Abbott Molecular Inc.
Stacy Ferguson
Director Regulatory Affairs
1300 E Touhy Ave,
Des Plaines, IL 60018,

Re: K233349
Trade/Device Name: Alinity m HSV 1 & 2 / VZV
Regulation Number: 21 CFR 866.3309
Regulation Name: Herpes Virus Nucleic Acid-Based Cutaneous And Mucocutaneous Lesion Panel
Regulatory Class: Class II
Product Code: PGI
Dated: March 26, 2024
Received: March 26, 2024

Dear Stacy Ferguson:

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,

Laura E. Ulitzky -S

Digitally signed by Laura E. Ulitzky -S
Date: 2024.05.03 13:24:17 -04'00'

Laura Ulitzky, Team Lead on behalf of:

Ryan Karsner, MD
Branch Chief
Deputy Assistant Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological HealthEnclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K233349

Device Name
Alinity m HSV 1 & 2 / VZV

Indications for Use *(Describe)*

The Alinity m HSV 1 & 2 / VZV assay is an in vitro real-time polymerase chain reaction (PCR) assay for the qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2) and Varicella Zoster Virus (VZV) DNA from clinician-collected cutaneous or mucocutaneous lesion swab specimens from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. The Alinity m HSV 1 & 2 / VZV assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster active cutaneous or mucocutaneous infections. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2 or varicella-zoster virus infections and should not be used as the sole basis for diagnosis, treatment or other management decisions.

The Alinity m HSV 1 & 2 / VZV assay is not intended for use with cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Alinity m HSV 1 & 2 / VZV assay is not intended for use in prenatal screening.

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

Submitter

Applicants Name and Address:	Abbott Molecular Inc. 1300 E. Touhy Ave Abbott Molecular Inc.
Contact Person:	Stacy Ferguson Director Regulatory Affairs Abbott Molecular, Inc. 1350 E. Touhy Avenue Des Plaines, IL 60018 Phone: 224-206-4081
Date Prepared:	May 1, 2024

Device Information

Trade Name	Regulation Name	Product Code	Regulation Number	Class
Alinity m HSV 1 & 2 / VZV	Herpes virus nucleic acid-based cutaneous and mucocutaneous lesion panel.	PGI	21 CFR 866.3309	II

Predicate Device

Predicate Device	Product Code	510(k)	Date Cleared
Lyra Direct HSV 1 + 2/VZV Assay	PGI	K133448	May 13, 2014

Intended Use

The Alinity m HSV 1 & 2 / VZV assay is an in vitro real-time polymerase chain reaction (PCR) assay for the qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2) and Varicella Zoster Virus (VZV) DNA from clinician-collected cutaneous or mucocutaneous lesion swab specimens from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. The Alinity m HSV 1 & 2 / VZV assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster active cutaneous or mucocutaneous infections. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2 or varicella-zoster virus

infections and should not be used as the sole basis for diagnosis, treatment or other management decisions.

The Alinity m HSV 1 & 2 / VZV assay is not intended for use with cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Alinity m HSV 1 & 2 / VZV assay is not intended for use in prenatal screening.

Device Description
The Alinity m HSV 1 & 2 / VZV assay is an in vitro real-time polymerase chain reaction (PCR) assay for the qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2) and Varicella Zoster Virus (VZV) DNA from clinician--collected cutaneous or mucocutaneous lesion swab specimens from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. This assay is intended for use with the automated Alinity m System.

The steps of the Alinity m HSV 1 & 2 / VZV assay consist of sample preparation, PCR assembly, amplification/detection, and result calculation and reporting. The steps involved in all stages of the Alinity m HSV 1 & 2 / VZV assay procedure are executed automatically by the Alinity m System. No intermediate processing or transfer steps are performed by the user. The Alinity m System is designed to be a random access analyzer that can perform the Alinity m HSV 1 & 2 / VZV assay in parallel with other Alinity assays on the same instrument.

The Alinity m HSV 1 & 2 / VZV assay requires two separate assay specific kits as follows:

1) The Alinity m HSV 1 & 2 / VZV AMP Kit (List No. 09N61-095) is comprised of 2 types of multi-well trays:

TRAY 1: Alinity m HSV 1 & 2 / VZV AMP TRAY 1
TRAY 2: Alinity m HSV 1 & 2 / VZV ACT TRAY 2.

TRAY 1 - Alinity m HSV 1 & 2 / VZV AMP is individually packed in a foil pouch and contains 48 unit-dose liquid amplification reagent wells and 48 unit-dose liquid IC wells. One well of each is used per test.

