

Product Instructions	English:	pages	2-7
Mode d'emploi	Français:	pages	8-14
Gebrauchsanweisung	Deutsch:	Seiten	15-21
Istruzioni per il prodotto	Italiano:	pagine	22-28
Instruções do Produto	Português:	páginas	29-35
Instrucciones	Español:	páginas	36-42
Produktvejledning	Dansk:	sider	43-48
Gebruiksaanwijzing voor het product	Nederlands:	pagina's	49-54
Produktanvisningar	Svenska:	sidor	55-60
Οδηγίες προϊόντος	Ελληνικά:	Σελίδες	61-66

NOW®

Legionella

Urinary Antigen Test

Test d'antigène urinaire

Urin-Antigentest

Prova Urinaria Dell'Antigene

Teste de Antigénio na Urina

Prueba Urinaria Del Antígeno

Urinprøve-antigentest

Urinary Antigen test

Test för urinantigen

Τεστ αντιγόνου ούρων

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ENGLISH

INTENDED USE

The Binax NOW® *Legionella* Urinary Antigen Test is an *in vitro* rapid immunochromatographic assay for the qualitative detection of *Legionella pneumophila* serogroup 1 antigen (*L. pneumophila* serogroup 1 antigen) in urine specimens from patients with symptoms of pneumonia. It is intended to aid in the presumptive diagnosis of *Legionella* infection (Legionnaires' Disease) caused by *L. pneumophila* serogroup 1 in conjunction with culture and other methods.

SUMMARY AND EXPLANATION OF THE TEST

Legionnaires' Disease, named after the outbreak in 1976 at the American Legion convention in Philadelphia, is caused by *Legionella pneumophila* and is characterized as an acute febrile respiratory illness ranging in severity from mild illness to fatal pneumonia.¹ The disease occurs in both epidemic and endemic forms and sporadic cases are not easily differentiated from other respiratory infections by clinical symptoms. An estimated 25,000² to 100,000³ cases of *Legionella* infection occur in the United States annually. The resulting mortality rate, ranging from 25% to 40%, can be lowered if the disease is diagnosed rapidly and appropriate antimicrobial therapy is instituted early. Known risk factors include immunosuppression, cigarette smoking, alcohol consumption and concomitant pulmonary disease.² The young and the elderly are particularly susceptible.^{4,6}

Legionella pneumophila is responsible for 80-90% of reported cases of *Legionella* infection with serogroup 1 accounting for greater than 70% of all legionellosis.^{2,7,8} Current methods for the laboratory detection of pneumonia caused by *Legionella pneumophila* require a respiratory specimen (e.g. expectorated sputum, bronchial washing, transtracheal aspirate, lung biopsy) or paired sera (acute and convalescent) for an accurate diagnosis. These techniques include *Legionella* culture, direct fluorescent antibody (DFA), DNA probe, and indirect fluorescent antibody (IFA). All of these rely on either obtaining an adequate respiratory specimen for sufficient sensitivity, or collecting sera at a two to six week interval. Unfortunately, one of the presenting signs of patients with Legionnaires' Disease is the relative lack of productive sputum.^{8,9} In many patients, this necessitates the use of an invasive procedure to obtain a respiratory specimen. Diagnosis by serological techniques is usually retrospective in nature, and even then, patient compliance in obtaining the necessary samples is poor.

The Binax NOW® *Legionella* Urinary Antigen Test allows for early diagnosis of *Legionella pneumophila* serogroup 1 infection through detection of a specific soluble antigen present in the urine of patients with Legionnaires' Disease.¹⁰ ¹⁴ *Legionella pneumophila* serogroup 1 antigen has been detected in urine as early as three days after the onset of symptoms.¹⁵ The test is rapid, giving a result within 15 minutes, and utilizes a urine specimen which is convenient for collection, transport, and subsequent detection of early, as well as later, stages of disease.¹⁵

PRINCIPLES OF THE PROCEDURE

The Binax NOW® *Legionella* Urinary Antigen Test is an immunochromatographic membrane assay to detect *Legionella pneumophila* serogroup 1 soluble antigen in human urine. Rabbit anti-*Legionella pneumophila* serogroup 1 antibody, the patient line, is adsorbed onto nitrocellulose membrane. Goat anti-rabbit IgG, the control line, is adsorbed onto the same membrane as a second stripe. Rabbit anti-*Legionella pneumophila* serogroup 1 antibodies are conjugated to visualizing particles that are dried onto an inert fibrous support. The resulting conjugate pad and the striped membrane are combined to construct the test strip. This test strip and a well to hold the swab specimen are mounted on opposite sides of a hinged, book-shaped test device.

