Hologic, Inc.
Vlada Rudenko
Regulatory Affair Specialist
10210 Genetic Center Dr.
San Diego, California 92121

Re: K241240
Trade/Device Name: Panther Fusion SARS-CoV-2/Flu A/B/RSV assay
Regulation Number: 21 CFR 866.3981
Regulation Name: Device To Detect And Identify Nucleic Acid Targets In Respiratory Specimens From Microbial Agents That Cause The SARS-Cov-2 Respiratory Infection And Other Microbial Agents When In A Multi-Target Test
Regulatory Class: Class II
Product Code: QOF
Dated: April 29, 2024
Received: May 3, 2024

Dear Vlada Rudenko:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

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

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

Sincerely,

Joseph Briggs -S

Joseph Briggs, Ph.D.
Deputy Branch Chief
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K241240

Device Name
Panther Fusion SARS-CoV-2/Flu A/B/RSV assay

Indications for Use *(Describe)*
The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a fully automated multiplexed real-time polymerase chain reaction (RT-PCR) in vitro diagnostic test intended for the qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (Flu A), influenza B virus (Flu B), and respiratory syncytial virus (RSV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens and anterior nasal (AN) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS- CoV-2, influenza, and RSV can be similar. This assay is intended to aid in the differential diagnosis of SARS-CoV-2, Flu A, Flu B, and RSV infections in humans and is not intended to detect influenza C virus infections.

Nucleic acids from the viral organisms identified by this test are generally detectable in NP and AN swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus and aids in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms. The organism(s) detected by the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections. This assay is designed for use on the Panther Fusion system.

The Hologic RespDirect Collection Kit is cleared for NP swab specimens only for testing with the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay.

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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510(k) SUMMARY

K241240

Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay

I. SUBMITTER

Hologic, Inc.
10210 Genetic Center Dr.
San Diego, CA 92121

Contact Person: Vlada Rudenko, MA
Regulatory Affairs Specialist
vlada.rudenko@hologic.com
Phone: 858-410-7967

Date Prepared: July 3, 2024

II. DEVICE

Proprietary/Trade Name:	Panther Fusion SARS-CoV-2/Flu A/B/RSV assay
Classification Name:	Multi-Target Respiratory Specimen Nucleic Acid Test Including SARS-CoV-2 And Other Microbial Agents
Regulation Number:	21 CFR 866.3981
Regulatory Class:	Class II
Product Code:	QOF
Secondary Product Code:	OOI

III. PREDICATE DEVICE

The predicate device is the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for testing with nasopharyngeal swab specimens. The purpose of this pre-market submission is to (1) add an anterior nasal swab collected in viral/universal transport medium (VTM/UTM), collected from symptomatic patients, as a validated specimen type to the currently marketed Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (K222736; cleared May 16, 2023) and (2) to implement an Adaptive Crosstalk Correction (ACC) factor in the Assay Definition Module (ADM) software to eliminate potential under correction of crosstalk between the SARS-CoV-2 (ROX) channel and the Flu B channel (RED647).

IV. DEVICE DESCRIPTION

Proprietary/Trade Name: Panther Fusion SARS-CoV-2/Flu A/B/RSV assay

The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is classified as a Class II *in vitro* diagnostic device per 21 CFR 866.3981 and has product code QOF. The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is designed for use on the fully automated Panther Fusion System.

The Panther Fusion system is a class II exempt device under 21CFR 862.2570 that has product code OOI.

Brief Description of Assay Principles

The assay principles are as follows and remain unchanged from the previous submission.
The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a multiplex real-time reverse transcriptase PCR (RT-PCR) *in vitro* diagnostic test developed for use on the fully automated Panther Fusion system to detect and differentiate SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV) directly from nasopharyngeal and anterior nasal swab specimens, from individuals exhibiting signs and symptoms of a respiratory tract infection.

