510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K231214

B Applicant

DiaSorin Inc.

C Proprietary and Established Names

LIAISON VZV IgG HT, LIAISON Control VZV IgG HT

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LFY	Class II	21 CFR 866.3900 - Varicella-Zoster Virus Serological Reagents	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:
Clearance of a new device.

B Measurand:
Human IgG antibodies specific to Varicella Zoster Virus (VZV).

C Type of Test:
Chemiluminescence Immunoassay (CLIA) Technology.

III Intended Use/Indications for Use:

A Intended Use(s):
The LIAISON VZV IgG HT assay uses chemiluminescent immunoassay (CLIA) technology for the in vitro qualitative detection of specific IgG antibodies to varicella-zoster virus (VZV) in human serum (with gel and without gel-SST), dipotassium EDTA (K2- EDTA), lithium heparin and sodium heparin plasma samples. This assay is intended as an aid in the determination of

previous infection of varicella-zoster virus. The test must be performed on the LIAISON XL Analyzer. The assay performance in detecting antibodies to VZV in individuals vaccinated with the FDA-licensed VZV vaccine is unknown. The user of this assay is responsible for establishing the performance characteristics with VZV vaccinated individuals.

B Indication(s) for Use:
See Intended Uses above.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
The LIAISON XL Analyzer.

IV Device/System Characteristics:

A Device Description:

The LIAISON VZV IgG HT assay requires the use of reagents specific for VZV IgG immunoassay and the recommended LIAISON Control VZV IgG HT. The reagent and calibrators are packaged together in the LIAISON VZV IgG HT kit, while the LIAISON Control VZV IgG HT is packaged separately. The assay is performed on the LIAISON XL Analyzer, a fully automated system with continuous loading system that performs the complete sample processing (sample pre-dilutions, sample and reagent dispensing, incubations, wash processes) and the measurement and evaluation.

The assay contains different components: reagent integral (magnetic particles, conjugate, assay buffer, and calibrator), and external controls (positive and negative).

B Principle of Operation:

The LIAISON VZV IgG HT assay is an indirect chemiluminescence immunoassay (CLIA) used for the qualitative detection of specific IgG antibodies to varicella-zoster virus (VZV). During the first incubation with the magnetic particles, anti-VZV antibodies, if present in calibrators, samples, or controls, bind to VZV antigen coated on magnetic particles (solid phase). During the second incubation, the antibody conjugate (anti-human mouse monoclonal antibody conjugated to isoluminol derivative) reacts with any human anti-VZV IgG already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate in the sample, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of absence of anti-VZV IgG antibodies in calibrators, samples, or controls.

Interpretation of Results: The presence or absence of VZV IgG antibodies in the specimens is determined by comparing the chemiluminescence reaction signal to the cut-off value provided by the assay calibration. The LIAISON XL analyzer automatically calculates the signal-to-cutoff (S/CO) ratios, and interprets the results as presented in **Table 1**.

Table 1: LIAISON VZV IgG HT Results Interpretation

S/CO	Result	Interpretation
< 1.00	Negative	A result below 1.00 S/CO may indicate the absence, or a level of IgG antibodies to VZV below the threshold.
≥1.00	Positive	A result above or equal to 1.00 S/CO generally indicates exposure of the subject to VZV.

C Instrument Description Information:

1. Instrument Name:
   LIAISON XL Analyzer

2. Specimen Identification:
   Specimen identification is automated using LIAISON XL Analyzer. The assay is intended for use with the following matrices: Serum (with gel and without gel-SST), dipotassium EDTA (K2- EDTA), lithium heparin and sodium heparin plasma.

