510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K162451

B. Purpose for Submission:

Clearance of new device

C. 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.

D. Type of Test:

Molecular diagnostic test using isothermal amplification technology (helicase-dependent amplification, HDA), for the qualitative detection and differentiation of HSV-1, HSV-2, and VZV DNA isolated and purified from cutaneous or mucocutaneous lesion samples.

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Solana® HSV 1+2/VZV Assay

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3309

2. Classification:

Class II

3. Product code:

PGI

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

The Solana® HSV 1+2/VZV Assay is an *in vitro* diagnostic test, using isothermal amplification technology (helicase-dependent amplification, HDA), for the 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 Solana® 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 Solana® HSV 1+2/VZV Assay is intended for use only with the Solana® instrument.

Warning: The Solana® 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 Solana® HSV 1 + 2/VZV Assay is not intended for use in prenatal screening.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only in accordance with 21 CFR 801.109

4. Special instrument requirements:

Solana® instrument

I. Device Description:

The Solana® HSV 1+2/VZV Assay amplifies and detects viral DNA isolated 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 assay consists of two (2) major steps: 1) specimen preparation, and 2) amplification and detection of target sequences specific to HSV-1, HSV-2 and/or VZV using isothermal Helicase-Dependent Amplification (HDA) in the presence of target-specific fluorescence probes.

The Solana® HSV 1+2/VZV Assay includes the following components in the kit.

Component	Quantity	Storage
Process Buffer Tubes	48 tubes/kit 1.6 mL	2°C to 8°C
Reaction Tubes	48 tubes/kit	2°C to 8°C

External controls for HSV-1, HSV-2, or VZV (e.g., Quidel Molecular HSV/VZV Control Set, which contains positive and negative controls) serve as external processing and extraction controls.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Lyra® Direct HSV 1+2/VZV Assay

2. Predicate 510(k) number(s):

K133448

3. Comparison with predicate:

Similarities

Item	New Device Solana® HSV 1+2/VZV Assay	Predicate Device Lyra® Direct HSV 1 + 2/VZV Assay (K133448)
Intended Use	The Solana® HSV 1+2/VZV Assay is an *in vitro* diagnostic test, using isothermal amplification technology (helicase-dependent amplification, HDA), for the qualitative detection and differentiation of herpes simplex virus type 1, herpes simplex virus type 2, and varicella-zoster virus	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

	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 Solana® 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 Solana® HSV 1+2/VZV Assay is intended for use only with the Solana® instrument. Warning: The Solana® 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 Solana® HSV 1 + 2/VZV Assay is not intended for use in prenatal screening.	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 Results	Qualitative	Qualitative
Detection Techniques	Multiplex assay using different reporter dyes for each target	Multiplex assay using different reporter dyes for each target
Identification of HSV-1, HSV-2, and VZV	Yes	Yes
Sample Types	Cutaneous or mucocutaneous lesion swab specimens obtained from symptomatic patients	Cutaneous or mucocutaneous lesion swab specimens obtained from symptomatic patients
Extraction Method	Not required	Not required

Differences

Item	New Device Solana® HSV 1+2/VZV Assay	Predicate Device Lyra® Direct HSV 1 + 2/VZV Assay (K133448)
Viral Target	HSV-1: US7: glycoprotein I HSV-2: noncoding region between UL47: VP13/14 and UL48: VP16 VZV: ORF6: DNA-helicase primase	HSV-1: glycoprotein G HSV-2: glycoprotein G VZV: ORF6: DNA-helicase primase
Assay Methodology	Helicase-Dependent Amplification (HDA) detecting the presence or absence of viral DNA in clinical specimens	PCR-based system for detecting the presence or absence of viral DNA in clinical specimens
Instruments	Solana® instrument	Life Technologies QuantStudio™ Dx, the Applied Biosystems® 7500Fast Dx, or the CepheidSmartCycler® II System

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

The Solana® HSV 1+2/VZV Assay amplifies and detects viral DNA isolated 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 Solana® instrument heats each reaction tube to 64°C. If present, the target sequence is amplified by HSV-1, HSV-2 and/or VZV specific primers and detected by HSV-1, HSV-2 and/or VZV specific fluorescence probes included in the Reaction Tube. Each probe has a fluorescent dye of specific wavelength. The target probes are labeled with a quencher on one end and a fluorophore on the other end. In addition, the target probes carry a ribonucleic acid. Upon annealing to the respective amplicons, the fluorescence probes are cleaved by RNaseH2 and the fluorescence signal increases due to physical separation of fluorophore from quencher. The Solana® instrument measures and interprets the fluorescent signal, using on-board method-specific algorithms. The Solana® instrument will then report the test results to the user on its display screen, and it can print out the results via a printer.

