

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

K091753

**B. Purpose for Submission:**

This 510(k) premarket notification describes modifications to the current in vitro diagnostic device, ELVIS<sup>®</sup> HSV ID/Typing Test System (k971662). The current intended use of the device has not been modified, although the exact wording of the indications for use statement has been edited to add clarity regarding appropriate specimen types. The changes to the device involve replacing the current monoclonal antibodies (MAbs) used for the typing of Herpes simplex virus type 1 (HSV-1) with two newly developed HSV-1 specific MAbs. Also, the number of HSV-2 specific MAbs will be increased.

**C. Measurand:**

Herpes simplex virus type 1 (HSV-1) and Herpes simplex virus type 2 (HSV-2)

**D. Type of Test:**

Cell culture system for viral identification

**E. Applicant:**

Diagnostic Hybrids, Inc.

**F. Proprietary and Established Names:**

ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System

**G. Regulatory Information:**

<b>Product Code</b>	<b>Classification</b>	<b>Regulation Section</b>	<b>Panel</b>
<u>GQL</u>	<u>Class II</u>	<u>21 CFR 866.3305</u>	<u>Microbiology (83)</u>

**H. Intended Use:**

The ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System provides Cells, Replacement Medium and Test Reagents for the culture, qualitative identification and typing of herpes simplex virus (HSV) from cutaneous or mucocutaneous specimens as an aid in the diagnosis of HSV type 1 (HSV-1) and HSV type 2 (HSV-2) infections. The performance characteristics of this assay have not been established for antiviral therapy, prenatal monitoring or use with cerebral spinal fluid specimens.

**I. Device Description:**

The ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System (D<sup>3</sup> ELVIS) is comprised of Cells, Replacement Medium and Test Reagents for the culture, qualitative identification and typing of HSV isolated from cutaneous or mucocutaneous specimens collected from patients with clinical suspicion of HSV infection. ELVIS<sup>®</sup> HSV Cells are genetically engineered Baby Hamster Kidney (BHK) cells, which, when infected with either HSV-1 or HSV-2, are induced to generate and accumulate an endogenous, intracellular bacterial enzyme,  $\beta$ -galactosidase. Other viruses within the herpesviridae family (e.g., Varicellazoster) are not capable of inducing the formation of this enzyme. HSV infection of the ELVIS<sup>®</sup> HSV Cells also results in the formation of HSV-type-specific proteins. The presence of these proteins can be detected microscopically when fluorescent labeled HSV-type-specific antibodies are used.

**J. Substantial Equivalence Information:**

Characteristics of the ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System and the cleared ELVIS<sup>®</sup> HSV ID/Typing Test System are described in the Table below:

<b>Subject Device and Predicate Device Characteristics</b>		
<b>Similarities</b>		
<b>Item</b>	<b>Subject Device</b>	<b>Predicate Device</b>
Intended Use	The ELVIS <sup>®</sup> HSV ID and D <sup>3</sup> Typing Test System provides Cells, Replacement Medium and Test Reagents for the culture, qualitative identification and typing of Herpes simplex virus (HSV).	Same
Assay Format	Shell vials or Multi-well plates	Same
Assay Principle	Genetically engineered Baby Hamster Kidney (BHK) cells, which, when infected with either HSV-1 or HSV-2, are induced to generate and accumulate an endogenous, intracellular bacterial enzyme, $\beta$ -galactosidase.	Same
Labeling Method	Direct Method – Using fluorescein isothiocyanate (FITC) to label HSV-2 Specific monoclonal antibodies, and goat-anti-mouse IgG antibody	Same
<b>Differences</b>		
<b>Item</b>	<b>Subject Device</b>	<b>Predicate Device</b>
Monoclonal Antibodies (MAbs)	HSV-1: non-labeled specific to epitopes on the HSV-1 protein UL42 HSV-2: FITC labeled specific for HSV-2 glycoproteins C, G, and a recombinant glycoprotein G	HSV-1: non-labeled specific to HSV-1 viral protein occurring in the nuclei of infected cells and an HSV-1 glycoprotein C HSV-2: FITC labeled specific for

