

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
DEVICE ONLY TEMPLATE**

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

k061820

**B. Purpose for Submission:**

New device clearance

**C. Measurand:**

Varicella-Zoster Virus (VZV) IgG

**D. Type of Test:**

Qualitative, CLIA

**E. Applicant:**

DiaSorin Inc.

**F. Proprietary and Established Names:**

DiaSorin LIAISON<sup>®</sup> VZV IgG

**G. Regulatory Information:**

**a) Regulation section:**

Varicella –zoster Virus, serological reagents (21 CFR 866.3900).

**b) Classification:**

Class II

**Product Code:**

LFY

**c) Panel:**

83 Microbiology

**H. Intended Use:**

**a) Intended use(s):**

The DiaSorin LIAISON<sup>®</sup> VZV IgG uses chemiluminescence immunoassay (CLIA) technology on the LIAISON<sup>®</sup> Analyzer for the qualitative detection of specific IgG antibodies to varicella-zoster virus (VZV) in human serum. This assay can be used as an aid in the determination of previous infection of varicella-zoster virus. .

**b) Indication(s) for use:**

The LIAISON<sup>®</sup> VZV IgG Assay. This assay can be used as an aid in the determination of previous infection with varicella-zoster virus.

**c) Special condition for use statement(s):**

The device is for prescription use only

**d) Special instrument Requirements:**

NA

**I. Device Description:**

Indirect chemiluminescence immunoassay

**J. Substantial Equivalence Information:**

**a) Predicate device name(s):**

Diamedix Is-VZV IgG Test System

**b) Predicate K number(s):**

K981867

Comparison with predicate:

Similarities		
Item	Device	Predicate
Same target population.	DiaSorin LIAISON <sup>®</sup> VZV IgG	<u>Diamedix Is-VZV IgG Test System</u>
Same sample matrix	Test persons who are pregnant or have signs or symptoms of VZV infection  Serum	Test persons who are pregnant or have signs or symptoms of VZV infection.  Serum
Differences		
Item	Device	Predicate
Different Methodology	Indirect chemiluminescence immunoassay	IgG Indirect ELISA
Different Indications for Use	Qualitative	Qualitative/Semiquantitative
Capture Reagent	Magnetic particles coated with antigen	Microtiter plate wells coated with antigen
Detector antibody Species	Mouse	Goat
Antigen	VZV ROD strain	VZV ELLEN strain

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

NA

**L. Test Principle:**

The method for the qualitative determination of specific IgG to varicella- zoster virus is an indirect chemiluminescence immunoassay (CLIA). All assay steps and incubations are performed by the LIAISON<sup>®</sup> Analyzer. Varicella-zoster virus antigen is used for coating magnetic particles (solid phase) and a mouse monoclonal antibody to human IgG is linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, anti-VZV IgG antibodies, present in calibrators, samples or controls, bind to the solid phase. After each incubation, the unbound material is removed with a wash

cycle. During the second incubation, the antibody conjugate reacts with anti-VZV IgG already bound to the solid phase. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is induced. The light signal, and the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of anti-VZV IgG concentration present in calibrators, samples or controls.

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

1. Analytical performance:

*a. Precision/Reproducibility:*

An assay reproducibility study was conducted at two external US laboratories and at DiaSorin, according to CLSI document EP15-A2. The study included 3 different kit lots. A coded panel comprised of 9 frozen repository samples was prepared by DiaSorin and provided to each site for testing by the LIAISON<sup>®</sup> VZV IgG assay. The panel contained samples prepared to represent negative levels, low to mid positive analyte levels and moderate to high positive levels. All panel members were divided into aliquots and stored frozen prior to testing. The same coded panel was tested at all three sites, in four replicates per run for five runs. The results are summarized in the following table.