The following is a summary of the procedure:

The patient specimen is transferred to a Process Tube, subjected to heat treatment at 95°C for 5 minutes and mixed and vortexed. The processed sample is transferred to a Reaction Tube and mixed. The Reaction Tube contains lyophilized HDA reagents, dNTPs, primers and probes. Once the Reaction Tube contents are rehydrated with the diluted sample, the Reaction Tube is placed in the Solana® instrument for amplification and detection of specific target sequences. In the Solana® instrument, the target sequences are amplified by HSV-1, HSV-2 and/or VZV specific primers and detected by HSV-1, HSV-2 and/or VZV specific fluorescence probes included in the Reaction Tube. A competitive process control (PRC) is included in the Process Tube to monitor sample processing,inhibitory substances in clinical samples, reagent failure or device failure. The PRC target is amplified by specific primers and detected by a PRC specific fluorescence probe.The target and PRC probes are labeled with a quencher on one end and a fluorophore on the other end. In addition, the target and PRC probes carry ribonucleic acid. Upon annealing to HSV-1, HSV-2, VZV or PRC amplicons, the fluorescence probes are cleaved by RNaseH2 and the fluorescence signal increases due to physical separation of fluorophore from quencher. The Solana® instrument measures and interprets the fluorescent signal, using on-board method-specific algorithms. The Solana® instrument will then report the test results to the user on its display screen, and the results can be printed via an attached printer.

Interpretation of Results

Samples	Assay Result	Interpretation
Patient specimen	HSV-1 Positive	HSV-1 DNA detected
	HSV-1 Negative	No HSV-1 DNA detected and other virus or PRC detected
	HSV-2 Positive	HSV-2 DNA detected
	HSV-2 Negative	No HSV-2 DNA detected and other virus or PRC detected
	VZV Positive	VZV DNA detected
	VZV Negative	No VZV DNA detected and other virus or PRC detected
	Invalid	No HSV-1, HSV-2, VZV DNA and No PRC detected; for invalid test results, retest the same processed sample first. If the test is invalid upon retesting with the processed sample, re-process another aliquot of the same sample or obtain a new sample and re-test.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Reproducibility:

The reproducibility of the Solana® HSV 1+2/VZV Assay was evaluated at three laboratory sites. A reproducibility panel containing 30 contrived samples, manufactured as high negative samples (n=3; 1/18x or 1/27x LOD (C_{20} – C_{80} concentration)) for HSV-1 MacIntyre, HSV-2 G, and VZV Ellen, low positive samples (n=3; near the assay limit of detection) for HSV-1, HSV-2 and VZV, moderate positive samples (n=3; 3x LOD) for HSV-1, HSV-2 and VZV and negative samples (n=3) was used for the study. The samples were randomized and blind-coded within each panel, and the operator tested one (1) panel, together with three (3) positive and three (3) negative external controls, in three runs. The panels were run by two operators at each testing site for five (5) non-consecutive days.

Results of the Reproducibility study for the Solana® HSV 1+2/VZV Assay performed at three sites are presented in the tables below.

Reproducibility Study Summary for HSV-1

HSV-1 MacIntyre	**Site**						**Overall Percent Agreement**		**95% Confidence Interval**
	Site #1		**Site #2**		**Site #3**				
	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	
High Negative (3.50×10^1 $TCID_{50}$/mL)	11/30	36.7	5/30	16.7	14/30	46.7	30/90	33.3	24.5 to 43.6
Low Positive (6.30×10^2 $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Moderate Positive (1.89×10^3 $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Negative	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100
Positive Control	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Negative Control	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100

Reproducibility Study Summary for HSV-2

HSV-2 G	Site						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	
High Negative (3.71×10^2 $TCID_{50}$/mL)	12/30	40	8/30	26.7	7/30	23.3	27/90	30.0	21.5 to 40.1
Low Positive (6.67×10^3 $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Moderate Positive (2.00×10^4 $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Negative	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100
Positive Control	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Negative Control	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100

Reproducibility Study Summary for VZV

VZV Ellen	[redacted]						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	
High Negative (5.50×10^{-3} $TCID_{50}$/mL)	11/30	36.7	2/30	6.7	8/30	26.7	21/90	23.3	15.8 to 33.1
Low Positive (1.49×10^{-1} $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Moderate Positive (4.46×10^{-1} $TCID_{50}$/mL)	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100
Negative	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100
Positive	30/30	100	30/30	100	30/30	100	90/90	100	95.9 to 100