		HSV-2 glycoproteins C, and G
ELVIS HSV Solution 3	Contains goat-anti-mouse IgG AND Evans Blue	Contains goat-anti-mouse IgG (NO Evans Blue)
Concentrated PBS solution	Provided	Not Provided

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

Not Applicable

**L. Test Principle:**

Specimens are inoculated onto the ELVIS<sup>®</sup>HSV Cells. After an overnight incubation period (17- to 24-hours), the inoculated monolayers are fixed using the supplied ELVIS<sup>®</sup>HSV Solution 1. The cells are then stained with the supplied ELVIS<sup>®</sup>HSV Solution 2T, which contains the chromogenic substrate for the induced  $\beta$ -galactosidase enzyme and the MAbs for typing isolates as HSV-1 or HSV-2. Those cells infected with HSV develop an indigo-blue precipitate, while non-infected cells remain colorless. Only monolayers containing the blue precipitate are examined for the presence of fluorescent cells. Monolayers containing fluorescent cells are reported as positive for HSV-2. Monolayers containing no fluorescent cells are rinsed and stained with the supplied ELVIS<sup>®</sup>HSV Solution 3. After a brief rinse step, the monolayers are examined for fluorescent cells. Monolayers containing fluorescent cells are reported as positive for HSV-1. Monolayers containing no fluorescent cells after staining with ELVIS<sup>®</sup>HSV Solution 3 are reported as positive for HSV, but not typeable.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

A study was undertaken to demonstrate the reproducibility of HSV identification and typing results obtained with the ELVIS HSV ID and D<sup>3</sup> Typing Test System.

A. Study Design

Ten panels of frozen virus suspensions were created for each testing site to stain and interpret. The vial number of each panel member was staggered for each scheduled run, such that the end-user did not come to expect a certain result for each vial number after the first run. Each panel was inoculated and stained once according to the ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System instructions for use. Two panels per day were tested on separate plates for 5-days (10 total runs). Testing was completed at each site on non-consecutive days over a 10-day period. Positive and negative control wells were

inoculated and stained according to the instructions for use and the results recorded with each run.

**Description of Panel Members:**

Panel Member	Description
<b>HSV-1 low level</b>	SF029* lab adapted QC strain; 200 TCID <sub>50</sub> /mL
<b>HSV-1 high level</b>	SF029 lab adapted QC strain; 1000 TCID <sub>50</sub> /mL
<b>HSV-2 low level</b>	SF028† lab adapted QC strain; 200 TCID <sub>50</sub> /mL
<b>HSV-2 high level</b>	SF028 lab adapted QC strain; 1000 TCID <sub>50</sub> /mL
<b>Negative</b>	EMEM with 10% Fetal Bovine Serum

\*Isolate confirmed as HSV-1 by 2 FDA cleared IVD devices

†Isolate confirmed as HSV-2 by 2 FDA cleared IVD devices

Panel members were manufactured by diluting high-titered master stocks. The dilutions were made with the same lot of EMEM with 10% Fetal Bovine Serum used as the negative control. These dilutions were frozen at -70°C and sent to the testing labs. The dilution’s titer was confirmed pre- and post freezing and found to fall within the expected infectivity range for the study: low level should exhibit less than 10% of the cells showing fluorescence; high level should exhibit greater than 10% but less than 50% of the cells showing fluorescence.

