SSI DIAGNOSTICA

IMMUVIEW®

S. pneumoniae Antigen Test

ENGLISH (UK)

Lateral flow test for qualitative detection of *S. pneumoniae* in urine and cerebrospinal fluid.

IMMUVIEW® *S. PNEUMONIAE* ANTIGEN TEST INSTRUCTIONS FOR USE

For *in vitro* diagnostic use

Intended use

The ImmuView® *S. pneumoniae* Antigen Test is intended for diagnosis of *Streptococcus pneumoniae (S. pneumoniae)* infections by detection of urinary antigens or antigens in cerebrospinal fluid (CSF). The test is a lateral flow test also known as a lateral flow immunochromatographic assay.

Description

ImmuView® *S. pneumoniae* Antigen Test is a rapid lateral flow test for qualitative detection of *S. pneumoniae* antigens in human urine and CSF samples.

The test is effective in presumptive diagnosis of pneumonia and meningitis caused by *S. pneumoniae*, in conjunction with culture and other methods. Correct and early treatment is vital for the prognosis and therefore quick methods to confirm the cause of diseases in the initial phase are very important in order to initiate the proper antibiotic treatment as soon as possible.

Principle

ImmuView® *S. pneumoniae* Antigen Test is a rapid lateral flow test for detection of *S. pneumoniae*.

Precautions

- The presence of partial lines and/or dots represent INVALID test results. The patient sample should be retested.

- Ensure that the test running buffer (RB) is added to all the test tubes and verified as present.
  False positive results can occur if no RB is added to the test tubes.

- Test results should be read within the recommended reading time.

- Do not use the test after the kit lot or components expiry date.

- Do not mix the components of the kit lot with components from other kit lots.

- Let the kit components equilibrate to room temperature before testing.

Materials Provided

- 1 tube with 22 test strips
- 0.5 mL positive control for *S. pneumoniae*
- 0.5 mL negative control for *S. pneumoniae*
- 2.5 mL running buffer
- 1 tweezer
- 22 transfer pipettes
- 22 test tubes
- 1 cardboard test tube holder
- Scorecard

Quick guide can be found on the inside of the box and on page seven.

Materials Required but not Provided

- Timer
- Sterile standard urine or CSF collection containers/ transport tubes.

Storage and stability

Please find the information on the box and labels.

Preservatives

The use of Boric Acid DO NOT interfere with the ImmuView® *S. pneumoniae* Antigen Test and can be used.

Sample Collection and Storage

Collect the urine sample in a sterile standard container (with or without boric acid preservative). If the sample is run within 24 hours, it can be stored at room temperature. Alternatively, the sample can be stored at 2-8˚C for 1 week or frozen at -20˚C (avoid multiple freeze/thaw circles). Make sure that samples always reach room temperature before testing. CSF samples should be tested as soon as possible after sampling or be stored frozen until testing is possible. Follow your laboratory procedures for long term storage of CSF samples.

Quality Control

The positive and negative controls provided with ImmuView® *S. pneumoniae* Antigen Test function as the kit quality control. Follow your local or state requirements for frequency of quality control testing.

Before using a new lot of a kit, or a new shipment of the same lot or by a new operator, please perform quality control testing before testing of clinical samples. The positive and negative controls within the kit are tested according to procedure described in this IFU.

