MIKROGEN DIAGNOSTIK

IVD

Instructions for use (English)

## 1 Purpose

The *recom*Line HSV-1 & HSV-2 is a qualitative in-vitro test for the detection of IgG antibodies against protein antigens of Herpes simplex viruses in human serum or plasma.

## 2 Intended use

An immuno-assay for detecting and differentiating IgG antibodies against the Herpes simplex virus Type 1 and Type 2. The use of joint and type-specific protein antigens for the Herpes simplex virus Type 1 (HSV-1) or Type 2 (HSV-2) allows for a differentiated diagnosis (clear distinction between the two serotypes).
By separately lining up the individual antigens, unlike ELISAs, the test principle allows the identification of specific antibodies against the individual antigens of HSV-1 and/or HSV-2 in a single test preparation.

## 3 Test principle

Highly purified HSV antigens (HSV lysate - virus lysate of HSV-1 and HSV-2, gG1 - a type-specific, recombinant antigen of HSV-1, gG2 - a type-specific, recombinant antigen of HSV-2) have been fixed on nitrocellulose membrane test strips.

1. The test strips are incubated with the diluted serum or plasma sample, with specific antibodies attached to the pathogen antigens on the test strip.
2. Unbound antibodies are then flushed away.
3. In a second step, the strips are incubated with anti-human immunoglobulin antibodies (IgG), which are coupled to horseradish peroxidase.
4. Unbound conjugate antibodies are then flushed away.
5. Specifically bound antibodies are detected by a peroxidase-catalysed colour reaction. If an antigen-antibody reaction has taken place, a dark band will appear on the strip at the corresponding point.

There are control bands at the upper end of the test strips:

a) The reaction control band under the strip number, which must show a reaction for every serum/plasma sample.
b) The conjugate controls (IgG) serve as a control for the conjugate and strip type used (Ig class-specific). If, for example, the IgG-specific test strip is used for the detection of IgG antibodies, the IgG conjugate control will show this clearly on the band.
c) "Cut-off control": The intensity of this band allows the assessment of the reactivity of each antigen band (see 9.2. Evaluation).

## 4 Reagents

### 4.1 Package contents

The reagents in one package are sufficient for 20 tests.

Each test kit contains:

| | |
|---|---|
| WASHBUF A 10 X | **100 ml** Wash Buffer A (**10 times concentration**)<br>Contains phosphate buffer, NaCl, KCl, detergent, preservative: MIT (0.1%) and Oxypyrion (0.2%) |
| SUBS TMB | **40 ml** Chromogenic substrate Tetramethylbenzidin (**TMB, ready-to-use**) |
| MILKPOW | **5 g** skimmed milk powder |
| INSTRU | **1** Instructions for use |
| EVALFORM | **1** Evaluation form |
| TESTSTR | **2** tubes, each with 10 numbered test strips |
| CONJ IgG | **500 µl** anti-human IgG conjugate **(100-fold concentration, green cap)**<br>From rabbit, containing NaN3 (<0.1%), MIT (0.1%) and chloroacetamide (0.1%) |

### 4.2 Materials required but not supplied

- Incubation trays (can be purchased as needed from MIKROGEN)
- Deionised water (high quality)
- Plastic forceps
- Horizontal shaker
- Vortex mixer or other rotators
- Vacuum pump or similar device
- Volumetric cylinders, 50 ml and 1000 ml
- Micropipettes with disposable tips, 20 µl and 1000 µl
- 10 ml pipette or dispenser
- Timer
- Absorbent paper towels
- Disposable protective gloves
- Waste container for bio-hazardous materials