- Amplification reagent wells consist of synthetic oligonucleotides, DNA Polymerase, dNTPs, and 0.15% ProClin® 950 in a buffered solution with a reference dye. IC wells consist of plasmid DNA with unrelated IC sequences and poly dA:dT in a TE buffer containing 0.15% ProClin 950 as a preservative.

TRAY 2 - Alinity m HSV 1 & 2 / VZV ACT is individually packed in a foil pouch and contains 48 unit-dose liquid activation reagent wells. One reagent well is used per test.

• Activation reagent wells consist of magnesium chloride, potassium chloride, and tetramethylammonium chloride. Preservative: 0.15% ProClin 950.

Alinity m HSV 1 & 2 / VZV Assay Kit	
Alinity m HSV 1 & 2 / VZV AMP Kit	**Quantity 192 Tests**
Alinity m HSV 1 & 2 / VZV AMP TRAY 1	4 Trays/48 Test Each
Alinity m HSV 1 & 2 / VZV ACT TRAY 2	4 Trays/48 Test Each

2) The Alinity m HSV 1 & 2 / VZV CTRL Kit (09N61-085) consists of negative controls and positive controls, each supplied as liquid in single-use tubes.

Alinity m HSV 1 & 2 / VZV Negative CTRL (List No. 9N61Z) consists of Negative Diluent / TE buffer (containing 0.085% Sodium Azide and 0.087% ProClin 950).

Alinity m HSV 1 & 2 / VZV Positive CTRL (List No. 9N61W) consists of linearized plasmid DNA containing HSV-1, HSV-2 and VZV DNA sequences in Negative Diluent / TE buffer (containing 0.085% Sodium Azide and 0.087% ProClin 950).

Alinity m HSV 1 & 2 / VZV Control Kit	
Alinity m HSV 1 & 2 / VZV Negative CTRL	12 Tube x 0.75 mL
Alinity m HSV 1 & 2 / VZV Positive CTRL	12 Tube x 0.75 mL

The Alinity m HSV 1 & 2 / VZV assay is to be run on the Alinity m System which is a fully integrated, sample to result automated system that performs real-time PCR test using the Alinity m HSV 1 & 2 / VZV AMP Kit along with the Alinity m HSV 1 & 2 / VZV CTRL Kit.

Similarities and Differences to Predicate Device

Device and Predicate	New Device K233349	Predicate Device K133448
Device Trade Number	**Alinity m HSV 1 & 2 / VZV Assay**	**Lyra Direct HSV 1 + 2/VZV Assay**
Similarities		
Intended Use	The Alinity m HSV 1 & 2 / VZV assay is an in vitro real-time polymerase chain reaction (PCR) assay for the qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2), and Varicella Zoster Virus (VZV) DNA from clinician-collected cutaneous or mucocutaneous lesion swab specimens from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster virus infection. The Alinity m HSV 1 & 2 / VZV assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster virus active cutaneous or mucocutaneous infections. Negative results do not preclude herpes simplex virus type 1, herpes simplex virus type 2 or varicella-zoster virus infections and should not be used as the sole basis for diagnosis, treatment or other management decisions. The Alinity m HSV 1 & 2 / VZV assay is not intended for use with cerebrospinal fluid (CSF) or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Alinity m HSV 1 & 2 / VZV assay is not intended for use in prenatal screening.	The Lyra Direct HSV 1 + 2/VZV Assay is an in vitro multiplex Real-Time PCR test for qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus DNA isolated and purified from cutaneous or mucocutaneous lesion samples obtained from symptomatic patients suspected of active herpes simplex virus 1, herpes simplex virus 2 and/or varicella-zoster infection. The Lyra Direct HSV 1 + 2/VZV Assay is intended to aid in the diagnosis of herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus active cutaneous or mucocutaneous infections. Negative results do not preclude herpes simplex virus 1, herpes simplex virus 2 and varicella-zoster virus infections and should not be used as the sole basis for diagnosis, treatment or other management decisions. The Lyra Direct HSV 1 + 2/VZV Assay is not intended for use with cerebrospinal fluid or to aid in the diagnosis of HSV or VZV infections of the central nervous system (CNS). The Lyra Direct HSV 1 + 2/VZV Assay is not intended for use in prenatal screening. The device is not intended for point-of-care use.
Assay Type	Qualitative	Same
Assay Targets	Viral DNA from HSV-1, HSV-2, and VZV	Same
Specimen Types	Cutaneous and Mucocutaneous (Lesion and Lesion swab specimens)	Same
Amplification Technology	Real-Time Polymerase Chain Reaction (PCR)	Same
Automated Analysis	Yes	Same
Assay Controls	• Negative Control • Positive Control	Same
Differences		