The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay involves the following steps: sample lysis, nucleic acid capture and elution transfer, and multiplex RT-PCR where analytes (when present) are simultaneously amplified, detected and differentiated. Nucleic acid capture and elution takes place in a single tube on the Panther Fusion system. The eluate is transferred to the Panther Fusion system reaction tube containing the assay reagents. Multiplex RT-PCR is then performed for the eluted nucleic acid on the Panther Fusion system.

Sample lysis, nucleic acid capture, and elution: Prior to processing and testing on the Panther Fusion system, specimens are transferred to a Specimen Lysis Tube containing specimen transport media (STM). Alternatively, samples can be collected with the RespDirect Collection kit which contains enhanced specimen transport media (eSTM). STM and eSTM lyse the cells, release target nucleic acid and protect them from degradation during storage.

The Internal Control-S (IC-S) is added to each test specimen and controls via the working Panther Fusion Capture Reagent-S (wFCR-S). The IC-S is the reagent used to monitor specimen processing, amplification and detection. Magnetic particles with covalently bound oligonucleotides mediate the nucleic acid capture. Capture oligonucleotides hybridize to nucleic acid in the test specimen. Hybridized nucleic acid is then separated from the lysed specimen in a magnetic field. Wash steps remove extraneous components from the reaction tube. The elution step elutes purified nucleic acid. During the nucleic acid capture and elution step, total nucleic acid is isolated from specimens.

Elution transfer and RT-PCR: During the elution transfer step, eluted nucleic acid is transferred to a Panther Fusion reaction tube already containing oil and reconstituted mastermix. Target amplification occurs via RT-PCR. A reverse transcriptase generates a DNA copy of the target sequence. Target specific forward and reverse primers and probes then amplify targets while simultaneously detecting and discriminating multiple target types via multiplex RT-PCR. The Panther Fusion system compares the fluorescence signal to a predetermined cut-off to produce a qualitative result for the presence or absence of the analyte. The positive result for each analyte will be accompanied by the cycle threshold (Ct value). The analytes and the channel used for their detection on the Panther Fusion system are summarized in the table below.

Analyte	Gene Targeted	Instrument Channel	Dye
SARS-CoV-2	ORF1ab	ROX	Cal Red 610
Influenza A Virus	Matrix	FAM	Fluorescein (FAM)
Respiratory Syncytial Virus A/B	Matrix	HEX	Cal Orange 560
Influenza B Virus	Matrix	RED647	Quasar 670 (Q670)
Internal Control	Not applicable	RED677	Quasar 705 (Q705)

The Panther Fusion system software has been updated from version 7.2.5 in the initial Panther Fusion SARS-CoV-2/Flu A/B/RSV assay with nasopharyngeal swab specimens collected in VTM/UTM or the RespDirect Collection Kit under 510(k) clearance K222736 (cleared May 16, 2023) to version 7.2.7 used in this submission, and the current on-market system software version 7.2.9. The Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay Definition Module (ADM) software has been updated from version 1.1.5.9 in the initial 510(k) clearance K222736 to ADM

software version 1.2.5.6 in the current submission supporting the addition of an anterior nasal swab specimen collected in VTM/UTM for processing on the Panther Fusion system and the introduction of the Adaptive Crosstalk Correction (ACC) factor explained below.

The ACC algorithm evaluates the correlation between the SARS-CoV-2 and Flu B fluorescence signals and applies crosstalk compensation when correlation of the fluorescence signals between the two analytes exceeds a pre-set threshold indicating the presence of measurable crosstalk signal. Implementation of the ACC software update reduces the potential for occasional Flu B false positives in presence of SARS-CoV-2 positives without adversely affecting safety and effectiveness of the device. Validation of the ACC ADM software update demonstrated through assay and software verification and analytical/clinical wet-testing demonstrates that the assay and system performance is equivalent to the released on-market assay performance.

V. INDICATIONS FOR USE

The intended use has been updated to include the anterior nasal swab specimen type claim. The updated intended use is as follows:

The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a fully automated multiplexed real-time polymerase chain reaction (RT-PCR) *in vitro* diagnostic test intended for the qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (Flu A), influenza B virus (Flu B), and respiratory syncytial virus (RSV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens and anterior nasal (AN) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza, and RSV can be similar. This assay is intended to aid in the differential diagnosis of SARS-CoV-2, Flu A, Flu B, and RSV infections in humans and is not intended to detect influenza C virus infections.

