. The results presented in the table below.

Influenza Virus		LoD (EID_{50}/ml)	% Reactive (No. of positive / Total No. of Replicates)
Type/Subtype	Strain		
A (H3N2)	A/Perth/16/2009	$3.2 \times 10^{4.9}$	100% (20/20)
	A/Singapore/INFIMH-16-0019/2016	$2.0 \times 10^{5.2}$	100% (20/20)
A (H1N1) pdm09	A/California/07/2009	$3.2 \times 10^{4.9}$	100% (20/20)
	A/Michigan/45/2015	$3.2 \times 10^{4.2}$	100% (20/20)
B (Victoria lineage)	B/Brisbane/60/2008	$2.0 \times 10^{5.5}$	95% (19/20)
	B/Colorado/06/2017	$1.6 \times 10^{6.4}$	100% (20/20)
B (Yamagata lineage)	B/Wisconsin/01/2010	$4.0 \times 10^{4.9}$	100% (20/20)
	B/Phuket/3073/2013	$1.6 \times 10^{5.5}$	100% (20/20)

EID_{50}= 50% Egg Infectious Dose

5.9.2. Analytical Sensitivity: Reactivity (Inclusivity)

To determine the detectability of *CareStart*™ Flu A&B *Plus*, fifteen strains of influenza A virus representing each of three common currently or recently circulating influenza A subtypes (i.e., H3N2, H3N2v, and H1N1 pdm09) and ten strains of influenza B virus representing each of two influenza B genetic lineages (i.e., Yamagata lineage and Victoria lineage) were tested in this study.

In this study, each influenza virus strain of the panel was serially diluted to the concentration at which at least one negative result was obtained from replicate testing. All viruses were detected in all three replicates at the concentrations shown below.

Influenza Virus		Lowest Concentration detected by *CareStart*™ Flu A&B *Plus*	Test Results (# of positives / # of replicates)	
Subtype	Virus Strain Name		Flu A Result	Flu B Result
A (H3N2)	A/Alaska/232/2015	2.6 x 10^6 $CEID_{50}$/ml	3/3	0/3
	A/California/02/2014	5.8 x 10^2 $TCID_{50}$/ml	3/3	0/3
	A/Hong Kong/4801/2014	9.6 x 10^5 $CEID_{50}$/ml	3/3	0/3
	A/Michigan/15/2014	9.3 x 10^4 FFU/ml	3/3	0/3
	A/Texas/71/2017	9.3 x 10^4 FFU/ml	3/3	0/3
A (H3N2)v	A/Indiana/08/2011	8.1 x 10^2 $TCID_{50}$/ml	3/3	0/3
	A/Minnesota/11/2010	2.2 x 10^4 $CEID_{50}$/ml	3/3	0/3
A (H1N1) pdm09	A/Bangladesh/3002/2015	1.3 x 10^5 $CEID_{50}$/ml	3/3	0/3
	A/Dominican Republic/7293/2013	5.0 x 10^3 $TCID_{50}$/ml	3/3	0/3
	A/Iowa/53/2015	2.9 x 10^6 $CEID_{50}$/ml	3/3	0/3
	A/Massachusetts/15/2013	1.6 x 10^6 $CEID_{50}$/ml	3/3	0/3
	A/Michigan/272/2017	9.6 x 10^3 $TCID_{50}$/ml	3/3	0/3
	A/New Hampshire/02/2010	1.8 x 10^6 $CEID_{50}$/ml	3/3	0/3
	A/South Carolina/2/2010	2.5 x 10^5 $CEID_{50}$/ml	3/3	0/3
	A/St. Petersburg/61/2015	9.3 x 10^5 $CEID_{50}$/ml	3/3	0/3
B (Victoria lineage)	B/New Jersey/1/2012	8.8 x 10^4 $TCID_{50}$/ml	0/3	3/3
	B/Colorado/6/2017	1.6 x 10^6 $CEID_{50}$/ml	0/3	3/3
	B/Florida/78/2015	1.7 x 10^6 $CEID_{50}$/ml	0/3	3/3
	B/Hong Kong/286/2017	2.7 x 10^3 $TCID_{50}$/ml	0/3	3/3
	B/Maryland/15/2016	1.3 x 10^3 $TCID_{50}$/ml	0/3	3/3
B (Yamagata lineage)	B/Guangdong-Liwan/1133/2014	1.8 x 10^6 $CEID_{50}$/ml	0/3	3/3
	B/Massachusetts/2/2012	1.0 x 10^7 $CEID_{50}$/ml	0/3	3/3
	B/Phuket/3073/2013	1.1 x 10^6 $CEID_{50}$/ml	0/3	3/3
	B/Texas/06/2011	6.2 x 10^6 $CEID_{50}$/ml	0/3	3/3
	B/Utah/09/2014	6.3 x 10^4 $CEID_{50}$/ml	0/3	3/3

