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NADAL® Legionella Test (test cassette)

REF 552020

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NADAL® Legionella Test (Ref. 552020)

1. Intended Use

The NADAL® Legionella Test is an *in-vitro* rapid chromatographic lateral flow immunoassay for the qualitative detection of *Legionella pneumophila (L. pneumophila)* serogroup 1 antigen in urine specimens from patients with symptoms of pneumonia. The NADAL® Legionella Test is intended to be used in conjunction with culture and other methods as an aid in the presumptive diagnosis of *Legionella* infection (Legionnaires' disease) caused by *L. pneumophila* serogroup 1.

2. Introduction and Clinical Significance

Legionnaires' disease is a serious form of pneumonia accompanied by a mortality rate in the range of 10-15% in otherwise healthy individuals. The symptoms are similar to those of a flu-like illness followed by a dry cough, and frequently progress to the symptoms of pneumonia. Approximately 30% of people infected may also develop diarrhoea and vomiting and around 50% may show signs of mental confusion. The incubation period normally ranges from 2-10 days, with symptoms typically being displayed from 3-6 days after exposure. Legionnaires' disease may occur as an outbreak of two or more cases following a limited temporal and spatial exposure to a single source. It may also appear as a series of independent cases in an area in which it is highly endemic. Moreover, Legionnaires' disease may occur as sporadic cases without any obvious temporal or geographical grouping. Outbreaks have occurred repeatedly in establishments such as hotels and hospitals.

The NADAL® Legionella Test allows an early diagnosis of *L. pneumophila* serogroup 1 infection through detection of a specific soluble antigen present in the urine of patients with Legionnaires' disease. The *L. pneumophila* serogroup 1 antigen has been detected in urine as early as three days after the onset of symptoms. The test is rapid, giving a result within 15 minutes, and is carried out using urine specimens which allow convenient collection, transportation and subsequent detection of the early as well as late stages of the disease.

3. Test Principle

The NADAL® Legionella Test is a chromatographic lateral flow immunoassay for the detection of *Legionella pneumophila* serogroup 1 antigen in human urine. Anti-*L. pneumophila* serogroup 1 antibodies are precoated onto the test line region. During testing, the sample reacts with particles precoated with further anti-*L. pneumophila* serogroup 1 antibodies which are pre-dried onto the internal test strip. The mixture then migrates along the membrane by capillary action.

The specific antibodies present on the membrane will react with the mixture conjugates and generate one or two coloured lines.

The appearance of a coloured line in the control line region serves as a procedural control, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

4. Reagents and Materials Supplied

- 10 NADAL® Legionella test cassettes (incl. disposable pipettes)
- 1 Positive Control: inactivated *L. pneumophila* swab, 1 Reagent Control + vial, 1 testing tube
- 1 Negative Control: *L. pneumophila* negative swab, 1 Reagent Control – vial, 1 testing tube
- 1 package insert

5. Additional Materials Required

- Specimen collection container
- Disposable gloves
- Timer

6. Storage & Stability

Store the test as packaged in the sealed foil pouch either refrigerated or at room temperature (2-30°C). The test and reagents are stable until the expiration date printed on the packaging. Do not use test kits beyond their expiration date.

7. Warnings and Precautions

- For professional *in-vitro* diagnostic use only.
- Carefully read through the test procedure prior to testing.
- Do not use the test beyond the expiration date indicated on the package.
- Do not use the test if the foil pouch is damaged.
- Do not reuse tests.
- Do not add samples to the reaction area (result area).
- In order to avoid contamination, do not touch the reaction area (result area).
- Do not substitute or mix components from different test kits.
- Do not eat, drink or smoke in the area where specimens and test kits are handled.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are being assayed.
- Handle all specimens as if they contain infectious agents. Observe established precautions for microbiological risks throughout all procedures and standard guidelines for the appropriate disposal of specimens.
- The test kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not completely guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious, and handled in accordance with usual safety precautions (e.g., do not ingest or inhale).
- After testing, used testing materials should be discarded in a proper biohazard container and according to local regulations.
- Humidity and temperature can adversely affect test results.

8. Specimen Collection and Preparation

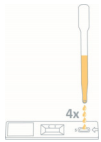
Urine specimens should be collected in standard containers. The samples can be stored at room temperature (15-30°C) if tested within 24 hours of collection. Alternatively, specimens can be stored at 2-8°C for up to 14 days or at -10°C to -20°C for longer periods of time before testing. Boric acid may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

Where necessary, urine specimens can be transported in leak-proof containers at 2-8°C or frozen. Bring all specimens to room temperature before testing.

9. Test Procedure

Procedure for patient samples (and other, liquid urine controls)

Bring patient samples and/or liquid urine control(s) to room temperature (15-30°C). Do not remove the test cassette from the foil pouch until the test sample or liquid urine control(s) has/have reached the room temperature. The test must be carried out within 2 hours of opening the sealed foil pouch.