VZV Ellen	[redacted]						[redacted]		95% Confidence Interval
	Site #1		Site #2		Site #3		Agreement		
	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	Rate of Detection	% Agreement	
Control									
Negative Control	0/30	100	0/30	100	0/30	100	0/90	100	95.9 to 100

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The Solana® HSV 1+2/VZV Control Set is available for use with the kit. These controls are manufactured by ZeptoMetrix according to Quidel Corporation specifications. The positive control uses a mixture of highly purified, inactivated strains of HSV-1, HSV-2 and VZV in a HSV-1, HSV-2 and VZV DNA-free matrix. The negative control is the same HSV-1, HSV-2 and VZV DNA-free matrix. The final concentration of HSV-1, HSV-2 and VZV is based on the assay's LOD for the viral strains, and is intended to be near LOD. The controls are used to monitor the assay performance as follows:

i. The *process control* is used to monitor sample processing, to detect HDA inhibitory specimens and to confirm the integrity of assay reagents and Solana® instrument functionality. The process control is included in the Process Buffer tube.

ii. The *external positive control* is treated as a patient specimen. The control should be sampled and tested as if it were a specimen and processed as described in the Assay Procedure. The external positive control is intended to monitor substantial reagent and instrument failure.

iv. The *external negative control* is treated as a patient specimen. The control should be sampled and tested as if it were a specimen and processed as described in the Assay Procedure. The external negative control is used to detect reagent or environmental contamination (or carry-over) by HSV 1+2/VZV DNA or amplicons.

d. Detection limit:

The analytical sensitivity (limit of detection or LOD) of the Solana® HSV 1+2/VZV

Assay was determined using quantified ($TCID_{50}$/mL) cultures of two (2) HSV-1 strains, two (2) HSV-2 strains, and two (2) VZV strains, serially diluted in negative matrix. Each dilution was run as 20 replicates in the Solana® HSV 1+2/VZV assay. Analytical sensitivity (LOD) is defined as the lowest concentration at which at least 95% of all replicates tested positive. The LOD for each virus strain tested is shown below:

LOD	
Virus Strains	**TCID50/mL**
HSV-1 MacIntyre	6.30×10^{2}
HSV-1 316	5.47×10^{4}
HSV-2 G	6.67×10^{3}
HSV-2 COMP	1.62×10^{5}
VZV Ellen	1.49×10^{-1}
VZV 9939	1.65×10^{2}

e. *Analytical Reactivity (Inclusivity*):

The inclusivity of the Solana® HSV 1+2/VZV Assay was further evaluated by functional testing of viral strains in addition to those strains used in the LOD study. The clinical panel consisted of two (2) strains of HSV-1, three (3) strains of HSV-2, and five (5) strains of VZV at concentrations near the level of detection (LOD) of the assay.

Inclusivity Strains	**$TCID_{50}$/mL**
HSV-1 Isolate #1	1.26×10^{3}
HSV-1 Isolate #3	1.26×10^{3}
HSV-2 Strain MS	1.33×10^{4}
HSV-2 Isolate #25	1.33×10^{4}
HSV-2 Isolate #32	1.33×10^{4}
VZV Strain 82	8.05×10^{0}
VZV Strain 130	2.41×10^{1}
VZV Strain 275	8.05×10^{0}
VZV Strain B	2.41×10^{1}
VZV Strain D	8.05×10^{0}

f. Analytical Specificity/Cross Reactivity:

A study was performed to evaluate the performance of the Solana® HSV 1+2/VZV Assay in the presence of sixty-four (64) microorganisms that could be found in lesion specimens. Each potentially cross-reactive microorganism was tested at a clinically relevant level. There was no cross reactivity observed with the sixty-four (64) microorganisms tested with the Solana® HSV 1+2/VZV Assay.

