

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

A. 510(k) Number:

K061239

B. Purpose for Submission:

New device(s)

C. Measurand:

Anti-HSV-1 IgG antibodies and Anti-HSV-2 IgG antibodies

D. Type of Test:

ELISA

E. Applicant:

EUROIMMUN US LLC

F. Proprietary and Established Names:

EUROIMMUN Anti-HSV-1 ELISA (IgG) Kit and EUROIMMUN Anti-HSV-2 ELISA (IgG) Kit

G. Regulatory Information:

1. Regulation section: 21CFR 866. 3305: Herpes Simplex Virus Serological Reagents
2. Classification: Class: II
3. Product code:
MXJ: Enzyme linked immunosorbent assay, herpes simplex virus, hsv-1
MYF: Enzyme linked immunosorbent assay, herpes simplex virus, hsv-2
4. Panel: 83 Microbiology

H. Intended Use:

HSV-1 Assay: The EUROIMMUN Anti-HSV-1 ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against Herpes simplex virus type 1 (HSV-1) specific glycoprotein C1 in human serum. It is intended for the

presumptive diagnosis of type specific HSV-1 infection in conjunction with EUROIMMUN Anti-HSV-2 ELISA (IgG) in persons suspected of herpes viral infection.

HSV-2 Assay: The EUROIMMUN Anti-HSV-2 ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against Herpes simplex virus type 2 (HSV-2) specific glycoprotein G2 in human serum. It is intended for the presumptive diagnosis of type specific HSV-2 infection in conjunction with EUROIMMUN Anti-HSV-1 ELISA (IgG) in persons suspected of herpes viral infection.

2. Indication(s) for use:

HSV-1 Assay: The EUROIMMUN Anti-HSV-1 ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against Herpes simplex virus type 1 (HSV-1) specific glycoprotein C1 in human serum. It is intended for the presumptive diagnosis of type specific HSV-1 infection in conjunction with EUROIMMUN Anti-HSV-2 ELISA (IgG) in persons suspected of herpes viral infection.

HSV-2 Assay: The EUROIMMUN Anti-HSV-2 ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against Herpes simplex virus type 2 (HSV-2) specific glycoprotein G2 in human serum. It is intended for the presumptive diagnosis of type specific HSV-2 infection in conjunction with EUROIMMUN Anti-HSV-1 ELISA (IgG) in persons suspected of herpes viral infection.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

None

I. Device Description:

HSV-1 Assay: The test kit contains microtiter wells coated with affinity purified glycoprotein C1 isolated from HSV-1. In the first reaction step, diluted patient samples, calibrators and controls are incubated in the wells. Anti-HSV-1 antibodies will bind to the antigens coated in the microtiter wells. The wells are washed to remove any unbound proteins and non-specific antibodies. In a second reaction step, rabbit anti-human IgG HRP enzyme conjugate is added to each well. The enzyme conjugate will bind to any wells that have human IgG binding to the HSV-1 antigen. The wells are washed to remove any unbound HRP enzyme conjugate. 3,3',5,5'-tetramethylbenzidine (TMB) enzyme substrate is added. If the HRP enzyme is present in the well (positive reaction), the HRP enzyme will react with the TMB substrate and produce a blue color.

HSV-2 Assay: The test kit contains microtiter wells coated with affinity purified

glycoprotein G2 isolated from HSV-2. In the first reaction step, diluted patient samples, calibrators and controls are incubated in the wells. Anti-HSV-2 antibodies will bind to the antigens coated in the microtiter wells. The wells are washed to remove any unbound proteins and non-specific antibodies. In a second reaction step, rabbit anti-human IgG HRP enzyme conjugate is added to each well. The enzyme conjugate will bind to any wells that have human IgG binding to the HSV-2 antigen. The wells are washed to remove any unbound HRP enzyme conjugate. 3,3',5,5'-tetramethylbenzidine (TMB) enzyme substrate is added. If the HRP enzyme is present in the well (positive reaction), the HRP enzyme will react with the TMB substrate and produce a blue color.