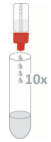


1 Remove the test cassette from the foil pouch immediately before use. Use a separate test cassette for each sample or control.
2 Place the test cassette on a flat surface. Use a separate pipette for each sample or control. Dispense exactly 4 drops of the sample/control into the circular sample well marked with an arrow. Start the timer.
3 Read the result after 15 minutes. Do not interpret the result after more than 15 minutes.

Procedure for positive and negative swab controls.

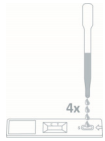
Do not remove the test cassette from the foil pouch until the reagents have reached the room temperature (15-30°C).

Perform the test as follows:



1 Holding the Reagent Control + vial vertically, slowly add 10 drops to the testing tube.
2 Immediately remove the positive control swab from the foil pouch and put the swab into the testing tube with the reagent. Mix for 1 minute and extract as much liquid as possible from the swab, squeezing the sides of the tube as the swab is withdrawn. Discard the swab.

3 Remove the test cassette from the sealed pouch.
4 Place the test cassette on a flat surface. Use a separate pipette and test cassette for each control. Dispense exactly 4 drops of the solution from the testing tube into the circular sample well marked with an arrow. Start the timer.



5 Read the result after 15 minutes. Do not interpret the result after more than 15 minutes.

Repeat the procedure for negative control swab using the Reagent Control - instead of the Reagent Control +.

10. Result Interpretation

Positive:

Two red lines appear in the result window. One line appears in the test line region (T) and the other line develops in the control line region (C).

Recommended report: Presumptive positive for *L. pneumophila* serogroup 1 antigen in urine, suggesting current or past infection.

Negative:

Only the red control line appears in the control line region (C).

Recommended report: Presumptive negative for the *L. pneumophila* serogroup 1 antigen in urine, suggesting no recent or current infection. Infection due to *Legionella* cannot be ruled out, since other serogroups and species may cause disease. Moreover, the antigen may not be present in urine in the early stages of infection and the level of antigen present in the urine may be below the detection limit of the test.

Invalid:

The control line fails to appear. Results from any test which has not produced a control line must be discarded, regardless of the presence or absence of the test line at the specified reading time. Please review the procedure and repeat the test with a new test cassette. If the problem persists, discontinue using the test kit immediately and contact your distributor.

11. Quality Control

Positive Procedural Control:

An internal positive procedural control is included in each test cassette:

A reddish line appearing in the control line region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Negative Procedural Control:

A clear background in the result window is an internal negative background control. The background colour in the result window should be light pink to white within 10-15 minutes and should not interfere with the reading of the test result.

Daily Quality Control:

The manufacturer's recommendation for daily quality control is to document these controls for each sample run.

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 the assay procedure. Positive and negative control swabs which monitor the entire assay are provided with the test kit.

To use liquid urine controls, follow the instructions for testing patient samples.

Positive and negative controls should be tested once with each new lot and as otherwise required by your laboratory's standard quality control procedures.

12. Limitations

- The NADAL® Legionella 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. drinking water).

- This test cannot 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 the 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 the *Legionella* antigen in urine may vary from patient to patient. Antigen excretion may begin as early as 3 days after the onset of symptoms and persist for up to 1 year afterwards. A positive result can occur due to current or past infection and is therefore not definitive proof of infection without other supporting evidence.
- The performance of the NADAL® Legionella Test on diuretic urine has not been evaluated. The NADAL® Legionella Test has been evaluated on hospitalised patients only. An outpatient population has not been tested.

13. Expected Values

Legionnaires' disease occurs in both epidemic and endemic forms. Sporadic cases are not easily differentiated from other respiratory infections by clinical symptoms. 25,000 to 100,000 cases of Legionella infection are estimated to occur in the United States annually. The resulting mortality rate, ranging from 25% to 40%, can be lowered if the disease is diagnosed quickly and an appropriate antimicrobial therapy is instituted early.

14. Performance Characteristics

Sensitivity and specificity

An evaluation was performed using the NADAL® Legionella Test with urine specimens in comparison with the immunoassay BinaxNOW® Legionella Urinary Antigen Test (ALERE, USA).

Sensitivity and specificity were determined using standard methods. The measure of concordance was calculated using Cohen's kappa coefficient. The interpretation should be as follow:

Kappa values (IK) <0.4 → weak concordance

Kappa values (IK) between 0.4 - 0.6 → high concordance

Kappa values (IK) >0.6 → excellent concordance

The results are presented in the following table

Method		BinaxNOW® *Legionella* Urinary Antigen Test (ALERE)		
		Positive	Negative	Results
NADAL® Legionella Test	Positive	17	0	17
	Negative	0	47	47
	Results	17	47	64

Sensitivity: >99%

Specificity: >99%

Positive predictive value: >99%

Negative predictive value: >99%

Kappa value: 1

The NADAL® Legionella Test was highly specific (>99%) and also sensitive (>99%) compared with the results of the Binax NOW® Legionella Urinary Antigen Test in the evaluation.

