Read this Instructions for Use carefully before testing.

For in vitro diagnostic use only

MIZUHO MEDY Co., Ltd.

Streptococcus pneumoniae antigen kit,
Legionella pneumophila antigen kit

Quick Chaser Streptococcus pneumoniae /Legionella

[Package]

70060: Quick Chaser Streptococcus pneumoniae/Legionella - 10 tests/kit

[Contents]

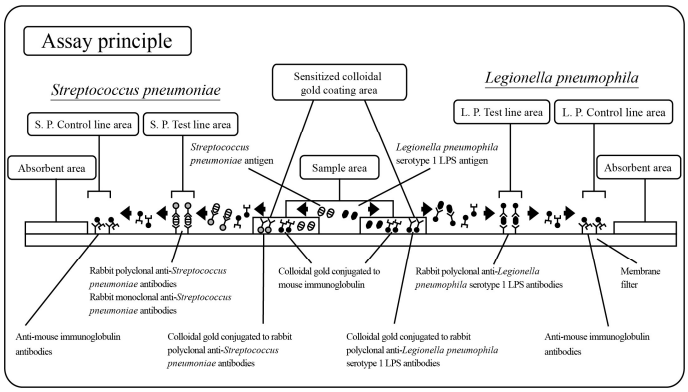
1) Test plate - 10 tests
   - Rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies
   - Rabbit monoclonal anti-*Streptococcus pneumoniae* antibodies
   - Rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS antibodies
   - Colloidal gold conjugated to rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies
   - Colloidal gold conjugated to rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS antibodies
2) Dropper - 10 pieces

[Intended use]

For qualitative detection of *Streptococcus pneumoniae* antigen in urine or cerebrospinal fluid (CSF)
(An aid in the diagnosis of *streptococcus pneumoniae* infection)
For qualitative detection of *Legionella pneumophila* serogroup 1LPS antigen in urine
(An aid in the diagnosis of legionellosis infection)

[Principle of the test]

"Quick Chaser Streptococcus Pneumoniae/Legionella" is the in vitro diagnostic reagent for qualitative detection of *Streptococcus pneumoniae* antigen and *Legionella pneumophila* serogroup 1LPS based on the immunochromatographic assay.
Colloidal gold conjugated to rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies or colloidal gold conjugated to rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS and colloidal gold conjugated to mouse immunoglobulins for control line are coated in sensitized colloidal gold coating area on a membrane filter which is set in test plate. Also, rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies and rabbit monoclonal anti-*Streptococcus pneumoniae* antibodies are immobilized in S. P. test line area and rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS antibodies are immobilized in L. P. test line area. Anti-mouse immunoglobulin antibodies for control line are immobilized in each control line area.
If *Streptococcus pneumoniae* antigens or *Legionella pneumophila* serogroup 1LPS antigens are present in the sample, according to the principle of immunochromatography, *Streptococcus pneumoniae* antibodies react with colloidal gold conjugated to rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies, *Legionella pneumophila* serogroup 1LPS antibodies react with colloidal gold conjugated to rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS antibodies as they migrate from the sample area. Moreover, they are captured in each test line area by reacting respectively with rabbit polyclonal anti-*Streptococcus pneumoniae* antibodies and rabbit monoclonal anti-*Streptococcus pneumoniae* antibodies, or rabbit polyclonal anti-*Legionella pneumophila* serogroup 1LPS antibodies. As a result, a purple-red line with the colloidal gold appears in each test line area.
At the same time, the colloidal gold conjugated to mouse immunoglobulin also migrate and are captured by the anti-mouse monoclonal immunoglobulin antibodies on each control line area, resulting in the appearance of a purple-red line in the control line area regardless of the presence or absence of *Streptococcus pneumoniae* antigens or *Legionella pneumophila* serogroup 1LPS antigens.