**Reproducibility Results:**

Panel Member		Day 1		Day 2		Day 3		Day 4		Day 5	
		Run 1	Run 2	Run 1	Run 2	Run 1	Run 2	Run 1	Run 2	Run 1	Run 2
<b>HSV-1 low level</b>	Site 1	+/-	+/-	+/-	+/-	1+	+/-	+/-	1+	1+	+/-
	Site 2	+/-	1+	1+	1+	+/-	1+	1+	1+	+/-	1+
	Site 3	1+	1+	1+	1+	1+	1+	1+	1+	+/-	1+
<b>HSV-1 high level</b>	Site 1	1+	1+	1+	1+	1 to 2+	1+	1+	1+	1+	1+
	Site 2	1+	1+	1+	2+	1+	1+	3+	2+	1+	2+
	Site 3	2+	2+	2+	2+	2+	2+	2+	3+	1+	2+
<b>HSV-2 low level</b>	Site 1	1+	+/-	1+	+/-	1+	+/-	+/-	+/-	1+	+/-
	Site 2	+/-	1+	1+	1+	1+	1+	2+	1 to 2+	1+	2+
	Site 3	1+	1+	1+	1+	1+	1+	1+	1+	+/-	1+
<b>HSV-2 high level</b>	Site 1	1+	+/-	1+	+/-	1+	1+	1+	1+	1+	1+
	Site 2	2+	2+	2+	2+	2+	1+	3+	3+	3+	2+
	Site 3	2+	3+	3+	3+	2+	3+	2+	3+	1+	2+
<b>Negative</b>	Site 1	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG
	Site 2	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG
	Site 3	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG

Key: +/- = Less than 10% of cells showing fluorescence  
 1+ = Between 10 to 30% of cells showing fluorescence  
 2+ = Between 30 to 50% of cells showing fluorescence  
 3+ = Between 50 to 75% of cells showing fluorescence  
 4+ = Between 75 to 100% of cells showing fluorescence

**Summary:**

The presence of HSV was reported in 100% (120/120) of the wells in which infected cells were present and the expected type was reported 100% (60/60) for HSV-1 and 100% (60/60) for HSV-2. The absence of HSV was reported in 100% (30/30) of the vials in which no virus was present. Controls performed as expected during each run

*b. Linearity/assay reportable range:*

Not Applicable

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

Shelf-life was determined for the device as a complete kit. The shelf-life of the device ELVIS<sup>®</sup> HSV ID and D3 Typing Test System was targeted at 6 months. Kits were stored at 2°C to 8°C and tested at the indicated time intervals. Characteristics monitored were performance, as well as pH, color and clarity. Acceptance criterion was “bright fluorescence” (as opposed to “dim fluorescence” or “no fluorescence”) observed in fixed, stained, infected cells [infected to a level of 2+ to 4+ (30-100%) cytopathic effect] using ELVIS<sup>®</sup> HSV Solution 2T reagent at 1/16 dilution. The table below summarizes the real-time stability testing results.

<b>Real-Time Stability 2-8<sup>o</sup>C Storage</b>			
<b>Stability Timepoint</b>	<b>Lot # Tested</b>	<b>Date Tested</b>	<b>Result (Pass/Fail)</b>
Time Zero	012909NA	2/5/2009	Pass
	012909NB	2/5/2009	Pass
	012909NC	2/5/2009	Pass
3 Month	012909NA	4/30/2009	Pass
	012909NB	4/30/2009	Pass
	012909NC	4/30/2009	Pass
6 Month	012909NA	7/30/2009	Pass
	012909NB	7/30/2009	Pass
	012909NC	7/30/2009	Pass

*d. Detection limit:*

Detection limit of the subject and predicate devices were determined using the ELVIS<sup>®</sup> HSV cell culture system. Analytical detection limits for HSV-1 and HSV-2 are reported in the table below as numbers of blue staining cells per cell monolayer. Each master stock (~1e7-TCID<sub>50</sub> per mL) virus preparation underwent a series of ten-fold dilutions, which were subsequently inoculated into a 96-well ELVIS<sup>®</sup> HSV cell culture plate. The plates were centrifuged at 700 x g for 60 minutes, and then incubated at 35°C to 37°C for 17-hours. Each well was stained with the subject and predicate devices then examined at

200X magnification and the number of blue staining cells counted.  
The table below lists the results for each virus strain tested.

