**OnSite™ HSV-2 IgG/IgM Rapid Test**

**INTENDED USE**

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

**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 herpes simplex virus-2 (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 infection. HSV 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 HIV. After primary infection, these viruses persist in a latent state for the rest of the infected host.

One of the biggest risks associated with HSV is neonatal transmission. The majority of the transmissions occur in the pregnant woman with primary HSV infection. Eighty-five to ninety percent of neonatal transmissions occur during the period of labor and delivery. 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 fatal death.

Serology is an effective means of diagnosing HSV because the manifestation of symptoms is transient and the infection is often undiagnosed. IgM anti-HSV can be detected 9-10 days after exposure and last for 7-14 days, although it may remain detectable for up to 8 weeks. IgG anti-HSV is often associated with primary infection but may be detectable during recurrences of the disease. IgM anti-HSV can be detected 21-28 days post exposure and detectable titers typically remain for life. Detection of IgM anti-HIV in the absence of IgG anti-HIV 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 CDC.

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 antibodies conjugated with colloidal gold; 2) a nitrocellulose 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 IgG anti-HSV-2; the M line is pre-coated with mouse anti-human IgM for detection of IgM anti-HSV-2, 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. IgM and IgG antibodies, 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 control line (indicating HSV-2 IgM positive test result). IgM anti-HSV-2, if present in the specimen, will also 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 test line (indicating HSV-2 IgG 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 immunocomplex 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 sample must be repeated with another device.

**MATERIALS MAY BE REQUIRED AND NOT PROVIDED**

- Positive control
- Negative control

**MATERIALS REQUIRED BUT NOT PROVIDED**

- Click or timer
- 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.
2. Do not open the sealed pouch until ready to conduct the assay.
3. Do not use expired devices or components.
4. Bring all reagents to room temperature (15-30°C) before use.
5. Do not use components from any other test kit as a substitute for the components in this kit.
6. Do not use hemolyzed blood for testing.
7. Wear protective clothing and disposable gloves while handling the kit reagents and clinical specimens. Wash hands thoroughly after performing the test.
8. Users of this test should follow the US CDC Universal Precautions for prevention of transmission of HIV, HBV and other blood-borne pathogens.
9. Do not smoke, drink or eat in areas where specimens or kit reagents are being handled.
10. Inaccurate test results may be obtained if the test is performed on specimens that were not stored properly.
11. Handle the positive and negative controls in the same manner as patient specimens.
12. The test result should be read within 10 minutes after a specimen is applied to the sample well of the device. Reading the result after 15 minutes may give erroneous results.
13. Do not perform the test in a room with strong air flow, i.e. an electric fan or strong air conditioning.

**REAGENT PREPARATION AND STORAGE INSTRUCTIONS**

All reagents are readily used as supplied. Store unused test devices unopened at 2-30°C. Store reagents at room temperature (15-30°C) before use.

**SPECIMEN COLLECTION AND HANDLING**

Consider any materials of human origin as infectious and handle using standard bio-safety procedures.

**Plasma**

**Step 1:** Collect blood specimen into a lavender, blue or green top collection tube (containing EDTA, citrate or heparin, respectively, in Vacutainer®) by puncture.

**Step 2:** Separate the plasma from the clot.

**Step 3:** Carefully withdraw the plasma into a new pre-labeled tube.

**Serum**

**Step 1:** Collect blood specimen into a lavender, blue or green top collection tube (containing no anticoagulants in Vacutainer®) by puncture.

**Step 2:** Allow the blood to clot.

**Step 3:** Separate the serum by centrifugation.

**Step 4:** Carefully withdraw the serum into a new pre-labeled tube.

**Test specimens**

Test specimens should be collected directly into a smear, smear onto glass with a toothpick, in stool, or in cerebrospinal fluid. Prior to testing, bring frozen specimens to room temperature slowly and minimize exposure to contaminants that could interfere with chlorination before testing.

