510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K233349

B Applicant

Abbott Molecular Inc.

C Proprietary and Established Names

Alinity m HSV 1 & 2 / VZV

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PGI	Class II	21 CFR 866,3309 - Herpes Virus Nucleic Acid-Based Cutaneous And Mucocutaneous Lesion Panel	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of a new device

B Measurand:

Target DNA sequences from conserved regions of the herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), and varicella-zoster virus (VZV) genes.

C Type of Test:

Molecular diagnostic test using real-time PCR (Polymerization Chain Reaction) technology for the direct qualitative detection and differentiation of HSV 1, HSV 2 and VZV DNA extracted and purified from cutaneous or mucocutaneous lesion samples.

III Intended Use/Indications for Use:

A Intended Use(s):

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.

B Indication(s) for Use:

Alinity m HSV 1 & 2 / VZV assay. See Intended Use (s)

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in vitro diagnostic Use only

D Special Instrument Requirements:

Alinity m System

IV Device/System Characteristics:

A 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 lesion swab specimens (including cutaneous or mucocutaneous lesion specimens).
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 HSV 1 & 2 / VZV assay procedure are executed automatically by the Alinity m System.

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

1) The Alinity m HSV 1 & 2 / VZV AMP Kit 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 11 & 2 / V 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% ProClin950 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. Each Alinity m HSV 1 & 2 / VZV ACT

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.

Table 1: 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 consists of negative controls and positive controls, each supplied as liquid in single-use tubes.

Alinity m HSV 1 & 2 / VZV Negative CTRL consists of Negative Diluent / TE buffer (containing 0.085% Sodium Azide and 0.087% ProClin 950).

Alinity m HSV 1 & 2 / VZV Positive CTRL 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).

Table 2. 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-1 that contains 2 types of multi-well trays (TRAY 1: Alinity m HSV 1 & 2 / VZV AMP) and (TRAY 2 - Alinity m HSV 11 & 2 / V ACT) described above. The external positive and negative controls from the Alinity m HSV 1 & 2 / VZV CTRL Kit -2 are run with the Alinity m HSV 1 & 2 / VZV assay.

The Alinity m HSV 1 & 2 / VZV assay also utilizes the following items:

Alinity m HSV 1 & 2 / VZV Application Specification Files
Alinity m Sample Prep Kit 2
Alinity m Tubes and Caps
Alinity m System Solutions
Alinity m Lysis Solution
Alinity m Diluent Solution
Alinity m Vapor Barrier Solution
Alinity m System

Interpretation of Results:
The Alinity m HSV 1 & 2 / VZV assay is a qualitative assay. For each analyte (HSV-1, HSV-2 or VZV) signal, the amplification CN (Cycle Number) is determined when the fluorescent signal is detected by the Alinity m System. Each signal is either reported as "Positive" if the CN is less than or equal to a fixed assay cutoff cycle for that signal or is reported as "Negative" if the CN is not generated, or the CN is greater than the assay cutoff cycle. The Alinity m System will automatically report a result and interpretation for each specimen. If applicable a message code or flag will be displayed.

Assay Result Interpretation

Assay	Result	Interpretation
HSV-1	HSV-1 XX.XX.CN	HSV-1 Positive
HSV-1	HSV-1 Target not detected (>31 CN)	HSV-1 Negative
HSV-2	HSV-2 XX.XX.CN	HSV-2 Positive
HSV-2	HSV-2 Target not detected (>33 CN)	HSV-2 Negative
VZV	VZV XX.XX.CN	VZV Positive
VZV	VZV Target not detected (>33 CN)	VZV Negative

B Principle of Operation:

Patient sample is dispensed into the Alinity m System which automates running of the assay and result reporting.

The Alinity m HSV 1 & 2 / VZV assay utilizes real-time polymerase chain reaction (PCR) to amplify and differentiate Herpes Simplex Virus 1 (HSV-1), Herpes Simplex Virus 2 (HSV-2) and Varicella Zoster Virus (VZV) DNA extracted from cutaneous or mucocutaneous lesion specimens. The steps of Alinity m HSV 1 & 2 / VZV assay consist of sample preparation, PCR assembly, amplification/detection, and result calculation and reporting. All stages of the Alinity m HSV 1 & 2 / VZV assay procedure are executed automatically by the Alinity m System. .

Assay controls are tested at or above an established minimum frequency to help ensure that instrument and reagent performance remain satisfactory. During each control event, a negative control and a positive control are processed through sample preparation and PCR procedures that are identical to those used for specimens. Assay controls are used to demonstrate proper sample processing and assay validity.