<b>Limit of Detection compared between ELVIS Subject (D<sup>3</sup> ELVIS) and Predicate (Current ELVIS Kit Formulation) Typing Systems</b>			
Virus strain	Virus per Inoculum	Blue staining cells/well	
		ELVIS Predicate	ELVIS Subject
HSV-1 Strain F ATCC VR-733	65-TCID <sub>50</sub>	74, 67, 65, 69, 70, 64	76, 70, 63, 68, 72, 71
	6.5-TCID <sub>50</sub>	9, 8, 11, 7, 7, 12	10, 9, 9, 11, 7, 13
	0.65-TCID <sub>50</sub>	1, 2, 1, 1, 3, 3	3, 2, 4, 3, 1, 1
	0.065-TCID <sub>50</sub>	0, 0, 3, 1, 1, 0	0, 0, 1, 2, 0, 0
	0.0065-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0
HSV-1 CWOH0062 Clinical Isolate Passage 2	85-TCID <sub>50</sub>	70, 79, 75, 72, 80, 67	82, 77, 72, 65, 76, 85
	8.5-TCID <sub>50</sub>	10, 7, 7, 6, 9, 6	11, 10, 8, 6, 7, 7
	0.85-TCID <sub>50</sub>	0, 1, 3, 0, 0, 1, 0	2, 0, 0, 0, 2, 2
	0.085-TCID <sub>50</sub>	0, 0, 0, 0, 1, 0	1, 0, 0, 0, 1, 0
	0.0085-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0
HSV-1 CWOH0085 Clinical Isolate Passage 2	60-TCID <sub>50</sub>	39, 47, 52, 41, 42, 48	46, 48, 37, 42, 47, 50
	6.0-TCID <sub>50</sub>	6, 10, 11, 8, 7, 15	7, 14, 9, 8, 11, 7
	0.6-TCID <sub>50</sub>	2, 0, 2, 0, 0, 1	1, 1, 0, 0, 0, 1
	0.06-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0
HSV-2 G Strain ATCC VR-734	100-TCID <sub>50</sub>	92, 102, 95, 91, 97, 90	95, 96, 97, 98, 89, 103
	10-TCID <sub>50</sub>	12, 11, 17, 9, 9, 10	12, 12, 7, 16, 13, 12
	1.0-TCID <sub>50</sub>	3, 2, 1, 1, 3, 4	5, 1, 2, 2, 1, 3
	0.1-TCID <sub>50</sub>	0, 1, 0, 1, 0, 0	1, 0, 0, 0, 1, 1
	0.01-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0
HSV-2 CWOH0082 Clinical Isolate Passage 2	80-TCID <sub>50</sub>	70, 67, 73, 78, 70, 62	76, 77, 64, 80, 70, 69
	8.0-TCID <sub>50</sub>	8, 7, 10, 11, 6, 5	7, 8, 14, 11, 11, 9
	0.8-TCID <sub>50</sub>	1, 0, 3, 3, 2, 2, 1	2, 1, 1, 3, 1, 0
	0.08-TCID <sub>50</sub>	0, 0, 1, 0, 0, 0	0, 1, 0, 0, 0, 0
	0.008-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0
HSV-2 CWOH0091 Clinical Isolate Passage 2	55-TCID <sub>50</sub>	53, 61, 55, 62, 67, 65	70, 62, 55, 57, 53, 59
	5.5-TCID <sub>50</sub>	3, 7, 7, 9, 2, 4	4, 4, 7, 8, 10, 3
	0.55-TCID <sub>50</sub>	1, 0, 0, 2, 2, 1	3, 1, 0, 0, 2, 2
	0.055-TCID <sub>50</sub>	0, 0, 0, 1, 0, 0	1, 0, 0, 0, 0, 0
	0.0055-TCID <sub>50</sub>	0, 0, 0, 0, 0, 0	0, 0, 0, 0, 0, 0