V Substantial Equivalence Information:

A Predicate Device Name(s):
LIAISON VZV IgG, LIAISON Control VZV IgG

B Predicate 510(k) Number(s):
K150375

C Comparison with Predicate(s):

Device & Predicate Device(s):	Predicate	Candidate Device
	K150375	K231214
Device Trade Name	LIAISON VZV IgG	LIAISON VZV IgG HT
General Device Characteristic Similarities		
Technology/ Assay Principle	Chemiluminescent Immunoassay (CLIA)	Same
Sample Handling/Assay Processing	Automated	Same
Manufacturing Process	No Change	Same
Storage	Store at 2-8º C until ready to use	Same
Measured	IgG antibodies to Varicella-zoster virus	Same
Sample Volume	20 µL	Same
	• Dispense calibrators, controls, or samples	

Device & Predicate Device(s):	Predicate K150375	Candidate Device K231214
Assay Procedure	• Dispense magnetic particles • Dispense specimen diluent • Incubate • Wash • Dispense conjugate • Incubate • Wash • Dispense starter reagent • Measure Light emitted (RLUs)	Same
Measurement System	Photomultiplier (flash chemiluminescence reader)	Same
Calibrators	Included with kit	Same
Open Use/On Board Stability	Eight (8) weeks at 2-8°C or onboard the analyzer	Same
Calibration Stability	Eight (8) weeks	Same
Controls	Provided Separately	Same
Sample Storage at	Seven (7) days	Same
Serum Storage Freeze-Thaw Cycles	5 freeze-thaw cycles	Same
General Device Characteristic Differences		
Intended Use/Indications For Use	The DiaSorin LIAISON VZV IgG uses chemiluminescence immunoassay (CLIA) technology on the LIAISON Analyzer family 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. The assay performance in detecting antibodies to VZV in individuals vaccinated with the FDA licensed VZV vaccine is unknown. The user of this assay is responsible for establishing the performance characteristics with VZV vaccinated individuals.	The LIAISON VZV IgG HT assay uses chemiluminescent immunoassay (CLIA) technology for the in vitro qualitative detection of specific IgG antibodies to varicella-zoster virus (VZV) in human serum (with gel and without gel-SST), dipotassium EDTA (K2- EDTA), lithium heparin and sodium heparin plasma samples. This assay is intended as an aid in the determination of previous infection of varicella-zoster virus. The test must be performed on the LIAISON XL Analyzer. The assay performance in detecting antibodies to VZV in individuals vaccinated with the FDA-licensed VZV vaccine is unknown. The user of this assay is responsible for establishing the performance characteristics with

Device & Predicate Device(s):	Predicate	Candidate Device
	K150375	K231214
		VZV vaccinated individuals.
Reagent Integral Configuration (1 compartment each reagent)	• Magnetic particles • Calibrator 1 • Calibrator 2 • Specimen Diluent • Conjugate	• Magnetic particles • Calibrator • Assay Buffer • Conjugate
Raw Materials	• Antigen: Inactivated varicella-zoster virus lysate (ROD strain) • Detector: Mouse monoclonal anti-human IgG conjugated to isoluminol derivative • Capture: Magnetic microparticles coated with varicella-zoster antigen	• Antigen: purified Varicella Zoster Virus glycoprotein • Detector: same • Capture: Magnetic particles coated with varicella Zoster Virus glycoprotein
Sample Type	Human Serum	Human Serum and Plasma
Tests per Kit	100	200
Cut-Off	150 Index value	1.00 S/CO
Equivocal Zone	135-165 Index Value	No equivocal zone
Reagent Volume Provided	Magnetic particles (2.5 mL) Conjugate (23 mL)	Magnetic particles (2.45 mL) Conjugate (28.5 mL)
Calibration	Two-point verification of stored master curve	Calibration by using fully qualitative approach with one calibrator
Unit of Measure	Index Value	Signal/Cut-off (S/CO)

VI Standards/Guidance Documents Referenced:

Standard/Guidance Documents referenced are below:

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline -Third Edition (2014).
- CLSI EP07 lnterference Testing in Clinical Chemistry; Approved Guideline-Third Edition (2018).
- CLSI EP37 Supplemental Tables for Interference Testing in Clinical Chemistry-First Edition.
- CLSI EP15-A3 User Verification of Precision and Estimation of Bias; Approved Guideline – Third Edition (Reaffirmed: September 2019).
- CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (2009).
- ISO 14971-Medical Devices-Application of risk management to medical devices-Third Edition. (2019).