**Do not use specimens demonstrating gross lipemia, gross hemolysis or turbidity in order to avoid interference with result interpretation.**

**Whole blood**

Drops of whole blood can be obtained by either finger tip puncture or venipuncture. Collect blood into a lavender, blue or green top collection tube (containing EDTA, citrate or heparin, respectively, in Vacutainer®). Do not use hemolyzed blood for testing.

Whole blood specimens should be stored in refrigeration (2-8°C) if not tested immediately. The specimens must be tested within 24 hours of collection.

**ASSAY PROCEDURE**

1. **Step 1:** Bring the specimen and test components to room temperature if refrigerated or frozen. Once the specimen is thawed, mix well prior to performing the assay.

2. **Step 2:** When ready to test, open the pouch at the notch and remove the device. Place the test device on a clean, flat surface.

3. **Step 3:** Be sure to label the device with the specimen’s ID number.

4. **Step 4:** Fill the capillary tube with specimen or non-reducing formamide solution containing the specimen. Avoid frothing.

For better precision, transfer specimen using a pipette capable of delivering a 10 µL volume.

Holding the capillary tube vertically, dispense the specimen into the sample well of the device.

Immediately add 2 drops (about 60-80 µL) of Sample Diluent to the sample well with bottle positioned vertically.

**Result**

10 µL serum or plasma
2 drops of sample diluent

10 µL whole blood
2 drops of sample diluent

10 minutes

Result


2. Performance on BBI Anti-Herpes Midget Titer Performance Panel

The performance of the OnSite HSV-2 IgG/IgM Rapid Test was evaluated using the BBI(Boston Biomedica Inc) Anti-Herpes Midget Titer Performance Panel (PHIQ2). 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>IgG HSV-2 Positive Only</td>
<td>10/10</td>
</tr>
<tr>
<td>IgG HSV-1 Positive Only</td>
<td>10/10</td>
</tr>
<tr>
<td>IgG HSV-2 Positive</td>
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<td>3/3</td>
</tr>
<tr>
<td>IgM HSV-1 Positive</td>
<td>3/3</td>
</tr>
</tbody>
</table>

3. Positive Rate on the Random Clinical Specimens

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

4. Cross-Reactivity

No false positive IgG and IgM HSV-2 results were observed on 3-10 specimens from the following disease states or special conditions, respectively:

- CMV
- Dengue
- HAV
- HBV
- HCV
- HAV
- HCV
- HAV
- HCV
- Malaria
- Rubella
- TB
- Toxoplasma
- Typhoid
- Syphilis
- ANA
- HAMA
- 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 did not affect the performance of the OnSite HSV-2 IgG/IgM Rapid Test.

List of potentially interfering substances and concentrations tested:

1. Albumin: 60 g/L
2. Bilirubin: 20 mg/dL
3. Creatinine: 442 µmol/L
4. EDTA: 3.4 µmol/L
5. Glucose: 55 mmol/L

EXPECTED VALUES

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

LIMITATIONS OF TEST

1. The assay is procedure and 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 specimens failure to follow these guidelines 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 a linear correlation with the titer of 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 HSV-2 antibody present in the specimen is below the level detectable by the assay or if HSV-2 antibody was present during the stage of disease in which the sample was collected.
4. A negative result does not rule out a infection with HSV-2. Samples collected early in the course of infection may not have detectable levels of IgM.
5. A positive result is highly specific. If the symptom persists, the result from OnSite HSV-2 IgG/IgM Rapid Test is assumed to be positive. It is recommended to test with an alternative test method or 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 titer 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

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<thead>
<tr>
<th>REF</th>
<th>For in vitro diagnostic use only</th>
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</thead>
<tbody>
<tr>
<td>Lot Number</td>
<td>Authorized Representative</td>
</tr>
<tr>
<td>Store between 2-30°C</td>
<td>Date of manufacture</td>
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</table>

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