In this study, the detection limit for the test is defined as the lowest inoculum level at which positive wells (i.e., containing blue staining cells) are observed, in terms of TCID<sub>50</sub>. The results presented in the table above indicate that detection limit for both subject and predicate devices averages between 0.65- and 8.5-TCID<sub>50</sub> for HSV-1 and 0.1 and 8.0-TCID<sub>50</sub> for HSV-2 depending on the strain.

e. *Analytical specificity:*

The specificity of the MABs used in the device was assessed using the organisms listed below. The subject device *Solution 2T* at 2X concentration was tested in duplicate on the prepared slides. After 1-hour at 37°C, the slides were rinsed with PBS and the subject device *Solution 3* secondary stain was added and incubated at 37°C for 15 minutes. After rinsing and applying *Mounting Fluid*, the slides were examined at 400X using a fluorescence microscope.

<b>Respiratory Cross-Reactivity Testing</b>			
Organism	Strain or Type	ELVIS HSV Typing Reagent at 2X concentration [Positive (+) or Negative (-) for Reactivity]	Concentrations of targets (viruses: TCID <sub>50</sub> inoculum level; bacteria: CFU)
<b>Viruses</b>			
Adenovirus	Type 1	-	1000-TCID <sub>50</sub>
	Type 3	-	1000-TCID <sub>50</sub>
	Type 5	-	1000-TCID <sub>50</sub>
	Type 6	-	1000-TCID <sub>50</sub>
	Type 7	-	1000-TCID <sub>50</sub>
	Type 8	-	1000-TCID <sub>50</sub>
	Type 10	-	1000-TCID <sub>50</sub>
	Type 13	-	1000-TCID <sub>50</sub>
	Type 14	-	1000-TCID <sub>50</sub>
	Type 18	-	1000-TCID <sub>50</sub>
Influenza A	Type 31	-	1000-TCID <sub>50</sub>
	Aichi (H3N2)	-	1000-TCID <sub>50</sub>
	Mal (H1N1)	-	1000-TCID <sub>50</sub>
	Hong Kong (H3N2)	-	1000-TCID <sub>50</sub>
	Denver (H1N1)	-	1000-TCID <sub>50</sub>
	Port Chalmers (H3N2)	-	1000-TCID <sub>50</sub>
	Victoria (H3N2)	-	1000-TCID <sub>50</sub>
	New Jersey (HSWN1)	-	1000-TCID <sub>50</sub>
	WS (H1N1)	-	1000-TCID <sub>50</sub>
PR (H1N1)	-	1000-TCID <sub>50</sub>	
Influenza B	Hong Kong	-	1000-TCID <sub>50</sub>
	Maryland	-	1000-TCID <sub>50</sub>
	Mass	-	1000-TCID <sub>50</sub>
	GL	-	1000-TCID <sub>50</sub>
	Taiwan	-	1000-TCID <sub>50</sub>
	JH-001 Isolate	-	1000-TCID <sub>50</sub>
	Russia	-	1000-TCID <sub>50</sub>
RSV	Long	-	1000-TCID <sub>50</sub>