Cross Reactivity

Potentially Cross-reactive Organisms			
Organism	**Test Concentration**	**Organism**	**Test Concentration**
Acholeplasma laidlawi	7.10E+06 CFU/mL	*Klebsiella pneumoniae*	1.61E+06 CFU/mL
Acinetobacter calcoaceticus	9.27E+06 CFU/mL	*Lactobacillus acidophilus*	2.49E+06 CFU/mL
Adenovirus 7	1.58E+05 $TCID_{50}$/mL	*Legionella pneumophila*	1.76E+06 CFU/mL
Bacteroides fragilis	1.19E+06 CFU/mL	Measles virus	1.95E+05 $TCID_{50}$/mL
Bordetella bronchiseptica	1.97E+06 CFU/mL	*Mobiluncus mulieris*	2.54E+06 CFU/mL
Bordetella pertussis	7.21E+06 CFU/mL	*Moraxella cartarrhalis*	1.26E+06 CFU/mL
Candida albicans	2.00E+06 CFU/mL	Mumps virus	5.89E+05 $TCID_{50}$/mL
Candida glabrata	3.93E+06 CFU/mL	*Mycoplasma hominis*	1.30E+06 CFU/mL
Chlamydia trachomatis	3.00E+06 CFU/mL	*Mycoplasma hyorhinis*	6.60E+06 CFU/mL
Chlamydophila pneumoniae	1.25E+06 IFU/mL	*Mycoplasma orale*	3.08E+06 CFU/mL
Clostridium perfringens	1.06E+06 CFU/mL	*Mycoplasma pneumoniae*	3.16E+06 CFU/mL
Coronavirus OC43	8.51E+05 $TCID_{50}$/mL	*Mycoplasma salivarium*	1.67E+06 CFU/mL
Corynebacterium diphtheriae	1.51E+06 CFU/mL	*Neisseria gonorrhoeae*	1.23E+06 CFU/mL
Coxsackievirus B4	3.16E+05 $TCID_{50}$/mL	Parainfluenza Type 1	3.97E+05 $TCID_{50}$/mL
Cytomegalovirus Towne VR-	2.14E+05 $TCID_{50}$/mL	Parainfluenza Type 2	3.15E+05 $TCID_{50}$ /mL
Echovirus 11	2.14E+05 $TCID_{50}$/mL	Parainfluenza Type 3	2.56E+05 $TCID_{50}$/mL
Enterococcus faecalis	3.45E+06 CFU/mL	Parainfluenza Type 4	1.37E+05 $TCID_{50}$/mL
Enterovirus 70	1.78E+05 $TCID_{50}$/mL	*Proteus mirabilis*	1.19E+06 CFU/mL
Epstein Barr Virus	1.34E+05 vp/mL	*Pseudomonas aeruginosa*	1.32E+06 CFU/mL
Escherichia coli	8.42E+06 CFU/mL	RSV A Long	1.95E+05 $TCID_{50}$/mL
Gardnerella vaginalis	1.20E+06 CFU/mL	RSV B Washington	3.43E+05 $TCID_{50}$/mL
Haemophilis influenza type A	5.33E+06 CFU/mL	Rubella Virus	2.09E+05 TCID50/mL
HBV synthetic DNA	6.80E+05 cp/mL	*Salmonella enteriditis*	5.40E+06 CFU/mL
HCV synthetic RNA	1.96E+05 cp/mL	*Salmonella typhimurium*	1.01E+06 CFU/mL
HHV-6	3.30E+05 TCID50/mL	*Staphylococcus aureus*	1.02E+06 CFU/mL
HHV-7	1.15E+05 TCID50/mL	*Staphylococcus*	2.00E+06 CFU/mL
HHV-8	1.26E+05 TCID50/mL	*Streptococcus agalactiae*	2.20E+06 CFU/mL
HIV purified RNA	1.60E+05 cp/mL	*Streptococcus pneumoniae*	2.18E+06 CFU/mL
hMPV A1	3.66E+05 TCID50/mL	*Streptococcus pyogenes*	1.29E+06 CFU/mL
HPV	4.30E+05 cp/uL	*Toxoplasma gondii*	1.06E+06 tachyzoites/mL
Influenza A/Mexico/ 4108/2009	2.88E+05 vp/mL	*Trichomonas vaginalis*	1.06E+06 tachyzoites/mL
Influenza B Hong Kong VR-791	1.91E+05 TCID50/mL	*Ureaplasma uralyticum*	1.23E+06 CFU/mL

Microbial Interference:

A study was performed to evaluate the performance of the Solana® HSV 1+2/VZV Assay in the presence of sixty-four (64) microorganisms that could be found in lesion specimens. Each potentially interfering microorganism was tested in the presence of at 2x LOD HSV-1, HSV-2 and VZV viruses, or negative matrix at clinically relevant levels of the microorganisms. The same microorganisms as listed above in the table for the Cross Reactivity Study were evaluated in the Microbial Interference Study and at the same levels listed in the table for Cross Reactivity. There was no interference observed with the sixty-four (64) organisms tested with the Solana® HSV 1+2/VZV Assay.

g. *Analytical Secificity/Interfering Substances:*

The performance of Solana® HSV 1+2/VZV Assay was evaluated with potentially interfering substances that may be present in lesion specimens. A panel composed of twenty-six (26) substances was tested in the absence or presence of HSV-1, HSV-2, or VZV (MacIntyre, G, Ellen strains, respectively) at 2X LOD in the Solana® 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.