[Warnings and Precautions]

1) For in vitro diagnostic use only.
2) Procedures not described in the Instructions for Use are not guaranteed.
3) This product can be interpreted both visually and with the dedicated device "Smart QC Reader". When interpreting with the dedicated device, use it according to the Instruction for Use and User Manual of the dedicated device.
4) Dropper included in this kit is not sterilized. When performing the culture test, please separate specimens in advance to avoid the contamination of specimens.
5) Add the specified volume (about 130 µl) of specimen to the center of the sample area. If the sample volume is not as specified, the reaction may not be accurate.
6) Bring test plate to 15 to 30°C prior to testing.
7) Strictly follow the interpretation time to avoid false-negative and false-positive.
8) Specimen may contain not only *Streptococcus pneumoniae* and *Legionella pneumophila* but also other infectious materials. Handle specimen with great care as there is a risk of infection during the test.
9) When using, wear protective equipment (glasses, disposable gloves, mask, etc.) and be careful not to let the sample (specimen) directly adhere to the skin or get into your eyes.
10) If a specimen accidentally gets into your eyes or mouth, take first-aid measures such as rinsing it thoroughly with water, and seek medical attention if necessary.
11) The material of the membrane used for the test plate is nitrocellulose. Do not perform tests near a fire as nitrocellulose is extremely flammable.
12) If the sample (specimen) spatters, wipe it off with alcohol for disinfection, etc.
13) Do not freeze this product. Store it in accordance with the description of storage. Do not use frozen reagents as they may change the quality and may not give correct results.
14) Do not use this product beyond the expiration date.
15) Use the test plate immediately after opening the aluminum foil pouch. If the test plate is left in a room for a long period of time, it could not react by exposure to moisture.
16) Do not touch sample area, test line area, and control line area by hand directly.
17) Do not perform the test in a place such as under an air conditioner where the dry wind directly blows the surface of the test plate to prevent uneven migration.
18) Do not use the reagents, accessories, etc. of this product for any purpose other than this test.
19) Test plates and droppers are intended for single use only.
20) Handle liquid waste and used utensils by any of the following disinfection and sterilization methods as sample (specimen) may contain infectious material such as HIV, HBV, and HCV, etc.
    a) Immerse in sodium hypochlorite solution (effective chlorine concentration of 1,000 ppm) for 1 hour or longer
    b) Immerse in 2% glutaraldehyde solution for 1 hour or longer
    c) Autoclave at 121°C for 20 minutes or longer
21) Regarding disposal of used reagents and utensils, dispose of them in accordance with the Local Regulation and Law of waste disposal.

[Storage and stability of the device]

Store kit at 1 to 30°C, out of direct sunlight or high humidity. Kit contents are stable until the expiration dates printed on the product box and packaging. Do not freeze.

[Specimen collection and handling]

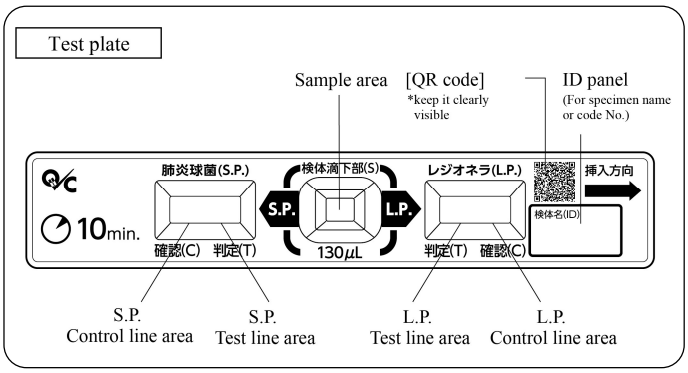
1. Urine
   Collect urine specimen in an aseptic container.
2. CSF
   Collect CSF specimen in an aseptic container according to standard procedures.

Collected urine specimen and CSF specimen should be tested as soon as possible. If the specimen cannot be tested immediately or needs to be stored for a long period of time, a test should be performed within 3 days if stored at 5 to 30℃ or within 14 days if stored at -80 to 4℃. Do not repeat freezing and thawing of the specimen three times or more. Specimen should be brought to 15 to 30℃ prior to use.