Assay Steps	All steps of the Alinity m HSV 1 & 2 / VZV assay procedure are executed automatically by the Alinity m System. No intermediate processing or transfer steps are performed by the user.	Assay processing steps are executed manually until placed on instrument for signal evaluation: • Life Technologies QuantStudio Dx • Applied Biosystems 7500 Fast Dx • Cepheid SmartCycler II System
Sample Preparation Instrument Components	Automated liquid handling and robotic manipulation platform. Automated process for sample processing using an internal control (IC)	Mechanical lysis and addition of Process Buffer. Manual process for sample processing using the processing control (PRC)
Reagent Kit Storage (Unopened) until expiration date	-25^{0}C to -15^{0}C	2^{0}C to 8^{0}C

Performance Data

The following performance data were provided in support of the substantial equivalence determination.

Analytical Studies

Analytical Sensitivity/Limit of Detection (LoD)

The limit of detection (LoD) for Alinity m HSV 1 & 2 / VZV assay for each analyte were determined by quantified ($TCID_{50}$/mL) cultures of HSV-1 (Maclntyre), HSV-2 (MS) or VZV (Ellen) viral strains diluted into pooled negative clinical swab specimens. The LoD of each analyte is presented below in **Table 1**.

Table 1. Limit of Detection

Analyte	Strain	LoD ($TCID_{50}$/mL)
HSV-1	MacIntyre	5.90
HSV-2	MS	2.07
VZV	Ellen	0.055

Inclusivity

The inclusivity for the Alinity m HSV 1 & 2 / VZV assay was determined by testing 5 HSV-1 strains / isolates, 3 HSV-2 strains / isolates and 5 VZV strains / isolates. The strains whose reported units of measure were in $TCID_{50}$/mL, were diluted to a concentration ≤ 3X LoD. For strains where concentration in $TCID_{50}$/mL was not available, a dilution series based on copies/mL was prepared and tested. The dilution series consisted of at least one concentration that resulted in positive results 100% of the time, and at least one concentration that resulted in positive results <100% of the time. The Alinity m HSV 1 & 2 / VZV assay detected all strains listed in **Table 2** at a level of 3X LoD.

Table 2. Inclusivity

Analyte	Strain	Concentration	Inclusive (Yes/No)
HSV-1	MacIntyre	17.7 $TCID_{50}$/mL	Yes
	HF	17.7 $TCID_{50}$/mL	Yes
	F	17.7 $TCID_{50}$/mL	Yes
	KOS	300 copies/mL[a]	Yes
	Vero 2 Isolate	17.7 $TCID_{50}$/mL	Yes
HSV-2	MS	6.21 $TCID_{50}$/mL	Yes
	G	6.21 $TCID_{50}$/mL	Yes
	Vero 2 Isolate	6.21 $TCID_{50}$/mL	Yes
VZV	Ellen	0.093 $TCID_{50}$/mL	Yes
	82	100 copies/mL[a]	Yes
	Oka	0.093 $TCID_{50}$/mL	Yes
	Webster	0.093 $TCID_{50}$/mL	Yes
	AV92-3:L	0.093 $TCID_{50}$/mL	Yes

[a] Lowest level that has 100% detection.

Analytical Specificity- Cross Reactivity and Microbial Interference

A total of 55 potential cross-reacting microorganisms (viruses, bacteria, and fungi) that are commonly encountered in lesion swab specimens were tested with Alinity m HSV 1 & 2 / VZV assay to assess analytical specificity. The microorganisms were tested at 10^5 Units/mL for viruses and fungi, and 10^6 Units/mL for bacteria or the highest titer available. No cross-reactivity was observed with the 55 microorganisms tested with the Alinity m HSV 1 & 2 / VZV assay. In addition, no interference was observed with 55 microorganisms when tested in the presence of each analyte at 3x LoD levels e,g., HSV-1, HSV-2 or VZV.