## 5 Shelf life and handling

- Store reagents at +2 to +8 °C before and after use, **do not freeze**.
- Subject all ingredients to room temperature (+18 to +25 °C) for at least 30 minutes before beginning the test. The test procedure is carried out at room temperature.
- Washing buffer, milk powder, dilution buffer, conjugate and TMB can be interchanged between the different *recom*Line and *recom*Blot test systems, if these components carry the same symbols. Consider the shelf life of these components.
- Mix the concentrated reagents and samples thoroughly before use. Avoid the build-up of foam.
- Only open the tube containing the test strip immediately before use to avoid condensation. Leave unused strips in the tube and continue to store at +2 °C to +8°C (reseal tube tightly, test strips must not become moist before the test!).
- The strips are marked with the serial number, as well as the test code.
- The packages bear an expiration date. After this has been reached no guarantee of quality can be offered.
- Protect kit components from direct sunlight throughout the entire test procedure. The substrate solution (TMB) is especially sensitive to light.
- The test should only be carried out by trained and authorised personnel.
- In case of substantial changes to the product or the regulations concerning use by the user, the application may lie outside the purpose given by MIKROGEN.
- Cross-contamination of patient samples or conjugates can lead to inaccurate test results. Add patient samples, test strips and conjugate solution carefully. Make sure that incubation solutions do not flow over into other wells. Carefully remove liquids.
- The strips must be completely wetted and immersed throughout the entire procedure.
- Automation is possible; you will receive further information from MIKROGEN.

## 6 Warnings and precautions

- For *In vitro* diagnostic use only.
- All blood products must be treated as potentially infectious.
- The test strips were prepared with inactivated whole cell lysates and/or recombinant bacterial, viral or parasitic antigens.
- After the addition of patient or control specimens the strip material must be considered infectious and treated as such.
- Suitable disposable gloves must be worn throughout the entire test procedure.
- The reagents contain the antimicrobial agents and preservatives sodium azide, MIT (methylisothiazolone), oxypyrion and chloroacetamide and hydrogen peroxide. Avoid contact with the skin or mucous membrane. Sodium azide can form an explosive azide upon contact with heavy metals such as copper and lead azide.
- All siphoned liquids must be collected. All collecting containers must contain suitable disinfectants for the inactivation of human pathogens. All reagents and materials contaminated with potentially infectious samples must be treated with disinfectants or disposed of according to your hygiene regulations. The concentrations and incubation periods stated by the manufacturer must be observed.
- Use incubation trays only once.
- Handle strips carefully using plastic forceps.
- Do not substitute or mix the reagents with reagents from other manufacturers.
- Read through the entire instructions for use before carrying out the test and follow them carefully. Deviation from the test protocol provided in the instructions for use can lead to erroneous results.

# 7 Sampling and preparation of reagents

## 7.1 Samples

The sample can be serum or plasma (citrate, EDTA, heparin, CPD), which needs to be separated from the blood clot as soon as possible after sampling so as to avoid haemolysis. Avoid Microbial contamination of the samples. Insoluble substances must be removed from the sample prior to incubation.
The use of heat-inactivated, icteric, haemolytic, lipemic or turbid samples is not recommended.
**Caution!**
**If the tests are not conducted immediately, the sample can be stored for up to 2 weeks at +2 to +8 °C. More extended storage of the samples is possible at -20 °C or lower. Repeated freezing and thawing of samples is not recommended due to the risk of producing inaccurate results. Avoid more than 3 cycles of freezing and thawing.**

## 7.2 Preparation of solutions

7.2.1 *Preparation of ready-to-use wash buffer A*
This buffer is required for serum and conjugate dilution as well as washing stages.
Prior to dilution, the volume of wash buffer A must be determined for the corresponding number of tests.
First, the skimmed milk powder is dissolved in wash buffer A concentrate, and then deionised water is added to bring the solution up to the final volume (dilution: 1 + 9). The quantities required for a defined number of test strips are to be mathematically determined according to the following formula (device-specific dead volume is not considered):

| Reagent | Formula | Example: 5 strips |
|---|---|---|
| Skimmed milk powder [g] | = number of strips x 0.1 | 0.5 g |
| Wash buffer A concentrate [ml] | = number of strips x 2 | 10 ml |
| Deionised water [ml] | = number of strips x 18 | 90 ml |
| Ready-to-use wash buffer A [ml] | = number of strips x 20 | 100 ml |

Ready-to-use wash buffer A can be stored for 4 weeks at +2°C to +8°C. The ready to use wash buffer A is odourless and easily marred.

7.2.2 *Preparation of conjugate solutions*
The conjugate solution must be prepared just before use. It is not possible to store the ready-to-use conjugate solution.
One part of the conjugate concentrate is diluted with 100 parts of the ready to use wash buffer A (1 + 100).