[Test procedure]

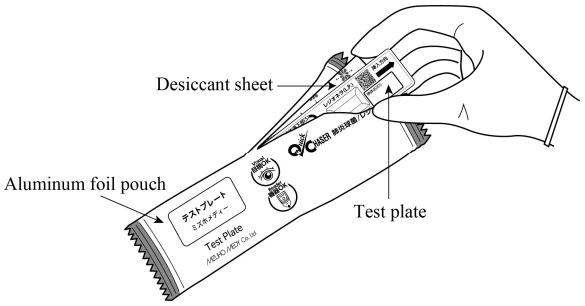
This product can be interpreted both visually and with a dedicated device.

· Details of test plate

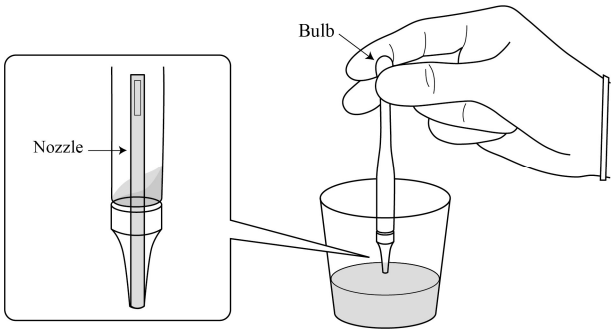


· Test procedure

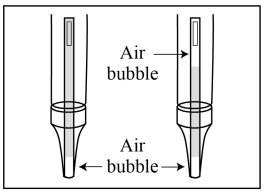
1) Preparation of reagent
   Test plate: No prior preparation required.
2) Test procedure
   1. Remove the test plate from the aluminum foil pouch. Discard the desiccant sheet included in the aluminum foil pouch.
      (Note) Please be careful not to stain the QR code when writing the sample name in the ID panel.



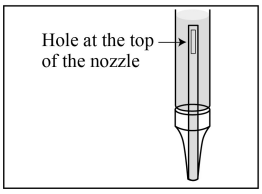
2. Squeeze the bulb of the dropper included in the kit and draw up a sufficient amount of specimen to fill the nozzle in one suction with the tip of the dropper completely immersed in the specimen. The excess specimen drawn up would overflow inside the dropper from the nozzle part and remains in the dropper.



Note) In the cases as shown below, the correct amount of the specimen cannot be dropped.

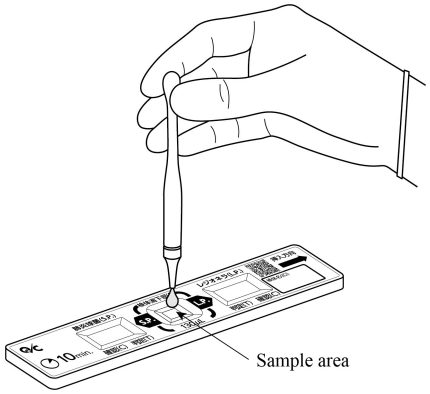


If air bubbles enter into the nozzle, discharge the specimen and fill the nozzle again.



Do not draw up the specimen repeatedly until the specimen overflowing from the nozzle exceeds the hole at the top of the nozzle. If the specimen exceeds the hole at the top of the nozzle, collect the specimen with a new dropper.

3. Drop the specimen on the sample area of the test plate by squeezing the bulb of the dropper. The required amount (about 130 μL) of the specimen is discharged.



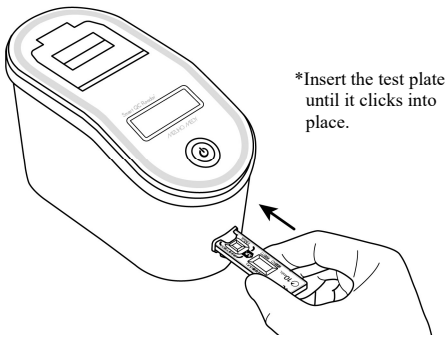
<When interpreting visually>

4.-1 Leave to react at 15 to 30°C.
   Interpret test results visually by reading lines in the test line area and control line area after 5 to 10 minutes.

<When interpreting with the dedicated device>

4.-2 A method of reading and interpreting the lines that appear in the test line area and control line area with the dedicated device.
After checking the insertion direction of the test plate, measure according to the operation method of "Mode 1" or "Mode 2".