Table 3. Cross-Reacting and Interfering Microorganisms Tested

Acinetobacter calcoaceticus	Herpes Virus 6A strain GS
Acinetobacter Iwoffii	Herpes Virus 6B strain Z29
Actinomyces israelii	HIV-1
Adenovirus type 1	HPV 16
Adenovirus type 7	HPV 18
Bacteroides fragilis	*Kingella kingae*
BK virus	*Klebsiella pneumoniae*
Bordetella pertussis	*Listeria monocytogenes*
Campylobacter jejuni	*Mobiluncus mulieris*
Candida albicans	*Moraxella catarrhalis*
Chlamydophila pneumoniae	*Mycobacterium tuberculosis*[a]
Chlamydia trachomatis serovar D	*Neisseria gonorrhoeae*
Chlamydia trachomatis serovar I	*Neisseria meningitidis*
Clostridioides difficile	*Proteus mirabilis*
Clostridium perfringens	*Proteus vulgaris*
Cryptococcus neoformans	*Pseudomonas aeruginosa*
Cutibacterium acnes	*Staphylococcus aureus*
Cytomegalovirus	*Staphylococcus epidermidis*
Enterobacter cloacae	*Staphylococcus saprophyticus*
Enterococcus faecalis	*Streptococcus agalactiae*
Enterococcus faecium	*Streptococcus mitis*
Epstein-Barr virus	*Streptococcus mutans*
Escherichia coli	*Streptococcus pneumoniae*
Fusobacterium nucleatum	*Streptococcus pyogenes*
Haemophilus ducreyi	*Streptococcus salivarius*
Haemophilus influenzae	*Treponema pallidum*
Hepatitis B virus	*Toxoplasma gondii*
Hepatitis C virus	

[a] *Mycobacterium tuberculosis* genomic DNA was used as target.

Interfering Substances

The performance of the Alinity m HSV 1 & 2 / VZV assay was evaluated with potentially interfering endogenous and exogenous substances that may be present in cutaneous or mucocutaneous lesion specimens. A panel composed of 24 substances listed in **Table 4** was tested in the absence or presence of HSV-1, HSV-2, or VZV (MacIntyre strain, MS strain, Ellen strain, respectively) at 3x LOD in the Alinity m HSV 1 & 2 / VZV assay. There was no evidence of interference (false positive or false negative results) caused by the substances tested at the concentrations shown below in **Table 4**.

Table 4. Interfering Substances Tested

Substance	Test Level
Blood (human)	5% v/v
Leukocytes	10^6 cells/mL
Mucin	0.3% v/v
Urine	5% v/v
Feces	0.1% w/v
Human Serum Albumin	1% w/v
Saliva	4% v/v
Seminal Fluid	5% v/v
K-Y Jelly (Personal Lubricant)	2.5% w/v
Vaginal Contraceptive Gel	2.5% w/v
Monistat (Miconazole Nitrate Vaginal Cream)	3% w/v
Preparation H (Hemorrhoidal Ointment)	2.5% w/v
Abreva (Cold Sore Cream)	2.5% w/v
Acyclovir	2.5% w/v
Vagisil (Anti-Itch Cream)	0.25% w/v
Vagicaine (Anti-Itch Cream)	2.5% w/v
Feminine Wash (Douche)	2.5% w/v
Denavir (Anti-retro viral cream)	2.5% w/v
Feminine Deodorant Spray	2.5% w/v
Lip Balm	3% w/v
Summer's Eve (Body Powder)	2.5% w/v
Toothpaste	2.5% w/v
Casein protein	0.7% w/v
Mouthwash	3% v/v

Competitive Interference

A competitive interference study was conducted to challenge the performance of the Alinity m HSV 1 & 2 / VZV assay. Each sample was prepared with 2 of the analytes (HSV-1, HSV-2 or VZV) at 3X LoD and the third analyte at 1000X LoD in negative simulated matrix.

The three Panel Members (PM) evaluated were:

- PM 1: HSV-1 and HSV-2 at 3X LoD and VZV at 1000X LoD
- PM 2: HSV-1 and VZV at 3X LoD and HSV-2 at 1000X LoD
- PM 3: HSV-2 and VZV at 3X LoD and HSV-1 at 1000X LoD

Across panel members, all replicates at the low concentration were detected for each of the 3 analytes. None of the analyte targets present at the high concentration interfered with the detection of the other 2 analyte targets at low levels. Results are presented in the **Table 5**.

Table 5. Competitive Interference Results

Panel Number	High Analyte	HSV-1 Positivity	HSV-2 Positivity	VZV Positivity
PM 1	HSV- 1 & 2 at 3X LoD and VZV at 1000X LoD	100.0% (24/24)	100.0% (24/24)	100.0% (24/24)
PM 2	HSV-1 and VZV at 3X LoD and HSV-2 at 1000X LoD	100.0% (23/23)	100.0% (23/23)	100.0% (23/23)
PM 3	HSV-2 and VZV at 3X LoD and HSV-1 at 1000X LoD	100.0% (24/24)	100.0% (24/24)	100.0% (24/24)

Carryover Contamination

The carryover rate for Alinity m HSV 1 & 2 / VZV assay was determined by testing 360 alternating replicates of negative and high-positive samples. High positive samples consisted of HSV-2 DNA targeted to a CN value of 10.00. The testing was performed across 3 different Alinity m Systems. All negative samples reported negative interpretations, resulting in an overall carryover rate of 0.0% (0/360, 95% CI: 0.0%, 1.1%).