	Wash	-	1000-TCID <sub>50</sub>
	9320	-	1000-TCID <sub>50</sub>
Parainfluenza 1	C-35	-	1000-TCID <sub>50</sub>
Parainfluenza 2	Greer	-	1000-TCID <sub>50</sub>
Parainfluenza 3	C-243	-	1000-TCID <sub>50</sub>
Parainfluenza 4	M-25	-	1000-TCID <sub>50</sub>
Parainfluenza 4b	CH-19503	-	1000-TCID <sub>50</sub>
CMV	AD169	-	Control Slide
Varicella-zoster	Webster	-	Control Slide
Echovirus 7	ODH-594684	-	Control Slide
Coxsackievirus A9	ODH-36685	-	Control Slide
Coxsackievirus B2	ODH-185	-	Control Slide
Enterovirus 71	ODH 02-89	-	Control Slide
<b>Bacteria*</b>			
<i>Acinetobacter calcoaceticus</i>		-	3.6x10 <sup>9</sup> CFU
<i>Bordetella bronchiseptica</i>		-	1.1x10 <sup>10</sup> CFU
<i>Bordetella pertussis</i>		-	4.3x10 <sup>9</sup> CFU
<i>Chlamydia trachomatis</i>	LGV-II	-	Control Slide
<i>Corynebacterium diphtheriae</i>		-	5.7x10 <sup>7</sup> CFU
<i>Escherichia coli</i>		-	7.5x10 <sup>8</sup> CFU
<i>Haemophilis influenzae type A</i>		-	4.1x10 <sup>9</sup> CFU
<i>Klebsiella pneumoniae</i>		-	1.2x10 <sup>9</sup> CFU
<i>Moraxella cartarrhalis</i>		-	1.2x10 <sup>10</sup> CFU
<i>Mycoplasma hominis</i>		-	3.5x10 <sup>10</sup> CFU
<i>Mycoplasma orale</i>		-	6.6x10 <sup>9</sup> CFU
<i>Mycoplasma pneumoniae</i>		-	7.9x10 <sup>9</sup> CFU
<i>Mycoplasma salivarium</i>		-	7.7x10 <sup>8</sup> CFU
<i>Proteus mirabilis</i>		-	3.6x10 <sup>9</sup> CFU
<i>Pseudomonas aeruginosa</i>		-	1.0x10 <sup>8</sup> CFU
<i>Salmonella enteritidis</i>		-	8.7x10 <sup>9</sup> CFU
<i>Salmonella typhimurium</i>		-	7.5x10 <sup>9</sup> CFU
<i>Staphylococcus aureus</i>		+ <sup>†</sup>	6.3x10 <sup>9</sup> CFU
<i>Streptococcus agalactiae</i>		-	5.5x10 <sup>8</sup> CFU
<i>Streptococcus pneumoniae</i>		-	6.7x10 <sup>9</sup> CFU
<i>Streptococcus pyogenes</i>		-	6.9x10 <sup>9</sup> CFU
<b>Yeast*</b>			
<i>Candida glabrata</i>		-	1.6x10 <sup>6</sup> CFU

\* Turbidity or a color change to yellow indicates possible bacterial contamination and may render a test result unreliable, due either to a technical contamination during the culture setup or to a contaminated specimen. We recommend the original specimen be filtered and re-cultured.

<sup>†</sup> Light background fluorescent staining may occur with specimens contaminated with *Staphylococcus aureus* strains containing large amounts of protein A. Protein A binds to the Fc portions of the conjugated antibodies. Such binding can be distinguished from viral

antigen binding on the basis of morphology, e.g., *S. aureus*-bound fluorescence appears as small (~1 micron diameter), bright dots.

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

*Method comparison with predicate device:*

Studies were performed at three locations using 735 specimens submitted, April through May, 2009, for HSV culture. The number of specimens cultured at each of the three sites: Study site 1 - 299 specimens; Study site 2 - 136 specimens; and Study site 3 - 300 specimens. The specimens were cultured in duplicate and stained concurrently with both devices. The data generated by each site was similar and has been combined for presentation. Of these 735 specimens, 16 were excluded from the final analysis for the reasons listed in the table below.

<b>Combined Study Sites Rejected Specimens/Samples</b>	
Exclusion criteria – Toxic to cell culture	13
Exclusion criteria - Contaminated	3
Grand Total	16

The table below shows the age and gender distribution for individuals included in the Study:

<b>Combined Study Sites - Age and Gender Distribution (720 Specimens)</b>			
<b>Age Range</b>	<b>Values are # Positive (based on Subject Device) / Total</b>		
	<b>Male</b>	<b>Female</b>	<b>Total</b>
0 to 1 month	0/9	1/9	1/18
>1 month to 2 years	0/1	0/1	0/2
>2 to 12 years	1/7	4/7	5/14
>12 to 21 years	4/22	54/110	58/132
22 to 30 years	9/34	71/146	80/180
31 to 40 years	10/37	44/121	54/158
41 to 50 years	8/22	18/64	26/86
51 to 60 years	3/14	15/50	18/64
>60 years	3/18	9/47	12/65
Unknown age	0/0	0/0	0/0
Grand Total	38/165	216/555	254/719

