OnSiteTM HSV-2 IgG/IgM Rapid Test

INTENDED USE

The OnSite HSV-2 IgG/IgM Rapid Test is a lateral flow chromatographic immunoassay for the qualitative detection and differentiation of IgG and IgM antibodies to herpes simplex virus 2 (HSV-2) in serum, plasma or whole blood. It is intended to be used by professionals as a screening test and provides a preliminary test result to aid in the diagnosis of infection with HSV-2.

Any use or interpretation of this preliminary test result must also rely on other clinical findings and the professional judgment of health care providers. Alternative test method(s) should be considered to confirm the test result obtained by this device.

SUMMARY AND EXPLANATION OF THE TEST

Herpes simplex viruses are two types of DNA viruses of the Herpesviridae family, herpes simplex virus-1 (HSV-1) and HSV-2. HSV-1 is generally acquired during childhood via non-sexual contact and affects mainly the orofacial area. HSV-2 is nearly always sexually transmitted and is the main cause of genital herpes. HSV-1 and HSV-2 can infect both genital and orofacial areas. Up to 50% of first-episode cases of genital herpes are caused by HSV-1, but recurrences are much less frequent for genital HSV-1 infection than genital HSV-2 infection8. HSV-2 subclinical viral shedding is less frequent for genital HSV-1 than genital HSV-2. Genital HSV infection has also been associated with increased risk for sexual transmission of HIV9,10. After primary infection, these viruses persist in a latent state for life1.

One of the biggest risks associated with HSV is neonatal transmission11. The majority of the transmissions occur in the pregnant woman with primary HSV infection. Eighty-five to ninety percent of neonatal transmission occurs at the time of delivery with only 5% of infections occurring intrauterine12. Clinical manifestations of neonatal infection with HSV range from local lesions of the skin, mouth, eye or central nervous system to severe, widespread dissemination involving visceral organs and potentially death8. Serology is an effective means of diagnosing HSV because the manifestation of symptoms is transient and the infection is often undiagnosed6. Anti-HSV IgM can be detected 9-10 days after exposure and last for 7-14 days, although it may remain detectable for up to 6 weeks6. Anti-HSV IgM is often associated with primary infection but may be detectable during recurrence of the disease6. Anti-HSV IgG can be detected 21-28 days post exposure and detectable titers typically remain for life6. Detection of anti-HSV IgM in the absence of anti-HSV IgG can be an effective tool in detecting early stages of HSV infection and as an indicator of potential primary infection.

HSV-1 and HSV-2 infections have different prognoses. Type-specific serological diagnosis is beneficial, which can be achieved by using glycoprotein G1 and glycoprotein G2 as recommended by the CDC7.

The OnSite HSV-2 IgG/IgM Rapid Test uses HSV-2 glycoprotein G2 for the specific detection and differentiation of IgG and IgM antibodies to HSV-2 in serum, plasma and whole blood. The test can be performed in 10 minutes by minimally skilled personnel without the use of laboratory equipment.

TEST PRINCIPLE

The OnSite HSV-2 IgG/IgM Rapid Test is a lateral flow chromatographic immunoassay. The test cassette consists of: 1) a burgundy colored conjugate pad containing HSV-2 type specific glycoprotein G2 antigens conjugated with colloidal gold (HSV-2 conjugates) and a control antibody conjugated with colloidal gold, 2) a microporous membrane strip containing two test lines (G and M lines) and a control line (C line). The G line is pre-coated with mouse anti-human IgG for detection of anti-HSV-2 IgG, the M line is pre-coated with mouse anti-human IgM for detection of anti-HSV-2 IgM, and the C line is pre-coated with a control line antibody.

When an adequate volume of test specimen and sample diluent are dispensed into the sample well, the specimen migrates by capillary action across the cassette. Anti-HSV-2 IgG, if present in the specimen, will bind to the HSV-2 conjugates. The immunocomplex is then captured on the membrane by the pre-coated mouse anti-human IgG forming a burgundy colored G line, indicating an HSV-2 IgG positive test result. Anti-HSV-2 IgM, if present in the specimen, will bind to the HSV-2 conjugates. The immunocomplex is then captured on the membrane by the pre-coated mouse anti-human IgM forming a burgundy colored M line, indicating an HSV-2 IgM positive test result.