The Alinity m HSV 1 & 2 / VZV amplification reagents include primers and probes that amplify and detect an exogenous internal control (containing plasmid DNA). Amplification and detection

of the internal control demonstrates proper sample processing. The internal control is used to demonstrate assay validity.

Results are reported as positive or negative based on the cycle number (CN) output for each target (HSV-1, HSV-2, VZV, and IC), which is based on threshold cycle (Ct) at which the fluorescent signal surpasses a threshold to indicate the detection target nucleic acids.

The Alinity m HSV 1 & 2 / VZV assay is a dual target assay for HSV-1 and HSV-2, and a single target assay for VZV. Identification of HSV-1, HSV-2, and VZV occurs by the target-specific primers and fluorescent-labeled probes that hybridize to conserved regions in the viral genomes.

C Instrument Description Information:

1. Instrument Name:
   Alinity m System

2. Specimen Identification:
   Specimen identification can be entered via barcode scanning.

3. Specimen Sampling and Handling:
   Lesion swab specimens, including cutaneous and mucocutaneous, collected in commercially available viral transport media (VTM) (Copan UTM, BD UVT, Remel M4RT) can be used with the Alinity m HSV 1+2/VZV assay on the Alinity m System.

4. Calibration:
   NA

5. Quality Control:
   There are two types of Quality Control for the Alinity m HSV 1 & 2 / VZV assay: Built-in Process Internal Control and External Controls.

   a) **Internal Control (IC)**:

   The Alinity m HSV 1 & 2 / VZV assay contains an internal control (IC) for each sample. The IC DNA sequences, unrelated to the Alinity m HSV 1 & 2 / VZV assay target sequences, are amplified and detected simultaneously with the target DNAs, serving as an internal control to demonstrate that the process has proceeded correctly for each sample.

   b) **External Controls**

   The Alinity m HSV 1 & 2 / VZV CTRL Kit consists of 12 filled tubes of Negative Control and 12 filled tubes of Positive Control. Assay controls are used to demonstrate proper sample processing and assay validity. A negative control and a positive control are processed through sample preparation and PCR procedures that are identical to those used for specimens.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Lyra Direct HSV 1 + 2 / VZV Assay

B Predicate 510(k) Number(s):
K133448

Comparison with Predicate(s):

Device & Predicate Device(s):	New Device K233349	Predicate K133448
Device Trade Name	**Alinity m HSV 1 & 2 / VZV**	**Lyra Direct HSV 1 + 2/VZV Assay**
General Device Characteristic Similarities		
Intended Use/Indication For 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 a 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 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.

	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.	
Amplification Technology	Real-Time Polymerase Chain Reaction (PCR)	Same
Qualitative	Yes	Same
Analyte	Viral DNA from HSV 1, HSV 2 and VZV	Same
Specimen Types	Cutaneous or mucocutaneous lesion swabs in transport medium	Same
Automated Analysis	Yes	Same
External Assay Controls	Positive and Negative Control	Same
General Device Characteristic Differences		
Assays 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 Quant Studio Dx • Applied Biosystems 7500 Fast Dx • Cepheid Smart Cycler II System
Sample Preparation Instrument Components	Automated liquid handling and robotic manipulation platform. Automated process for sample processing using Internal control (IC)	Mechanical lysis and addition of Process Buffer. Manual process for sample processing using processing control (PRC)
Reagent Kit Storage (Unopened) until expiration date	-25^0C to -15^0C	2^0C to 8^0C

VI Standards/Guidance Documents Referenced:

Not Applicable

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

1a. Within-Laboratory Precision:

The 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) for each assay analyte. The positive panel members were prepared by spiking HSV-1, HSV-2, and VZV stocks into negative matrix to achieve the targeted level of Moderate Positive (3X LoD), Low Positive (1X to 2X LoD), and High Negative (<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 precision results for HSV-1, HSV-2, and VZV are summarized below in Table 3.

Table 3. Within-laboratory Precision

Analyte	Sample	Agreement with Expected Results (N^a/N^b)	Mean CN	Within Run		Between Run		Between Day		Within laboratory[c]		Between instrument Lot/Operator		Total[d]	
				SD	% CV	SD	% CV	SD	%CV	SD	% CV	SD	% CV	SD	% CV
HSV-1	3x LoD	100% (90/90)	26.31	0.233	0.9	0.000	0.0	0.000	0.0	0.233	0.9	0.178	0.7	0.287	1.1
	1 - 2x LoD	100% (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
	Negative	100% (90/90)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-2	3x LoD	100% (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
	1 - 2x LoD	100% (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% (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
	Negative	100% (90/90)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
VZV	3x LoD	100% (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
	1 - 2x LoD	100% (90/90)	28.77	0.305	1.1	0.204	0.7	0.000	0.0	0.387	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	2.4	0.315	1.0	0.753	2.4
	Negative	100% (90/90)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

[a] Number of replicates with expected 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.