Within-Laboratory Precision

Alinity m HSV 1 & 2 / VZV assay within-laboratory Precision was evaluated by testing a 4 member precision panel consisting of 4 target levels (Moderate Positive, Low Positive, Sub-LoD, and Negative). Each positive panel member was prepared by spiking HSV-1, HSV-2, and VZV stocks into simulated negative matrix to achieve the targeted level at Moderate Positive (3X LoD), Low Positive (1X to 2X LoD), sub-LoD (<1X LoD). Each panel member was tested with 3 replicates in a run, 2 runs on each of 5 days, on 3 Alinity m Systems operated by 3 operators (one operator per system), using 3 Alinity m HSV 1 & 2 / VZV AMP Kit lots (one lot per system) for a total of 90 replicates of each panel member. The results for HSV-1, HSV-2, and VZV are described in **Table 6**. For the negative panel member, no HSV-1, HSV-2, or VZV was detected in any replicate.

Table 6. Precision

				Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory[c]		Between-Instrument/ Lot/Operator Component		Total[d]	
Analyte	Panel Description	Rate of Detection (n^a/N^b)	Mean (CN)	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
HSV-1	3X LoD	100.0% (90/90)	26.31	0.233	0.9	0.000	0.0	0.000	0.0	0.233	0.9	0.178	0.7	0.293	1.1
	1X - 2X LoD	100.0% (90/90)	26.82	0.181	0.7	0.060	0.2	0.089	0.3	0.210	0.8	0.245	0.9	0.323	1.2
	<1X LoD	78.9% (71/90)	30.26	0.418	1.4	0.095	0.3	0.000	0.0	0.428	1.4	0.125	0.4	0.446	1.5
HSV-2	3X LoD	100.0% (90/90)	29.03	0.265	0.9	0.000	0.0	0.024	0.1	0.266	0.9	0.233	0.8	0.354	1.2
	1X - 2X LoD	100.0% (90/90)	29.60	0.270	0.9	0.156	0.5	0.000	0.0	0.311	1.1	0.243	0.8	0.395	1.3
	<1X LoD	90.0% (81/90)	32.07	0.474	1.5	0.219	0.7	0.000	0.0	0.522	1.6	0.063	0.2	0.526	1.6
VZV	3X LoD	100.0% (90/90)	27.38	0.257	0.9	0.118	0.4	0.000	0.0	0.283	1.0	0.104	0.4	0.301	1.1
	1X - 2X LoD	100.0% (90/90)	28.77	0.305	1.1	0.204	0.7	0.000	0.0	0.367	1.3	0.125	0.4	0.388	1.3
	<1X LoD	88.9% (80/90)	31.92	0.586	1.8	0.353	1.1	0.000	0.0	0.684	2.1	0.315	1.0	0.753	2.4

[a] Number of replicates with positive results used in the Mean and SD calculation.

[b] Total Number of replicates.

[c] Within-Laboratory includes Within-Run, Between-Run and Between-Day Components.

[d] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument/Lot/Operator Components.

Reproducibility Study

Reproducibility performance of the Alinity m HSV 1 & 2 / VZV assay was evaluated by testing a 4-member reproducibility panel consisting of 4 target levels (Positive, Low Positive, High Negative, and Negative). Each positive panel members were prepared by spiking HSV-1, HSV-2 and VZV stocks into simulated negative matrix to achieve the targeted level at 5X LoD (Positive), 1X to 2X LoD (Low Positive), sub-LoD (High Negative), and Negative panel member. A total of 3 Alinity m HSV 1 & 2 / VZV AMP Kit lots were used. Each of 3 external sites tested 2 Alinity m HSV 1 & 2 / VZV AMP Kit lots, on 5 non-consecutive days for each lot. Six replicates of each panel member were tested on each of 5 days. Each of the 3 external sites used different lots of Alinity m HSV 1 & 2 / VZV CTRL Kits and Alinity m Sample Prep Kit 2. The reproducibility results for HSV-1, HSV-2 and VZV are summarized in **Table 7**.