The table below shows the specimen source distribution for the Study:

<b>Combined Study Sites - Specimen Source Distribution (719 Specimens) Values are # Positive (based on Subject Device) / Total</b>																
Source	Total Specimens	Unknown +/-	Genital +/-	Penis +/-	Vaginal +/-	Labia +/-	Cervical +/-	Wound +/-	Perineum * +/-	Vulva +/-	Urethra +/-	Lesion +/-	Face <sup>##</sup> +/-	Mouth <sup>**</sup> +/-	Skin <sup>#</sup> +/-	Bartholin Cyst +/-
	254/ 719	66/ 175	18/ 50	14/ 44	45/ 105	23/ 47	18/ 50	0/4	16/ 40	23/ 66	0/ 12	5/ 14	4/ 32	9/ 37	13/ 42	1/1
* Perineum: anal, groin, buttock, perianal, tailbone ** Mouth: mouth, lip, throat, NP Wash, Tongue # Skin: skin, arm, back, breast, finger, foot, leg, thigh, breast, abdomen, hand ## Face: cheek, chin, eye, nasal																

The table below shows the comparison of the Subject device with the Predicate device for the isolation and detection of HSV at Study Sites Combined:

<b>Combined Study Sites - Subject Device compared to Predicate Device for the Isolation of HSV</b>			
Specimen (719 specimens)		Predicate Device (Current ELVIS Kit Formulation)	
		Pos	Neg
Subject Device (D <sup>3</sup> ELVIS)	Pos	250	5
	Neg	1	463
Positive Percent Agreement (PPA)		99.6% (250/251)	
95% CI-PPA		97.8 – 100%	
Negative Percent Agreement (NPA)		98.9% (463/468)	
95% CI-NPA		97.5 – 99.7%	

The table below shows the comparison of the Subject device with the Predicate device for the identification of HSV-2 at Study Sites Combined:

<b>Combined Study Sites - Subject Device compared to Predicate Device for the Typing of HSV-2</b>			
Specimen (106 specimens)		Predicate Device HSV-2 (Current ELVIS Kit Formulation)	
		Pos	Neg
Subject Device HSV-2 (D <sup>3</sup> ELVIS)	Pos	145	6
	Neg	1	98
Positive Percent Agreement (PPA)		99.3% (145/146)	
95% CI-PPA		96.2 – 100%	
Negative Percent Agreement (NPA)		94.2% (98/104)	
95% CI-NPA		87.9 – 97.9%	

The table below shows the comparison of the Subject device with the

Predicate device for the identification of HSV-2 at Study Sites Combined:

<b>Combined Study Sites - Subject Device compared to Predicate Device for the Typing of HSV-1</b>			
<b>Specimen</b> (36 specimens)		<b>Predicate Device HSV-1</b> (Current ELVIS Kit Formulation)	
		Pos	Neg
<b>Subject Device HSV-1</b> (D <sup>3</sup> ELVIS)	Pos	90	1
	Neg	0	7
Positive Percent Agreement (PPA)		100% (32/32)	
95% CI-PPA		96.0 – 100%	
Negative Percent Agreement (NPA)		87.5% (7/8)	
95% CI-NPA		47.3 – 99.7%	

*Shell Vial versus Multi-Well Plate Method Comparison Data for the ELVIS® HSV ID and D3 Typing System:*

Each master stock (~5e6-TCID<sub>50</sub> per mL) virus preparation was diluted to an inoculum titer of ~100-TCID<sub>50</sub> per mL. Three wells of a 24-well ELVIS® HSV cell culture plate and three shell vials with coverslips were inoculated with 1-mL inoculum per isolate. The cultures were centrifuged at 700 xg for 60 minutes, and then incubated at 35°C to 37°C for 17-hours. Each well was stained with the subject device then examined at 200X magnification and the number of blue staining cells and fluorescent plaques counted. The table below lists the virus along with each well's counts.

