INTENDED USE

The StrongStep® HSV 1 and 2 antigen Rapid Test Device is a rapid visual immunobase for the qualitative presumptive detection of HSV 1 and 2 antigen in cutaneous specimens. This kit is intended to be used as an aid in the diagnosis of HSV infection.

INTRODUCTION

HSV is an envelop, DNA-containing virus morphologically similar to the other members of the genus Herpesviridae. Two antigenically distinct types are recognized, designated type 1 and type 2. HSV type 1 and 2 are frequently implicated in superficial infections of the oral cavity, the skin, the eye and the genitalia. Infections of the central nervous system (meningoencephalitis) and severe generalized infection in the neonate of immunocompromised patient are also seen, though more rarely. After the primary infection been resolved, the virus may exist in a latent form in nervous tissue, from where it may re-emerge, under certain conditions, to cause a recurrence of the symptoms.

The classical clinical presentation of genital herpes starts with widespread multiple painful macules and papules, which then mature into clusters of clear, fluid-filled vesicles and pustules. The vesicles rupture and form ulcers. Skin ulcers crust, whereas lesions on mucous membranes heal without crusting. In women, the ulcers occur at the introitus, labia, perineum, or perianal area. Men usually develop lesions on the penial shaft or glans. The patient usually develops tender inguinal adenopathy. Perianal infections are also common in MSM. Pharyngitis may develop with oral exposure. Serology studies suggest that 50 million people in the United States have genital HSV infection. In Europe, HSV-2 is found in 8-15% of the general population. In Africa, the prevalence rates are 40-50% in 20-year-olds. HSV is the leading cause of genital ulcers. HSV-2 infections at least doubles the risk of sexual acquisition of human immunodeficiency virus (HV) and also increases transmission.

Until recently, viral isolation in cell culture and determination of the type of HSV with fluorescent staining has been the mainstay of herpes testing in patients presenting with characteristic genital lesions. Besides PCR assay for HSV DNA has been shown to be more sensitive than viral culture and has a specificity that exceeds 99.9%. But these methods in clinical practice are currently limited, because the cost of the test and the requirement for experienced, trained technical staff to perform the testing restrict their use.

There are also commercially available blood tests used for detecting Type Specific HSV antibodies, but these serological testing cannot detect primary infection so they can be used only to rule out recurrent infections. This novel antigen test can differentiate other genital ulcer diseases with genital herpes, such as syphilis and chancroid, to help the early diagnosis and therapy of HSV infection.

PRINCIPLE

The HSV antigen Rapid Test Device has been designed to detect HSV antigen through visual interpretation of color development in the internal strip. The membrane was immobilized with anti HSV simplex virus monoclonal antibody on the test region. During the test, the specimen is allowed to react with colored monoclonal anti-HSV antibody colored particles conjugates, which were precoated on the sample pad of the test. The mixture then moves on the membrane by capillary action, and interacts with reagents on the membrane. If there were enough HSV antigens in specimens, a colored band will form at the test region of the membrane. Presence of this colored band indicates a positive result, while its absence indicates a negative result. Appearance of a colored band at the control region serves as a procedural control. This indicates that proper volume of specimen has been added and membrane wicking has occurred.

KIT COMPONENTS

20 Individually packed test devices

Each device contains a strip with colored conjugates and reactive reagents pre-coated at the corresponding regions.
4. Prepare swab specimens:
   • Place a clean extraction tube in the designated area of the workstation.
   • Add 15 drops of Extraction Buffer to the extraction tube.
   • Immerse the patients swab into the Extraction Tube and extract 2 minutes at room temperature. During extraction, use a circular motion to roll the swab against the side of the extraction tube so that the liquid is expressed from the swab and can reabsorb. Discard the swab following guidelines for handling infectious agents.
   • The specimens extracted can retain at room temperature for 60 minutes without affecting the result of the HSV test.

2. Remove the test from its sealed pouch, and place it on a clean, level surface. Label the device with patient or control identification. To obtain a best result, the assay should be performed within one hour.

3. Add 3 drops (approximately 100 µl) of extracted sample from the Extraction Tube to the sample well on the test cassette.

Avoid trapping air bubbles in the specimen well (S), and do not drop any solution in observation window.

As the test begins to work, you will see color move across the membrane.

4. Wait for the colored band(s) to appear. The result should be read at 15 minutes. Do not interpret the result after 20 minutes.

**INTERPRETATION OF RESULTS**

**POSITIVE RESULT:**

- Two colored bands appear on the membrane. One band appears in the control region (C) and another band appears in the test region (T).