Table 7. Reproducibility

Analyte	Panel Description	Rate of Detection (n^a/N^b)	Mean (CN)	Within-Run/Day Component		Between-Run/Day Component		Between-Lot Component		Between-Site/Instrument Component		Total[c]	
				SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
HSV-1	5X LoD	100.0% (180/180)	27.21	0.322	1.2	0.140	0.5	0.097	0.4	0.000	0.0	0.364	1.3
	1X-2X LoD	98.9% (178/180)	28.96	0.413	1.4	0.000	0.0	0.041	0.1	0.066	0.2	0.421	1.5
	<1X LoD	49.4% (89/180)	30.52	0.406	1.3	0.000	0.0	0.000	0.0	0.037	0.1	0.408	1.3
HSV-2	5X LoD	100.0% (180/180)	29.53	0.311	1.1	0.142	0.5	0.054	0.2	0.105	0.4	0.362	1.2
	1X-2X LoD	100.0% (180/180)	30.56	0.391	1.3	0.102	0.3	0.192	0.6	0.084	0.3	0.455	1.5
	<1X LoD	35.6% (64/180)	32.38	0.421	1.3	0.000	0.0	0.115	0.4	0.000	0.0	0.437	1.3
VZV	5X LoD	100.0% (180/180)	27.38	0.409	1.5	0.154	0.6	0.000	0.0	0.184	0.7	0.474	1.7
	1X-2X LoD	100.0% (180/180)	29.22	0.438	1.5	0.152	0.5	0.057	0.2	0.133	0.5	0.486	1.7
	<1X LoD	62.2% (112/180)	32.21	0.577	1.8	0.000	0.0	0.000	0.0	0.097	0.3	0.585	1.8

[a] Number of replicates with positive results used in the Mean and SD calculation.

[b] Total Number of replicates.

[c] Total includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Components.

Clinical Performance Evaluation

Performance characteristics of the Alinity m HSV 1 & 2 / VZV assay were established in prospective and retrospective clinical studies conducted in the United States.

Prospective Study

The multicenter, prospective clinical study was conducted using swab specimens from lesions (including cutaneous and mucocutaneous) of symptomatic individuals suspected of HSV-1, HSV-2, and/or VZV infection at geographically diverse locations in the US. All lesion swab specimens were prospectively collected in BD UVT, COPAN UTM, or Remel M4RT collection media. The subjects were male and female individuals of all ages, including pediatric and geriatric populations.

The swab specimens included in the study were categorized as cutaneous (e.g., skin lesion), mucocutaneous (e.g., anorectal, vaginal/cervical, and oral lesion), and uncategorized (lesion type could not be determined). A total of 1,258 results were included in the clinical performance analysis for each analyte (1,257 results for HSV-1, 1,257 results for HSV-2, and 1,257 results for VZV).

The gender and age demographics for each lesion type are listed in **Table 8**.

Table 8. Prospective Study - Age and Gender Distribution by Lesion Type

		Number of Specimens		
Lesion Type	Age	Female Subjects (# Lesions)	Male Subjects (# Lesions)	Total (# Lesions)
Cutaneous	≤ 5 Years	10 (11)	15 (16)	25 (27)
	6 to 21 Years	24 (28)	27 (28)	51 (56)
	22 to 59 Years	176 (195)	163 (183)	339 (378)
	≥ 60 Years	82 (95)	78 (86)	160 (181)
	Total	292 (329)	283 (313)	575 (642)
Mucocutaneous	≤ 5 Years	13 (20)	14 (29)	27 (49)
	6 to 21 Years	33 (34)	12 (13)	45 (47)
	22 to 59 Years	219 (240)	120 (170)	339 (410)
	≥ 60 Years	62 (80)	21 (27)	83 (107)
	Total	327 (374)	167 (239)	494 (613)
Uncategorized	≤ 5 Years	0 (0)	0 (0)	0 (0)
	6 to 21 Years	0 (0)	0 (0)	0 (0)
	22 to 59 Years	0 (0)	0 (0)	0 (0)
	≥ 60 Years	3 (3)	0 (0)	3 (3)
	Total	3 (3)	0 (0)	3 (3)
Total	Total	622 (706)	450 (552)	1072 (1258[a])

[a]One specimen did not have a result for HSV-1 and HSV-2 but did have a result for VZV; another specimen did not have result for VZV but did have result for HSV-1 and HSV-2; therefore, a total of 1,257 results were included for each analyte.

The Alinity m HSV 1 & 2 / VZV assay results for each analyte were directly compared to commercially available NAAT comparator method (NAAT 1). For specimens with discordant results between Alinity m and the comparator method, testing with a second commercially available RT-PCR comparator method was performed (NAAT 2). Results of testing on discordant samples were not included in the analysis of device performance and are considered for information purposes only.