Note) • Do not attach labels etc. on the test plate.
• Be careful not to touch the sample area when inserting the test plate.
• Insert the test plate by keeping it horizontal to prevent the sample from spilling or splashing into the instrument.
• Insert the test plate all the way.



*Insert the test plate until it clicks into place.

1) Mode 1 [Read Now]
This mode interprets the test plate after the reaction time has elapsed.
1. Leave to react at 15 to 30°C.
2. After 10 minutes, insert the test plate into the test plate insertion slot of the dedicated device.
3. The lines appearing in the test line area and control line area are read inside the dedicated device.

2) Mode 2 [Walk Away]
This mode automatically interprets the test plate after dropping the sample inside the dedicated device.
1. Immediately after dropping the sample, insert the test plate into the test plate insertion slot of the dedicated device.
2. The measurement starts automatically, and the lines appearing in the test line area and control line area are read every minute after 5 minutes inside the dedicated device.

[Interpretation]

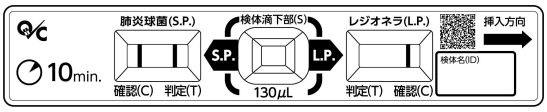
<When interpreting visually>

Interpretation by the existence of red-purple lines in the test line area and control line area.

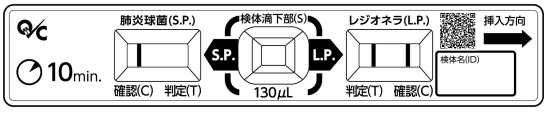
<Positive>

Both test line and control line appear.

S.P. Positive
L.P. Negative



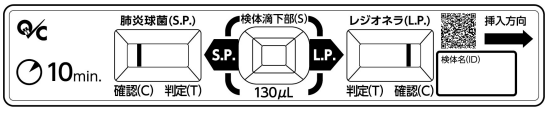
S.P. Negative
L.P. Positive



<Negative>

Only control lines appear.

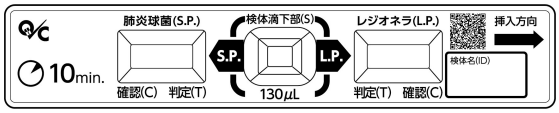
S.P. Negative
L.P. Negative



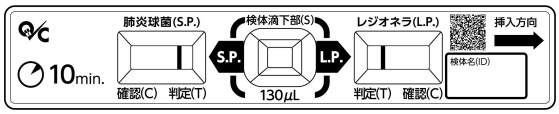
<Retest>

If both test line and control line do not appear or no control line appears, an operational error such as insufficient sample volume may be considered. Recheck test procedure and retest with the new test plate. If the same result comes out in the retest again, confirm it with other methods.

Retest



Retest



<When interpreting with the dedicated device>

Both Mode 1 [Read Now] and Mode 2 [Walk Away] are automatically interpreted according to the interpretation method of < When interpreting visually> based on the result of reading the lines with the dedicated device. Interpretation and display on the device screen are the same in Mode 1 [Read Now] and Mode 2 [Walk Away].

Interpretation	Display on the device screen
S.P Positive L.P Negative	S.P : ＋ L.P : －
S.P Negative L.P Positive	S.P : － L.P : ＋
S.P Negative L.P Negative	S.P : － L.P : －
Retest	S.P : ＊ #03 L.P : ＊ #03

*Error code #03: Error when the control line is not detected.
*For error codes other than error code #03, refer to the User Manual of the dedicated device.