$CEID_{50}$= 50% Chicken Embryo Infectious Dose
$TCID_{50}$= 50% Tissue Culture Infectious Dose
FFU= Focus Forming Assay Unit

5.9.3. Analytical Specificity: Cross-Reactivity (Exclusivity) and Microbial Interference

The potential cross-reactivity (exclusivity) of a panel of common organisms was evaluated with influenza negative samples using the *CareStart*™ Flu A&B *Plus*.

Potential microbial interference was evaluated with samples containing influenza A or influenza B at approximately 2x LoD. A total of 31 bacteria were tested at a target concentration of approximately 10^7 cfu/ml with the exception of *Mycoplasma pneumoniae*, which was tested at a final concentration of 1.5 x 10^3 cfu/ml. The 15 non-influenza viruses were tested at concentrations between $10^{5.86}$ and $10^{4.2}$ $TCID_{50}$/ml. All influenza negative samples gave negative results at the concentrations of the potentially cross-reactive common organisms tested showing no cross-reactivity with *CareStart*™ Flu A&B *Plus* assay. All samples with influenza A or influenza B tested positive showing no microbial interference at the concentrations of the potentially interfering common organisms tested.

Bacteria	ATCC#	Stock Concentration (cfu/ml)	Testing Concentration (cfu/ml)	Results of triplicate without influenza virus (# of positives / # of replicates)	Results of triplicate in presence of influenza A virus (# of positives / # of replicates)	Results of triplicate in presence of influenza B virus (# of positives / # of replicates)
Acinetobacter calcoaceticus	17902	10^9	10^7	0/3	3/3	3/3
Bordetella pertussis	9340	10^9	10^7	0/3	3/3	3/3
Candida albicans	11006	10^9	10^7	0/3	3/3	3/3
Chlamydophila pneumoniae	53592	10^9	10^7	0/3	3/3	3/3
Corynebacterium diphtheriae	296	10^9	10^7	0/3	3/3	3/3
Enterococcus faecalis	4079	10^9	10^7	0/3	3/3	3/3
Escherichia coli	26	10^9	10^7	0/3	3/3	3/3
Gardnerella vaginalis	14018	10^9	10^7	0/3	3/3	3/3
Haemophilus influenzae	49144	10^9	10^7	0/3	3/3	3/3
Klebsiella pneumoniae	33495	10^9	10^7	0/3	3/3	3/3
Lactobacillus casei	393	10^9	10^7	0/3	3/3	3/3
Legionella pneumophila	33152	10^9	10^7	0/3	3/3	3/3