The prospective clinical agreement of Alinity m HSV 1 & 2 / VZV assay compared to a commercially available NAAT comparator method is summarized in **Table 9**. Overall, for HSV-1, positive percent agreement (PPA) was 97.6% and negative percent agreement (NPA) was 98.9%. For HSV-2, PPA was 99.2% and NPA was 99.2%. For VZV, PPA was 97.7% and NPA was 99.8%. Clinical performance by the lesion type is also shown in **Table 9.**

Table 9. Clinical Agreement by Analyte and Lesion Type - Prospective Study

Analyte	Sample Type	N	NAAT 1 + Alinity +	NAAT 1 + Alinity -	NAAT 1 - Alinity -	NAAT 1 - Alinity +	PPA (%) with 95% CI	NPA (%) with 95% CI
HSV-1	Cutaneous	641	36	0	600	5	100.0 (36/36) (90.4, 100.0)	99.2 (600/605) (98.1, 99.6)
	Mucocutaneous	613	87	2	517	7	97.8 (87/89) (92.2, 99.4)	98.7 (517/524) (97.3, 99.4)
	Uncategorized[a]	3	0	1	2	0	0.0 (0/1) (0.0, 79.3)	100.0 (2/2) (34.2, 100.0)
	Total	1257	123	3[b]	1119	12[c]	97.6 (123/126) (93.2, 99.2)	98.9 (1119/1131) (98.2, 99.4)
HSV-2	Cutaneous	641	61	1	575	4	98.4 (61/62) (91.4, 99.7)	99.3 (575/579) (98.2, 99.7)
	Mucocutaneous	613	60	0	548	5	100.0 (60/60) (94.0, 100.0)	99.1 (548/553) (97.9, 99.6)
	Uncategorized[a]	3	1	0	2	0	100.0 (1/1) (20.7, 100.0)	100.0 (2/2) (34.2, 100.0)
	Total	1257	122	1[d]	1125	9[e]	99.2 (122/123) (95.5, 99.9)	99.2 (1125/1134) (98.5, 99.6)
VZV	Cutaneous	641	38	0	601	2	100.0 (38/38) (90.8, 100.0)	99.7 (601/603) (98.8, 99.9)
	Mucocutaneous	613	5	1	607	0	83.3 (5/6) (43.6, 97.0)	100.0 (607/607) (99.4, 100.0)
	Uncategorized[a]	3	0	0	3	0	-	100.0 (3/3) (43.9, 100.0)
	Total	1257	43	1[f]	1211	2[g]	97.7 (43/44) (88.2, 99.6)	99.8 (1211/1213) (99.4, 100.0)

[a] The lesion type for these swabs could not be determined.
[b] 3 out of 3 NAAT 1+/Alinity m HSV-1 negative results were negative by NAAT 2.
[c] 2 out of 12 NAAT 1-/Alinity m HSV-1 positives were positive by NAAT 2.
[d] 1 out of 1 NAAT 1+/Alinity m HSV-2 negative results were negative by NAAT 2.
[e] 3 out of 9 NAAT 1-/Alinity m HSV-2 positives were positive by NAAT 2.
[f] 1 out of 1 NAAT 1+/Alinity m VZV negative results were negative by NAAT 2.
[g] 0 out of 2 NAAT 1-/Alinity m VZV positives were positive by NAAT 2.

Retrospective Study

The retrospective study was conducted using archived, leftover lesion swab specimens from routine clinical testing, collected from male and female individuals of all ages, including pediatric and geriatric populations. All lesion swab specimens were previously collected in BD UVT, COPAN UTM, or Remel M4RT collection media per standard of care. One lesion swab specimen was obtained from each individual.

The swab specimens included in the study were categorized as cutaneous (eg, skin lesion), mucocutaneous (eg, anorectal, vaginal/cervical, and oral lesion), and uncategorized (lesion type could not be determined or categorized). A total of 411 specimens were included in the clinical performance analysis that had results for at least one of the analytes (410 results for HSV-1, 410 results for HSV-2, and 411 results for VZV).

The gender and age demographics for each lesion type are listed in **Table 10**.