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Within-Laboratory Precision: A 20-day within-laboratory precision study was performed using 3 lots of LIAISON VZV IgG HT reagent integrals and LIAISON Control VZV IgG HT. Study was conducted within a single calibration cycle. Within laboratory precision results are reported in table below.

Table 2: LIAISON VZV IgG HT Assay Within-Laboratory Precision

Sample ID	N	Mean (S/CO)	Repeatability		Between Run		Between Day		Between-Lot		Total	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Negative Control A	240	0.0166	0.0012	7.3%	0.0017	10.4%	0.0021	13.0%	0.0021	12.8%	0.0034	20.7%
Negative Control B	240	0.0150	0.0018	11.9%	0.0014	9.6%	0.0020	13.2%	0.0023	15.3%	0.0035	23.5%
Positive Control A	240	3.73	0.069	1.8%	0.076	2.0%	0.211	5.7%	0.206	5.5%	0.285	7.6%
Positive Control B	240	3.57	0.079	2.2%	0.089	2.5%	0.216	6.1%	0.193	5.4%	0.289	8.1%
Positive Control C	240	3.49	0.070	2.0%	0.078	2.2%	0.199	5.7%	0.210	6.0%	0.279	8.0%
Sample 1	240	0.120	0.005	3.8%	0.003	2.8%	0.005	4.2%	0.009	7.1%	0.010	8.5%
Sample 2	240	0.669	0.021	3.1%	0.023	3.4%	0.029	4.4%	0.027	4.0%	0.047	7.0%
Sample 3	240	0.850	0.019	2.3%	0.021	2.4%	0.036	4.3%	0.065	7.7%	0.070	8.2%
Sample 4	240	1.26	0.030	2.4%	0.021	1.7%	0.055	4.4%	0.037	2.9%	0.072	5.7%
Sample 5	240	3.33	0.071	2.1%	0.053	1.6%	0.151	4.5%	0.099	3.0%	0.190	5.7%
Sample 6	240	6.84	0.13	1.8%	0.17	2.5%	0.26	3.9%	0.20	3.0%	0.37	5.4%
Sample 7	240	12.6	0.25	2.0%	0.44	3.5%	0.22	1.8%	0.40	3.1%	0.64	5.0%

Reproducibility Study (multi-site precision): A 5-day reproducibility study was performed at 3 US sites, using 1 test lot. Results of the Reproducibility study for the LIAISON VZV IgG HT Assay performed across three sites are presented in the tables below.

Table 3: LIAISON VZV IgG HT Assay Reproducibility

Sample ID	N	Mean (S/CO)	Repeatability		Between Day		Between Site		Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%
Negative Control	90	0.017	0.002	9.1%	0.001	7.6%	0.001	7.3%	0.002	13.0%
Positive Control	90	3.55	0.115	3.2%	0.135	3.8%	0.121	3.4%	0.201	5.7%
Sample 1	90	0.108	0.007	6.7%	0.010	9.4%	0.000	0.4%	0.011	10.4%
Sample 2	90	0.638	0.029	4.6%	0.042	6.6%	0.019	3.0%	0.050	7.8%
Sample 3	90	0.783	0.041	5.2%	0.054	6.9%	0.019	2.4%	0.064	8.1%
Sample 4	90	1.18	0.047	4.0%	0.079	6.7%	0.063	5.4%	0.104	8.8%
Sample 5	90	3.31	0.143	4.3%	0.176	5.3%	0.172	5.2%	0.267	8.1%
Sample 6	90	6.95	0.279	4.0%	0.187	2.7%	0.240	3.5%	0.388	5.6%
Sample 7	90	13.2	0.446	3.4%	0.427	3.2%	0.509	3.9%	0.756	5.7%

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

a. Potential Cross-Reactivity:

Potential cross-reactivity for the LIAISON VZV IgG HT assay was determined by testing specimens (serum, K2 EDTA plasma and Li Heparin plasma samples) from individuals with antibodies to different microorganisms or with other medical conditions unrelated to VZV (bacterial and viral infections as well as autoimmune disorders). No false positive results were observed. The data provided showed no cross-reactivity with the potential cross-reactants tested.