Listeria monocytogenes	7302	10^9	10^7	0/3	3/3	3/3
Moraxella catarrhalis	25238	10^9	10^7	0/3	3/3	3/3
Mycobacterium tuberculosis	NR-122	10^9	10^7	0/3	3/3	3/3
Mycoplasma pneumoniae	29342	1.5×10^5	1.5×10^3	0/3	3/3	3/3
Neisseria gonorrhoeae	19424	10^9	10^7	0/3	3/3	3/3
Neisseria meningitidis	13077	10^9	10^7	0/3	3/3	3/3
Neisseria sicca	9913	10^9	10^7	0/3	3/3	3/3
Proteus vulgaris	33420	10^9	10^7	0/3	3/3	3/3
Pseudomonas aeruginosa	9721	10^9	10^7	0/3	3/3	3/3
Staphylococcus aureus	12600	10^9	10^7	0/3	3/3	3/3
Staphylococcus epidermidis	14990	10^9	10^7	0/3	3/3	3/3
Serratia marcescens	13880	10^9	10^7	0/3	3/3	3/3
Streptococcus mutans	25175	10^9	10^7	0/3	3/3	3/3
Streptococcus pneumoniae	49136	10^9	10^7	0/3	3/3	3/3
Streptococcus pyogenes	19615	10^9	10^7	0/3	3/3	3/3
Streptococcus sp. Group B	12386	10^9	10^7	0/3	3/3	3/3
Streptococcus sp. Group C	12388	10^9	10^7	0/3	3/3	3/3
Streptococcus sp. Group F	700231	10^9	10^7	0/3	3/3	3/3
Streptococcus sanguinis	10556	10^9	10^7	0/3	3/3	3/3

cfu/ml: colony-forming units per milliliter

Viruses	ATCC#	Stock Concentration ($TCID_{50}$/ml)	Testing Concentration ($TCID_{50}$/ml)	Results of triplicate without influenza virus (# of positives / # of replicates)	Results of triplicate in presence of influenza A virus (# of positives / # of replicates)	Results of triplicate in presence of influenza B virus (# of positives / # of replicates)
Adenovirus 1	VR-1	$10^{7.20}$	$10^{5.20}$	0/3	3/3	3/3
Adenovirus 7	VR-7	$10^{6.45}$	$10^{5.45}$	0/3	3/3	3/3
Coronavirus (OC43)	VR-1558	$10^{5.45}$	$10^{5.45}$	0/3	3/3	3/3
Coronavirus (229E)	VR-740	$10^{4.45}$	$10^{4.45}$	0/3	3/3	3/3
Cytomegalovirus	VR-538	$10^{5.95}$	$10^{4.95}$	0/3	3/3	3/3
Human Coxsackievirus B4	VR-184	$10^{7.45}$	$10^{5.45}$	0/3	3/3	3/3
Human metapneumovirus	NR-22227	2.8×10^{6}	2.8×10^{5}	0/3	3/3	3/3
Measles	VR-24	$10^{4.20}$	$10^{4.20}$	0/3	3/3	3/3
Mumps (Enders)	VR-106	$10^{5.20}$	$10^{5.20}$	0/3	3/3	3/3
Parainfluenza virus type 1	VR-94	$10^{7.86}$	$10^{5.86}$	0/3	3/3	3/3
Parainfluenza virus type 2	VR-92	$10^{7.20}$	$10^{5.20}$	0/3	3/3	3/3
Parainfluenza virus type 3	VR-93	$10^{7.20}$	$10^{5.20}$	0/3	3/3	3/3
Respiratory Syncytial Virus Type B	VR-1400	$10^{6.20}$	$10^{5.20}$	0/3	3/3	3/3
Rhinovirus 1A	VR-1559	$10^{7.20}$	$10^{5.20}$	0/3	3/3	3/3
Rubella	VR-315	$10^{6.20}$	$10^{5.20}$	0/3	3/3	3/3

$TCID_{50}$= 50% Tissue Culture Infectious Dose

5.9.4. Analytical Specificity: Interfering Substances Effect

To assess the potential interference effects, the *CareStart*™ Flu A&B *Plus* was evaluated with thirty substances naturally or artificially present in the respiratory specimen or nasal cavity/nasopharynx.

The positive samples were prepared using the influenza A and B virus strains diluted to

a concentration approximately two times the respective LoD levels. Each influenza strain combined with each interfering substance was evaluated separately. Negative samples were prepared by adding each interfering substance to the Universal Transport Medium (UTM). Each positive and negative sample, combined with each interfering substance, was tested in triplicate. None of the thirty potential interfering substances tested produced false positive or false negative test results using *CareStart*™ Flu A&B *Plus* with influenza positive and negative samples at the concentrations specified below.