1b. Reproducibility Study (multi-site precision):

The reproducibility of the Alinity m HSV 1 & 2 / VZV assay was evaluated by testing a 4 - member panel, including a 5X LoD (Positive), 1-2X LoD (Low Positive), <1X LoD (High Negative), and Negative panel member. The positive panel members were prepared by spiking cultured viral particles HSV-1, HSV-2 and VZV into the negative matrix.
A total of 3 Alinity m HSV 1 & 2 / VZV kit lots were used for the reproducibility study. Each of external sites used 2 different lots of reagent kits and a different Alinity m system. Six replicates of each panel member were tested with 3 reagent lots at 3 external sites on 5 non-consecutive days (6 replicates x 2 kit lots/site x 3 sites x 5 days = 180). The reproducibility results of the Alinity m HSV 1 & 2 / VZV assay for HSV-1, HSV-2, and VZV are presented below in Table 4**.**

Table 4. Reproducibility

Analyte	Panel Member	Agreement with Expected Results (N^a/N^b)	Mean CN	Within Run/Day		Between Run/Day		Between Lot		Between Site/Instrument		Total[c]	
				SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
HSV-1	5x LoD	100% (180/180)	27.21	0.322	1.2	0.140	0.5	0.097	0.4	0.000	0.0	0.364	1.3
	1 - 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
	Negative	100% (180/180)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HSV-2	5x LoD	100% (180/180)	29.53	0.311	1.1	0.142	0.5	0.054	0.2	0.105	0.4	0.362	1.2
	1 - 2x LoD	100% (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
	Negative	100% (180/180)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
VZV	5x LoD	100% (180/180)	27.38	0.409	1.5	0.154	0.6	0.000	0.0	0.184	0.7	0.474	1.7
	1 - 2x LoD	100% (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)	35.21	0.577	1.8	0.000	0.0	0.000	0.0	0.097	0.3	0.585	1.8
	Negative	100% (180/180)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

[a]Number of replicates with expected 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.

2. Linearity:
   Not applicable

3. Analytical Specificity/Interference:

a. Cross-Reactivity:

A study was performed to evaluate the performance of the Alinity m HSV 1 & 2 / VZV assay in the presence of 55 potential cross-reactivity microorganisms that could be found in lesion swab specimens. 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. There was no cross reactivity observed with the 55 microorganisms tested with the Alinity m HSV 1 & 2 / VZV assay tested at the concentrations indicated below in Table 5.

Table 5. Cross-Reactivity

Organism	Organism Type	Concentration of the Microorganism	Unit of Concentration
Acinetobacter calcoaceticus	Bacteria	1.10E+06	cfu/mL
Acinetobacter lwoffii	Bacteria	1.10E+06	cfu/mL
Actinomyces israelii	Bacteria	1.10E+06	cfu/mL
Adenovirus type 1	Virus	1.10E+05	TCID50/mL
Adenovirus type 7	Virus	1.10E+05	TCID50/mL
Bacteroides fragilis	Bacteria	1.10E+06	cfu/mL
BK virus	Virus	1.10E+05	copies/mL
Bordetella pertussis	Bacteria	1.10E+06	cfu/mL
Campylobacter jejuni	Bacteria	1.10E+06	cfu/mL
Candida albicans	Fungi	1.10E+05	cfu/mL
Chlamydophila pneumoniae	Bacteria	1.10E+06	IFU/mL
Chlamydia trachomatis serovar D	Bacteria	1.10E+06	IFU/mL
Chlamydia trachomatis serovar I	Bacteria	1.10E+06	IFU/mL
Clostridium difficile	Bacteria	1.00E+06	cfu/mL
Clostridium perfringens	Bacteria	1.10E+06	cfu/mL
Cryptococcus neoformans	Fungi	1.10E+05	cfu/mL
Cytomegalovirus	Virus	1.10E+05	copies/mL
Enterobacter cloacae	Bacteria	1.10E+06	cfu/mL
Enterococcus faecium	Bacteria	1.10E+06	cfu/mL
Enterococcus faecalis	Bacteria	1.10E+06	cfu/mL
Epstein-Barr virus	Virus	1.10E+05	copies/mL
Escherichia coli	Bacteria	1.10E+06	cfu/mL
Fusobacterium nucleatum	Bacteria	1.10E+06	cfu/mL