The quantities required for a defined number of test strips are to be calculated according to the following formula:

| Reagent | Formula | Example: 5 strips |
|---|---|---|
| Conjugate concentrate [µl] | = number of strips x 20 | 100 µl |
| Ready-to-use wash buffer A [ml] | = number of strips x 2 | 10 ml |

The conjugate quantities are calculated without dead volume. Depending on handling (manual or on a device), please mix additional conjugate for 1 to 3 strips.

# 8 Test procedure

## 8.1 One-hour serum incubation

| No. | Execution | Note |
|---|---|---|
| 1 | Temper all reagents for at least 30 minutes at 18°C - 25° (room temperature) before beginning the test. | The test procedure is carried out at room temperature. |
| 2 | Prepare test strips<br>Place the strips in **2 ml** of ready-to-use **wash buffer A**. | Do not touch the strips with bare hands - use tweezers instead. The strip number points upward. Place each strip in a separate well in the incubation tray (see 4.2).The strips must be completely immersed. |
| 3<br>a)<br><br><br><br>b) | Incubation of samples<br>**20 µl** of undiluted sample (human serum or plasma) is pipetted on to the test strip for each incubation mixture. (Dilution 1 + 100)<br><br>Incubate for **1 hour** with gentle shaking | <br>Pipette the sample at one end of the immersed strip in the wash buffer A and mix as quickly as possible by carefully shaking the tray.<br>Cover the incubation tray with plastic cover and place in the shaker. |
| 4<br><br>a)<br><br>b)<br><br><br><br>c) | Washing<br><br>Carefully remove the plastic cover from the incubation trays.<br>Gently siphon serum dilution from the individual wells.<br><br><br><br>Pipette **2 ml** of ready to use **wash buffer A** into each well, wash for 5 minutes with gentle shaking and then siphon off the wash buffer A. | Carry out washing stages 8.4a-8.4c three times in total.<br>Avoid cross-contamination.<br><br><br>The manufacturer's instructions must be followed during automatic processing. |
| 5 | Incubation with conjugate<br>Add **2 ml** of ready-to-use **conjugate solution** and incubate for **45 minutes** while shaking gently. | Cover the incubation tray with plastic cover and place in the shaker. |
| 6 | Washing<br>see under 8.4 | Carry out washing stages three times in total (see 8.4a-8.4c) |
| 7 | Substrate reaction<br>Add **1.5 ml** of **substrate solution** and incubate for **5-10 minutes** while shaking gently. | |
| 8 | Stopping the reaction<br>Remove substrate solution<br>Wash at least three times **briefly** with **deionisied water**. | |
| 9 | Drying the strips<br>Dry strip between 2 layers of absorbent paper for **2 hours** before analysis. | Carefully remove strips from water using plastic forceps. Store strip away from light. |
| **Caution!**<br>**Incubation solutions must not flow into other wells. Splashing must be avoided especially when opening and closing the lid.** | | |

# 9 Results

Caution:
Please do not use automated interpretation without consideration of the information on interpretation given below.

## 9.1 Validation – Quality Control

An analysis of the test can be carried out if the following criteria have been fulfilled:
1. Reaction control band (top line) with clearly visible stain, dark band
2. Antibody class (second band): the IgG conjugate control band must show a clear staining.
3. Cut-off control (third band): weak, but visible staining

## 9.2 Evaluation

The analysis of the test strips can be visual or computer-assisted - using the test strip analysis software *recom*Scan. The *recom*Scan software is designed to support the evaluation of test strips. Further information and related instructions for the computer-assisted analysis is available on request from MIKROGEN. The following instructions relate to visual analysis.

9.2.1 *Assessment of band intensity*
1. Note the date and batch number, as well as the detected antibody class, on the attached evaluation form.
2. Enter the sample identification numbers to the evaluation sheet.
3. Now stick the corresponding test strip onto the appropriate fields on the evaluation form using a glue stick. Align the test strip with the reaction control bands along the marked lines. Then use a transparent adhesive tape to attach the test strip to the left of the marked lines (do not tape over the reaction control band!). Sticking the entire test strip down flat using glue or tape can lead to changes in colour.
4. Now identify the bands of the developed test strip on the basis of the printed control strip of the evaluation sheet and enter this in the evaluation sheet. For each corresponding immunoglobulin class, assess separately the intensity of the bands occurring on the basis of Table 1.