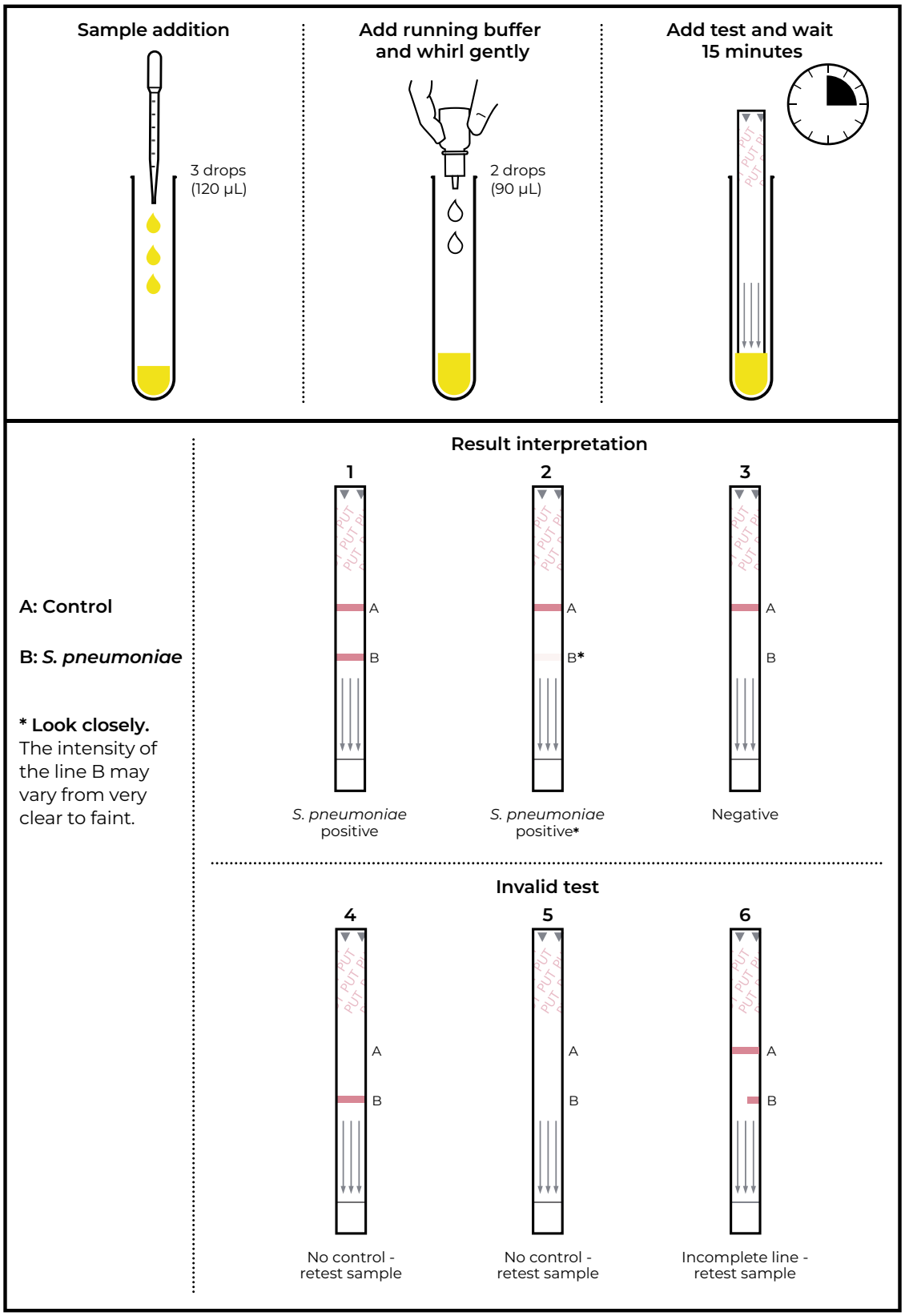
Procedure

The positive and negative controls should follow the same procedure as if it was a urine or a CSF sample. The positive control should be visible at the control test line and the *S. pneumoniae* test line. The negative control should only be visible at the control line.

1. Bring the patient urine or CSF sample to room temperature.*
2. Apply a test tube in the cardboard holder.
3. Fill the transfer pipette with urine or CSF and add 3 drops (120 µL) of sample to the test tube (hold the pipette vertically).
4. Add 2 drops (90 µL) of running buffer to the test tube (hold the buffer bottle vertically).
5. Whirl the test tube gently.
6. Take the container with test, open it and take out the number of test strips needed, and close it firmly afterwards.
7. Insert the test strip into the test tube.
8. Wait 15 minutes.
9. Lift the test strip out of the test tube. Read the result within 5 minutes. **
10. Discard the test strip after interpretation of the result.

* If the urine sample contains visible blood, please confirm a positive result by boiling the sample for 5 minutes and retest [1,2].
** Otherwise the test result may be inaccurate.

Quick guide


Sample addition
3 drops
(120 µL)
Add running buffer
and whirl gently
2 drops
(90 µL)
Add test and wait
15 minutes
A: Control
B: S. pneumoniae
* Look closely.
The intensity of
the line B may
vary from very
clear to faint.
Result interpretation
1
2
3
A
B
B*
S. pneumoniae
positive
S. pneumoniae
positive*
Negative
Invalid test
4
5
6
No control -
retest sample
No control -
retest sample
Incomplete line -
retest sample

Interpretation of results

A **positive sample for *S. pneumoniae*** will show a red line for *S. pneumoniae* positive in the bottom half of the test, and at the top of the test a red control test line will appear (see test result number 1 and 2, page 7).

