Please read this package insert carefully before use.

Capilia™ Strep A

INTENDED USE

To detect group A beta-hemolytic streptococcal (GABHS) antigens in pharyngeal swab (to assist in the diagnosis of GABHS infection).

SUMMARY AND EXPLANATION

Group A beta-hemolytic streptococci are the principal bacteria causing pharyngitis and tonsillitis in children, and are transmitted from human to human by droplet infection.

If the infection persists for a long period of time, glomerulonephritis, rheumatic fever and other complications may occur. In addition, it has been reported that fulminant hemolytic streptococcal infection leads to a fatal outcome within a short time.

It has also been reported that oral antibiotic therapy with penicillin can reduce fever promptly and render the bacteria almost non-infectious within 24 hours after medication.

Considering GABHS are highly contagious, rapid diagnosis and prompt treatment of these infections can have a positive effect on public health.

However, the rapid diagnosis of these infections is difficult because the initial symptoms can be similar to those caused by other infectious agents.

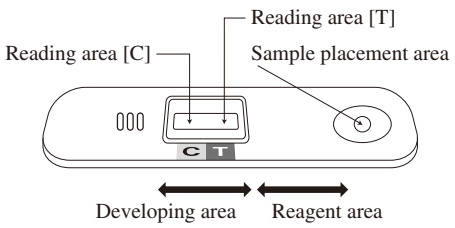
Capilia Strep A can provide rapid and accurate detection of antigens of GABHS (*Streptococcus pyogenes*) from symptomatic patients. No special techniques or instruments are required.

PRINCIPLE OF THE TEST

Measurement using this product is based on an immunochromatography assay using a polyclonal antibody that recognizes GABHS antigens.

This product comprises a test plate with a carrier strip containing a sample placement area, a reagent area including a colloidal platinum-gold labeled anti-GABHS polyclonal antibody (rabbit) (hereinafter referred to as "colloidal platinum-gold labeled antibody"), and a reading area [T] that fixes the anti-GABHS polyclonal antibody (rabbit) (hereinafter referred to as "anti-GABHS antibody"), and a reading area [C] that fixes an anti-rabbit immunoglobulin antibody.

Names of each area of the test plate



When a sample is placed on the sample placement area of the test plate, the colloidal platinum-gold labeled antibody dissolves and forms an immune complex with GABHS antigens in the sample. This immune complex migrates through the developing area by capillary action, is captured by the anti-GABHS antibody fixed in the reading area [T], and forms a black line of colloidal platinum-gold in the reading area [T]. The black line visually displays the existence of GABHS antigen in the sample.

Regardless of the existence of GABHS antigens in the sample, excess colloidal platinum-gold labeled antibodies further migrate through the developing area, are captured by anti-rabbit immunoglobulin antibodies fixed in the reading area [C], and form a black line in the reading area [C]. This means the colloidal platinum-gold labeled antibodies have migrated normally.

REAGENTS AND MATERIALS PROVIDED

REF CAST1170 Capilia Strep A (20 Tests)

Test plates

・Components

Colloidal platinum-gold labeled anti-GABHS polyclonal antibody (rabbit)
Anti-GABHS polyclonal antibody (rabbit)

Reagent 1 (sodium nitrite solution)

Reagent 2 (acetic acid solution)

Nozzles

MATERIALS REQUIRED BUT NOT PROVIDED

Timer,sterile swab (as listed here)

Recommended Swab

The following swabs are recommended for use with the kit.

For Pharyngeal Swab

①FLOQSwabs ™ (Cat No. 502CS01, Copan Italia S.p.A, Italy)

②Sterilized Swab PL6S 10 pcs (Cat No. 4371, HEIWA MEDIC. CO., LTD, Japan)

Acceptable Swab

The following swabs are acceptable for use with the kit.

・Tip material
Rayon, flocked nylon and polyester

・Standard tip size
Plain dry swab: maximum diameter 6 mm, length 14 mm
Flocked swab: maximum diameter 6 mm, length 16 mm

・Shaft material
Paper, plastic (PS, nylon), aluminum

Unacceptable Swab

Do not use calcium alginate swabs.

WARNING AND PRECAUTIONS

1. Precautions when handling (including hazard control)

1) Handle all the specimens as if they contain infectious agents.
2) In consideration of the risk of infection, wear protective clothes such as a mask and gloves and handle the specimens and samples carefully during the test.
3) Reagent 1 contains sodium nitrite and Reagent 2 contains acetic acid. If these reagents get into your eyes, or come into contact with your hands or clothes, immediately flush with a large quantity of water. If you still feel some abnormality, see a doctor for treatment.