**NEGATIVE RESULT:**

- Only one colored band appears in the control region (C). No apparent colored band appears in the test region (T).

**INVALID RESULT:**

- Control band fails to appear. Results from any test which has not produced a control band at the specified reading time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.

**NOTE:**

1. The intensity of the color in test region (T) may vary depending on the concentration of aimed substances present in the specimen. But the substances level can not be determined by this qualitative test.

2. Insufficient specimen volume, incorrect operation procedure, or performing expired tests are the most likely reasons for control band failure.

**QUALITY CONTROL**

- Internal procedural controls are included in the test. A colored band appearing in the control region (C) is considered as an internal positive procedural control. It confirms sufficient specimen volume and correct procedural technique.

- External procedural controls may provided(on request only) in the kits to ensure that the tests are functioning properly. Also, the Controls may be used to demonstrate proper performance by the test operator. To perform a positive or negative control test, complete the steps in the Test Procedure section treating the control swab in the same manner as a specimen swab.

**LIMITATIONS OF THE TEST**

1. The HSV antigen Rapid Test Device is for professional in vitro diagnostic use, and should be used for the qualitative detection of HSV only. There is no meaning attributed to line color intensity or width.

2. Detection of HSV antigen is dependent on the number of organisms present in the specimen. This may be affected by specimen collection methods and patient factors such as age, history of STD, presence of symptoms, etc.

3. The likelihood of detecting HSV decreases with time following the onset of disease and the development of lesions. The probability of viral isolation decreases as the lesion ulcerates, crusts and heals. Specimens should be collected as soon as possible after the appearance of lesions. It is reported that there is a 90% chance of obtaining a positive culture when the specimen is obtained from the base of a freshly unroofed vesicle or pustule, but that sensitivity decreases to 70% when the specimen is obtained from an existing herpes ulcer and drops to only 27% when a crusted lesion is used as a specimen source.

4. The tests have only been evaluated with cutaneous specimens and genital swabs, other specimen such as cerebrospinal fluids, eye swabs, urines, respiratory specimens do not have clinical data yet.

5. As with all diagnostic tests, a confirmed diagnosis should only be made by a physician after all clinical and laboratory findings have been evaluated.

**PERFORMANCE CHARACTERISTICS**

**Table: HSV antigen Rapid Test vs. PCR**

<table>
<thead>
<tr>
<th>Clinical Specimens</th>
<th>Relative Sensitivity</th>
<th>Relative Specificity</th>
<th>Overall Agreement</th>
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<tbody>
<tr>
<td></td>
<td>89.1% (77.7%-95.9%)*</td>
<td>95.9% (89.9%-98.9%)*</td>
<td>92.3% (88.3%-96.9%)*</td>
</tr>
</tbody>
</table>

*95% Confidence Interval: 55 98 153

The antibody used in the HSV test has been shown to detect all HSV serovars. Cross reactivity with other organisms has been studied using suspensions of 10^7 org/ml. The following organisms were not detected using the test:

- Achroplasma laidlawi
- Mycoplasma spp
- Actinobacteria spp
- Neisseria gonorrhoeae
- Aeromonas spp
- Peptococcus spp
- Bacteroides spp
- Peptostreptococcus spp
- Campylobacter jejuni
- Proteus spp
- Candida spp
- Pseudomonas spp
- Citrobacter freundii
- Salmonella spp
- Chlamydia trachomatis
- Serratia spp
- Clostridium spp
- Shigella spp
- Cyto megalovirus
- Staphylococcus aureus (cowan 1 strain)
- Enterobacter spp
- Staphylococcus spp (coag. neg)
- Epstein Barr Virus
- Staphylococcus spp (coag. pos)
- Escherichia coli
- Sphingomonas spp
- Gardnerella spp
- Treponema pallidum
- Haemophilus influenzae
- Ureaplasma urealyticum
- Klebsiella spp
- Varicella zoster virus
- Lactobacilli spp
- Vellonella spp
- Listeria spp

**LITERATURE REFERENCES**


**GLOSSARY OF SYMBOLS**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>REF</td>
<td>Temperature limit</td>
</tr>
<tr>
<td>LOT</td>
<td>Batch code</td>
</tr>
<tr>
<td>IDV</td>
<td>Use by</td>
</tr>
<tr>
<td>MAN</td>
<td>Contains sufficient for &lt;n&gt; tests</td>
</tr>
<tr>
<td>DNT</td>
<td>Authorized in the European Community</td>
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