

**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[®] 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[®] VZV IgG uses chemiluminescence immunoassay (CLIA) technology on the LIAISON[®] 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[®] 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 [®] 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[®] 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[®] 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 (100% serum)</i> | 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.”

| Organism/condition | Number of Expected Negative Samples | LIAISON[®] Positive or equivocal Result |
|---------------------------|--|---|
| 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) |
| Total | 183 | (0/183) |

No positive result was found for the samples when tested by LIAISON[®] VZV IgG.

f. Assay cut-off:

The cut-off for the LIAISON[®] 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[®] 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[®] 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.