Nucleic acids from the viral organisms identified by this test are generally detectable in NP and AN swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus and aids in diagnosis if used in

conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Positive results do not rule out coinfection with other organisms. The organism(s) detected by the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections. This assay is designed for use on the Panther Fusion system.

The Hologic RespDirect Collection Kit is cleared for NP swab specimens only for testing with the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The predicate device is the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for use with nasopharyngeal (NP) swab specimens collected in Viral/Universal Transport Medium (VTM/UTM) or Enhanced Specimen Transport Medium (eSTM) (RespDirect Collection Kit) (K222736, cleared May 16, 2023, Hologic, San Diego, CA)).

Both the predicate and subject devices utilize the same technology, run on the automated Panther Fusion system, and have similar intended uses. The only difference is that this premarket submission adds (1) an anterior nasal swab specimen collected in VTM/UTM to the intended use and (2) implements an Adaptive Crosstalk Correction (ACC) factor in the Assay Definition Module (ADM) software to eliminate potential under correction of crosstalk between the SARS-CoV-2 (ROX) channel and the Flu B channel (RED647).

A comparison of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for use with NP and AN swab specimens to the predicate device (cleared for NP swab specimens only) is summarized in **Table 1** (similarities) and **Table 2** (differences).

Table 1: Similarities Between Predicate Device and Subject Device

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect), K222736))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM and anterior nasal swab in VTM/UTM)
Technology/ Principle of Operation	Reverse transcriptase multiplexed polymerase chain reaction test	Same
Platform	Automated Panther Fusion System	Same
Assay Targets	4 targets: SARS-CoV-2, Flu A, Flu B, RSV (RSV A/RSV B)	Same
Assay Results	Qualitative	Same
Function	Detection of RNA from SARS-CoV-2, Flu A, Flu B, and RSV	Same

Table 2: Differences Between Predicate Device and Subject Device

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect), K222736))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM and anterior nasal swab in VTM/UTM)
Intended Use	The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a fully automated multiplexed real-time polymerase chain reaction (RT-PCR) *in vitro* diagnostic test intended for the qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (Flu A), influenza B virus (Flu B), and respiratory syncytial virus (RSV). Nucleic acids are isolated and	The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is a fully automated multiplexed real-time polymerase chain reaction (RT-PCR) *in vitro* diagnostic test intended for the qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (Flu A), influenza B virus (Flu B), and respiratory syncytial virus (RSV). Nucleic acids are isolated and

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect), K222736))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM and anterior nasal swab in VTM/UTM)
	purified from nasopharyngeal (NP) specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza, and RSV can be similar. This assay is intended to aid in the differential diagnosis of SARS-CoV-2, Flu A, Flu B, and RSV infections in humans and is not intended to detect influenza C virus infections. Nucleic acids from the viral organisms identified by this test are generally detectable in NP specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus and aids in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms. The organism(s) detected by the Panther Fusion SARS-CoV-	purified from nasopharyngeal (NP) swab specimens and anterior nasal (AN) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza, and RSV can be similar. This assay is intended to aid in the differential diagnosis of SARS-CoV-2, Flu A, Flu B, and RSV infections in humans and is not intended to detect influenza C virus infections. Nucleic acids from the viral organisms identified by this test are generally detectable in NP and AN swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus and aids in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms. The organism(s) detected by

