

**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).

$$\begin{aligned}\text{Specificity} &= 35 / 35 = 100 \% \\ \text{Sensitivity} &= 65 / 65 = 100 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity} &= 62 / 62 = 100 \% \\ \text{Sensitivity} &= 187 / 187 = 100 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity} &= 5 / 7 = 71.4 \% \\ \text{Sensitivity} &= 14 / 14 = 100 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity} &= 5 / 5 = 100 \% \\ \text{Sensitivity} &= 13 / 13 = 100 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity} &= 10 / 13 = 76.9 \% \\ \text{Sensitivity} &= 9 / 9 = 100 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity} &= \text{N/A} \\ \text{Sensitivity} &= 17 / 18 = 94.5 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Specificity Agreement} &= 20 / 20 = 100 \% \\ \text{Sensitivity} &= 4 / 4 = 100 \%\end{aligned}$$

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

$$\begin{aligned}\text{Negative Agreement} &= 44 / 50 = 88.0 \% \\ \text{Positive Agreement} &= 49 / 50 = 98.0 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Negative Agreement} &= 188 / 193 = 97.4 \% \\ \text{Positive Agreement} &= 62 / 66 = 93.9 \%\end{aligned}$$

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.

$$\begin{aligned}\text{Negative Agreement} &= 133 / 137 = 97.1 \% \\ \text{Positive Agreement} &= 30 / 31 = 96.8 \%\end{aligned}$$

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.