Cross-reactivity

An evaluation was performed to determine the cross-reactivity of the NADAL® Legionella Test. No cross-reactivity with the pathogens *Streptococcus pneumonia,* occasionally present in urine, was demonstrated.

15. References

1. Roig, J., X. Aquiler, J. Ruiz, et. al. Comparative study of Legionella pneumophila and other nosocomial-acquired pneumoniaes. Chest. 1991;99:344-50.
2. Berdal, B.P., C.E. Farshy, and J.C. Feeley. Detection of Legionella pneumophila antigen in urine by enzyme-linked immunospecific assay. J. Clin. Microbiol. 1979;9:575-578.
3. White A., et al. Rapad diagnosis of Legionnaires' disease. Trans Am Clin. Climatol. Assoc.l 1982;93:50-62
4. Bibb, W.F., P.M. Arnow, L. Thacker, and R.M. McKinney. Detection of soluble Legionella pneumophila antigens in serum and urine specimens by enzyme-linked immunosorbent assay with monoclonal and polyclonal antibodies. J. Clin. Microbiol. 1984;20:478-482.
5. Tang, P.W., and S. Toma. Broad-spectrum enzyme-linked immunosorbent assay for detection of Legionella soluble antigens. J. Clin. Microbiol. 1986;24:556-558.
6. Kohler, R.B., W.C. Winn, Jr., and L.J. Wheat. Onset and duration of urinary antigen excretion in Legionnaires' disease. J. Clin. Microbiol. 1984;20:605-607.

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Symbol	Deutsch	English	Français	Español	Italiano	Polski
CE	CE Konformitätszeichen	CE marking of conformity	Conformité aux normes européennes	Conformidad europea	Conformità europea	Znak zgodności CE
	Gebrauchsanweisung beachten	Consult instructions for use	Consulter la notice d'utilisation	Consúltense las instrucciones de uso	Consultare le istruzioni per l'uso	Przestrzegać instrukcji obsługi
IVD	In-vitro-Diagnostika	In-vitro diagnostic medical device	Dispositif médical de diagnosticc in vitro	Producto sanitario para diagnóstico in vitro	Dispoitivo medico-diagnostico in vitro	Tylko do diagnostyki in vitro
	Temperaturbegrenzung	Temperature limitation	Limites de température	Límites de temperatura	Limiti di temperatura	Temperatura przechowywania
LOT	Chargenbezeichnung	Batch code	Code du lot	Código de lote	Codice lotto	Numer serii
	Nicht zur Wiederverwendung	Do not reuse	Ne pas réutiliser	No reutilizar	Non riutilizzare	Tylko do jednorazowego użytku
	Verwendbar bis	Use by	Utiliser jusqu'au	Fecha de caducidad	Utilizzare entro	Data ważności
REF	Bestellnummer	Catalogue Number	Référence du catalogue	Número de catálogo	Riferimento di Catalogo	Numer katalogowy
	Hersteller	Manufacturer	Fabricant	Fabricante	Fabbricante	Producent
	Ausreichend für <n> Ansätze	Sufficient for <n> tests	Suffisant pour pour "n" tests	Suficiente para <n> utilizaciones	Sufficiente per "n" saggi	Wystarczający na <n> Powtórzeń

Symbol	Português	Český	Suomi	Svenskt	Nederlands	Dansk
CE	Conformidade com as normas europeias	CE certifikát	CE-merkitty	CE-märkning	CE-markering	CE-mærkning
	Consultar as instruções de utilização	Viz návod k použití	Katso käyttöohjetta	Läs bruksanvisningen	Raadpleeg de gebruiksaanwijzing	Se brugsanvisningen
IVD	Dispositivo médico para diagnóstico in vitro	Diagnostický zdravotnický prostředek in vitro	In vitro - diagnostiikkaan tarkoitettu lääkinnällinen laite	Medicinteknisk produkt avsedd för in vitro-diagnostik	Medisch hulpmiddel voor in-vitrodiagnostiek	Medicinsk udstyr til in vitro-diagnostik
	Limites de temperatura	Teplotní omezení	Lämpötilarajat	Temperaturbegränsning	Temperatuurlimiet	Temperaturbegrænsning
LOT	Código do lote	Kód šarže	Eräkoodi	Satsnummer	Code van de partij	Batchkode
	Não reutilizar	Pro jednorázové použití	Kertakäyttöinen	Får inte återanvändas	Niet opnieuw gebruiken	Må ikke genbruges
	Prazo de validade	Spotřebujte do	Käytettävä viimeistään	Används före	Houdbaar tot	Udløbsdato
REF	Número de catálogo	Katalogov éčíslo	Luettelonumero	Listnummer	Catalogus nummer	Best il l ingsnummer
	Fabricante	Výrobce	Valmistaja	Tillverkare	Fabrikant	Fabrikant
	Suficiente para <n> test	Dostačuje pro <n> testů	Lukumäärä <n> test	Räcker till <n> test	Voldoende voor <n> test	Tilstrækkeligt til <n> test

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