Table 10. Retrospective Study - Age and Gender Distribution by Lesion Type

		Number of Specimens		
Lesion Type	Age	Female Subjects (# Lesions)	Male Subjects (# Lesions)	Total (# Lesions)
Cutaneous	≤ 5 Years	8 (8)	17 (17)	25 (25)
	6 to 21 Years	9 (9)	9 (9)	18 (18)
	22 to 59 Years	60 (60)	25 (25)	85 (85)
	≥ 60 Years	9 (9)	10 (10)	19 (19)
	Total	86 (86)	61 (61)	147 (147)
Mucocutaneous	≤ 5 Years	31 (31)	28 (28)	59 (59)
	6 to 21 Years	18 (18)	13 (13)	31 (31)
	22 to 59 Years	78 (78)	33 (33)	111 (111)
	≥ 60 Years	20 (20)	13 (13)	33 (33)
	Total	147 (147)	87 (87)	234 (234)
Uncategorized	≤ 5 Years	5 (5)	4 (4)	9 (9)
	6 to 21 Years	2 (2)	1 (1)	3 (3)
	22 to 59 Years	8 (8)	8 (8)	16 (16)
	≥ 60 Years	0 (0)	2 (2)	2 (2)
	Total	15 (15)	15 (15)	30 (30)
Total	Total	248 (248)	163 (163)	411 (411)

The Alinity m HSV 1 & 2 / VZV assay results for each analyte were directly compared to commercially available NAAT comparator method (NAAT 1). For specimens with discordant results between Alinity m and the comparator method, testing with a second commercially available RT-PCR comparator method was performed (NAAT 2). Results of testing on discordant samples were not included in the analysis of device performance and are considered for information purposes only.

The retrospective clinical agreement of Alinity m HSV 1 & 2 / VZV assay compared to the comparator method is summarized in Table 11. For HSV-1, positive percent agreement (PPA) was 100.0% and negative percent agreement (NPA) was 96.2%. For HSV-2, PPA was 98.7% and NPA was 95.8%. For VZV, PPA was 97.8% and NPA was 98.4%. Clinical performance by the lesion type is also shown in **Table 11.**

Table 11. Clinical Agreement by Analyte and Lesion Type - Retrospective Study

Analyte	Sample Type	N	NAAT 1 + Alinity +	NAAT 1 + Alinity -	NAAT 1 - Alinity -	NAAT 1 - Alinity +	PPA (%) with 95% CI	NPA (%) with 95% CI
HSV-1	Cutaneous	147	16	0	124	7	100.0 (16/16) (80.6, 100.0)	94.7 (124/131) (89.4, 97.4)
	Mucocutaneous	234	51	0	178	5	100.0 (51/51) (93.0, 100.0)	97.3 (178/183) (93.8, 98.8)
	Uncategorized[a]	29	5	0	23	1	100.0 (5/5) (56.6, 100.0)	95.8 (23/24) (79.8, 99.3)
	Total	410	72	0	325	13[b]	100.0 (72/72) (94.9, 100.0)	96.2 (325/338) (93.5, 97.7)
HSV-2	Cutaneous	147	23	1	115	8	95.8 (23/24) (79.8, 99.3)	93.5 (115/123) (87.7, 96.7)
	Mucocutaneous	234	44	0	186	4	100.0 (44/44) (92.0, 100.0)	97.9 (186/190) (94.7, 99.2)
	Uncategorized[a]	29	7	0	20	2	100.0 (7/7) (64.6, 100.0)	90.9 (20/22) (72.2, 97.5)
	Total	410	74	1[c]	321	14[d]	98.7 (74/75) (92.8, 99.8)	95.8 (321/335) (93.1, 97.5)
VZV	Cutaneous	147	20	0	125	2	100.0 (20/20) (83.9, 100.0)	98.4 (125/127) (94.4, 99.6)
	Mucocutaneous	234	17	0	214	3	100.0 (17/17) (81.6, 100.0)	98.6 (214/217) (96.0, 99.5)
	Uncategorized[a]	30	7	1	21	1	87.5 (7/8) (52.9, 97.8)	95.5 (21/22) (78.2, 99.2)
	Total	411	44	1[e]	360	6[f]	97.8 (44/45) (88.4, 99.6)	98.4 (360/366) (96.5, 99.2)

[a] The lesion type for these swabs could not be determined or categorized.

[b] 0 out of 13 NAAT 1-/Alinity m HSV-1 positives were positive by NAAT 2.

[c] 1 out of 1 NAAT 1+/Alinity m HSV-2 negative results were negative by NAAT 2.

[d] 0 out of 14 NAAT 1-/Alinity m HSV-2 positives were positive by NAAT 2.

[e] 1 out of 1 NAAT 1+/Alinity m VZV negative results were negative by NAAT 2.

[f] 0 out of 6 NAAT 1-/Alinity m VZV positives were positive by NAAT 2.

Conclusions Drawn from the Studies

The analytical and clinical study results demonstrate that the Alinity m HSV 1 & 2 / VZV assay on the Alinity m System performs comparably to the predicate device in detecting HSV 1 & 2 / VZV and supports a substantial equivalence decision.