Haemophilus ducreyi	Bacteria	1.10E+06	copies/mL
Haemophilus influenzae	Bacteria	1.10E+06	cfu/mL
Hepatitis B virus	Virus	1.10E+05	IU/mL
Hepatitis C virus	Virus	1.10E+05	IU/mL
Herpes Virus 6A strain GS	Virus	1.10E+05	copies/mL
Herpes Virus 6B strain Z29	Virus	1.10E+05	copies/mL
HIV-1	Virus	1.10E+05	IU/mL
HPV 16	Virus	1.10E+05	copies/mL
HPV 18	Virus	1.10E+05	copies/mL
Kingella kingae	Bacteria	1.00E+06	cfu/mL
Klebsiella pneumoniae	Bacteria	1.10E+06	cfu/mL
Listeria monocytogenes	Bacteria	1.10E+06	cfu/mL
Mobiluncus mulieris	Bacteria	1.10E+06	cfu/mL
Moraxella catarrhalis	Bacteria	1.10E+06	cfu/mL
Mycobacterium tuberculosisa[a]	Bacteria	1.10E+06	copies/mL
Neisseria gonorrhoeae	Bacteria	1.10E+06	cfu/mL
Neisseria meningitidis	Bacteria	1.10E+06	cfu/mL
Propionibacterium acnes	Bacteria	1.10E+06	cfu/mL
Proteus mirabilis	Bacteria	1.10E+06	cfu/mL
Proteus vulgaris	Bacteria	1.10E+06	cfu/mL
Pseudomonas aeruginosa	Bacteria	1.10E+06	cfu/mL
Staphylococcus aureus	Bacteria	1.10E+06	cfu/mL
Staphylococcus epidermidis	Bacteria	1.10E+06	cfu/mL
Staphylococcus saprophyticus	Bacteria	1.10E+06	cfu/mL
Streptoccoccus agalactiae	Bacteria	1.10E+06	cfu/mL
Streptococcus mitis	Bacteria	1.10E+06	cfu/mL
Streptococcus mutans	Bacteria	1.10E+06	cfu/mL
Streptococcus pneumoniae	Bacteria	1.10E+06	cfu/mL
Streptococcus pyogenes	Bacteria	1.10E+06	cfu/mL
Streptococcus salivarius	Bacteria	1.10E+06	cfu/mL
Treponema pallidum	Bacteria	1.00E+06	cells/mL
Toxoplasma gondii	Bacteria	1.10E+06	copies/mL

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

b. Microbial Interference Study:

The microbial interference study was performed with a list of microorganisms listed above in the Table 5 for the Cross Reactivity Study.

Each potentially interfering microorganism was tested in the presence of 3X LoD levels for each analyte e.g., HSV-1, HSV-2 and VZV viruses spiked into negative matrix. All positive samples reported positive results for HSV-1, HSV-2, and VZV in the presence of these microorganisms. There was no interference observed with the 55 microorganisms tested with the Alinity m HSV 1 & 2 / VZV Assay.

c. 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 twenty -four (24) substances listed in Table 6 was tested in the absence or presence of HSV-1, HSV-2, or VZV (Isolate 2, G strain, Ellen strain, respectively) viruses 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 6.

Table 6. Interference

Interfering Substance	Test Concentration
Blood (human)	5% v/v
Leukocytes	4.0×10^5 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

d. Competitive Interference: A competitive interference study was performed to evaluate the performance of the Alinity m HSV 1 & 2 / VZV assay in the presence of the 3 target analytes. Each sample was prepared with 2 of the analytes (HSV-1, HSV-2 or VZV viruses) at 3X LoD and the third analyte at 1000X LoD in negative simulated swab matrix.

The three Panel Members (PM) were evaluated as follow:

- 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 below in Table7.

Table 7. 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)

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Not applicable

6. Limit of Detection:

The limit of detection (LoD) for Alinity m HSV 1 & 2 / VZV assay for each analyte were determined by quantified (TCID50/mL) cultures of HSV-1 (Maclntyre), HSV-2 (MS) or VZV (Ellen) viral strains diluted into pooled negative clinical swab specimens. The LoD was established in 2 phases as follows:

Phase 1: LoD Range Finding - A dilution series was made from viral stocks of HSV-1, HSV-2 and VZV into negative clinical matrix (CM). For each panel member (PM), a total of 72 replicates of each dilution (panel member) were tested across 3 Alinity m HSV 1 & 2 / VZV AMP Kit lots and 3 Alinity m Systems (one lot per system) over 3 days (8 replicates x 3 days x 3 instruments/lot = 72 replicates per each panel member).