		Mean	Within-run	Within-run	Between-run	Between-run	Between-site	Between-site	Overall	Overall
ID#	N	Index	sd	%CV	sd	%CV	sd	%CV	sd.	%CV
DiaSorin Neg Ctl	60	30.3	2.97	9.0	4.52	7.87	3.88	12.8	5.64	18.6
DiaSorin Pos Ctl	60	434	42.6	9.81	48.9	9.21	40.3	9.29	62.4	14.4
011006 (Cutoff Ctl)	60	246	22.8	9.44	26.4	10.2	13.6	5.54	33.9	13.8
<i>BR Neg Ctl</i> (100% serum)	60	<10	15.0	5.53	18.0	6.15	4.0	1.62	23.0	8.24
BR Pos Ctl (100% serum)	60	863	86.4	10.2	70.6	8.05	27.8	3.22	108	12.6
3314	60	60.2	3.81	6.54	3.74	5.42	1.04	4.01	5.75	9.54
3360	60	265	19.5	7.35	29.3	7.59	6.88	9.75	34.2	12.9
3385	60	242	22.0	8.98	26.1	7.63	4.67	9.63	33.5	13.8
3403	60	164	8.23	4.86	13.1	5.73	0.73	6.96	14.9	9.14
3492	60	276	24.8	9.08	24.4	7.62	7.89	6.08	33.9	12.3
3515	60	252	27.4	10.6	24.9	8.42	7.12	6.25	36.5	14.5
3554	60	291	26.0	8.68	28.6	7.94	14.0	5.83	41.5	14.3
Pos 5	60	1530	227	14.6	184	10.2	138	7.02	291	19.0
Pos 9	60	679	60.6	9.06	57.1	7.79	38.8	1.20	82.7	12.2

*BR Neg Ctl Index was below the reading range of the assay therefore; the precision calculations are based on signal (RLU) for this sample.*

*b. Linearity/assay reportable range:*

NA

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

NA

*d. Detection limit:*

NA

*e. Analytical specificity:*

The cross-reactivity study for the LIAISON® VZV IgG assay was designed to evaluate potential interference from closely-related members of the herpesviridae family (EBV, HSV CMV), other organisms that may cause symptoms similar to VZV infection (Rubella virus, Measles, Mumps), other organisms that may cause infectious disease (*Toxoplasma gondii*, *Borrelia burgdorferi*) and from other conditions that may result from atypical immune system activity (antinuclear autoantibodies ANA. Samples for these studies were pre-screened with another commercially available VZV IgG assay. If found negative for VZV IgG antibodies they were used for potentially cross-reactive viruses.”

<b>Organism/condition</b>	<b>Number of Expected Negative Samples</b>	<b>LIAISON<sup>®</sup> Positive or equivocal Result</b>
Anti-Measles IgG	23	(0/23)
Anti-Mumps IgG	20	(0/20)
Anti-VCA IgG	24	(0/24)
Anti-EBNA IgG	25	(0/25)
Anti-CMV IgG	26	(0/26)
Anti-Rubella IgG	22	(0/22)
Anti-Toxo IgG	2	(0/2)
Anti-Borrelia IgG	2	(0/2)
Anti-HSV1/2 IgG	25	(0/25)
ANA	14	(0/14)
<b>Total</b>	<b>183</b>	<b>(0/183)</b>

No positive result was found for the samples when tested by LIAISON<sup>®</sup> VZV IgG.

*f. Assay cut-off:*

The cut-off for the LIAISON<sup>®</sup> VZV IgG assay was determined during European clinical trials in which 393 samples were tested. The samples consisted of single samples from different selected populations (subjects never infected with VZV, routine VZV IgG samples, transplant recipients, pregnant patients, blood donors and pediatric patients). Based on available clinical and laboratory data, the samples were classified as expected negative or positive for VZV IgG and evaluated with the LIAISON<sup>®</sup> VZV IgG assay. A cut-off of 150 Index was determined to provide the best balance of sensitivity and specificity for the tested clinical samples. An equivocal zone of 135-165 Index was applied to the assay to account for normal measurement imprecision.

2. Comparison studies:

*a. Method comparison with predicate device:*

DiaSorin LIAISON<sup>®</sup> VZV IgG assay was compared to the Diamedix Is-VZV IgG Test System, K981867

*b. Matrix comparison:*

NA

3. Clinical studies:

*a. Clinical Sensitivity:*

NA

*b. Clinical specificity:*

NA

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

### PERFORMANCE CHARACTERISTICS

A total of 1434 prospectively collected samples of which 689 were from pregnant women, were tested in the U.S for the presence of VZV IgG antibodies using the LIAISON® VZV IgG assay and a commercially available ELISA test kit at two independent sites as well as DiaSorin Inc., Stillwater, MN. Site #1 is a university hospital laboratory located in Philadelphia, PA and site #2 is a clinical laboratory located in Minneapolis, MN. Site #1 tested 340 of the routine VZV samples and site #2 tested 405 of the routine VZV samples. DiaSorin Inc., tested all of the samples from pregnant women. The following tables compare the results obtained for the LIAISON® VZV IgG assay and the commercially available ELISA.