Potentially Interfering Substances			
Substance	**Test Concentration**	**Substance**	**Test Concentration**
Abreva	7%	Female Urine	7%
Acetamidophenol	10 mg/mL	KY Jelly	7%
Acyclovir	7 mg/mL	Lanacane	3.50%
Albumin	3.3 mg/mL	Leukocytes	$2.5x10^5$ cells/mL
Blood/EDTA	0.63%	Listerine	7%
Carmex	7%	Male Urine	7%
Casein	7 mg/mL	Miconazole 1	7%
Chlorpheniramine	5 mg/mL	Miconazole 3	7%
Colgate	7%	Mucin	60 µg/mL
Cornstarch	2.5 mg/mL	Preparation H	7%
Dextromethorphan	5 mg/mL	Releev	7%
Douche	7%	Seminal Fluid	2%
Feces	0.22%	Tioconazole 1	7%

h. *Competitive Interference Study:*

A study was performed to demonstrate that detection of near LOD levels of each of HSV-1, HSV-2, or VZV is not impacted by high levels ($\geq 10^5$ $TCID_{50}$/mL) of the other two viruses when tested with the Solana® HSV 1+2/VZV assay.

Near LOD HSV-1 (Strain MacIntyre, 2x LOD, 1.26×10^3 $TCID_{50}$/mL) detection was not impacted by high levels of HSV-2 (Strain G, 1.00×10^5 $TCID_{50}$/mL) or VZV (Isolate D, 1.23×10^5 $TCID_{50}$/mL).

Near LOD HSV-2 (Strain G, 2x LOD, 1.26×10^3 $TCID_{50}$/mL) detection was not impacted by high levels of HSV-1 (Isolate #17, 1.15×10^5 $TCID_{50}$/mL), but was impacted by high levels of VZV (Isolate D, 1.23×10^5 $TCID_{50}$/mL). Near LOD HSV-2 detection was observed after a 100-fold reduction of the VZV test concentration (1.23×10^3 $TCID_{50}$/mL).

Near LOD VZV (Strain Ellen, 2x LOD, 2.97×10^{-1} $TCID_{50}$/mL) detection was not impacted by high levels of HSV-1 (Isolate #17, 1.15×10^5 $TCID_{50}$/mL) or HSV-2 (Strain G, 1.00×10^5 $TCID_{50}$/mL).

i. Assay cut-off:

Not applicable

j. Sample Stability Studies:

Transport Media (Swab) Compatibility and Stability*:*
HSV-1, HSV-2, and VZV virus stocks (HSV-1 MacIntyre, HSV-2 G, and VZV Ellen) were diluted to their respective 2x LOD concentrations in each in of five (5) transport medium pooled negative matrix (Remel M4, Remel M4-RT, Remel M5, Remel M6, or UTM transport medium).

The transport media systems containing the contrived samples were stored at three different conditions: Condition 1) = room temperature (30 ± 2°C) for 50 hours, Condition 2) = 2° to 8°C for 8 days, and Condition 3) = -20°C for 8 days.

HSV-1, HSV-2, and VZV samples at 2x LOD were stable when stored in M4, M4-RT, M5, M6, and UTM negative matrix for up to 50 hours at 30°C ± 2°C. HSV-1, HSV-2, and VZV samples were stable when stored in M4, M4-RT, M5, M6, and UTM negative matrix for up to 8 days at 2° to 8°C. HSV-1, HSV-2, and VZV samples were stable when stored in M4, M4-RT, M5, M6, and UTM negative matrix for up to 8 days at -20°C.

These stability data support the claim in the Package Insert that specimens can be stored at room temperature (up to 30 °C) for up to 48 hours, 2° to 8°C or –20°C for up to 7 days prior to processing.

Processed Specimen Stability*:*
HSV-1, HSV-2, and VZV virus stocks (HSV-1 MacIntyre, HSV-2 G, and VZV

Ellen) were diluted to their respective 2x LOD concentrations in negative matrix. Each sample was added to Process Buffer tubes, which were stored at 2° to 8°C either before or after heat lysis and tested at 0, 24, 48, 72, and 73 hours post-storage.

Samples are stable in process buffer up to 73 hours at 2° to 8°C before and after the heat step.

These data support the claim in the Package Insert that specimens in Process Buffer Tubes may be stored at 2°C to 8°C for up to 72 hours before and after the heat step.

Processed Specimen Stability - 95°C Lysis Time Flex Study*:*
HSV-1, HSV-2, and VZV virus stocks (HSV-1 MacIntyre, HSV-2 G, and VZV Ellen) were diluted to their respective 2x LOD concentrations in pooled negative matrix and tested in 3 replicates for each condition. The heat time conditions were 2 minutes, 3 minutes, 5 minutes, 10 minutes and 11 minutes.