To perform the test, a swab is dipped into the urine specimen, removed, and then inserted into the test device. Reagent A is added from a dropper bottle. The device is then closed, bringing the sample into contact with the test strip. *L. pneumophila* serogroup 1 urinary antigen captured by immobilized anti-*L. pneumophila* serogroup 1 antibody reacts to bind conjugated antibody. Immobilized goat anti-rabbit IgG also captures visualizing conjugate, forming the control line. A positive test result is read visually in 15 minutes or less depending on the concentration of antigen present in the urine specimen. A negative Binax NOW® *Legionella* Urinary Antigen Test result, read in 15 minutes, indicates that *L. pneumophila* serogroup 1 antigen was not detected in the urine sample.

The test is interpreted by the presence or absence of visually detectable pink-to-purple colored lines. A positive result will include the detection of both a patient and a control line, while a negative assay will produce only the control line. Failure of the control line to appear, whether the patient line is present or not, indicates an invalid assay.

REAGENTS AND MATERIALS

Materials Provided

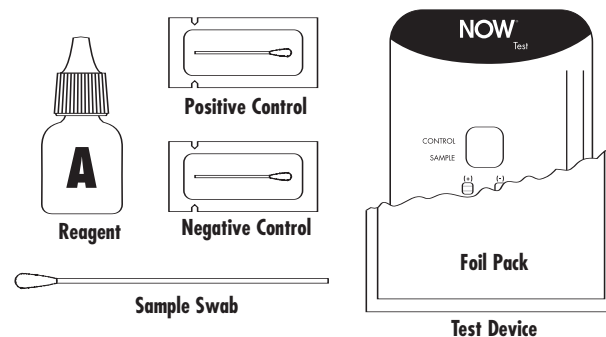
Test Devices – A membrane coated with rabbit antibody specific for *Legionella pneumophila* serogroup 1 antigen and with goat anti-rabbit IgG is combined with rabbit anti-*Legionella pneumophila* serogroup 1 antigen conjugate in a hinged test device.

Reagent A – Citrate / Phosphate with Tween® 20 and Azide.

Swabs – Designed for use in the Binax NOW® *Legionella* Urinary Antigen Test. **Do not use other swabs.**

Positive Control Swab – Heat inactivated *L. pneumophila* dried onto swab.

Negative Control Swab – *L. pneumophila* negative swab.



Materials Not Provided

Clock, timer, or stopwatch, standard urine collection containers

Accessory Item

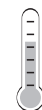
Binax NOW® *Legionella* Urinary Antigen Control Swab Pack containing 5 positive and 5 negative control swabs.

PRECAUTIONS

1. **INVALID RESULTS**, indicated by no control line, can occur when an insufficient volume of Reagent A is added to the test device. To insure delivery of an adequate volume, hold vial vertically, 1/2 - 1 inch above the swab well, and add drops slowly.
2. For *In Vitro* Diagnostic Use.
3. The test device is sealed in a protective foil pouch. Do not use if pouch is damaged or open. Remove test device from pouch just prior to use. Do not touch the reaction area of the test device.
4. Do not use kit past its expiration date.
5. Do not mix components from different kit lots.
6. Swabs in the kit are approved for use in the Binax NOW® test. **Do not use other swabs.**
7. Solutions used to make the control swabs are inactivated using standard methods. However, patient samples, controls, and test devices should be handled as though they could transmit disease. Observe established precautions against microbial hazards.

STORAGE AND STABILITY

Store kit at room temperature (59-86°F, 15-30°C). The Binax NOW® *Legionella* Urinary Antigen Test kit and reagents are stable until the expiration dates marked on their outer packaging and containers. Do not use the kit beyond its labeled expiration date.



**59-86°F
15-30°C
STORAGE
TEMPERATURE**

SPECIMEN COLLECTION

Urine specimens should be collected in standard containers. The samples can be stored at room temperature (59-86°F, 15-30°C) if assayed within 24 hours of collection. Alternatively, specimens may be stored at 2-8°C for up to 14 days or at -10°C to -20°C for longer periods before testing. Boric acid may be used as a preservative.

When necessary, urine specimens should be shipped in leakproof containers at 2-8°C or frozen.

Allow all specimens to equilibrate to room temperature before testing in the Binax NOW® *Legionella* Urinary Antigen Test.

QUALITY CONTROL

Daily Quality Control:

The Binax NOW® *Legionella* Urinary Antigen Test contains built-in control features. The manufacturer's recommendation for daily quality control is to document these controls for each sample run.