2. Precautions when using

1) This product is a rapid test for detecting GABHS antigens.
A definite diagnosis should be made by an attending physician, in combination with the clinical symptoms, the result of bacterial isolation culture test and other test results.
2) This product should be used in accordance with the test procedure stated in the package insert.
3) In order to prevent deterioration, this product should be stored between 2°C and 30°C, avoiding high temperatures, high humidity and direct sunlight.
4) If this product has been refrigerated, it must be removed from the refrigerator at least 30 minutes before use to be acclimatized to room temperature.
5) **The aluminum pouch containing a test plate should not be opened until the test plate is about to be used.**
6) The sample placement area and the reading area of the test plate should not be touched with the hands.
7) Do not use a swab if it is broken, bent partially whitened, or stained.
8) Avoid the following when using the swab since they may cause the breakage of the shaft. (Please read the package insert of the swab.)
・To use the swab in a manner such that the shaft (especially the narrow part of the shaft) receives too much force, pressure or torsional load at the time of specimen collection.
・To intentionally deform the shaft, more specifically, to bend, arch or break the shaft.
9) Particularly at the time of specimen collection from a child, firmly retain the upper body of the child to be tested lest he or she should act up, bite or break the swab and swallow the broken part, and collect the specimen with great caution.
10) Do not use any products beyond the expiration date.
11) Do not use enclosed reagents for any purpose other than intended with this kit. Do not mix any enclosed reagents with other samples, other extracts of specimens, etc.
12) **The mixed solution (extraction reagent) of Reagents 1 and 2 cannot be preserved. It should be used immediately after mixed.**
13) All specimens should be handled as potentially infectious, and special precautions should be exercised.

3. Precautions for disposal

1) Reagent 1 of this product contains sodium nitrite. When sodium nitrite is mixed with ammonium salts or cyanides, an explosion may occur. Therefore, it should be discarded with a large quantity of water.
2) Because used test plates, swabs and nozzles, containers containing samples, remaining samples, etc. may cause infections, they should be autoclaved (121°C, 20 min) or soaked in 2% glutaraldehyde for more than one hour. When reagents or their accessories are disposed of, they should be treated in accordance with the laws and regulations concerning medical waste disposal and water pollution control.
3) When remaining samples used in the test are disposed of, do not use sodium hypochlorite. **The use of sodium hypochlorite may cause the generation of chlorine gas.**
4) If you spill the specimen, wipe it and disinfect the area with an alcohol spray, etc.

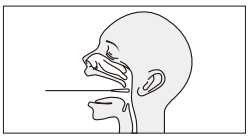
STORAGE CONDITIONS

Storage : Store at 2 to 30°C. **DO NOT FREEZE.**
Keep away from direct sunlight.
Do not use test plate or reagent 1, reagent 2 after expiration date.

SPECIMEN COLLECTION AND PREPARATION

1. Methods of specimen collection

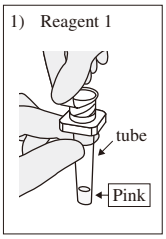
Use pharyngeal swabs as specimens. At the collection of specimens.



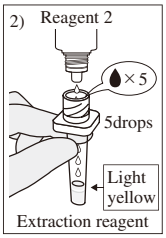
Firmly insert the pharyngeal swab into the pharynx through the oral cavity, and collect the mucosal epithelium by swabbing the posterior wall of the pharynx and the palatine tonsil several times, centering around the rubefacient portion. Avoid touching the inside of the mouth (e.g., the tongue, gum, inside of cheeks, and saliva), except for the pharynx, with the tip of the swab.

With a collected specimen, prepare the sample according to the procedure specified in the following "Sample preparation" section and perform the test as quickly as possible.

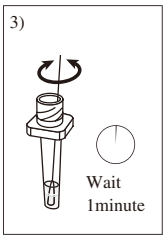
2. Sample preparation



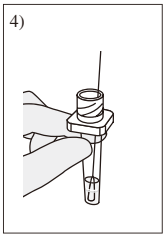
1) Remove the aluminum sealing cap from the tube of Reagent 1 (sodium nitrite solution), while taking care not to spill the liquid.
Color of reagent: Pink



2) Remove the cap from the bottle of Reagent 2 (acetic acid solution), and hold the bottle perpendicularly with the tip down. **Add 5 drops of Reagent 2 to Reagent 1**, and use this as the extraction reagent.
Color of reagent: Changed to light yellow

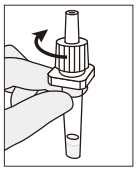


3) Soak the swab that collected the specimen in the extraction reagent, stir well, and **allow to stand for 1 minute**.
Note: An inadequate standing time may result in the inadequate extraction of antigens into the extraction reagent, which may lead to a false result.



