November 15, 2024

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

Re: K242465
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, OOI
Dated: August 19, 2024
Received: August 20, 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.

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

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

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

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Anna M. Mielech -S

Anna Mielech, Ph.D.
Deputy Branch Chief (Acting)
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)*
K242465

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.

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.

510(k) SUMMARY

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: October 15, 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 and anterior nasal swab specimens collected in UTM/VTM. The purpose of this pre-market submission is to add an anterior nasal swab collected in Enhanced Transport Medium (eSTM), collected from patients with signs and/or symptoms of respiratory infection, as a validated specimen type to the currently marketed Panther Fusion SARS-CoV- 2/Flu A/B/RSV assay (K241240; cleared July 18, 2024).

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)

V. INDICATIONS FOR 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 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 specimen 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.

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) and anterior nasal (AN) swab specimen collected in VTM/UTM (K241240, cleared July 18, 2024, 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 an anterior nasal swab specimen collected in eSTM to the intended use.

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 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) and AN Swab in VTM/UTM, K241240))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP and AN Swab in VTM/UTM or eSTM)
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) and AN Swab in VTM/UTM, K241240))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP and AN Swab in VTM/UTM or eSTM
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	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

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect) and AN Swab in VTM/UTM, K241240))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP and AN Swab in VTM/UTM or eSTM
	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.	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

Item	Predicate Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP Swab in VTM/UTM or eSTM (RespDirect) and AN Swab in VTM/UTM, K241240))	Subject Device Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay (NP and AN Swab in VTM/UTM or eSTM
	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.	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.
Specimen Types	• Nasopharyngeal (NP) swab specimens collected in VTM/UTM or eSTM (RespDirect) and anterior nasal (AN) specimens collected in VTM/UTM	• Nasopharyngeal and anterior nasal swab specimens collected in VTM/UTM or eSTM (RespDirect)

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 previously submitted in K22276 and K241240 were performed to demonstrate the performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay with nasopharyngeal swab specimens and anterior nasal swabs in UTM/VTM collected from individuals exhibiting signs and symptoms of a respiratory tract infection.

- 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

Summary of Performance Testing – Clinical

Clinical Performance with Prospectively Collected Anterior Nasal Swab Specimens collected in eSTM (RespDirect)

A non-interventional, prospective, multicenter study was conducted. One thousand thirty three (1033) 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/or symptoms of respiratory infection consistent with COVID-19, influenza, or RSV were enrolled in the prospective study between January 2023 and May 2023. Two (2) anterior nasal (AN) swab specimens were collected from each individual: one specimen for comparator testing was always collected by a healthcare professional (HCP) using a synthetic flocked swab and placed into UTM/VTM, and one specimen for Panther Fusion SARS-CoV-2/Flu A/B/RSV assay testing alternated between collection by the HCP or by the individual (under HCP supervision) using the RespDirect flocked swab in eSTM. Patient-collected specimens from minors were collected either by the minor or a guardian. AN swab specimens were tested either fresh (Category I specimens) or frozen (Category II specimens) with the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay at three U.S. testing sites.

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.

There were 1033 individuals enrolled in the prospective study. Four individuals were withdrawn, and 10 individuals were not evaluable for at least one target: one individual had their Panther Fusion SARS-CoV-2/Flu A/B/RSV specimen withdrawn, seven did not have a valid final Panther Fusion SARS-CoV-2/Flu A/B/RSV assay result, and two had unknown CCA results.

A total of 1032 nasal swab specimens from the prospective study were tested in valid Panther Fusion SARS-CoV-2/Flu A/B/RSV assay runs, including 11 (1.1%) with initial invalid results.

Upon retest, four specimens yielded valid results and seven yielded invalid results, for a total of 1025 (99.3%) specimens with final valid results.

The final data set consisted of 1021 evaluable AN swab specimens in the prospective study, of which 1011 were tested fresh (Category I specimens) with the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay and 10 were tested after freezing (Category II specimens); not all were evaluable for all analytes.

The performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for the detection of SARS-CoV-2, Flu A, Flu B, and RSV for prospective AN swab specimens in RespDirect eSTM is described in **Table 3**.

Table 3. Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay Performance in Prospectively Collected Anterior Nasal Swab Specimens in RespDirect eSTM

Target Virus	Prevalence[1] (%)	PPA		NPA	
		TP/(TP+FN)	% (95% CI)[2]	TN/(TN+FP)	% (95% CI)[2]
SARS-CoV-2	10.8	109/110	99.1 (95.0, 99.8)	900/909	99.0 (98.1, 99.5)
Flu A	1.1	11/11	100 (74.1-100)	1009/1010	99.9 (99.4, 100)
Flu B	0.6	5/6	83.3 (43.6, 97.0)	1013/1015	99.8 (99.3, 99.9)
RSV	0.1	1/1	100 (20.7, 100)	1019/ 1020	99.9 (99.4, 100)

CI = confidence interval, FN = false negative, FP = false positive, NPA = negative percent agreement, PPA = positive percent agreement, TP = true positive, TN = true negative.
[1]Study prevalence reported.
[2]Score CI.