**Table 1:** Assessment of band intensity in relation to the cut-off band

| Stain intensity of the bands | Assessment |
|---|---|
| No reaction | - |
| Very low intensity (lower than the cut-off band) | +/- |
| Low intensity (equivalent to the cut-off band) | + |
| High intensity (higher than the cut-off band) | ++ |
| Very strong intensity | +++ |

## 9.3 Interpretation of test results

An assessment schedule for Herpes simplex virus antigens was developed in the *recom*Line HSV-1 & HSV-2 for safe and easy test evaluation on the basis of clinical evaluations (see Table 2). Based on this,

the positive, borderline or negative assessment can be read off by comparing the individual results with -, +/-, +, ++ or +++-rated bands. The interpretation of the recomLine HSV-1 & HSV-2 is primarily based on the positive or negative reactivity of the lysate bands.

Step 1: When lysate has **-** or **+/-** ⇨ the result is HSV-negative
When lysate has **+**, **++**, **+++** ⇨ the result is HSV-positive or borderline (continue with Step 2)

In the second step, the reactivity of the type-specific bands is interpreted in the light of the results of the first step (when the HSV lysate has **+**, **++**, **+++**).

Step 2: When gG-1 has **+**, **++**, **+++** ⇨ HSV-1-positive
When gG-2 has **+**, **++**, **+++** ⇨ HSV-2-positive
When gG-1 and gG-2 has **+**, **++**, **+++** ⇨ the result is HSV-1-positive and HSV-2-positive
When gG-1 and gG-2 have **-** or **+/-** ⇨ HSV-borderline

**Table 2:** Assessment of the bands in *recom*Line HSV-1 & HSV-2 IgG

| Assessment of bands | | | Interpretation of patient samples |
|---|---|---|---|
| **Lysate** | **gG-1** | **gG-2** | |
| Total antigen HSV-1 and HSV-2 | Type-specific antigen HSV-1 | Type-specific antigen HSV-2 | |
| **-** or **+/-** | **-** or **+/-** or **+, ++, +++** | **-** or **+/-** or **+, ++, +++** | **negative**<br>No indication of HSV-1 and HSV-2 |
| **+, ++, +++** | **+, ++, +++** | **-** or **+/-** | **HSV-1-positive**<br>Suspicion of HSV-1 |
| **+, ++, +++** | **-** or **+/-** | **+, ++, +++** | **HSV-2-positive**<br>Suspicion of HSV-2 |
| **+, ++, +++** | **+, ++, +++** | **+, ++, +++** | **HSV-1-positive + HSV-2-positive**<br>Suspicion of HSV-1 and HSV-2 |
| **+, ++, +++** | **-** or **+/-** | **-** or **+/-** | **HSV-borderline**<br>Strips that are only lysate-positive may indicate an early HSV infection, as IgG antibodies against the gG protein in the immune response are only formed in a late state (late sero-conversion).<br>It must also be taken into account that approximately 0.2% of all Herpes simplex viruses do not have gG. A follow-up test is recommended. |