Interfering Substances	Concentration Tested	Test Results (# of positives / # of replicates)				
		A/Perth/16/2009	A/Michigan/45/2015	B/Colorado/06/2017	B/Phuket/3073/2013	Negative Samples
Acetaminophen	10 mg/ml	3/3	3/3	3/3	3/3	0/3
Acetyl salicylic acid	15 mg/ml	3/3	3/3	3/3	3/3	0/3
Beclomethasone	0.5 mg/ml	3/3	3/3	3/3	3/3	0/3
Benzocaine	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Budesonide	2 mg/ml	3/3	3/3	3/3	3/3	0/3
Chlorpheniramine maleate	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Dexamethasone	1 mg/ml	3/3	3/3	3/3	3/3	0/3
Dextromethorphan HBr	2 mg/ml	3/3	3/3	3/3	3/3	0/3
Diphenhydramine HCl	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Ephedrine HCl	10 mg/ml	3/3	3/3	3/3	3/3	0/3
Flunisolide	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Fluticasone	1 mg/ml	3/3	3/3	3/3	3/3	0/3
Guaiacol Glyceryl Ether	20 mg/ml	3/3	3/3	3/3	3/3	0/3
Histamine Dihydrochloride	10 mg/ml	3/3	3/3	3/3	3/3	0/3

Interfering Substances	Concentration Tested	Test Results (# of positives / # of replicates)				
		A/Perth/16/2009	A/Michigan/45/2015	B/Colorado/06/2017	B/Phuket/3073/2013	Negative Samples
Menthol	10 mg/ml	3/3	3/3	3/3	3/3	0/3
Mometasone	1 mg/ml	3/3	3/3	3/3	3/3	0/3
Mucin	2%	3/3	3/3	3/3	3/3	0/3
Mupirocin	1 mg/ml	3/3	3/3	3/3	3/3	0/3
OTC Throat drop (Halls)	15%	3/3	3/3	3/3	3/3	0/3
OTC Throat drop (Ricola)	15%	3/3	3/3	3/3	3/3	0/3
OTC Nasal spray (Afrin)	15%	3/3	3/3	3/3	3/3	0/3
OTC Nasal spray (Vicks Sinex)	15%	3/3	3/3	3/3	3/3	0/3
OTC Nasal spray (Zicam)	15%	3/3	3/3	3/3	3/3	0/3
Oxymetazoline HCl	10 mg/ml	3/3	3/3	3/3	3/3	0/3
Phenylephrine HCl	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Phenylpropanolamine	5 mg/ml	3/3	3/3	3/3	3/3	0/3
Tobramycin	1 mg/ml	3/3	3/3	3/3	3/3	0/3
Triamcinolone	1 mg/ml	3/3	3/3	3/3	3/3	0/3
Whole Blood	2%	3/3	3/3	3/3	3/3	0/3
Zanamivir	1 mg/ml	3/3	3/3	3/3	3/3	0/3

The interfering effects of biotin concentrations ranging between 125 ng/mL and 2 µg/mL were tested in a separate study. Biotin concentrations up to 500 ng/ml did not lead to false results. Biotin concentrations >500 ng/ml can cause false negative influenza A results with the *CareStart*™ Flu A&B *Plus*.

5.9.5. Expected Values

The prevalence of influenza varies from year to year, with outbreaks occurring during the fall and winter months. The influenza positivity rate is dependent upon many factors, including specimen collection, test method, and geographic location. Prevalence varies throughout the flu season and from location to location. The *CareStart*™ Flu A&B *Plus* prospective clinical study was conducted during the 2018-2019 influenza season. The following tables show the number of influenza A and influenza B positive cases and its percentage in four subject age categories, as observed during the clinical study.