Item	Predicate Device **Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect), K222736))**	Subject Device **Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM and anterior nasal swab in VTM/UTM)**
	2/Flu A/B/RSV assay may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections. This assay is designed for use on the Panther Fusion system. The Hologic RespDirect Collection Kit can be used to collect NP specimens for testing with the Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay. Additionally, other NP swabs (not provided with the Hologic RespDirect Collection Kit) may be used to collect NP specimens in 3mL of VTM or UTM. **Ancillary Collection Kit:** Hologic RespDirect Collection Kit The Hologic RespDirect Collection Kit is intended to be used for the collection of nasopharyngeal (NP) swab specimens (collected by a healthcare provider) for testing with the Panther Fusion SARS-CoV-2/ Flu A/B/RSV assay.	the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections. This assay is designed for use on the Panther Fusion system. The Hologic RespDirect Collection Kit is cleared for NP swab specimens only for testing with the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay.
Specimen Types	• Nasopharyngeal swab specimen collected in VTM/UTM or eSTM (RespDirect)	• Nasopharyngeal swab specimen collected in VTM/UTM or eSTM (RespDirect) • Anterior nasal swab specimen collected in VTM/UTM

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect), K222736))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM and anterior nasal swab in VTM/UTM)
Adaptive Crosstalk Correction Implemented	• No	• Yes

VII. GUIDANCE DOCUMENTS REFERENCED

- The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], issued July 28, 2014
- Guidance for Industry and FDA Staff: Content of Premarket Submissions for Device Software Functions, issued June 14, 2023
- Electronic Submission Template for Medical Device 510(k) Submissions, issued October 2, 2023
- Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions, September 27, 2023
- Respiratory Viral Panel Multiplex Nucleic Acid Assay – Class II Special Controls Guidance for Industry and FDA Staff, October 9, 2009

VIII. PERFORMANCE DATA

Summary of Performance Testing – Bench (Analytical Studies)

The following analytical studies were performed to demonstrate the performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay with nasopharyngeal swab specimens collected from individuals exhibiting signs and symptoms of a respiratory tract infection. Analytical results for NP swabs represent results from the most challenging claimed clinical matrix type. With the exception of one study (i.e., Cutoff Study), all data from the analytical studies performed in NP swab matrix that were previously submitted with initial 510(k) submission K222736 (cleared

May 16, 2023) were reprocessed with validated Results Processor Tool version 3.1.1.0 (RP tool) and Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay Sequence File version 1.2.4.6 with the Adaptive Crosstalk Compensation factor. Data produced in the Cutoff study were generated with single target panels/samples which are not affected by Adaptive Crosstalk Correction since cross talk only impacts results where SARS-CoV-2 and Flu B are present. Since the Cutoff study data did not contain that condition, re-analysis was not required.

The same testing and acceptance criteria were utilized in the reanalysis of NP swab matrix studies previously submitted in K222736. The implementation of the ACC software update affectively resolves the potential for unexpected Flu B positive results in the presence of SARS-CoV-2. The validation of the ACC ADM software change demonstrated through assay and software verification and analytical/clinical wet-testing demonstrates that the assay and system performance is equivalent to the released on-market assay performance.

The following studies previously submitted in K222736 were reprocessed with validated Results Processor Tool version 3.1.1.0 (RP tool) and Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay Sequence File version 1.2.4.6 with the Adaptive Crosstalk Compensation factor. No changes to the previously performed study conclusions occurred after the reanalysis with ACC.

- Limit of Detection (LOD)
- Analytical Reactivity (Inclusivity)
- Analytical Exclusivity
- Cross Reactivity of Microorganisms
- Interfering Substances
- Competitive Interference/Co-Infection
- Within Laboratory Precision-Repeatability
- Matrix Equivalency
- Specimen Stability (VTM/UTM)
- Shipping Stability
- On-Board Stability
- Shelf-Life Stability

Additional supplemental analytical testing was performed to ensure that the Adaptive Crosstalk Correction factor added to the ADM software is effective in eliminating occasional occurrence of false Flu B positive results in the presence of SARS-CoV-2 positives and to verify that the software update does not impact the performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay when processed with the Assay Sequence File version 1.2.4.6. Studies included confirmation of the Limit of Detection (LoD) for Flu B, confirmation of no Competitive Interference between high SARS-CoV-2 concentration and low Flu B concentration co-infections and testing of SARS-CoV-2 positive clinical specimens that are representative of those that yielded false positive Flu B results in the field. A representative thermocycler that previously demonstrated unexpected Flu B positive results in the presence of SARS-CoV-2 using assay sequence file version 1.2.5.3 due to under correction of crosstalk between SARS-CoV-2 and Flu B channels (Red647/Q670) was used in these studies.