Table 4: LIAISON VZV IgG HT Assay Cross-Reactivity study

ID	Potential Cross reactants	Number of tested samples
1	CMV (anti-CMV positive)	10
2	Epstein-Bar Virus (anti-EBV positive)	10
3	Herpes Simplex Virus (anti-HSV 1 positive)	10
4	Herpes Simplex Virus (anti-HSV 2 positive)	10
5	Rubella (anti-Rubella positive)	10
6	Hepatitis C Virus (anti-HCV positive)	10
7	Human Immunodeficiency Virus (anti-HIV antibodies)	10
8	Hepatitis A Virus (anti-HAV positive)	10
9	*Borrelia burgdorferi (anti-B. burgorferi antibodies)*	10
10	*Toxoplasma. Gondii* (anti-*T. gondii* antibodies)	11
11	Parvovirus B19 (anti-Parvovirus B19 positive)	16
12	Measles virus (anti-Measles antibodies)	11
13	Mumps virus (anti-Mumps antibodies)	12
14	Adenovirus (anti-Adenovirus antibodies)	10
15	Anti-Influenza A antibodies	11
16	Anti-Influenza B antibodies	10
17	*Mycoplasma pneumonia* (anti-*M. pneumonia* antibodies)	10
18	Respiratory syncytial virus (RSV) antibodies	11
19	Rheumatoid Factor	10
20	Human anti-mouse antibodies (HAMA)	14
21	Anti-nuclear antibodies (ANA)	10
	TOTAL	**226**

b. Endogenous and Exogenous Interfering Substances:

The LIAISON VZV IgG HT assay was evaluated for potential interference caused by endogenous and exogenous substances using VZV IgG antibody-negative, high negative, around the cut-off, low positive, and high positive samples. No interference was observed with the endogenous and exogenous interference substances at the concentration listed in the table below.

Table 5: Endogenous and Exogenous Interfering Substances Evaluated

Substance	Concentrations tested
Endogenous Substances	
Unconjugated bilirubin	40 mg/dL
Conjugated bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Triglycerides	3000 mg/dL
Human Serum Albumin	6000 mg/dL
Cholesterol	400 mg/dL
Total IgG	2000 mg/dL
Total IgM	400 mg/dL
Total protein (high)	≥ 120 g/L
Total protein (low)	≤ 60 g/L
Human anti-mouse antibody (HAMA)	820 ng/mL
Rheumatoid Factor (RF)	2000 IU/mL
Exogenous Substances	
Biotin	3500 ng/mL
Vitamin A	800 µg/dL
Vitamin B12	2850 pg/mL
Vitamin C	20 mg/dL
Vitamin D	450 ng/mL
Vitamin E	120 mg/L
Folic Acid	160 ng/mL
Acetaminophen	15.6 mg/dL
Ibuprofen	21.9 mg/dL
Acetylsalicylic acid	50 mg/dL
Naproxen	36.0 mg/dL
Penicillin	110 mg/dL
Streptomycin (sulphate)	25.8 mg/dL
Erythromycin	13.8 mg/dL

4. Assay Reportable Range:

   Not Applicable.

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

   Not Applicable.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   The study was performed to determine the LIAISON VZV IgG HT assay S/CO cutoff. A total of 90 samples with 42 VZV IgG antibody negative samples, and 48 VZV IgG antibody positive samples were included. A receiver-operator curve analysis showed a clear separation of the non-reactive and reactive results using a cut-off of 1.00 S/CO value.