HSV-1, HSV-2, VZV and the process control were detected for 3 of 3 replicates with all tested heat lysis times, indicating that the Solana® HSV 1+2/VZV Assay tolerates heat lysis times between 2 to 11 minutes at 95°C.

Processed Specimen Stability - 95°C Lysis Temperature Flex Study:
HSV-1, HSV-2, and VZV virus stocks (HSV-1 MacIntyre, HSV-2 G, and VZV Ellen) were diluted to their respective 2x LOD concentrations in pooled negative matrix and tested in 3 replicates for each condition. The heat lysis temperature conditions were 92°C, 93°C, 95°C, 97°C and 98°C.

HSV-1, HSV-2, VZV and the process control were detected for 3 of 3 replicates with all tested heat lysis temperatures, indicating that the Solana® HSV 1+2/VZV tolerates heat lysis temperatures between 92° to 98°C for 5 minutes.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not Applicable. Refer to the Clinical Section below.

   b. *Matrix comparison:*

      Not Applicable.

3. Clinical studies:

   a. *Clinical Sensitivity:*

Not Applicable.

b. Clinical specificity:

Not Applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Clinical Performance:

Performance characteristics of the Solana® HSV 1+2/VZV Assay were established during a prospective study. One thousand and sixty-two (1062) fresh lesion specimens, collected for herpes simplex/varicella-zoster detection and identification, were tested at three (3) sites across the United States. A single specimen was collected per patient. The specimens were processed and tested with the Solana® HSV 1+2/VZV Assay on the Solana® instrument at the sites. Each specimen was also processed and inoculated into two (2) different cell culture systems within 72 hours of collection. The isolation and identification of HSV-1 and HSV-2 was performed using the FDA-cleared ELVIS HSV ID and D³ Typing Test. This testing was performed according to the manufacturer's product insert. The detection and isolation of VZV was performed by staining cells present in the specimen with an FDA-cleared VZV detection reagent (DSFA) and by culturing the specimen for 96-hours using commercially available mixed cell culture (H&V mixed cells from Diagnostic Hybrids, a Quidel Company) consisting of MRC-5 cells (human diploid fibroblast) and CV-1 cells (african green monkey kidney), and staining the cultures with the same FDA-cleared reagent used for DSFA. A specimen was considered positive for VZV if either the DSFA or the culture with DFA was positive. Testing of the comparator methods (culture with DFA) were performed at one central location.

The gender and age demographics of the patients enrolled in the study are shown below.

Combined Study – Age and Gender Distribution (Cutaneous)		
Gender	Female	Male
Total	111	164
Age/Years		
≤ 5	4	5
6 to 21	10	33
22 to 59	68	112
≥ 60	29	14

Combined Study – Age and Gender Distribution (Mucocutaneous)		
Gender	Female	Male
Total	552	69
Age/Years		
≤ 5	5	16
6 to 21	141	18
22 to 59	366	22
≥ 60	40	13

Combined Study – Age and Gender Distribution (Uncategorized Lesion Source)		
Gender	Female	Male
Total	129	37
Age/Years		
≤ 5	5	6
6 to 21	20	8
22 to 59	75	14
≥ 60	29	9

Cutaneous Lesions

HSV-1: Two-hundred and seventy-five (275) active cutaneous lesion specimens were cultured for HSV-1, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-1 viral DNA. Samples which gave HSV-2 positive results from the ELVIS method were excluded from the HSV-1 performance calculation because of the inability of the ELVIS method to distinguish an HSV-1 positive sample when HSV-2 was detected first (n=26). The table below details the HSV-1 results for the remaining two-hundred and forty-nine (249) specimens.

HSV-1 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	22	5*	27
Negative	0	222	222
Total	22	227	249
			95% CI
Sensitivity	22/22	100%	85.1% to 100%
Specificity	222/227	97.8%	95.0% to 99.1%

* Three (3) of the five (5) positives was positive by an additional RT-PCR assay.

HSV-2: Two-hundred and seventy-five (275) active cutaneous lesion specimens were cultured for HSV-2, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-2 viral DNA. The table below details the HSV-2 results for the two-hundred and seventy-five (275) specimens.

HSV-2 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	24	14*	28
Negative	2**	235	237
Total	26	249	275
			95% CI
Sensitivity	24/26	92.3%	75.9% to 97.9%
Specificity	235/249	94.4%	90.8% to 96.6%

*Thirteen (13) of the fourteen (14) positives were positive by an additional RT-PCR assay.
** Two (2) of the two (2) negatives were positive by an additional RT-PCR assay.