Absence of any test lines (G or M) suggests a negative result. The test contains an internal control (C line) which should exhibit a burgundy colored line of the immunocomplexes of the control antibodies, regardless of color development on the test lines (G and M). If no control line (C line) develops, the test result is invalid and the specimen must be retested with another device.

REAGENTS AND MATERIALS PROVIDED
1. Individually sealed foil pouches containing:
   a. One cassette device
   b. One desiccant
2. 10 µL capillary tubes
3. Sample diluent (14-SB-R0213, 5 mL/bottle)
4. One package insert (instruction for use)

MATERIALS MAY BE REQUIRED AND NOT PROVIDED
1. Positive control
2. Negative control

MATERIALS REQUIRED BUT NOT PROVIDED
1. Clock or timer
2. Lancing device for whole blood testing

WARNINGS AND PRECAUTIONS
For in vitro Diagnostic Use
1. This package insert must be read completely before performing the test. Failure to follow the insert may lead to inaccurate test results.

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OnSite HSV-2 IgG/IgM Rapid Test - Cassette (Serum / Plasma / Whole Blood)

QUALITY CONTROL

1. **Internal Control**: This test contains a built-in control feature, the C line. The C line develops after adding the specimen and the sample diluent. If the C line does not develop, review the entire procedure and repeat the test with a new device.

2. **External Control**: Good Laboratory Practice recommends using external controls, positive and negative, to assure the proper performance of the assay, particularly under the following circumstances:
   a. A new operator uses the kit, prior to performing the testing of the specimens.
   b. A new lot of test kits is used.
   c. A new shipment of test kits is used.
   d. The temperature used during storage of the kits falls outside of 2-30°C.
   e. The temperature of the test area falls outside of 15-30°C.
   f. A new operator uses the kit, prior to performing the testing of the specimens.
   g. To verify a higher than expected frequency of positive or negative results.

   **INTERPRETATION OF ASSAY RESULT**

1. **NEGATIVE RESULT**: If only the C line develops, the test indicates that anti-HSV-2 antibodies are not detected in the specimen. The result is negative or non-reactive.

2. **POSITIVE RESULT**: In addition to the presence of the C line, if only the G line develops, the test result indicates the presence of anti-HSV-2 IgG; the result is HSV-2 IgG positive or reactive.

   **2.1** In addition to the presence of the C line, if only the G line develops, the test indicates the presence of anti-HSV-2 IgG. The result is H SV-2 IgG positive or reactive.

   **2.2** In addition to the presence of the C line, if only the M line develops, the test indicates the presence of anti-HSV-2 IgM. The result is HSV-2 IgM positive or reactive.

   **2.3** In addition to the presence of C line, if both the G and M lines develop, the test indicates the presence of anti-HSV-2 IgG and IgM. The result is HSV-2 IgG and HSV-2 IgM positive or reactive.

   **Positive interpretation according to the C line**

   **3. INVALID**: If no C line develops, the assay is invalid regardless of any color development on the test lines (G and M) as indicated below. Repeat the assay with a new device.

   **PERFORMANCE CHARACTERISTICS**

1. **Accuracy of IgG Detection**

   A total of 214 specimens were collected and tested with the OnSite HSV-2 IgG/IgM Rapid Test and by a commercial anti-HSV-2 IgG ELISA. Comparison for all subjects is shown in the following table:

<table>
<thead>
<tr>
<th>Reference</th>
<th>OnSite HSV-2 IgG/IgM Rapid Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>HSV-2 IgG</td>
<td>60</td>
</tr>
<tr>
<td>HSV-1 and HSV-2</td>
<td>10</td>
</tr>
<tr>
<td>HSV-2 IgM</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
</tr>
</tbody>
</table>

   Relative Sensitivity: 93.8%, Relative Specificity: 96.0%, Overall Agreement: 95.3%.

2. **Performance on BBI Anti-Herpes Mixed Titer Performance Panel**

   The performance of the OnSite HSV-2 IgG/IgM Rapid Test was evaluated using the BBI (Boston Biomedica Inc) Anti-Herpes Mixed Titer Performance Panel (P7H202). The results are shown in the following table:

<table>
<thead>
<tr>
<th>BBI Reference Panel</th>
<th>OnSite HSV-2 IgG/IgM Rapid Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-2 IgG Positive</td>
<td>Number of Numbers of Agreement</td>
</tr>
<tr>
<td>Only</td>
<td>7</td>
</tr>
<tr>
<td>HSV-1 and HSV-2 Positive</td>
<td>10</td>
</tr>
<tr>
<td>HSV-2 Positive</td>
<td>2</td>
</tr>
<tr>
<td>HSV-1 and HSV-2 Positive</td>
<td>4</td>
</tr>
<tr>
<td>HSV-2 Positive</td>
<td>4</td>
</tr>
<tr>
<td>HSV-1 and HSV-2 Positive</td>
<td>4</td>
</tr>
</tbody>
</table>

3. **Positive Rate on the Random Clinical Specimens**

   Ten thousand random, clinical specimens were tested with the OnSite HSV-2 IgG/IgM Rapid Test. The positive rate was 4.6% for anti-HSV-2 IgG and 1.7% for anti-HSV-2 IgM.

4. **Cross-Reactivity**

   No false positive anti-HSV-2 IgG and IgM results were observed on 3-10 specimens from the following disease states or special conditions, respectively:
   - CMV
   - HEV
   - Malaria
   - Syphilis
   - Dengue
   - HIV
   - Rubella
   - HIV
   - HCV
   - hCG
   - TB
   - ANA
   - HBV
   - H. pylori
   - HAMA
   - Typhoid
   - RF (up to 2.500 IU/mL)

5. **Interference**

   Common substances (such as pain and fever medication and blood components) may affect the performance of the OnSite HSV-2 IgG/IgM Rapid Test. This was studied by spiking these substances into negative, IgG positive and IgM positive specimens, respectively. The results demonstrate that at the concentrations tested, the substances studied do not affect the performance of the OnSite HSV-2 IgG/IgM Rapid Test.

   List of potentially interfering substances and concentrations tested:
   1. Albunin 60 µg/mL
   2. Bilirubin 20 mg/dL
   3. Creatinine 442 µmol/L
   4. EDTA 3.4 µmol/L
   5. Glucose 55 mmol/L
   6. Hemoglobin 2 g/L
   7. Heparin 3.000 U/L
   8. Saliicylic acid 4.24 mmol/L
   9. Sodium citrate 3.8%

   **EXPECTED VALUES**

   HSV-2 infects over 500 million people worldwide, with an estimated 23 million new infections annually. Seroprevalence ranges from 3.2% in some Chinese populations to over 80% in some areas of sub-Saharan Africa. Seroprevalence in women is up to twice as high as men, and increases with age. Most people are not aware of the infection, and infection is widespread even among people with low or moderate levels of sexual activity.

   **LIMITATIONS OF TEST**

   1. The assay procedure and the interpretation of assay result sections must be followed closely when testing for the presence of antibodies to HSV-2 in serum, plasma or whole blood from individual subjects. Failure to follow the procedure may lead to inaccurate results.

   2. The OnSite HSV-2 IgG/IgM Rapid Test is limited to the qualitative detection of antibodies to HSV-2 in human serum, plasma or whole blood. The intensity of the test line does not have linear correlation with the titer of anti-HSV-2 antibody in the specimen.

   3. A negative or non-reactive test result does not preclude the possibility of exposure to or infection with HSV-2. A negative or non-reactive result can occur if the titer of anti-HSV-2 antibody present in the specimen is below the level detectable by the assay or if anti-HSV-2 antibody was not present during the stage of disease in which the sample was collected.

   4. A negative result does not rule out an infection with HSV-2. Samples collected too early in the course of an infection may not have detectable levels of IgM.

   5. Infection may progress rapidly. If the symptom persists, while the result from OnSite HSV-2 IgG/IgM Rapid Test is negative or non-reactive, it is recommended to test with an alternative test method or to re-test the patient a few days later.

   6. The OnSite HSV-2 IgG/IgM Rapid Test has not been validated on specimens from neonates.

   7. Specimens from patients with infectious mononucleosis or high titers of heterophile antibodies, rheumatoid factor (>2.500 IU/mL) may affect expected results.

   8. Any use or interpretation of this preliminary test results must also rely on other clinical findings and the professional judgment of health care providers. Alternative test method(s) should be considered to confirm the test result obtained by this device.

   **REFERENCES**


   **Index of CE Symbols**

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Date of manufacture</th>
<th>Authorized Representative</th>
</tr>
</thead>
<tbody>
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<td>POWAY, CA 92064, USA</td>
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<td>E-mail: <a href="mailto:info@ctkbiotech.com">info@ctkbiotech.com</a></td>
<td>Tel: 858-457-8698</td>
<td></td>
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