4) Then, pinch the tip of the swab firmly with the soft wall of the tube of the extraction reagent with your fingers and squeeze out the swab. Use this squeezed-out liquid as the sample.

TEST PROCEDURE



1) Firmly attach the nozzle (with a filter) provided in the kit to the top of the tube containing the prepared sample.
2) Hold the middle of the tube containing the prepared sample with the fingers and dispense **3 drops of the sample (80 to 120 µL)** onto the sample placement area of the test plate. Hold the tube perpendicularly and take care not to let the tip of the nozzle touch the sample placement area.
3) Observe the reading area of the test plate after **5 minutes** and interpret the result according to the "READING TEST RESULTS".

READING TEST RESULTS

Allow the samples to react according to the test procedure and read the black lines that appear in the reading area.

Positive

When black lines are seen at both [T] and [C] in the reading area (two lines), the result is read as positive.
When a very faint black line is seen in the reading area [T], the result is interpreted as positive.

Negative

When no black line is seen at [T] in the reading area but a line is seen only at [C] in the reading area (one line), the result is read as negative.
When the black line at [C] in the reading area is faint but visually recognizable, chromatographic development has occurred normally.

Retesting

When no line is seen at [C] in the reading area, there may be some problem with the test procedure or the reagent quality. The test should be performed again, using another test plate.

A line that appears anywhere within the section of the reading area, which are separated by color, is considered valid.

(Note)

1. Black lines seen both at [T] and [C] in the reading area 5 minutes after sample dripping are read as positive. No black line at [T] in the reading area even 5 minutes after sample dripping indicates a negative result.
2. Do not use the test plate for a reading result beyond the judgment time as the result may change due to drying, etc.
3. A black line may not appear at [C] in the reading area due to problems with the test procedure or the reagent quality. In this case, the test should be performed again, using another test plate.
4. If the amount of antigen is very high, a very thick line may be seen at [T] in the reading area and no line may be seen at [C] in the reading area. In that case, dilute the sample with more extraction reagent (5 drops of Reagent 2 are added to one bottle of Reagent 1) and perform the test again.
   Example) Method for dilution of sample: Dispense 3 drops of the sample to the newly prepared extraction reagent, mix thoroughly, and use the solution as the test sample.
5. The line is valid even if there is unevenness in depth and there are breaks in the line.

LIMITATIONS

1. This product is a rapid test for detecting antigens of group A beta-hemolytic streptococci (GABHS) (*Streptococcus pyogenes*). A definite diagnosis should be made by an attending physician, in combination with the clinical symptoms and other test results.
2. The test plate should be used immediately after opening the packaging. When it absorbs moisture, the quality deteriorates and an accurate result cannot be obtained.
3. This product should be used for *in vitro* diagnosis only and should not be used for any other purposes.
4. Please use this product following the test procedure and precautions described in this package insert. We cannot guarantee results obtained from any other operations and for any other purposes that are not described in the package insert.

PERFORMANCE CHARACTERISTICS

1. Correlation data

1) Correlation with the bacterial isolation culture method

		Culture method		
		Positive	Negative	Total
This product	Positive	67	0	67
	Negative	5	69	74
	Total	72	69	141

Sensitivity: 93.1% (67/72)
Specificity: 100% (69/69)
Accuracy: 96.5% (136/141)

2) The result of the clinical performance evaluation in Japan (Comparison with control products (Rapid Test))

		Control product A		
		Positive	Negative	Total
This product	Positive	66	1[Note1]	67
	Negative	0	74	74
	Total	66	75	141

Sensitivity: 100% (66/66)
Specificity: 98.7% (74/75)
Accuracy: 99.3% (140/141)

Note 1: Positive when tested by either the culture method or the PCR method.

		Control product B		
		Positive	Negative	Total
This product	Positive	66	1[Note2]	67
	Negative	4[Note3]	70	74
	Total	70	71	141

Sensitivity: 94.3% (64/70)
Specificity: 98.6% (70/71)
Accuracy: 96.5% (136/141)

Note 2: Positive when tested by either the culture method or the PCR method.
Note 3: All 4 specimens are negative when tested by either the culture method or the PCR method.

2. Detection limit

The minimum detection limit of this product is 3.9×10^3 cfu/test.