<b>Evaluation of the subject ELVIS® HSV ID and D3 Typing System with shell vial versus multi-well plates cell cultures</b>				
<b>Virus Type and Isolate Number</b>	<b>Shell Vial Cultures</b>		<b>Multi-well Plate Cultures</b>	
	Blue Cell Counts	Fluorescent Plaque Counts	Blue Cell Counts	Fluorescent Plaque Counts
HSV-1 CWOH-0072	34-29-29	7-6-9	25-31-29	6-8-9
HSV-1 CWOH-0062	53-67-65	30-29-27	74-69-68	23-21-29
HSV-1 CWOH-0076	489-495-501	214-252-249	470-436-502	242-236-252
HSV-1 CWOH-0061	60-63-70	32-39-40	67-65-66	35-36-38
HSV-1 CWOH-0092	587-575-602	394-387-410	635-595-599	375-402-415
HSV-1 CWOH-0094	42-42-46	27-31-36	43-46-40	31-29-35
HSV-1 CWOH-0081	302-325-310	179-170-164	300-296-325	182-167-179
HSV-1 CWOH-0017	76-93-89	49-48-51	85-96-92	54-46-49
HSV-1 CWOH-0041	146-153-155	71-67-77	158-164-154	70-75-81

HSV-1 CWOH-0085	68-72-73	46-43-49	71-86-77	50-47-51
HSV-1 CWOH-0084	46-65-62	37-30-27	55-61-52	31-34-36
HSV-2 CWOH-0099	70-61-57	23-30-29	62-65-64	37-29-34
HSV-2 CWOH-0093	72-77-69	35-31-39	75-68-80	49-42-38
HSV-2 CWOH-0086	176-182-169	90-72-81	185-190-178	82-71-72
HSV-2 CWOH-0070	117-121-110	54-59-55	96-120-110	59-63-62
HSV-2 CWOH-0073	71-72-81	46-42-35	69-81-75	47-45-41
HSV-2 CWOH-0078	112-120-125	54-69-63	125-121-135	64-65-74
HSV-2 CWOH-0034	127-126-123	72-64-64	134-121-112	69-64-70
HSV-2 CWOH-0091	122-119-117	69-61-70	119-120-129	70-78-64
HSV-2 CWOH-0025	131-114-123	62-59-69	121-125-118	69-65-63
HSV-2 CWOH-0024	86-90-92	39-42-44	93-91-88	47-41-43
HSV-2 CWOH-0095	191-204-207	101-113-105	191-205-197	112-95-110
HSV-2 CWOH-0074	204-197-187	137-123-140	240-243-229	175-183-167

3. Clinical studies:

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Clinical studies were performed at three sites with 735 specimens using a legally-marketed device and the ELVIS<sup>®</sup> HSV ID and D<sup>3</sup> Typing Test System. Sixteen specimens were either toxic or contaminated in cell culture, leaving 719 specimens for analysis.

Specimens used in the studies were obtained from a variety of sources. The table below shows the specimen source distribution at the combined Study Sites:

<b>Combined Study Sites Specimen Source Distribution Values are # Positive (based on Subject Device)/ Total</b>															
Total Specimens	Unknown +/-	Genital† +/-	Penis +/-	Vaginal +/-	Labia +/-	Cervical +/-	Perineum * +/-	Vulva +/-	Urethra +/-	Face +/-	Mouth ** +/-	Skin † +/-	Lesion +/-	Bartholin Cyst +/-	Wound +/-
719	94/175	18/50	14/44	45/105	23/47	18/50	16/40	23/66	0/12	4/32	9/37	13/42	5/14	1/1	0/4
† Genital: specific area of genitalia is unknown * Perineum: anal, buttock, tailbone, groin ** Mouth: mouth, lip, throat, tongue, nasopharynx † Skin: skin, breast, leg, arm, abdomen, thigh, ankle, back, finger, hand															

**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.