8. Analytical Sensitivity at cutoff:

   The analytical sensitivity of the LIAISON VZV IgG HT assay was determined using a series of serial dilutions of the WHO *First International Standard for varicella zoster immunoglobulin (1987), NIBSC code: W1044* in negative serum matrix. Three lots of the LIAISON VZV IgG HT assay were used. The data was analyzed by regression analysis, considering the best fit. The cut-off in mIU/mL was identified as the corresponding to 1.00 S/CO on the regression analysis. The analytical sensitivity at the cutoff is the higher concentration among the 3 lots for the reference standard that corresponds to the cut-off value of 1.00 S/CO for LIAISON VZV IgG HT assay is 0.1524 IU/mL (152.4 mIU/mL).

9. Accuracy (Instrument):

   Not applicable

10. Sample Carry-Over:

    The LIAISON VZV IgG HTis not susceptible to within-assay sample carry-over.

B Comparison Studies:

1. Method Comparison Study:

Clinical Agreement Study:

A multisite clinical agreement study was conducted to evaluate the clinical performance of the LIAISON VZV IgG HT test. One thousand five hundred and forty-four (1544) clinical human serum samples were used for this study, including 125 known positive specimens, 200 known

negative specimens, 135 pregnant women specimens and 1084 specimens sent to the laboratory for testing.
The samples were collected within the United States and tested at three independent external laboratories. Each sample, was tested with the LIAISON VZV IgG HT test and the comparator. The positive and negative percent agreements were calculated and presented below for normal laboratory routine (all), normal laboratory routine pediatric, and pregnant women. Specimens which were repeatedly equivocal by the predicate device were graded against the performance of the LIAISON VZV IgG HT assay which does not have an equivocal zone. The results for all populations are shown in the tables below.

Table 6: Known Positive Specimens (n=125)

LIAISON VZV IgG HT	**Comparator**			
	Positive	**Equivocal**	**Negative**	**Total**
Positive	123	0	0	123
Negative	1	0	1	2
Total	124	0	1	125
PPA	99.2% (123/124)		95%CI= 95.6% to 99.9%	
NPA	100% (1/1)		95% CI= 20.7% to 100.0%	

Table 7: Known Negative Specimens (n= 200)

LIAISON VZV IgG HT	**Comparator**			
	Positive	**Equivocal***	**Negative**	**Total**
Positive	0	1	3	4
Negative	0	6	190	196
Total	0	7	193	200
PPA*	0.0% (0/6)		95%CI= 0.0% to 39.0%	
NPA*	97.9% (190/194)		95%CI= 94.8% to 99.2%	

* Equivocal results are counted against candidate device performance

Table 8: Pregnant Women Specimens (n=135)

LIAISON VZV IgG HT	Comparator			
	Positive	Equivocal*	Negative	Total
Positive	108	0	1	109
Negative	0	2	24	26
Total	108	2	25	135
PPA*	98.2% (108/110)		95%CI= 93.6% to 99.5%	
NPA*	96.0% (24/25)		95%CI= 80.5% to 99.3%	

* Equivocal results are counted against candidate device performance

Table 9: Laboratory Routine Specimens (n= 1083**)

LIAISON VZV IgG HT	Comparator			
	Positive	Equivocal*	Negative	Total
Positive	556	4	5	565
Negative	10	5	503	518
Total	566	9	508	1083**
PPA*	556/571	97.4%	95%CI= 95.7% to 98.4%	
NPA*	503/512	98.2%	95%CI= 96.7% to 99.1%	

* Equivocal results are counted against candidate device performance
** 1 out of 1084 samples was excluded due to insufficient volume for testing on the candidate device.

2. Matrix Comparison:

A matrix equivalency study was conducted including 87 sets of matched reactive and nonreactive samples of different matrices (serum, with and without gel STT, dipotassium EDTA plasma, lithium-heparin plasma, and sodium heparin plasma) that were evaluated with the LIAISON VZV IgG HT assay. Data was analyzed using Passing Bablok fit regression comparing mean value results of all matrices to serum.

The following tube types are acceptable for use with the LIAISON VZV IgG HT assay:
• Serum (with and without gel STT)
• Plasma (dipotassium EDTA, lithium heparin, sodium heparin).

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

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

   Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not Applicable

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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