[Limitations]

1) Diagnosis of *Streptococcus pneumoniae* infection and legionellosis should not be based solely on the test results of this product but should be comprehensively made in consideration of other test results and clinical symptoms.
2) CSF should be used only for the detection of *Streptococcus pneumoniae*, not for *Legionella pneumophila*.
3) Use urine or CSF as a specimen. Do not use serum, sputum, or oropharyngeal swab, etc.
4) Do not use the turbid specimen containing pus or blood, etc.
5) When *Streptococcus pneumoniae* vaccine is inoculated, vaccine-derived antigens excrete in urine for a few days, possibly resulting in positive result.
6) In the case *Streptococcus pneumoniae* test line or *Legionella pneumophila* test line, and each control line appear at 5 to 10 minutes after dropping the sample, it can be interpreted as *Streptococcus pneumoniae* positive or *Legionella pneumophila* positive. Negative should be interpreted at 10 minutes after dropping the sample. The streak line might appear before 10 minutes temporarily. Do not interpret the temporal streak line as the appearance of the test line. After 10 minutes, colloidal gold can appear like a line due to the drying of the test plate with time. Therefore, please interpret test results at 10 minutes.
7) This product is used as an aid in the diagnosis for *Streptococcus pneumoniae* infection and legionellosis. In case *Streptococcus pneumoniae* antigens or *Legionella pneumophila* serotype 1LPS antigen amount in the specimen are below the detection limit of the test, test result could be interpreted as negative, even though the patient is infected by *Streptococcus pneumoniae* or *Legionella pneumophila*. In addition, a non-specific reaction may occur depending on the factors in the sample and a negative specimen may be interpreted as positive. The final definitive diagnosis should be made comprehensively from clinical symptoms and other test results.
8) *Streptococcus mitis* and *Streptococcus pseudopneumoniae* have a common antigen with *Streptococcus pneumoniae*, hence false positive result may be obtained.
9) Regarding infants and toddlers, if *Streptococcus pneumoniae* habitually resides in the nasopharynx, *Streptococcus pneumoniae* antigens excrete in urine and possibly resulting in positive result.

10) It is said that the quantity of the urinary *Streptococcus pneumoniae* antigen and *Legionella pneumophila* antigen reaches and exceeds the detectable amount after 3 days from an appearance of a pneumonia symptom, but it varies from case to case. In addition, the antigen may be excreted in urine from a few days to several weeks after the infection. When interpreting the results, consider the past medical history and clinical symptoms carefully and do not use it to determine the treatment effect.

11) This product uses rabbit antibody as a raw material. Please note that patients receiving treatment with rabbit antiserum may cause false positives.

12) The results of the visual interpretation and the interpretation with the dedicated device may not match. In such a case, make a comprehensive judgement based on both results, clinical symptoms, and other test results.

13) When interpreting with the dedicated device, if the control line area or test line area of the test plate is scratched or foreign matter (dust) is attached, it may be mistakenly detected as a line.

14) When using Mode 1 [Read Now] in the interpretation with the dedicated device, be sure to perform the measurement 10 minutes after the sample is dropped. If measured within 10 minutes, correct results may not be obtained.

[Performance characteristics]

1) Performance

1. Sensitivity
   - When in-house *Streptococcus pneumoniae* positive control [Note 1)] was tested, *Streptococcus pneumoniae* positive result was obtained.
   - When in-house *Legionella pneumophila* positive control [Note 2)] was tested, *Legionella pneumophila* positive result was obtained.

2. Accuracy
   - When in-house *Streptococcus pneumoniae* positive control was tested, *Streptococcus pneumoniae* positive result was obtained.
   - When in-house *Legionella pneumophila* positive control was tested, *Legionella pneumophila* positive result was obtained.
   - When in-house negative control [Note 3)] was tested, negative result was obtained.

3. Reproducibility
   - When in-house *Streptococcus pneumoniae* positive control was tested three times simultaneously, *Streptococcus pneumoniae* positive result was obtained in all cases.
   - When in-house *Legionella pneumophila* positive control was tested three times simultaneously, *Legionella pneumophila* positive result was obtained in all cases.
   - When in-house negative control was tested three times simultaneously, negative result was obtained in all cases.

Note 1) *Streptococcus pneumoniae* antigen control solution diluted with in-house negative control to be equivalent to 6.25×10^1 CFU/mL of the calibration reference standard.

Note 2) *Legionella pneumophila* antigen control solution diluted with in-house negative control to be equivalent to 2×10^4CFU/mL of the calibration reference standard.