Look closely. Even if there is a very faint line for *S. pneumoniae* the test result is positive (see test result number 2, page 7). The enclosed "Scorecard" can help to determine if the test result is positive or negative.

A **negative sample** will show a single red control line in the top of the test (see test result number 3, page 7).

If no control line is observed and/or incomplete test lines are present the test is **invalid** and the sample should be retested (see test results number 4, 5, and 6, page 7).

Limitations

- ImmuView® *S. pneumoniae* Antigen Test has not been validated to be used with urine samples from children under 8 years.

- ImmuView® *S. pneumoniae* Antigen Test has been validated using urine and CSF specimens only. Other specimens (e.g. serum or other body fluids) that may contain antigen have not been validated.

- The diagnosis of an *S. pneumoniae* infection cannot be based on clinical or radiological evidence alone.

- A negative result does not exclude an *S. pneumoniae* infection. The result of this test as well as culture, serology or other antigen detection methods should be used in conjunction with clinical findings to make an accurate diagnosis.

- *S. pneumoniae* vaccine may cause false positive results in urine in ImmuView® *S. pneumoniae* Antigen Test up to 10 days after vaccination.

- The test is not intended to replace culture.

- High concentrations of personel lubricant can cause invalid test results.

CLINICAL SENSITIVITY AND SPECIFICITY FOR URINE SAMPLES

(Retrospective study)

In a population of thirty (30) culture positive *S. pneumoniae* urine samples, 28/30 were *S. pneumoniae* positive with the ImmuView® *S. pneumoniae* Antigen Test using visual interpretation for a sensitivity of 93.3% (95% CI 78.7-98.2%). In the negative control population 119/121 were *S. pneumoniae* negative with the ImmuView® *S. pneumoniae* Antigen Test using visual interpretation for a specificity of 98.4% (95%CI 94.2-99.6%).

	Blood culture *S. pneumoniae*		
ImmuView®	Positive	Negative	Total
Positive	28	2	30
Negative	2	119	121
Total	30	121	151

ImmuView®	*S. pneumoniae*
Sensitivity	93.3% (28/30 CI: 79-98%)
Specificity	98.4% (119/121 CI: 94-100%)

ANALYTICAL STUDIES - URINE

Specificity (Cross-Reactivity)

The panel was tested with bacteria at 10^7 CFU/mL.

Organisms tested for interference	
E. faecium	*S. parasanquis*
L. pneumophila (SG 3)	*H. influenzae* (11)
Streptococcus Gr. A	*G. vaginalis*
Streptococcus Gr. B	*Acinetobacter anitratum*
Streptococcus Gr. C	*Acinetobacter* (3)
Streptococcus Gr. F	*S. mutans*
Streptococcus Gr. L	*K. pneumoniae* (3)
Streptococcus Gr. G	*Streptococcus Gr. A (colindale)*
E. cloacea (3)	*H. parainfluenzae*
E. faecalis (7)	*Streptococcus mitis*
E. coli (10)	*S. parasanguinis*
Enterococcuc durans	*S. sanguinis*

None of the organisms in the table cross-reacted with the ImmuView® *S. pneumoniae* Antigen Test.

Sensitivity (Limit of detection (LOD))

Antigen or whole cell	LOD
S. pneumoniae Antigen	125 pg/mL
S. pneumoniae type 1 whole cell	$0.5x10^5$ CFU/mL

The limit of detection for *S. pneumoniae* antigen (CWPS) is found to be 125pg/mL using the ImmuView® *S. pneumoniae* Antigen Test. For whole-cell organisms the limit of detection is $0.5x10^5$ CFU/mL. Boiling and preservatives might lower the LOD if whole-cell organisms are present in the urine due to the accessibility of the antigens.

Strain Reactivity

ImmuView® *S. pneumoniae* Antigen Test was able to detect 92 serotypes at 10^8 CFU/mL and 60 of those at 10^6 CFU/mL

Interfering Substances

ImmuView® *S. pneumoniae* Antigen Test was tested with forty-two (42) interfering agents at different concentrations in urine samples.