VZV: Two-hundred and seventy-five (275) active cutaneous lesion specimens were cultured for VZV using the H&V mixed cells with DFA cell culture systems and were also tested with the subject device for VZV viral DNA. Due to the presence of either HSV-1 or HSV-2, fifty-one (51) specimens were excluded from analysis. Two (2) specimens were contaminated or had toxic cultures. These fifty-three (53) specimens have been excluded from analysis. The table below details the VZV results for the remaining two-hundred and twenty-two (222) specimens.

VZV Results			
	Comparator: DSFA and Culture with DFA		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	22	7*	29
Negative	0	193	193
Total	22	200	222
			95% CI
Sensitivity	22/22	100%	85.1% to 100%
Specificity	193/200	96.5%	93.0% to 98.3%

* Six (6) of the seven (7) positives were positive by an additional RT-PCR assay.

Mucocutaneous Lesions

HSV-1: Six-hundred and twenty-one (621) active mucocutaneous lesion specimens were cultured for HSV-1, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-1 viral DNA. Seven (7) specimens were

contaminated in the ELVIS cell culture. Two (2) specimens were invalid in the Solana® HSV 1 + 2/VZV Assay. Two (2) specimens were contaminated and invalid. Samples which gave HSV-2 positive results from the ELVIS method were excluded from the HSV-1 performance calculation because of the inability of the ELVIS method to distinguish an HSV-1 positive sample when HSV-2 was detected first (n=109). Thus, one hundred and twenty (120) specimens were excluded from further analysis. The table below details the HSV-1 results for the remaining five hundred and one (501) specimens.

HSV-1 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	113	14*	127
Negative	0	374	374
Total	113	388	501
			95% CI
Sensitivity	113/113	100%	96.7% to 100%
Specificity	374/388	96.4%	94.0% to 97.8%

* Six (6) of the fourteen (14) positives were positive by an additional RT-PCR assay.

HSV-2: Six-hundred and twenty-one (621) active mucocutaneous lesion specimens were cultured for HSV-2, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-2 viral DNA. Seven (7) specimens were contaminated in the ELVIS cell culture. Two (2) specimens were invalid in Solana® HSV 1 + 2/VZV Assay. Two (2) specimens were contaminated and invalid. These eleven (11) specimens were excluded from further analysis. The table below details the HSV-2 results for the remaining six-hundred ten (610) specimens.

HSV-2 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	108	14*	122
Negative	1**	487	488
Total	109	501	610
			95% CI
Sensitivity	108/109	99.1%	95.0% to 99.8%
Specificity	487/501	97.2%	95.4% to 98.3%

* Eleven (11) of the fourteen (14) positives were positive by an additional RT-PCR assay.

** One (1) of one (1) negative was positive by an additional RT-PCR assay.

VZV: Six-hundred twenty and one (621) active mucocutaneous lesion specimens

were cultured for VZV using the H&V mixed cells with DFA cell culture system and were also tested with the subject device for VZV viral DNA. Due to the presence of either HSV-1 or HSV-2, two hundred and thirty-six (236) specimens were excluded from analysis. Nine (9) specimens were contaminated in culture, and four (4) specimens were invalid in the Solana® HSV 1 + 2/VZV Assay. These two hundred forty-nine (249) specimens have been excluded from analysis. The table below details the VZV results for the remaining three hundred and seventy-two (372) specimens.

VZV Results			
	Comparator: DSFA and Culture with DFA		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	4	5*	9
Negative	0	363	363
Total	4	368	372
			95% CI
Sensitivity	4/4	100%	51.0% to 100%
Specificity	363/368	98.6%	96.9% to 99.4%

* One (1) of the five (5) positives was positive by an additional RT-PCR assay.

Note: The data presented for the detection of VZV is consistent with the limited presence of VZV in mucocutaneous lesions. The use of mucocutaneous lesions has no discernible impact on the performance characteristics of Solana® HSV 1 + 2/VZV Assay.

Uncategorized Lesions

HSV-1: One hundred and sixty-six (166) active lesion specimens (not categorized as cutaneous or mucocutaneous) were cultured for HSV-1, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-1 viral DNA. Samples which gave HSV-2 positive results from the ELVIS method were excluded from the HSV-1 performance calculation because of the inability of the ELVIS method to distinguish an HSV-1 positive sample when HSV-2 was detected first (n=18). The table below details the HSV-1 results for the remaining one hundred and forty-eight (148) specimens.

HSV-1 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	25	3*	28
Negative	0	120	120
Total	25	123	148

			95% CI
Sensitivity	22/22	100%	86.7% to 100%
Specificity	120/123	97.6%	93.1% to 99.2%

* Three (3) of the three (3) positives was positive by an additional RT-PCR assay.