Positive Procedural Control

The pink-to-purple line at the "Control" position can be considered an internal positive procedural control. If capillary flow has occurred, this line will always appear.

Negative Procedural Control

The clearing of background color in the result window provides a negative background control. The background color in the window should be light pink to white within 15 minutes and should not interfere with the reading of the test result.

External Positive and Negative Controls:

Good Laboratory Practice recommends the use of positive and negative controls to assure functionality of reagents and proper performance of assay procedure. Positive and negative control swabs that will monitor the entire assay are provided in the kit. Additional Binax NOW® *Legionella* Positive and Negative Control Swabs are available separately. Alternatively, additional controls may be tested according to the guidelines or requirements of local, state, and/or federal regulations or of accrediting organizations. To use liquid urine controls, simply process as you would a patient sample.

Positive and negative controls should be tested once for each new test kit opened and as otherwise required by your laboratory's standard quality control procedures.

If expected control results are not obtained, do not report patient results. Repeat control testing or contact Binax Technical Service by phone within the US: **1-800-257-9525**, Outside US: **+1-609-627-8000** or by facsimile at **+1-207-730-5710**.

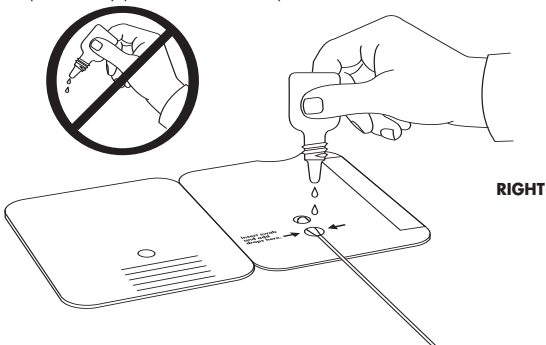
ASSAY PROCEDURE

Procedure for Patient Samples (and liquid urine controls):

Do not remove device from pouch until test sample has reached room temperature.

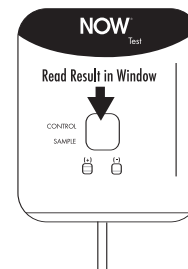
1. Bring patient urine and/or liquid urine control(s) to room temperature (59-86°F, 15-30°C). Remove device from its pouch **just before use** and lay flat.
2. Dip a Binax swab into the urine sample to be tested, completely covering the swab head. If the swab drips, touch swab to side of urine container to remove excess liquid.
3. There are two holes on the inner right panel of the device. Insert swab into the **BOTTOM** hole (swab well). Firmly push upwards so that the swab tip is fully visible in the top hole. **DO NOT REMOVE SWAB.**
4. Hold Reagent A vial vertically, 1/2 to 1 inch above the device. Slowly add **two (2)** free falling drops of **Reagent A** to the **BOTTOM** hole.
5. Immediately peel off adhesive liner from the right edge of the test device. Close and securely seal the device. Read result in window 15 minutes after closing the device. Results read beyond 15 minutes may be inaccurate. However, some positive patients may produce a visible sample line in less than 15 minutes.

WRONG



RIGHT

NOTE: For convenience, the swab shaft has been scored and may be snapped off **after** closing the device. Avoid dislodging the swab from the well when doing so.



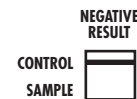
Procedure for Binax NOW® Swab Controls:

Remove device from the pouch **just before use**. Lay device flat and run test as follows:

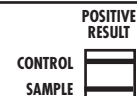
1. There are two holes on the inner right panel of the device. Insert swab into the **BOTTOM** hole. Firmly push upwards so that the swab tip is fully visible in the top hole. **DO NOT REMOVE SWAB.**
2. Hold Reagent A vial vertically, 1/2 to 1 inch above the device. Slowly add **six (6)** free falling drops of **Reagent A** to the **BOTTOM** hole.
3. Immediately peel off adhesive liner from the right edge of the test device. Close and securely seal the device. Read result in window 15 minutes after closing the device. Results read beyond 15 minutes may be inaccurate. However, the positive control swab/sample line may be visible in less than 15 minutes.

INTERPRETATION OF RESULTS

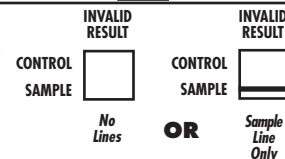
A **negative sample** will give a single pink-to-purple colored Control Line in the top half of the window, indicating a presumptive negative result. This Control Line means that the detection part of the test was done correctly, but no *L. pneumophila* serogroup 1 antigen was detected.