Phase 2: LoD Confirmation – The LoD determined for each analyte from Phase I Study was further confirmed in negative clinical matrix. For each target analyte, a total of 32 replicates of each PM in clinical negative matrix were tested across 2 Alinity m HSV 1 & 2 / VZV AMP kit lots and 2 Alinity m Systems, with each lot of reagents assigned to a specific instrument. A total of 16 replicates were tested for each PM on each of the 2 instrument/lot pair, resulting in a total of 32 replicates per PM (16 replicates × 2 instrument/lot = 32 replicates per PM).

Probit analysis of the data determined that the concentration detected with 95% probability (LoD by Probit) for HSV-1, HSV-2, and VZV was 5.90 TCID50/mL, 2.07 TCID50/mL, and 0.055 TCID50/mL respectively shown below in Table 8.

Table 8. Limit of Detection

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

7. Analytical Reactivity (Inclusivity):

Analytical reactivity or inclusivity of the Alinity m HSV 1 & 2 / VZV assay was further evaluated by functional testing of clinically relevant strains/isolates, in addition to those strains used in the LoD study. 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 at a level near LoD in Table 9.

Table 9: Inclusivity Test Results

Analyte	Strain/Isolate	Analyte 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	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.

8. Carry-Over:

The carry-over 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 carry-over rate of 0.0% (0/360, 95% CI: 0.0%, 1.1%).

9. Fresh/Frozen Specimen Stability

Study 1: Fresh/frozen specimen stability was evaluated by testing a panel member (PM) targeted to 2X LoD for HSV-1 and HSV-2 and 1.13X LoD for VZV prepared in pooled negative clinical specimens using Alinity m HSV 1 & 2 / VZV assay reagents and the Alinity m System. The PM was tested immediately (control condition) and after 1 freeze-thaw (FT1) and 3 freeze-thaw (FT2) test conditions. The PM were frozen at -70°C and thawed at 5°C± 3°C for at least 1 hr before testing. A total of 40 replicates were tested for each PM at each storage condition. The study results support that HSV-1/HSV-2/VZV positive panel member are stable undergoing 3 freeze/thaw cycles prior to testing shown below in Table 10.

Table 10: Freeze Thaw Stability (Study 1)

Analyte	Condition	Positive Rate	Mean	SD
HSV-1 (2X LoD)	No Freeze/Thaw	40/40 (100%)	27.04	0.332
	1 Freez/Thaw (FT1)	40/40 (100%)	27.09	0.271
	3 Freez/Thaw (FT2)	40/40 (100%)	27.07	0.182
HSV-2 (2X LoD)	No Freeze/Thaw	40/40 (100%)	29.81	0.323
	1 Freez/Thaw (FT1)	40/40 (100%)	29.74	0.293
	3 Freez/Thaw (FT2)	40/40 (100%)	29.69	0.316
VZV (1X LoD)	No Freeze/Thaw	40/40 (100%)	28.62	0,262
	1 Freez/Thaw (FT1)	40/40 (100%)	28.58	0.410
	3 Freez/Thaw (FT2)	40/40 (100%)	28.52	0.251

Study 2*:* Fresh/frozen specimen stability was evaluated by testing panel members (PMs) prepared in pooled negative clinical specimens using Alinity m System. The PMs were prepared by spiking HSV-1, HSV-2, and VZV virus stock into pooled negative clinical specimens to achieve the targeted final concentration of 4X Limit of Detection (LoD) for the respective analytes for Panel Member 1, 100X LoD for Panel Member 2, and 1000X LoD for Panel Member 3. All 3 targets (HSV-1, HSV-2, VZV) were spiked together in a given PM. For PM1, a total of 20 replicates were tested at each condition. For PM2 and PM3, a total of 10 replicates were tested at each condition. Negative clinical matrix was prepared by pooling HSV-1/HSV-2/VZV negative clinical swab specimens. The concentrations of PM for each analyte are listed below in Table 11.