HSV-2: One hundred and sixty-six (166) active lesion specimens (not categorized as cutaneous or mucocutaneous) were cultured for HSV-2, using the FDA-cleared ELVIS cell culture system and were also tested with the subject device for HSV-2 viral DNA. The table below details the HSV-2 results for the one hundred sixty-six (166) specimens.

HSV-2 Results			
	Comparator: ELVIS® HSV ID and D³ Typing Test		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	18	5*	23
Negative	0	143	143
Total	18	148	166
			95% CI
Sensitivity	18/18	100%	82.4% to 100%
Specificity	143/148	96.6%	92.3% to 98.6%

* Five (5) of the five (5) positives were positive by an additional RT-PCR assay.

VZV: One hundred sixty-six (166) active lesion specimens (not categorized as cutaneous or mucocutaneous) were cultured for VZV using the H&V mixed cells with DFA cell culture systems and were also tested with the subject device for VZV viral DNA. Due the presence of either HSV-1 or HSV-2, forty-six (46) specimens have been excluded from analysis. One (1) specimen was contaminated in culture. These forty-seven (47) specimens have been excluded from analysis. The table below details the VZV results for the remaining one hundred nineteen (119) specimens.

VZV Results			
	Comparator: DSFA and Culture with DFA		
Solana® HSV 1 + 2/VZV Assay	Positive	Negative	Total
Positive	17	6*	23
Negative	0	96	96
Total	17	102	119
			95% CI
Sensitivity	17/17	100%	81.6% to 100%
Specificity	96/102	94.1%	87.8% to 97.3%

*Five (5) of the six (6) positives were positive by an additional RT-PCR assay.

4. Clinical cut-off**:**

Not Applicable.

5. Expected Values:

The expected values of the Solana® HSV 1+2/VZV Assay were established during a prospective study conducted between February and May 2016. One thousand and sixty-two (1062) specimens were included in this study at three (3) sites across the United States. A single specimen was collected per patient. The specimens were processed and tested with the Solana® HSV 1+2/VZV Assay on the Solana® instrument at the sites.

The expected values for HSV-1, HSV-2, and VZV with the Solana® HSV 1+2/VZV Assay were calculated for the combined sites based on the category of specimen (cutaneous, mucocutaneous, or unknown lesion source) and the age of the patient.

Combined Study – Expected Values (Cutaneous) (N=275)									
Age/ Years	**HSV-1**			**HSV-2**			**VZV**		
	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
≤ 5	9	1	11.1%	9	0	N/A	9	4	44.4%
6 to 21	43	10	23.3%	43	4	9.3%	43	0	N/A
22 to 59	180	16	8.9%	180	26	14.4%	180	19	10.6%
≥ 60	43	0	N/A	43	8	18.6%	43	6	14.0%

Expected Values (Cutaneous) (~~N=275~~)									
Specimen Source	**HSV-1**			**HSV-2**			**VZV**		
	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
Skin lesion	105	10	9.5%	105	19	18.1%	105	1	1.0%
Genital	170	17	10.0%	170	19	11.2%	170	28	16.5%

Combined Study – Expected Values (Mucocutaneous) (N=617)*									
Age/ Years	**HSV-1**			**HSV-2**			**VZV**		
	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
≤ 5	21	4	19.0%	21	0	N/A	21	1	4.8%
6 to 21	158	41	25.9%	158	29	18.4%	158	0	N/A
22 to 59	385	74	19.2%	385	89	23.1%	385	8	2.1%
≥ 60	53	11	20.8%	53	5	9.4%	53	1	1.9%

* Four (4) specimens were invalid and removed from analysis

Combined Study – Expected Values (Mucocutaneous) (N=617)*									
Specimen Source	**HSV-1**			**HSV-2**			**VZV**		
	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence

Anorectal	26	7	26.9%	26	7	26.9%	26	1	3.8%
Genital – vaginal/ cervical	449	80	17.8%	449	112	24.9%	449	5	1.1%
Nares	23	5	21.7%	23	1	4.3%	23	3	13.0%
Ocular	7	2	28.6%	7	0	N/A	7	1	14.3%

* Four (4) specimens were invalid and removed from analysis

Combined Study – Expected Values (Uncategorized Lesion Source) (N=166)									
Age/ Years	**HSV-1**			**HSV-2**			**VZV**		
	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
≤ 5	11	1	9.1%	11	0	N/A	11	0	N/A
6 to 21	28	10	35.7%	28	0	N/A	28	2	7.1%
22 to 59	89	15	16.9%	89	18	20.2%	89	14	15.7%
≥ 60	38	2	5.3%	38	5	13.2%	38	8	21.1%

N. Proposed Labeling:

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

O. Conclusion:

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