3. Cross-reactivity

No cross-reactivity was found for any of the following bacteria and fungi and viruses listed below:

1) Bacteria and fungi
- *Acinetobacter baumannii*
- *Aspergillus niger*
- *Bordetella pertussis*
- *Burkholderia cepacia*
- *Candida albicans*
- *Enterococcus faecalis*
- *Enterococcus galliarum*
- *Escherichia coli*
- *Haemophilus aphrophilus*
- *Haemophilus parainfluenzae*
- *Haemophilus paraphorphilus*
- *Kingella kingae*
- *Legionella anisa*
- *Legionella bozemanii*
- *Legionella dumoffii*
- *Legionella gormanii*
- *Legionella jordanis*
- *Legionella longbeachae*
- *Legionella micdadei*
- *Legionella pneumophila* SG-1
- *Legionella pneumophila* SG-2
- *Legionella pneumophila* SG-3
- *Legionella pneumophila* SG-4
- *Legionella pneumophila* SG-5
- *Legionella pneumophila* SG-6
- *Legionella pneumophila* SG-7
- *Legionella pneumophila* SG-8
- *Legionella pneumophila* SG-9
- *Legionella pneumophila* SG-10
- *Legionella pneumophila* SG-11
- *Legionella pneumophila* SG-12
- *Legionella pneumophila* SG-13
- *Legionella pneumophila* SG-14
- *Legionella pneumophila* SG-15
- *Listeria monocytogenes*
- *Moraxella catarrhalis*
- *Mycobacterium fortuitum*
- *Mycobacterium kansasii*
- *Mycobacterium marinum*
- *Proteus mirabilis*
- *Proteus vulgaris*
- *Pseudomonas aeruginosa*
- *Serratia marcescens*
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Streptococcus mitis*
- *Streptococcus mutans*
- *Streptococcus* sp. Group B
- *Streptococcus* sp. Group C
- *Streptococcus* sp. Group F
- *Streptococcus* sp. Group G
- *Streptococcus salivarius*
- *Streptococcus pneumoniae* Type 1
- *Streptococcus pneumoniae* Type 3
- *Streptococcus pneumoniae* Type 5

2) Viruses
- Influenza virus A (H1N1)
- Influenza virus A (H3N2)
- Influenza virus B
- Adenovirus Type 1
- Adenovirus Type 2
- Adenovirus Type 3
- Adenovirus Type 4
- Adenovirus Type 6
- Adenovirus Type 11
- Adenovirus Type 19
- Adenovirus Type 37

Cross reactivity was found with some bacterial strains of *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE), which is an oral bacterium and has group A streptococcal polysaccharide antigens present in *Streptococcus pyogenes*.

INTERFERING SUBSTANCES

The following substances were found to have no effect on the results at the concentrations indicated.

Whole blood (0.10%), acetylsalicylic acid (20mg/mL), ambroxol hydrochloride (375ng/mL), dequalinium hydrochloride (6.25ng/mL), oxymetazoline hydrochloride (100ng/mL), powdered Platycodon root (555ng/mL), disodium cromoglycate (5mg/mL), zanamivir (500ng/mL), diphenhydramine hydrochloride (10mg/mL), cyproheptadine hydrochloride hydrate (200ng/mL), cefixime (0.5mg/mL), dextromethorphan hydrobromide monohydrate (10mg/mL), naphazoline nitrate (125ng/mL), (R)-(-)-phenylephrine hydrochloride (1mg/mL), fluticasone propionate (127.5ng/mL), and chlorpheniramine maleate (5mg/mL).

REFERENCES

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3) Liu D: Rapid identification of *Streptococcus pyogenes* with PCR primers from a putative transcriptional regulator gene. *Res Microbiol*, 156(4), 564-567, 2005.
4) McMillan DJ. Molecular markers for discriminating *Streptococcus pyogenes* and *S. dysgalactiae* subspecies *equisimilis. Eur J Clin Microbiol Infect Dis*, 29(5), 585-589, 2010.
5) Karasawa T (Central Clinical Laboratory, Tokyo Women's Medical University Hospital). Groups A and B hemolytic streptococci. *Clin Microbiol*, 34 (suppl), 499-502, 2007.

INQUIRES

TAUNS Laboratories, Inc.
761-1, Kamishima, Izunokuni,
Shizuoka, 410-2325 Japan

FAX : +81-558-76-0022

EC REP Emergo Europe
Prinsessegracht 20
2514 AP The Hague
The Netherlands

GLOSSARY OF SYMBOLS

CE	CE Marking (European directive 98/79/EC on *in vitro* diagnostic medical devices)	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device		Do not reuse
2℃ 30℃	Temperature limitation		Manufacturer/Manufactured by
	Use by YYYY-MM		Consult instructions for use
LOT	Batch code		Caution, consult accompanying documents
REF	Catalog number		Keep away from sunlight
Σ n	Contents sufficient for <n> tests		Fragile, handle with care
	Open here		