Table 11. Target Concentration of the Panel Member

Panel Member	Target concentration	Analyte	Target concentration ($TCID_{50}$/mL)
1	4X LoD	HSV-1	23.60
		HSV-2	8.28
		VZV	0.22
2	100X LoD	HSV-1	590
		HSV-2	207
		VZV	5.5
3	1000X LoD	HSV-1	5900
		HSV-2	2070
		VZV	55

The panel members were tested at the following storage conditions:

- Control Conditions: Not frozen or thawed before testing (Fresh)
- Test Conditions: 3 freeze/thaws (frozen at -70^{0}C or colder for 24 hours, thawed at 5^{0}C + 3^{0}C for a minimum of 1 hour, repeat 3X before testing.

Results are presented below in Table 12.

Table 12: Freeze Thaw Stability (Study 2)

Analyte	Target Concentration	Condition	Positive Rate	Mean (CN)	SD
HSV-1	3-4X LoD	No FreezeThaw	20/20 (100%)	26.56	0.170
		3 Freeze/Thaw	20/20 (100%)	26.91	0.161
	100X LoD	No Freeze/Thaw	10/10 (100%)	22.93	0.161
		3 Freeze/Thaw	10/10 (100%)	22.90	0.160
	1000X LoD	No Freeze/Thaw	10/10 (100%)	19.49	0.190
		3 Freeze/Thaw	10/10 (100%)	19.33	0.307
HSV-2	3-4X LoD	No Freeze/Thaw	20/20 (100%)	29.16	0.208
		3 Freeze/Thaw	20/20 (100%)	29.43	0.236
	100X LoD	No Freeze/Thaw	10/10 (100%)	25.44	0.157
		3 Freeze/Thaw	10/10 (100%)	25.47	0.121
	1000X LoD	No Freeze/Thaw	10/10 (100%)	21.96	0.193
		3 Freeze/Thaw	10/10 (100%)	21.91	0.152
VZV	3-4X LoD	No Freeze/Thaw	20/20 (100%)	27.28	0.454
		3 Freeze/Thaw	20/20 (100%)	27.62	0.408
	100X LoD	No Freeze/Thaw	10/10 (100%)	23.28	0.261
		3 Freeze/Thaw	10/10 (100%)	23.56	0.147
	1000X LoD	No Freeze/Thaw	10/10 (100%)	19.65	0.217
		3 Freeze/Thaw	10/10 (100%)	19.84	0.261

10. Specimen Storage/Onboard Stability Study: Storage conditions and on-board stability of HSV-1, HSV-2 and VZV clinical swab specimens were evaluated by 2 different studies:

Study 1 – Specimen Stability Study with Pooled Negative Clinical Matrix: The study was executed by spiking HSV-1, HSV-2 and VZV in clinical swab matrix that was prepared by pooling HSV-1, HSV-2 and VZV negative specimens followed by testing with the Alinity m HSV 1 & 2 / VZV assay at the following storage conditions.

Specimen Storage/Onboard Stability conditions evaluated:

- 20°C ±5°C for 35, 61, 91, and 99 days
- 2°C to 8°C for 4.4, 5.5, 8.8, and 15.5 days
- 26°C for 1.1, 2.2, and 4.4 days
- 30°C for 2.2, 3.3 and 4.4 days

The positive specimens were prepared by spiking all three targets at a concentration of 3X LoD in pooled negative clinical matrix. A minimum of 5 replicates for each specimen were evaluated for each control condition (baseline), test conditions, and at different timepoints and temperature. The study was conducted using 1 lot of reagent kit and 1 lot of control kit reagent.

Data supported specimen stability storage at -20°C ±5°C for 99 days, and at 2°C to 8°C for up to 15 days and at 26°C for 1 day.

Study 2 - Specimen Stability Study with individual clinical swab samples: The study was executed by spiking HSV-1, HSV-2 and VZV in individual negative clinical swab matrix rather than a pooled HSV-1, HSV-2 and VZV negative specimens followed by testing with the Alinity m HSV 1 & 2 / VZV assay at the storage conditions indicated below. This study represents the actual use of the test.

Ten positive samples were prepared by spiking each analyte from positive patient specimen to a target concentration of 3X LoD in individual negative clinical swab specimens. Replicates of spiked specimens were tested immediately (control condition or baseline) and specimen stability conditions (test conditions) described as follows:

- Baseline (Control Condition)
- Specimens stored for 2.2 days at 26°C + storage-on board for 4 hrs.
- Specimens stored 4.4 days at 26°C + storage-on board for 4 hrs.