Table 4 Supplemental Analytical and Clinical Testing with Adaptive Crosstalk Correction

Title	Description of Testing
Confirmation of the Limit of Detection (LoD) for Flu B	Flu B LoD was confirmed with single target spiked and co-spiked panels. Panels consisted of cultured virus for one Victoria and one Yamagata strain for Flu B that is identical to that used to originally establish the LoD. Testing was performed at 1xLoD as well as half a log above and below the LoD. Testing also consisted of a co-spiked panel that is positive for one strain of SARS-CoV-2, Flu A, Flu B, and RSV at 3xLoD each. Pooled negative clinical nasopharyngeal (NP) swab in VTM/UTM matrix was used. 28 replicates were tested per panel. All panels were made in pooled negative clinical NP swab VTM/UTM processed into STM matrix at a 1:1.56 ratio. Negative NP samples were screened for negativity using the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay and pooled. Flu B Yamagata was detected at 96% (27/28) and Flu B Victoria was detected at 100% (28/28) at 1xLoD; both strains had <95% detection at half log below their respective LoDs. At 3x LoD, all analytes were detected at 100% (28/28). The LoD's for both strains of Flu B were confirmed to be the same as previously established. All analytes in the co-spiked samples were confirmed at 3x LoD.
Competitive interference with high SARS-CoV-2 and low Flu B	Testing consisted of one SARS-CoV-2 strain and one Flu B strain. Flu B was tested at 3x LoD and SARS-CoV-2 at 1e4 $TCID_{50}$/mL. Pooled negative clinical nasopharyngeal (NP) swab in VTM/UTM matrix was used. The panel was tested at three replicates. Flu B was 100% positive at 3x LoD in the presence of high titer SARS-CoV-2 at 1e4 $TCID_{50}$/mL, demonstrating no competitive interference. These

Title	Description of Testing
	results align with data originally produced without the ACC.
Resolution of unexpected Flu B positives in the presence of SARS-CoV-2	Resolution of unexpected Flu B positives in the presence of SARS-CoV-2 with Adaptive Crosstalk Correction in assay version 1.2.4.6 was demonstrated with individual NP swab in VTM/UTM clinical specimens naturally positive for SARS-CoV-2. Ten individual clinical specimens were tested at one replicate each to produce ten unexpected Flu B positive results using assay sequence file version 1.2.5.3. All specimens that produced unexpected Flu B positive results were retested at one replicate each using assay sequence file version 1.2.4.6 which has Adaptive Crosstalk Correction implemented. One replicate per specimen was tested in each assay sequence file version for a total of two replicates per specimen or panel. Resolution of unexpected Flu B positives in the presence of SARS-CoV-2 with ACC in assay version 1.2.4.6 was demonstrated for all ten clinical specimens.

Summary of Performance Testing – Clinical

Clinical Performance with Prospectively Collected Anterior Nasal Swab Specimens

A non-interventional, prospective, multicenter study was conducted. One thousand two hundred and sixty-eight (1,268) male and female individuals of all ages attending one of nine participating medical facilities (collection sites) in the US and who were exhibiting signs and symptoms of respiratory viral infection consistent with COVID-19, influenza, or RSV were enrolled during the 2022-2023 respiratory infection season. Two (2) anterior nasal swab (AN) swab specimens were collected from each consented individual using synthetic flocked swabs and stored in tubes containing universal/viral transport medium (UTM/VTM). All specimens for candidate testing were tested fresh (i.e., never frozen before testing).