## 10 Limitations of the method - restrictions

- Serological test results must always be considered in the context of other medical assessments of the patient. Therapeutic consequences of the serological findings must always be taken in context with the clinical data.
- Strips that are only lysate-positive may indicate an early HSV infection, as IgG antibodies against gG in the immune response are only formed in a late state (late sero-conversion). It must also be taken into account that approximately 0.2% of all Herpes simplex viruses do not have gG. It is recommended to repeat the test after 4-12 weeks by carrying out a follow-up test.
- No serological test can provide a statement about the location - genital or oral - of a detected HSV infection. A method of direct virus detection, e.g. a virus culture, is recommended for clarification, keeping in mind that this frequently leads to false negative results (the sensitivity of the virus culture is 51% for HSV-1 and 53% for HSV-2).
- A positive serological HSV-2 result in the absence of symptoms nearly always indicates an asymptomatic or subclinical HSV-2 infection. HSV-2 infections of the oral cavity without a simultaneous HSV-2 infection are possible, but extremely rare. HSV-2-positive serology does not exclude a simultaneous genital infection with HSV-1.
- As is the case with all serological tests, false positive results may occur, e.g. in patients with a low probability of an HSV-2 infection. In such cases, a repeat test should be carried out or a different test should be used.
- Samples with inconclusive or borderline results should be followed up after 4-12 weeks, subject to the clinical situation.
- A negative result does not entirely exclude the possibility of an HSV infection in general. False negative results may occur when sampling has taken place before sero-conversion. The rate of sero-reversion when using gG-based tests is very low. It cannot be excluded, however, that a negative test result may be ascribed to this.
- For all test interpretations, especially in the case of slightly positive results, the incorporation of possible clinical information is essential. Once again, close cooperation between the laboratory and the attending physician is recommended.
- The intensity of the invididual antigen bands does not mean any conclusions can be drawn about the antibody titre of a patient. In addition, neither antibody titres nor the known antibody classes allow any conclusions to be drawn about specific infection stages such as primary infection, active relapses or latency.
- The use of serums from fresh EBV infections may result in a reduced gG reactivity or an unspecific reaction of the lysate.
- Dark test strips: Some patient samples can produce dark, uniform or patterned staining across the entire nitrocellulose strip. Various factors in each patient serum are responsible for this. The evaluation of these strips is usually only partly feasible. Thus, "inverse" bands (white bands on dark background), for example, should be evaluated as negative. The respective serum should always be examined using other serological methods.

## 11 Test performance

### 11.1 Diagnostic sensitivity and specificity

**Table 3:** Routine diagnosis: Comparison with a reference ELISA (HSV without type differentiation)

| Total HSV | | Reference ELISA positive / borderline | Reference ELISA negative | sensitivity | Specificity |
|---|---|---|---|---|---|
| *recom*Line HSV-1 & HSV-2 | positive/ borderline | 153 | 5* | 99.4 % | 91.1 % |
| | negative | 1 | 51 | | |

* Two samples were graded as positive / borderline in a reference immunoblot; the remaining three samples on which the *recom*Line HSV-1 & HSV-2 was used only reacted HSV-borderline (isolated lysate).

**Table 4:** Comparison with a type-specific immunoblot (HSV-1)

| HSV-1 | | Reference immunoblot positive / borderline | Reference immunoblot negative | sensitivity | Specificity |
|---|---|---|---|---|---|
| *recom*Line HSV-1 & HSV-2 | positive / borderline | 98 | 6[+] | 99 % | 88.7 % |
| | negative | 1 | 47 | | |

[+] All samples evaluated as HSV-1-positive in the *recom*Line HSV-1 & HSV-2 had poor bands in the reference immunoblot;' two serums responded only HSV-borderline in the *recom*Line HSV-1 & HSV-2 (isolated lysate).

**Table 5:** Routine diagnosis: Comparison with a type-specific immunoblot (HSV-2)

| HSV-2 | | Reference immunoblot positive / borderline | Reference immunoblot negative | sensitivity | Specificity |
|---|---|---|---|---|---|
| *recom*Line HSV-1 & HSV-2 | positive / borderline | 30 | 9[++] | 93.8 % | 92.5 % |
| | negative | 2[+++] | 111 | | |

[++] In the *recom*Line HSV-1 & HSV-2, two samples reacted HSV-borderline (without type differentiation) and were classified as HSV-1-positive, HSV-2-negative in the reference immunoblot; three other samples evaluated as HSV-2-positive in the *recom*Line HSV-1 & HSV-2 showed poor bands in the reference immunoblot.
[+++] These two samples reacted HSV-borderline in the reference immunoblot (without type differentiation) and were assessed as HSV-1-positive, HSV-2-negative in the recomLine HSV-1 & HSV-2.