A **positive sample** will give two pink-to-purple colored lines. This means that antigen was detected. Specimens with low levels of antigen may give a faint Sample Line. **Any visible line is positive.**



If no lines are seen, or if just the Sample Line is seen, the assay is **invalid**. Invalid tests should be repeated. If the problem persists, contact Binax Technical Service by phone within the US: **1-800-257-9525**, Outside US: **+1-609-627-8000** or by facsimile at **+1-207-730-5710**.



REPORTING OF RESULTS

Result	Recommended Report
Positive	Presumptive positive for <i>L. pneumophila</i> serogroup 1 antigen in urine, suggesting current or past infection.
Negative	Presumptive negative for <i>L. pneumophila</i> serogroup 1 antigen in urine, suggesting no recent or current infection. Infection due to <i>Legionella</i> cannot be ruled out since other serogroups and species may cause disease, antigen may not be present in urine in early infection, and the level of antigen present in the urine may be below the detection limit of the test.

LIMITATIONS

The Binax NOW® *Legionella* Urinary Antigen Test has been validated using urine samples only. Other samples (e.g., plasma, serum or other body fluids) that may contain *Legionella* antigen have not been evaluated. The test cannot be used on environmental samples (i.e. potable water).

This test will not detect infections caused by other *L. pneumophila* serogroups and by other *Legionella* species. A negative antigen result does not exclude infection with *L. pneumophila* serogroup 1. Culture is recommended for suspected pneumonia to detect causative agents other than *L. pneumophila* serogroup 1 and to recover *L. pneumophila* serogroup 1 when antigen is not detected in urine.

The diagnosis of Legionnaires' disease cannot be based on clinical or radiological evidence alone. There is no single satisfactory laboratory test for Legionnaires' disease. Therefore, culture results, serology and antigen detection methods should be used in conjunction with clinical findings to make an accurate diagnosis.

Excretion of *Legionella* antigen in urine may vary depending on the individual patient. Antigen excretion may begin as early as 3 days after onset of symptoms and persist for up to 1 year afterwards.¹⁵ A positive Binax NOW® *Legionella* Urinary Antigen Test result can occur due to current or past infection and therefore is not definitive for infection without other supporting evidence.

Performance of the NOW® test on diuretic urine has not been evaluated.

The Binax NOW® *Legionella* Urinary Antigen Test has been evaluated on hospitalized patients only. An outpatient population has not been tested.

PERFORMANCE DATA

Clinical Sensitivity and Specificity (Retrospective Study):

The Binax NOW® *Legionella* Urinary Antigen Test was used to evaluate 300 frozen archived patient urine specimens at a large University. One hundred (100) of these patients were positive for *Legionella pneumophila* serogroup 1 infection as determined by culture, DFA, RIA and/or IFA (4X titer).

Overall agreement of the NOW® test with laboratory diagnosis was 95%. Sensitivity and specificity were each 95%. Ninety five percent (95%) confidence intervals are listed below:

		Laboratory Diagnosis			
		+	-		
NOW® + Result -		95	10	Sensitivity	= 95% (88.7% - 98.4%)
		5	190	Specificity	= 95% (91.0% - 97.6%)
				Accuracy	= 95% (91.9% - 97.2%)

Clinical Specificity (Prospective Study):

In a multi-site study, 93 fresh urine specimens collected from hospitalized patients with lower respiratory symptoms or sepsis were tested in the Binax NOW® test. One hundred percent (100%) of these presumed negative patients produced negative NOW® test results, indicating that the Binax NOW® *Legionella* Urinary Antigen Test is highly specific in the population for which it is intended.

Cross-Reactivity:

Of the 200 negative urine specimens tested, 85 were from patients with bacteremic pneumonia (other than *Legionella* spp.), 84 with urinary tract infections, 14 with mycobacterial infections, 5 with empyema, 11 with other pulmonary conditions, and 1 with pneumonia caused by a transtracheal aspirate.

One hundred ninety (190) of these patient specimens produced negative results in the NOW® test yielding a specificity of 95%.

Reproducibility Study:

A blind study of the Binax NOW® *Legionella* Urinary Antigen Test was conducted at 3 separate sites using a panel of coded specimens. The proficiency panels contained negative, low positive, moderate positive, and high positive specimens. Specimens both with and without boric acid were tested. Each specimen was tested multiple times at each site on 3 different days. Six hundred twenty-nine (629) of the 630 total specimens tested produced the expected result.

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ORDERING INFORMATION

Reorder numbers:

852-012: Binax NOW® *Legionella* Urinary Antigen Test (12 test kit)
852-000: Binax NOW® *Legionella* Urinary Antigen Test (22 test kit)
852-010: Binax NOW® *Legionella* Urinary Antigen Control Swab Pack

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