The Panther Fusion SARS-CoV-2/Flu A/B/RSV assay was evaluated for SARS-CoV-2 performance by comparing the candidate device testing results to a composite comparator algorithm (CCA) consisting of up to three highly sensitive US FDA EUA SARS-CoV-2 molecular tests. A final CCA result was assigned when two of the three composite comparator assays were in concordance. The comparator method utilized to establish performance for the Flu A, Flu B, and RSV targets was a US FDA-cleared molecular Flu A/B/RSV assay.

Of the 1,268 subjects, (2) subjects were withdrawn. A total of 1230 nasal swab specimens in VTM/UTM were tested in valid Panther Fusion SARS-CoV-2/Flu A/B/RSV assay runs, including 10 (0.8%) with initial invalid results. Upon retest, 6 of the 10 specimens yielded valid results and 4 yielded invalid results, for a total of 1226 (99.7%) specimens with final valid results.

The final data set consisted of 1189 evaluable nasal swab specimens in VTM/UTM; not all were evaluable for all analytes. Non-evaluable specimens were excluded from the performance analyses for the following reasons: withdrawn Panther Fusion SARS-CoV-2/Flu A/B/RSV assay specimen (40 VTM/UTM), invalid or missing Panther Fusion SARS-CoV-2/Flu A/B/RSV assay result (4 VTM/UTM), unknown comparator method result (33 VTM/UTM each for SARS-CoV-2, Flu A, Flu B, and RSV).

The performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for the detection of all target viruses in prospective AN swab specimen is summarized in Table 5.

Table 5: Clinical Performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay in Prospectively Collected AN Swab Specimens in UTM/VTM

Target Virus	PPA	NPA
	% (95% CI) [n/N]	
SARS-CoV-2	94.8 (90.1, 97.3) [146/154]	98.8 (98.0, 99.3) [1023/1035]
Flu A	91.8 (80.8, 96.8) [45/49]	99.6 (99.0, 99.8) [1135/1140]
Flu B	66.7 (20.8, 93.9) [2/3]	99.7 (99.3, 99.9) [1183/1186]
RSV	94.4 (74.2, 99.0) [17/18]	99.8 (99.4, 100) [1169/1171]

Clinical Performance with Retrospective Anterior Nasal Swab Specimens

Flu B and RSV were of lower prevalence during the prospective clinical study and were therefore not encountered in large enough numbers to adequately demonstrate assay performance in AN swab specimens in VTM/UTM. Testing of 175 preselected retrospective specimens was performed to supplement the results of the prospective specimen population. In addition to evaluating Flu B and RSV positive specimens, Flu A positive specimens were included in the study. All known positive specimens underwent confirmatory testing using a US FDA-cleared molecular Flu A/B/RSV assay. Two (2) specimens were not included in the performance analyses because of a missing comparator result.

The performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for the detection of influenza A, influenza B, and RSV viruses in retrospective AN swab specimen is summarized in Table 6.

Table 6: Clinical Performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay in Retrospective AN Swab Specimens in UTM/VTM

Target Virus	PPA	NPA
	% (95% CI) [n/N]	
Flu A	97.9 (89.1, 99.6) [47/48]	98.4 (94.4, 99.6) [123/125]
Flu B	97.2 (90.3, 99.2) [69/71]	100 (96.4, 100) [102/102]
RSV	98.0 (89.5, 99.6) [49/50]	99.2 (95.5, 99.9) [122/123]

Conclusion Drawn from Clinical Results

This study was conducted to establish the performance characteristics of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay on the Panther/Panther Fusion system using anterior nasal swab specimens in UTM/VTM from symptomatic male and female subjects.

The conclusion drawn from the clinical study demonstrates that the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay is as safe and effective for the evaluation of the additional anterior nasal swab specimen type and performs comparably to the predicate device currently marketed for the intended use with nasopharyngeal swab specimens.

IX. CONCLUSIONS

The analytical and clinical study results demonstrate that the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for testing anterior nasal swab specimens on the Panther Fusion system performs comparably to the currently marketed predicate device with a nasopharyngeal swab claim. Hardware and software verification and validation demonstrate that the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay on the Panther Fusion system will perform as intended.