Ten replicates for each condition were tested. For each analyte (HSV-1, HSV-2 and VZV) a total of 34 results were generated in the study. There were 4 valid control results and 30 valid sample results included in the analyses for each analyte. All positive samples for each analyte were tested 100% positive. The results support that individual specimens are stable at 26°C±1°C for 4 days and Onboard for 4 hours.

Based on Study 1 and Study 2, the data supports the following specimen storage conditions:

- 15°C to 25°C (4 days)
- 2°C to 8°C (14 days)
- -25°C to -15°C (90 days)
- -70°C or colder (90 days)

10. **Comparison Studies:**

a. Method Comparison with Predicate Device:

See Section B Clinical Studies 3 below.

b. Matrix Equivalency Study:

i). Equivalency between Clinical Swab Matrix and Simulated Swab Matrix:

The matrix equivalency was established between clinical swab matrix (CM) and simulated swab matrix (SM) for the Alinity m HSV 1 & 2 / VZV assay. Four panel members for each analyte were prepared by spiking with HSV-1, HSV-2 and VZV stock to achieve the targeted level at 3X LoD, 1X LoD, <1X LoD, <0.1X LoD. For each target analyte, a total of 32 replicates of each PM in each matrix were tested across 2 Alinity m HSV 1 & 2 / VZV AMP kit lots and 2 Alinity m Systems, with each lot of reagents assigned to a specific instrument. For each matrix, a total of 16 replicates were tested for each PM on each of the 2 instrument/lot pair, resulting in a total of 32 replicates per PM (16 replicates × 2 instrument/lot = 32 replicates per PM).

The data supports that the simulated swab matrix (SM) is found to be equivalent to the clinical swab matrix (CM).

ii). Compatibility between Transport Media (Swab) and Simulated swab matrix:

The study was conducted for transport media compatibility and simulated swab matrix equivalency. The samples were prepared as follow:

1) Remel M4RT: Thirty (30) samples were tested in duplicate for a total of 60 replicates. All 30 samples were prepared by pooling 2 or 3 individual clinical specimens. Pooling was performed to ensure there was enough volume per sample for duplicate testing and for any potential repeat testing needed due to invalid results. Each of the 30 samples was spiked with HSV-1, HSV-2 and VZV stock to achieve the targeted final concentration of 3X LOD.

2) COPAN UTM/BD UTV media: Thirty (30) samples were tested in duplicate for a total of 60 replicates. Out of these 30 samples, 8 samples were individual clinical specimens, and the remaining 22 samples were prepared by pooling 2 individual specimens. Pooling was performed to ensure that there was enough volume per sample for duplicate testing and for any potential repeat testing needed due to invalid results. Each of the 30 samples was spiked with HSV-1, HSV-2 and VZV stock to achieve the approximate targeted final concentration of 3X LOD.

3) Simulated Swab Matrix (SM) was spiked with HSV-1, HSV-2 and VZV stock to achieve the approximate targeted final concentration of 3X LOD. For each matrix, a total of 60 replicates were tested. The results demonstrated that the performance of Alinity m HSV 1 & 2 / VZV assay is equivalent in Remel M4RT, COPAN UTM/BD UTV and Simulated Swab Matrix. The results demonstrated that the Alinity m HSV 1 & 2 / VZV assay is equivalent in Remel M4RT, COPAN UTM/BD UTV, and simulated swab matrix. Results are presented below in Table 13.

Table 13. Matrix Equivalency Results

Analyte	Matrix	Positive Rate	Mean CN	SD
HSV-1	Remel M4RT	100% (60/60)	26.89	0.465
	COPAN/BD	100% (60/60)	26.44	0.389
	Simulated Swab matrix (SM)	100% (60/60)	26.30	0.186
HSV-2	Remel M4RT	100% (60/60)	29.82	0.544
	COPAN/BD	100% (60/60)	29.43	0.407
	Simulated Swab matrix (SM)	100% (60/60)	29.34	0.245
VZV	Remel M4RT	100% (60/60)	28.97	0.669
	COPAN/BD	100% (60/60)	28.06	0.472
	Simulated Swab matrix (SM)	100% (60/60)	27.96	0.238

B. Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

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

   The swab specimens for prospective and retrospective studies were categorized as cutaneous (eg, skin lesion), mucocutaneous (eg, anorectal, vaginal/cervical, and oral lesion), and uncategorized (lesion type could not be determined).

   The clinical performance of the Alinity m HSV 1 & 2 / VZV assay was established by comparing to an FDA-cleared nucleic acid amplification test (NAAT 1). For specimens with discordant results between Alinity m and NAAT 1, testing with another FDA-cleared nucleic acid test (NAAT 2) was performed. Results of testing on discordant samples were not included in the analysis of device performance and are considered for information purposes only.