J. Substantial Equivalence Information:

1. Predicate device name(s):
HerpeSelect® 1 ELISA IgG
HerpeSelect® 2 ELISA IgG
2. Predicate 510(k) number(s):
K021429 (HSV-1)
K021486 (HSV-2)
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
<u>HSV-1 Assay</u> Specimen Type Method and type	Human serum Qualitative ELISA	Human serum Qualitative ELISA
<u>HSV-2 Assay</u> Method and type Specimen Type Antigen used	Qualitative Human serum Glycoprotein G-2	Qualitative Human serum Glycoprotein G-2
Differences		
Item	Device	Predicate
<u>HSV-1 Assay</u> Antigen used	Glycoprotein C-1	Glycoprotein G-1

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

Not applicable

L. Test Principle:

Enzyme linked immunosorbent assay, ELISA

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

HSV-1 Assay: The reproducibility of the HSV-1 test was investigated by determining the intra- and inter-assay coefficients of variation using 3 sera. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on 4 determinations performed in 4-6 different test runs. The inter-assay CV ranged from 2.5 to 7.2% for positive specimens.

HSV-2 Assay: The reproducibility of the HSV-2 test was investigated by determining the intra- and inter-assay coefficients of variation using 4 to 6 different sera. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on 4 determinations performed in 4 different test runs. The inter-assay CV ranged from 2.3 to 8.4% for positive specimens.

b. *Linearity/assay reportable range:*

Not applicable

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

Not applicable

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

HSV-1 Assay: This ELISA showed no serological cross reactivity with sera positive for the following: EBV-CA (n = 12), CMV (n = 6), VZV (n = 12), Adenovirus (n = 12), RSV (n = 12), Parainfluenza types 1-4 (n = 12), Influenza A (n = 12), Influenza B (n = 12), Mycoplasma pneumoniae (n = 8), Mumps (n = 12), Measles (n = 12), Rubella (n = 12), Chlamydia pneumoniae (n = 4), Helicobacter pylori (n = 7).

HSV-2 Assay: This ELISA showed no serological cross reactivity with sera positive for the following: HSV-1 (n = 12); EBV-CA (n = 12); CMV (n = 12); VZV (n = 12); Adenovirus (n = 12); RSV (n = 12); Parainfluenza types 1-4 (n = 12); Influenza A (n = 12); Influenza B (n = 12); Mycoplasma pneumoniae (n = 12); Mumps (n = 12); Measles (n = 12); Rubella (n = 12); Toxoplasma (n = 12); Chlamydia pneumoniae (n = 12); Helicobacter pylori (n = 12).

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

HSV-1 Assay

Sensitivity and specificity: In 4 clinical studies, 397 samples were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method.

Study 1: Hundred (100) prospective samples from the US were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method. This group consisted of 38 men and 57 women (and 5 unknown) with an average age of 36 years (range: 19-84 years).

$$\text{Specificity} = 35 / 35 = 100 \%$$

$$\text{Sensitivity} = 65 / 65 = 100 \%$$

Study 2: Two-hundred-fifty-four (254) samples, consisting of 186 samples from a risk group and 68 routine samples (both Muenster, Germany) were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity} = 62 / 62 = 100 \%$$

$$\text{Sensitivity} = 187 / 187 = 100 \%$$

Study 3: Twenty-five (25) member performance panel obtained commercially from Boston Biomedica Inc. were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity} = 5 / 7 = 71.4 \%$$

$$\text{Sensitivity} = 14 / 14 = 100 \%$$

Study 4: Eighteen (18) characterized samples obtained from INSTAND (Institute for Standardization and Documentation in Medical Laboratory) were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity} = 5 / 5 = 100 \%$$

$$\text{Sensitivity} = 13 / 13 = 100 \%$$

CDC panel: A panel of hundred (100) characterized samples obtained from the CDC were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG).