Note 3) Aqueous solution containing urea and sodium chloride

4. Detection limit

Streptococcus pneumoniae

1.56×10^1 CFU/mL (ATCC49619)

Legionella pneumophila

5.0×10^3CFU/mL (ATCC33152)

5. *Streptococcus pneumoniae* serotype and reactivity

It is confirmed that this product reacts with *Streptococcus pneumoniae* serotypes 1, 2, 3, 4, 5, 6A, 6B, 6C, 6D, 7F, 7C, 8, 9N, 9V, 10A, 11A/E, 12F, 13, 14, 15A, 15B, 15C, 16F, 17F, 18C, 19F, 19A, 20, 22F, 23F, 23A, 24F, 24B, 28F, 29, 31, 33F, 34, 35B, 37, 38.

6. *Legionella pneumophila* serogroup and reactivity

The reactivity with *Legionella pneumophila* serogroups is shown in the following table:

Specimen	Specimen concentration CFU/mL)			
	Quick Chaser Streptococcus pneumoniae/Legionella			
	1×10^9	1×10^8	1×10^7	1×10^4
Legionella pneumophila SG1	Positive	Positive	Positive	Positive
Legionella pneumophila SG 2	Positive	Positive	Negative	Negative
Legionella pneumophila SG 3	Positive	Negative	Negative	Negative
Legionella pneumophila SG 4	Positive	Positive	Negative	Negative
Legionella pneumophila SG 5	Positive	Positive	Negative	Negative
Legionella pneumophila SG 6	Positive	Negative	Negative	Negative
Legionella pneumophila SG 7	Positive	Positive	Positive	
Legionella pneumophila SG 8	Negative	Negative	Negative	Negative
Legionella pneumophila SG 9	Positive	Positive	Negative	Negative
Legionella pneumophila SG 10	Positive	Negative	Negative	Negative
Legionella pneumophila SG 11	Negative	Negative	Negative	Negative
Legionella pneumophila SG 12	Negative	Negative	Negative	Negative
Legionella pneumophila SG 13	Negative	Negative	Negative	Negative
Legionella pneumophila SG 15	Positive	Positive	Negative	Negative

Referring the table, cross reactivity was observed in *Legionella pneumophila* serotypes 2, 3, 4, 5, 6, 7, 9, 10, 15. Articles by Barthe et al. and Dagmar et al. have shown that the LPS antigens of *Legionella pneumophila* have a common antigen regardless of serotype[1),2)].

2) Correlations

- Urine

< *Streptococcus pneumoniae* >

Comparison with existing approved products (immunochromatographic assay)

Other product (1)

	Quick Chaser Streptococcus pneumoniae/Legionella		
	Positive	Negative	Total
Positive	51	0	51
Negative	8[*1]	118	126
Total	59	118	177

Positive agreement rate : 100%(51/51)
Negative agreement rate : 93.7%(118/126)
Total agreement rate : 95.5%(169/177)

*1 Five out of eight discrepant cases were determined as positive by Other product (2).

Other product (2)

	Quick Chaser Streptococcus pneumoniae/Legionella		
	Positive	Negative	Total
Positive	56	1[*3]	57
Negative	3[*2]	117	120
Total	59	118	177

Positive agreement rate : 98.2%(56/57)
Negative agreement rate : 97.5%(117/120)
Total agreement rate : 97.7%(173/177)

*2 Three discrepant cases were determined as negative by Other product (1).

*3 One discrepant case was determined as negative by Other product (1).

< *Legionella pneumophila* >

Comparison with existing approved products
(immunochromatographic assay)

Quick Chaser
Streptococcus pneumoniae/Legionella

Other product (3)	Positive	Negative	Total
Positive	53	0	53
Negative	0	124	124
Total	53	124	177

Positive agreement rate : 100%(53/53)
Negative agreement rate : 100%(124/124)
Total agreement rate : 100%(177/177)

Quick Chaser
Streptococcus pneumoniae/Legionella

Other product (4)	Positive	Negative	Total
Positive	51	0	51
Negative	2[*4]	124	126
Total	53	124	177

Positive agreement rate : 100%(51/51)
Negative agreement rate : 98.4%(124/126)
Total agreement rate : 98.9%(175/177)
*4 Two discrepant cases were also determined as positive by Other product (3).