Prospective samples: Routine Samples

LIAISON® VZV IgG Results	VZV IgG ELISA Results			
	Positive	Equivocal	Negative	Total
Positive	659	7	4	670
Equivocal	1	1	1	3
Negative	3	4	65	72
Total	663	12	70	745

	Percent Agreement	Exact 95% confidence interval
Positive	98.8% (659/667)	97.7 – 99.5%
Negative	84.4% (65/77)	74.4 – 91.7%

Specimens that were equivocal by both assays were not included in the percent agreement calculation. Positive or negative results from the LIAISON® VZV IgG assay were considered as non-agreements in the calculation of percent positive agreement and percent negative agreement when the corresponding reference assay result was equivocal.

Compares number of samples positive on both assays to sum of all positive samples on the reference assay + samples equivocal on the reference assay and negative on the LIAISON® VZV IgG.

Compared number of samples negative on both assay to sum of all negative samples on the reference assay + samples equivocal on the reference assay and positive on the LIAISON® VZV IgG

## Prospective samples: Pregnant Women

LIAISON® VZV IgG Results	VZV IgG ELISA Results			
	Positive	Equivocal	Negative	Total
Positive	645	11	3	659
Equivocal	3	0	0	3
Negative	2	0	25	27
Total	650	11	28	689

	Percent Agreement		Exact 95% confidence interval
Positive	99.2%	(645/650)	98.2 – 99.7%
Negative	64.1%	(25/39)	47.6 – 78.8%

Specimens that were equivocal by both assays were not included in the percent agreement calculation. Positive or negative results from the LIAISON® VZV IgG assay were considered as non-agreements in the calculation of percent positive agreement and percent negative agreement when the corresponding reference assay result was equivocal.

Compares number of samples positive on both assays to sum of all positive samples on the reference assay + samples equivocal on the reference assay and negative on the LIAISON® VZV IgG.

Compared number of samples negative on both assay to sum of all negative samples on the reference assay + samples equivocal on the reference assay and positive on the LIAISON® VZV IgG

3. Clinical cut-off:

NA

4. Expected values/Reference range:

The prevalence of VZV antibodies can vary depending on age, geographical location, socioeconomic status, race and vaccine usage. The prevalence of VZV antibodies generally varies from about 15% positive in 2 year olds to about 95% in persons over 40 years of age. The LIAISON® VZV IgG Assay was tested with prospectively collected samples from U.S. subjects sent to the laboratory for varicella- zoster virus testing (n=745) and from pregnant women (n=689) to evaluate the assays' performance in these populations. The samples sent to the laboratory for VZV IgG testing were 71.9% female (536), 27.7% male (206), 0.40% unknown (3) from the Northeastern U.S. The pregnant woman population was collected from the mid-Atlantic and Northeastern US areas. The distribution of results for IgG antibodies to varicella-zoster virus in these populations as determined by the LIAISON® VZV IgG Assay summarized as follows.

Prospectively-collected Samples from Subjects sent to the Laboratory for VZV IgG Testing:

	N	Negative	Equivocal	Positive	Prevalence
Total	745	72	3	670	89.9%
Gender					
Female	536	49	2	485	90.5%
Male	206	23	1	182	88.3%
Unknown	3	0	0	3	100%
Age (years)					
< 10	9	2	0	7	77.8%
10 – 14	60	13	0	47	78.3%
15 – 19	87	10	1	76	87.4%
20 – 29	219	23	1	195	89.0%
30 – 39	177	19	0	158	89.3%
40 – 49	101	1	1	99	98.0%
50 – 59	60	3	0	57	95.0%
60 – 69	22	1	0	21	95.4%
≥ 70	10	0	0	10	100.0%



Prospectively-collected Samples from Pregnant Women					
	LIAISON® VZV IgG				
	N	Negative	Equivocal	Positive	Prevalence
Total	689	27	3	659	95.6%
Age (years)					
15 – 19	55	2	1	52	94.5%
20 – 29	303	14	1	286	94.3%
30 – 39	297	10	1	286	96.9%
40 – 47	34	1	0	33	97.0%

#### **N. Proposed Labeling:**

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

#### **WARNINGS:**

1. Assay interference due to circulating antibodies against HIV, Hepatitis A, Hepatitis B and Hepatitis C virus, HAMA and Rheumatoid Factor has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents and antibodies.

The recommended LIAISON® VZV IgG quality control material contains a 5% serum matrix. It may not adequately control the DiaSorin LIAISON® VZV IgG assay for serum specimens. The user must provide quality control material for serum specimens. Alternative materials for the control of serum specimens include commercial quality control materials or your laboratory's own pooled serum specimens. Choose control levels that check assay performance at all clinically relevant points (e.g., assay cutoff). The recommendation is to run a positive and negative control close to the assay's decision point. It is the responsibility of the user to validate the use of alternative control materials with this assay and to establish appropriate control ranges

#### **O. Conclusion:**

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