**Table 6:** Blood donor: Comparison with a type-specific immunoblot (HSV-1)

| HSV-1 | | Reference immunoblot positive / borderline | Reference immunoblot negative | sensitivity | Specificity |
|---|---|---|---|---|---|
| *recom*Line HSV-1 & HSV-2 | positive / borderline | 113 | 2 | 100 % | 94.6 % |
| | negative | 0 | 35 | | |

**Table 7:** Blood donor: Comparison with a type-specific immunoblot (HSV-2)

| HSV-2 | | Reference immunoblot positive / borderline | Reference immunoblot negative | sensitivity | Specificity |
|---|---|---|---|---|---|
| *recom*Line HSV-1 & HSV-2 | positive / borderline | 15 | 1[#] | 75%[##] | 100 % |
| | negative | 5[##] | 129 | | |

[#] This sample tested HSV-borderline in the *recom*Line (without type differentiation) and HSV-1-positive, HSV-2-negative in the reference immunoblot.
[##] Four serums tested HSV-1-positive and HSV-2-negative in the *recom*Line HSV-1 & HSV-2, but HSV-borderline in the reference immunoblot (without type differentiation).

### 11.2 Clinically defined samples

**Table 8:** Examination of clinically defined samples using the recomLine HSV-1 & HSV-2 IgG

| Culture or PCR (smear) | *recom*Line HSV-1 & HSV-2 IgG (n = 58 serums) | | | | | |
|---|---|---|---|---|---|---|
| | HSV-1 positive / borderline | | HSV-2 positive / borderline | | negative | |
| | n | [%] | n | [%] | n | [%] |
| HSV-1-positive (n = 35) | 29 | 83 | 2* | 6 | 5 | 14 |
| HSV-2-positive (n = 22) | 14* | 64 | 22 | 100 | 0 | 0 |

**Table 9:** Examination of clinically defined samples using the reference immunoblot

| Culture or PCR (smear) | Reference immunoblot (IgG) (n = 58 serums) | | | | | |
|---|---|---|---|---|---|---|
| | HSV-1 positive / borderline | | HSV-2 positive / borderline | | negative | |
| | n | [%] | n | [%] | n | [%] |
| HSV-1-positive (n = 35) | 14 | 40 | 2* | 6 | 20 | 57 |
| HSV-2-positive (n = 22) | 13* | 59 | 20 | 91 | 2 | 9 |

* These are mainly samples with HSV-1- or HSV-2-positive smears, which returned a serological double-positive result (HSV-1 and HSV-2), which is why the addition of all immunoblot events exceeds the number of smears.

### 11.3 Analytical specificity

The analytical specificity is defined as the capacity of the test to precisely determine the analytes in the presence of potential interference factors in the sample matrix or cross-reactions with potentially interfering antibodies.

a) Interferences: Control studies on potentially interfering factors have shown that anticoagulants (CPD, sodium citrate, EDTA, heparin), haemolysis (up to 1,000 mg/dl haemoglobin), lipaemia, bilirubinaemia (up to 20 mg/dl bilirubin) or cycles of freezing and thawing do not affect the performance of the test.

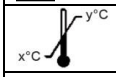
b) Cross-reactions: In control studies, the potential interferences of antibodies against other organisms (e.g. CMV, EBV, VZV) were examined. Also tested were conditions caused by atypical activity of the immune system (antinuclear autoimmune antibodies, rheumatoid factor, pregnancy, fresh herpes simplex infection). There was no evidence of any significant cross-reactions.