Age Group	Positivity Rates for Influenza A with the *CareStart*™ Flu A&B *Plus* during the Clinical Study		
	Number of Nasopharyngeal Swab Specimens	Number of **Influenza A** Positives	**Influenza A** Positivity Rate
≤5 Years of Age	174	61	35.1%
6-21 Years of Age	333	143	42.9%
22-59 Years of Age	394	101	25.6%
≥60 Years of Age	43	11	25.6%
Total	944	316	33.5%

Age Group	Positivity Rates for Influenza B with the *CareStart*™ Flu A&B *Plus* during the Clinical Study		
	Number of Nasopharyngeal Swab Specimens	Number of **Influenza B** Positives	**Influenza B** Positivity Rate
≤5 Years of Age	174	2	1.1%
6-21 Years of Age	333	7	2.1%
22-59 Years of Age	394	5	1.3%
≥60 Years of Age	43	1	2.3%
Total	944	15	1.6%

5.9.6. Prospective Clinical Study

The clinical performance characteristics of *CareStart*™ Flu A&B *Plus* were evaluated in a multi-site prospective study during the 2018-2019 influenza season in the U.S. against an FDA-cleared influenza A and B molecular assay. A total of 10 Point-of-Care investigational sites throughout the U.S. participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with flu-like symptoms and meet inclusion/exclusion criteria.

Two nasopharyngeal swabs were collected from one nostril from each subject using standard collection methods. At all sites, the first collected nasopharyngeal swab was eluted in 3 ml of viral transport media and transported to the central laboratory for testing using the FDA-cleared molecular assay as a comparator method. The second collected nasopharyngeal swab was tested directly on *CareStart*™ Flu A&B *Plus* according to product instructions.

A total of 955 subjects were enrolled in this study. Of those, 11 specimens are unevaluable (i.e., four samples failed to meet inclusion criteria, two samples were not collected due to subject refusal after enrollment, one sample was transported to the central laboratory in damaged and leaking state, and four samples transported to the central laboratory were mislabeled). A total of 944 nasopharyngeal swab specimens were considered evaluable. The performance of the *CareStart*™ Flu A&B *Plus* for influenza A and influenza B as compared to the comparator method is presented in the tables below.

All discrepant results were investigated by testing using an alternative FDA-cleared molecular assay at the same central laboratory. The results of this testing are captured in the footnotes but were not included in the calculations of the performance estimates shown below.

CareStart™ Flu A&B *Plus* Influenza A Performance against the Comparator Method

CareStart™ Flu A&B *Plus* – Influenza A	Molecular Comparator		
	Positive	Negative	Total
Positive	307	9[a]	316
Negative	77[b]	551	628
Total	384	560	944
Positive Percent Agreement (PPA)	79.9% (95% CI: 75.7% – 83.7%)		
Negative Percent Agreement (NPA)	98.4% (95% CI: 97.0% – 99.2%)		

[a] *Influenza A was detected in 2/9 false positive specimens using an alternative FDA-cleared molecular influenza A/B assay*

[b] *Influenza A was not detected in 15/77 false negative specimens using an alternative FDA-cleared molecular influenza A/B assay*

CareStart™ Flu A&B *Plus* Influenza B Performance against the Comparator Method

CareStart™ Flu A&B *Plus* – Influenza B	Molecular Comparator		
	Positive	Negative	Total
Positive	15	0	15
Negative	2[a]	927	929
Total	17	927	944
Positive Percent Agreement (PPA)	88.2% (95% CI: 65.7% – 96.7%)		
Negative Percent Agreement (NPA)	100.0% (95% CI: 99.6% – 100.0%)		

[a] *Influenza B was detected in 2/2 false negative specimens using an alternative FDA-cleared molecular influenza A/B assay*

CareStart™ Flu A&B *Plus* Influenza A and B Performance against the Comparator Method (Percent Agreement) by Age Group

		Prospective Study during the 2018-2019 influenza season	
		Influenza A	Influenza B
≤5 Years of Age	PPA	83.3% (55/66) 95% CI: 72.6% – 90.4%	100% (2/2) 95% CI: 34.2% – 100%
	NPA	94.4% (102/108) 95% CI: 88.4% – 97.4%	100% (172/172) 95% CI: 97.8% – 100%
6-21 Years of Age	PPA	82.5% (141/171) 95% CI: 76.1% – 87.4%	87.5% (7/8) 95% CI: 52.9% – 97.8%
	NPA	98.8% (160/162) 95% CI: 95.6% – 99.7%	100% (325/325) 95% CI: 98.8% – 100%
22-59 Years of Age	PPA	74.1% (100/135) 95% CI: 66.1% – 80.7%	83.3% (5/6) 95% CI: 43.7% – 97.0%