Negative Agreement = $35 / 45 = 77.8 \%$
Positive Agreement = $51 / 52 = 98.1 \%$

INSTAND samples: 28 clinically characterized patient samples (Inter-laboratory test samples of the INSTAND, Germany) were examined with the EUROIMMUN Anti-HSV-1 ELISA (IgG). The test shows an agreement of 100%.

Negative Agreement = $8 / 8 = 100 \%$
Positive Agreement = $20 / 20 = 100 \%$

Comparison to predicate kit: A study was conducted at a hospital clinical laboratory comparing the performance of the EUROIMMUN Anti-HSV-1 IgG ELISA and a kit in current distribution. 259 prospective samples from the US were tested.

Negative Agreement = $83 / 86 = 96.5 \%$
Positive Agreement = $170 / 173 = 98.3 \%$

Type specificity: Type specificity was confirmed using sera of patients serologically positive for Anti-HSV-1 IgG and negative for Anti-HSV-2 IgG and vice versa. 168 samples were tested with the EUROIMMUN Anti-HSV-1 ELISA and with another FDA-cleared ELISA as reference method. A type specificity of 97.6% was observed.

Negative Agreement = $30 / 31 = 96.8 \%$
Positive Agreement = $134 / 137 = 97.8 \%$

HSV-2 Assay

Sensitivity and specificity: In 5 clinical studies, 421 samples were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG) and Western blot as the reference method.

Study 1: Hundred (100) prospective samples from the US were tested with the EUROIMMUN Anti-HSV-1 ELISA (IgG) and Western blot as the reference method. This group consisted of 38 men and 57 women (and 5 unknown) with an average age of 36 years (range: 19-84 years).

Specificity = $64 / 64 = 100 \%$
Sensitivity = $36 / 36 = 100 \%$

Study 2: Two-hundred-fifty-four (254) samples, consisting of 186 samples from a risk group and 68 routine samples (both Muenster, Germany) were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG) and Western blot as the reference method.

Specificity = $148 / 160 = 92.5 \%$
Sensitivity = $87 / 87 = 100 \%$

Study 3: Twenty-five (25) member performance panel obtained commercially from

Boston Biomedica Inc. were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity} = 10 / 13 = 76.9 \%$$

$$\text{Sensitivity} = 9 / 9 = 100 \%$$

Study 4: Eighteen (18) characterized samples obtained from INSTAND (Institute for Standardization and Documentation in Medical Laboratory) were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity} = \text{N/A}$$

$$\text{Sensitivity} = 17 / 18 = 94.5 \%$$

Study 5: Twenty-four (24) stored samples (Chennai, India) were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG) and Western blot as the reference method.

$$\text{Specificity Agreement} = 20 / 20 = 100 \%$$

$$\text{Sensitivity} = 4 / 4 = 100 \%$$

CDC panel: A panel of hundred (100) characterized samples obtained from the CDC were tested with the EUROIMMUN Anti-HSV-2 ELISA (IgG).

$$\text{Negative Agreement} = 44 / 50 = 88.0 \%$$

$$\text{Positive Agreement} = 49 / 50 = 98.0 \%$$

Comparison to predicate kit: A study was conducted at a hospital clinical laboratory comparing the performance of the EUROIMMUN Anti-HSV-2 IgG ELISA and a kit in current distribution. 259 prospective samples from the US were tested.

$$\text{Negative Agreement} = 188 / 193 = 97.4 \%$$

$$\text{Positive Agreement} = 62 / 66 = 93.9 \%$$

Type specificity: Type specificity was confirmed using sera of patients serologically positive for Anti-HSV-1 IgG and negative for Anti-HSV-2 IgG and vice versa. 168 samples were tested with the EUROIMMUN Anti-HSV-2 ELISA and with another FDA-cleared ELISA as reference method. A type specificity of 97.0% was observed.

$$\text{Negative Agreement} = 133 / 137 = 97.1 \%$$

$$\text{Positive Agreement} = 30 / 31 = 96.8 \%$$

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):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

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.