Agent	Concentration	Agent	Concentration
Acetaminophen	0.1 mg/mL	Itraconazole	0.22 mg/mL
Acetylsalicyclic acid	0.1 mg/mL	Miconazole	5%
Amantadine	0.03, 0.02, 0.01 mg/mL	Mix*	-
Amoxicillin	0.075 mg/mL	Mucin	0.086 mg/mL
Amphotericin B	0.22, 0.11, 0.06, 0.03 mg/mL	Oseltamivir (Tamiflu)	0.03 mg/mL
Antihistamine	0.22 mg/mL	Oxalic acid	0.01%
Ascorbic acid (c-vitamin)	1 mg/mL	pH (acidic)	4,7,9,
Augmentin (Amoxicillin Clavulanate)	0.22 mg/mL	Plasma	60%, 50%, 40%
Azithromycin	0.012 mg/mL	Prednisone	0.22 mg/mL
Beet root	0.01%	Protein (albumin) (Low)	0.6, 5, and 10 mg/mL
Bilirubin	0.2 mg/mL	Pyridium	1 mg/mL
Bromhexin/Cough drops/cough syrup	0.22 mg/mL	Rifampicin	0.09 mg/mL
Caffeine	15 mg/mL	Spinach	1%
Chlorophyll	0.81 mg/mL	Tobacco, purified	0.4 mg/mL
Ciprofloxacin	0.22 mg/mL	Triglycerides	5 mg/mL
Cold and flu tablet+decongestant	5%, 10%, 20%, 50%	Urea 50%	20 mg/mL
Corticosterone (Corticosteroids)	0.015 mg/mL	Urea 75%	20 mg/mL
Erythromycin	0.067 mg/mL	Vancomycin	0.1 mg/mL
Glucose	3, 10, 20 mg/mL	Water-based personal lubricant	1%, 5%, 10%, 15%
Hemoglobin	5 mg/mL	Washed red blood cells	10%
Ibuprofen	0.1 mg/mL	Whole blood	5%, 10%, 15%

*(pH, whole blood, protein and glucose)

Red blood cells may result in difficult correct visual interpretation of the results. Thus, it is recommended to boil the urine sample if excessive color on the strip is present.

Furthermore, water-based personal lubricant might cause invalid results (no control line) when tested at high concentrations (10% or higher).

Clinical Sensitivity and Specificity for CSF

In a population of eleven (11) culture positive *S. pneumoniae* CSF samples, 11/11 were *S. pneumoniae* positive with the ImmuView® *S. pneumoniae* Antigen Test using visual interpretation for a sensitivity of 100% (95%CI 74.1-100%). In the negative control population 161/163 were *S. pneumoniae* negative with the ImmuView® *S. pneumoniae* Antigen Test using visual interpretation for a specificity of 98.8% (95%CI 95.6-99.7%).

	Blood culture *S. pneumoniae*		
ImmuView®	Positive	Negative	Total
Positive	11	0	11
Negative	2	161	163
Total	13	161	174

ImmuView®	***S. pneumoniae***
Sensitivity	93.3% (28/30 CI: 79-98%)
Specificity	98.4% (119/121 CI: 94-100%)

Analytical Studies - CSF

Sensitivity (Limit of detection (LOD))

The LOD of ImmuView® *S. pneumoniae* Antigen Test in CSF was 10^5 CFU/mL using *S. pneumoniae* type one.

CSF	LOD
S. pneumoniae type 1 whole cell	10^5 CFU/mL

Co-infection

Escherichia coli, Streptococcus gr. B, *Haemophilus influenzae* Type B, and *Neisseria meningitidis* Type B tested at concentration of 10^7CFU/mL in artificial CSF samples did not cross react with the ImmuView® *S. pneumoniae* Antigen Test.

Repeatability

The repeatability is 80/80 or one hundred percent (100%) (CI 95% 95-100%) using ImmuView® *S. pneumoniae* Antigen Test.

Quality Certificate

SSI Diagnostica's development, production and sales of *in vitro* diagnostics are quality assured and certified in accordance with ISO 13485.

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References

1 Rota MC, Fontana S, Montaño-Remacha C, et al.; Legionnaires' disease pseudoepidemic due to falsely positive urine antigen test results. J Clin Microbiol. 2014;52(6):2279-2280. doi:10.1128/JCM.00493-14

2 Briones ML, Blanquer J, Ferrando D, Blasco ML, Gimeno C, Marín J.; Assessment of analysis of urinary pneumococcal antigen by immunochromatography for etiologic diagnosis of community-acquired pneumonia in adults. Clin Vaccine Immunol. 2006;13(10):1092-1097. doi:10.1128/CVI.00090-06

Information and Ordering

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