	NPA	99.6% (258/259) 95% CI: 97.8% – 99.9%	100% (388/388) 95% CI: 99.0% – 100%
≥60 Years of Age	PPA	91.7% (11/12) 95% CI: 64.6% – 98.5%	100% (1/1) 95% CI: 20.7% – 100%
	NPA	100% (31/31) 95% CI: 89.0% – 100%	100% (42/42) 95% CI: 91.6% – 100%

5.9.7. **Retrospective Study**

Due to extremely low prevalence of influenza B observed during the 2018-2019 influenza season in the U.S., the prospective clinical study performance data were supplemented with data from a retrospective study testing 162 swab samples prepared from archived respiratory specimens that were obtained from patients with influenza-like symptoms and were confirmed positive or negative by an FDA-cleared molecular assay for influenza A and influenza B. These swab samples (112 samples positive for influenza B and 50 negative samples) were distributed (blinded and randomized) among four of the investigational sites and the testing was incorporated into the daily workflow at each site during the prospective clinical study period.

All of the 162 swab specimens enrolled in the retrospective study were considered evaluable to supplement the prospective clinical performance data for influenza B. The performance of the *CareStart*™ Flu A&B *Plus* for influenza B with archived samples as compared to the FDA-cleared molecular method is presented in the table below.

***CareStart*™ Flu A&B *Plus* Influenza B (swab specimens prepared from frozen archived respiratory specimens) Performance against the Comparator Method**

CareStart™ Flu A&B *Plus* – Influenza B (swab specimens prepared from frozen archived respiratory specimens)	Molecular Comparator		
	Positive	Negative	Total
Positive	113	1	114
Negative	4	44	48
Total	117	45	162
Positive Percent Agreement (PPA)	96.6% (95% CI: 91.5% – 98.7%)		
Negative Percent Agreement (NPA)	97.8% (95% CI: 88.4% – 99.6%)		

5.9.8. Reproducibility Study

The reproducibility study was performed to evaluate the reproducibility of the *CareStart*™ Flu A&B *Plus* with contrived swab samples at three Point-of-Care sites in the U.S. The test sample panels consisted of seven samples at various virus concentrations including near the respective LoD (i.e., true negative, high negative influenza A, low positive influenza A, moderate positive influenza A, high negative influenza B, low positive influenza B, and moderate positive influenza B). The sample panel was tested in a blinded manner by three operators at each of three test sites on five non-consecutive days. Agreement of obtained results with expected results was 100% across all sites, operators, and days.

Reproducibility by Study Site

Sample Category	Site 1		Site 2		Site 3		Overall % Agreement and 95% CI
	%	Count	%	Count	%	Count	
True Negative[a] (no virus)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
High Negative A[a] (0.1x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
Low Positive A (1x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
Moderate Positive A (3x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
High Negative B[a] (0.1x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
Low Positive B (1x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)
Moderate Positive B (3x LoD)	100.0%	45/45	100.0%	45/45	100.0%	45/45	100.0% (135/135) (97.2% - 100.0%)

[a] *The expected results for true negative and high negative samples are negative results.*

5.9.9. Lot-to-Lot Precision

Three different lots of the *CareStart*™ Flu A&B *Plus* were evaluated for precision. Agreement of observed results with expected results was 100%. No variability was observed between reagent lots.

Sample Category	Reagent Lot 1		Reagent Lot 2		Reagent Lot 3		Overall % Agreement and 95% CI
	%	Count	%	Count	%	Count	
True Negative[a] (no virus)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
High Negative A[a] (0.1x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
Low Positive A (1x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
Moderate Positive A (3x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
High Negative B[a] (0.1x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
Low Positive B (1x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)
Moderate Positive B (3x LoD)	100%	9/9	100%	9/9	100%	9/9	100% (27/27) (87.5% - 100%)

[a] *The expected results for true negative and high negative samples are negative results.*

5.10. Conclusion

Based on the data submitted in this traditional 510(k) submission, the *CareStart*™ Flu A&B *Plus* has been shown to be substantially equivalent in terms of intended use, technological characteristics, and assay performance to the predicate device.