## 12 Literature

1. Whitley, RJ: Sect. 2. 68, Herpesviruses. In: Baron, S (Hrsg). Medical Microbiology. 4th ed., Galveston (TX): University of Texas Medical Branch; 1996.
2. Riley, LE: Herpes simplex virus. Semin Perinatol. 1998 Aug; 22(4):284-92.
3. Modrow S, Falke D, Truyen U: Molekulare Virologie. Eine Einführung für Biologen und Mediziner. Spektrum Akademischer Verlag; Auflage: 2. Aufl. (Dez. 2002), 19.5.7 Humanpathogene Herpesviren, Die Herpes-simplex-Viren, 583-587.
4. Koelle DM, Wald A: Herpes simplex virus: the importance of asymptomatic shedding. J Antimicrob Chemother. 2000 Apr; 45 Suppl T3: 1-8.
5. Hellenbrand W, Thierfelder W, Muller-Pebody B, Hamouda O, Breuer T: Seroprevalence of herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) in former East and West Germany, 1997-1998. Eur J Clin Microbiol Infect Dis. 2005 Feb; 24(2):131-5.
6. Ashley RL, Wald A: Genital Herpes: Review of the Epidemic and Potential Use of Type-Specific Serology. Clinical Microbiology Reviews, January 1999, p. 1-8, Vol. 12, No. 1.
7. Malkin JE: Epidemiology of genital herpes simplex virus infection in developed countries. Herpes. 2004 Apr; 11 Suppl 1: 2A-23A.
8. Enders, G: 4. Herpes simplex. In: Enders, G: Infektionen und Impfungen in der Schwangerschaft. 2nd. ed., Urban & Schwarzenberger, München 1991, 54-67.
9. Strick L, Wald, A: Type-specific testing für herpes simplex virus. Expert Rev. Diagn. 4(4), (2004).
10. Corey L, Simmons A: The Medical Importance of Genital Herpes Simplex Virus Infection. On behalf of the IHMF, 1998.
11. Strick LB, Wald A: Diagnostics for herpes simplex virus: is PCR the new gold standard? Mol Diagn Ther. 2006; 10(1): 17-28.
12. Mertens T, Haller, O, Klenk HD: Humanpathogene Viren. Herpes-simplex-Virus. In: Diagostik und Therapie von Viruserkrankungen. Leitlinien der Gesellschaft für Virologie. 2. Auflage, Elsevier, Urban & Fischer. 2003, S. 126-137.
13. Ashley RL: Sorting out the new HSV type specific antibody tests. Sex Transm Infect. 2001 Aug; 77(4): 232-7.
14. Gorander S, Svennerholm B, Liljeqvist JA: Secreted portion of glycoprotein g of herpes simplex virus type 2 is a novel antigen for type-discriminating serology. J Clin Microbiol. 2003 Aug; 41(8): 3681-6.
15. Liljeqvist JA, Svennerholm B, Bergstrom T: Typing of clinical herpes simplex virus type 1 and type 2 isolates with monoclonal antibodies. J Clin Microbiol. 1999 Aug; 37(8): 2717-8.
16. Ashley RL: Performance and use of HSV type-specific serology test kits. Herpes. 2002 Jul; 9(2):3 8-45.
17. Cherpes TL, Ashley RL, Meyn LA, Hillier SL: Longitudinal reliability of focus glycoprotein G-based type-specific enzyme immunoassays for detection of herpes simplex virus types 1 and 2 in women. J Clin Microbiol. 2003 Feb; 41(2): 671-4.

We will gladly send you further literature on the diagnosis of HSV on request.

## 13 Explanation of symbols

| | |
|---|---|
| Σ | Content is sufficient for <n> applications<br>Number of applications |
| WASHBUF A 10 X | Wash Buffer A (ten-fold concentration) |
| SUBS TMB | Tetramethylbenzidine chromogenic substance |
| MILKPOW | Skimmed milk powder |
| INSTRU | Instructions for use |
| EVALFORM | Evaluation form |
| TESTSTR | Test strips |
| CONJ IgG | Anti-human IgG conjugate |
|  | See instructions for use |
| CONT | Content, includes |
| IVD | In-vitro diagnostic device |
| LOT | Batch/version number |
|  | Do not freeze |
| REF | Order number |
|  | Use by<br>Expiry date |
|   | Store at x°C to y°C |
|  | Manufacturer |

## 14 Manufacturer and version information

| | | |
|---|---|---|
| ***recom*Line HSV-1 & HSV-2 IgG** | | Item no. **5372** |
| **Instructions for use**<br>valid from | | GARLHS005EN<br>2023-03 |
|  | **MIKROGEN** GmbH<br>Anna-Sigmund-Str. 10<br>82061 Neuried<br>Germany<br>Tel. +49 89 54801-0<br>Fax +49 89 54801-100<br>E-mail mikrogen@mikrogen.de<br>Internet www.mikrogen.de | |
| | | CE |

GARLHS005