Supplemental Clinical Data for Low Prevalence Analytes (Category III Specimens) - Anterior Nasal Swab Specimens in RespDirect eSTM

Flu A, Flu B and RSV were of lower prevalence and were not encountered in sufficiently large numbers during the prospective clinical study to adequately demonstrate assay performance with AN swab specimens collected with the RespDirect Collection Kit in eSTM media.

To supplement the results of the prospective clinical study, an enrichment phase of the study

was initiated. Two hundred and ten (210) male and female individuals of all ages attending one of six participating medical facilities (collection sites) in the US and who were exhibiting signs and/or symptoms of respiratory infection consistent with COVID-19, influenza, or RSV and had a positive standard of care (SOC) test result for Flu A, Flu B, and/or RSV were enrolled in the enrichment study between October 2023 and February 2024. Two (2) nasal swab specimens were collected from each individual: one specimen for comparator testing was always collected by a healthcare professional (HCP) using a synthetic flocked swab and placed into UTM/VTM, and one specimen for Panther Fusion SARS-CoV-2/Flu A/B/RSV assay testing alternated between collection by the HCP or by the individual (under HCP supervision) using the RespDirect flocked swab in eSTM. Patient-collected specimens from minors were collected either by the minor or a guardian. All enrichment study specimens were frozen prior to testing with the Panther Fusion SARS-CoV-2/ Flu A/B/RSV assay at one U.S. site.

Testing results from a U.S. FDA-cleared molecular Flu A/B/RSV assay were used to establish performance for Flu A, Flu B, and RSV targets for the enrichment study. Enrichment study specimens were collected to supplement the data for Flu A/B/RSV only because of the low prevalence of these viruses in prospective specimens, and therefore underwent comparator testing only for Flu A/B/RSV.

There were 210 individuals enrolled in the enrichment study. Six individuals were withdrawn.

A total of 205 nasal swab specimens from the enrichment study were tested in valid Panther Fusion SARS-CoV-2/Flu A/B/ RSV assay runs. Two (2) of these specimens were invalid by the candidate device during testing, for an initial invalid rate of 1.0% (2/205). Upon retesting, both specimens obtained valid results for a total of 205/205 (100%) specimens with final valid results.

The performance of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay for the detection of Flu A, Flu B, and RSV for AN swab specimens in RespDirect eSTM for the enrichment study is described in **Table 4**. PPA was calculated for enrichment study specimens that were confirmed positive for at least one target analyte. NPA was calculated for specimens that had a

negative result on the comparator assay although they were confirmed positive for one of the other targets.

Table 4. Panther Fusion SARS-CoV-2/Flu A/B/RSV Assay Performance for the Enrichment Study with AN Swab Specimens in RespDirect eSTM

Target Virus	PPA			NPA[1]		
	TP/ (TP+FN)	%	95% CI	TN/ (TN+FP)	%	95% CI
Flu A	69/71	97.2	90.3-99.2	124/133	93.2	87.6-96.4
Flu B	44/45	97.8	88.4-99.6	158/159	99.4	96.5-99.9
RSV	60/61	98.4	91.3-99.7	137/143	95.8	91.2-98.1

CI = confidence interval; FN = false negative; FP = false positive; NPA = negative percent agreement; PPA = positive percent agreement, TN = true negative; TP = true positive;
[1]All samples enrolled in the enrichment study were SOC positive for Flu A, Flu B, and/or RSV. The NPA for the enrichment study was calculated using results from all evaluable samples with a negative comparator result for the analyte of interest.

Conclusion Drawn from the Clinical Performance Studies

The data from the prospective and the enrichment studies demonstrate that the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay performs as expected for detecting SARS-CoV-2, Flu A, Flu B, and RSV nucleic acids in AN swab sample collected with the RespDirect Collection Kit in eSTM.

IX. CONCLUSIONS

The prospective study and enrichment study were conducted to establish the performance characteristics of the Panther Fusion SARS-CoV-2/Flu A/B/RSV assay on the Panther Fusion System using AN swab specimens in eSTM from individuals exhibiting signs and/or symptoms of respiratory infection.

The results from the clinical study demonstrate that the Panther Fusion SARS-CoV- 2/Flu A/B/RSV assay performs comparably to the predicate device currently marketed for the intended use with nasopharyngeal swab specimens collected in VTM/UTM or eSTM (RespDirect) and anterior nasal (AN) swab specimens collected in VTM/UTM.