   Prospective Clinical Study #1

   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 ages >1 to <90 years.

   A total of 1,257 prospective specimens (1017 fresh + 240 frozen) were included for each analyte (HSV-1, HSV-2, and VZV), for clinical performance analysis, excluding 1 sample that did not have complete history information.

   The gender and age demographics for each category are listed below in Table 14.

Table 14. Prospective Study - Age and Gender Distribution by Sample Type

		Number of Specimens from		
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)

The Clinical Study #1 performance is summarized in Table 15.

Table 15. Clinical Agreement by analyte and Lesion Type (Prospective Clinical study #1)

Analyte	Specimen Type	Total	True Positive	False Negative	True Negative	False Positive	PPA % with 95% CI	NPA % with 95% CI
HSV1	Cutaneous Lesion	641	36	0	600	5	100% (36/36) (90.4 % -100%)	99.2% (600/605) (98.1% -99.6%)
	Mucocutaneous Lesion	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% (2/2) (34.2% - 100%)
	All	1257	123	3[b]	1119	12[c]	97.6% (123/126) (93.2% - 99.2%)	98.9% (1119/1131) (98.2% - 99.4%)
HSV2	Cutaneous Lesion	641	61	1	575	4	98.4% (61/62) (91.4 % - 99.7%)	99.2% (600/605) (98.1% -99.6%)
	Mucocutaneous Lesion	613	60	0	548	5	100% (60/60) (94.0 % -100%)	99.1% (548/553) (98.1% -99.6%)
	Uncategorized[a]	3	1	0	2	0	100% (1/1) (20.7% - 100%)	100% (2/2) (34.2% - 100%)
	All	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 Lesion	641	38	0	601	2	100% (38/38) (90.8 % -100%)	99.7% (601/603) (98.8% -99.9%)
	Mucocutaneous Lesion	613	5	1	607	0	83.3% (5/6) (43.6% - 97.0%)	100% (607/607) (99.4% - 100%)
	Uncategorized[a]	3	0	0	3	0	0/0	100% (3/3) (43.9% - 100%)
	All	1257	43	1[f]	1211	2[g]	97.7% (43/44) (88.2% - 99.6%)	99.8% 91211/1213) (99.4% - 100%)

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

Retrospective Clinical Study #2

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 ages >1 to <90 years. 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.

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 category are listed below in Table 16.

Table 16. Retrospective Study - Age and Gender Distribution by Sample Type

		Number of Samples from		
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 Clinical Study #2 performance is summarized in Table 17.

Table 17. Clinical Agreement by analyte and Lesion Type (Retrospective Clinical study #2)

Analyte	Specimen Type	Total	True Positive	False Negative	True Negative	False Positive	PPA % with 95% CI	NPA % with 95% CI
HSV1	Cutaneous Lesion	147	16	0	124	7	100% (16/16) (80.6 % -100%)	94.7% (124/131) (89.4% - 97.4%)
	Mucocutaneous Lesion	234	51	0	178	5	100% (51/51) (93.0% - 100%)	97.3% (178/183) 93.8% - 98.8%)
	Uncategorized[a]	29	5	0	23	1	100% (5/5) (56.6% - 100%)	95.8% (23/24) (79.8% - 99.3%)
	All	410	72	0	325	13[b]	100% (72/72) (94.9% - 100%)	96.2% (325/338) (93.5% - 97.7%)
HSV2	Cutaneous Lesion	147	23	1	115	8	95.8% (23/24) (79.8% - 99.3%)	93.5% (115/123) (87.7% - 96.7%)
	Mucocutaneous Lesion	234	44	0	186	4	100% (44/44) (92.0% - 100%)	97.9% (186/190) (2094.7% - 99.2%)
	Uncategorized[a]	29	7	0	20	2	100% (7/7) (64.6% - 100%)	90.9% (20/22) (72.2% - 97.5%)
	All	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 Lesion	147	20	0	125	2	100% (20/20) (83.9 % -100%)	98.4% (125/217) (94.4% - 99.6%)
	Mucocutaneous Lesion	234	17	0	214	3	100% (17/17) (81.6% -100%)	98.6% (214/127) (96.6% - 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%)
	All	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.

B Clinical Cut-Off:

Not applicable

C Expected Values/Reference Range:

Not applicable

VIII Proposed Labeling:

The labeling is sufficient, and it satisfies the requirements of 21 CFR Part 809.10.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.