• CSF

< *Streptococcus pneumoniae* >

Comparison with existing approved product
(immunochromatographic assay)

Quick Chaser
Streptococcus pneumoniae/Legionella

Other product (1)	Positive	Negative	Total
Positive	27	0	27
Negative	0	54	54
Total	27	54	81

Positive agreement rate : 100%(27/27)
Negative agreement rate : 100%(54/54)
Total agreement rate : 100%(81/81)

Comparison with existing approved product
(latex agglutination method)

Quick Chaser
Streptococcus pneumoniae/Legionella

Other product (5)	Positive	Negative	Total
Positive	15	0	15
Negative	12[*5]	54	66
Total	27	54	81

Positive agreement rate : 100%(15/15)
Negative agreement rate : 81.8%(54/66)
Total agreement rate : 85.2%(69/81)
*5 Twelve discrepant cases were determined as positive by Other product (1).

3) Calibration reference material (Standard material)
Streptococcus pneumoniae (ATCC49619)
Legionella pneumophila (ATCC33152)

4) Interfering substances and medications
Following substances and blood did not interfere with the performance of this product at the concentration listed below.
- Glucose (5000 mg/dL)
- Albumin (2000 mg/dL)
- Ascorbic acid (500mg/dL)
- Acetylsalicylic acid (2000 mg/dL)
- Ibuprofen (500 mg/dL)
- Sodium chloride (3000 mg/dL)
- Calcium chloride (110 mg/dL)
- Urea (5000 mg/dL)
- Cold medicine (acetaminophen concentration) (500mg/dL)
- Blood (2%)
- Bilirubin(10mg/dL)

5) Cross reactivity
Cross reactivity was not observed with the following bacteria and viruses.
- Bacteria

Candida albicans, Chlamydophila (Chlamydia) pneumoniae, Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Enterococcus faecalis, Escherichia coli, Haemophilus influenzae a*, Haemophilus influenzae* b*, Haemophilus influenzae* c*, Haemophilus influenzae* d*, Haemophilus influenzae* e*, Haemophilus influenzae* f*, Klebsiella pneumoniae, Legionella pneumophila, Listeria monocytogenes, Moraxella catarrhalis, Mycoplasma pneumoniae, Neisseria gonorrhoeae, Neisseria meningitidis* A*, Neisseria meningitidis* B*, Neisseria meningitidis* C*, Neisseria meningitidis* Y*, Neisseria meningitidis* W-135*, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus anginosus, Streptococcus* Group A*, Streptococcus* Group B*, Streptococcus* Group C*, Streptococcus* Group F*, Streptococcus* Group G*, Streptococcus mutans*

- Viruses

Adenovirus 3, Adenovirus 11, Adenovirus 19, Adenovirus 37, Coronavirus, Coxsackievirus A7, Coxsackievirus B3, Echovirus, Epstein-Barr virus, Herpes simplex virus 2, Influenza virus A, Influenza virus B, Measles virus, Mumps virus, Parainfluenza virus 1, Respiratory syncytial virus A, Respiratory syncytial virus B, Rhinovirus 8, Rotavirus, Rubella virus, Varicella zoster virus

In addition, cross reactions were observed with *Streptococcus mitis* at 1×10^7 CFU/mL or more and *Streptococcus pseudopneumoniae* at 1×10^4 CFU/mL or more.

[Shelf life]

24 months from the date of manufacture
(As indicated on the product box and packaging)

[Reference]

1) Barthe C. et al. : Common epitope on the lipopolysaccharide of *Legionella pneumophila* recognized by a monoclonal antibody, J. Clin. Microbiol. 26(5) : 1016-1023,1988
2) Dagmar J et al. : Cross-reacting lipopolysaccharide antigens in *Legionella pneumophila* serogroups 1 to 14, Infection and Immunity 63(6) : 2180-2184, 1995
3) Kohler RB et al., J Clin Microbiol,20(4),605-607(1984)
4) Elaine R.Keith,et al.:Jcin Microbiol, 44(3), 923-927(2006)

Technical information
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https://www.mizuho-m.co.jp/en