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NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (test cassette)

REF 243502N-20

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NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (Ref. 243502N-20)

1. Intended Use

The NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2, influenza A and B as well as respiratory syncytial virus (RSV) antigens in nasopharyngeal swab specimens from individuals with a suspected SARS-CoV-2/influenza/RSV infection in conjunction with clinical presentation and the results of other laboratory tests. The NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test is designed for *in-vitro* diagnostic and professional use only. It is intended for use in clinical laboratories and by healthcare professionals for point-of-care testing only. Not for home-use.

2. Introduction and Clinical Significance

COVID-19 (coronavirus disease) is a disease caused by the SARS-CoV-2 virus. It is highly contagious and spreads quickly. COVID-19 most often causes respiratory symptoms that can feel much like a cold, the flu, or pneumonia. COVID-19 may affect more than the lungs and respiratory system.

Influenza is an acute viral infection of the upper or lower respiratory tract marked by fever, chills, and a generalised feeling of weakness and pain in the muscles, along with varying degrees of soreness in the head and abdomen.

Respiratory syncytial virus, or RSV, is a common respiratory virus that usually causes mild, cold-like symptoms. Most people recover in a 1-2 weeks, but RSV can be serious. Infants and older adults are more likely to develop severe RSV symptoms and more likely to require hospitalisation. Vaccines are available to protect older adults from a severe course of RSV. Preventative options are also available to protect infants and young children from severe RSV symptoms.

3. Test Principle

The NADAL® SARS-CoV-2 Ag Test has one line of anti-SARS-CoV-2 antibodies in the test line region 'T' and one line of anti-mouse IgG antibodies in the control line region 'C'. When an extracted specimen is added to the specimen well, it reacts with the labeled antibodies to form complexes. The mixture then migrates along the membrane by capillary action and interacts with the precoated anti-SARS-CoV-2 antibodies in the test line region 'T'. If the specimen contains SARS-CoV-2 antigens, a red test line 'T' will appear, indicating a positive SARS-CoV-2 antigen result. Otherwise, the test result is to be considered negative. The test cassette also contains a control line 'C', which should turn red for all valid tests. If the quality control line 'C' does not appear, the test result is to be considered invalid, even if the test line 'T' appears.

The NADAL® Influenza A+B Ag Test has one line of anti-influenza A antibodies in the test line region 'A', one line of anti-influenza B antibodies in the test line region 'B' and one line of anti-mouse IgG antibodies in the control line region 'C'. When an extracted specimen is added to the specimen well, it reacts with the labeled antibodies to form complexes. The mixture then migrates along the membrane by capillary action and interacts with the precoated anti-influenza A antibodies and anti-influenza B antibodies in the corresponding test line regions. If the specimen contains influenza A or influenza B antigens, a red test line will appear, indicating the presence of influenza A or influenza B antigens. Otherwise, the test result is to be considered negative. The test cassette also contains a control line 'C' which should turn red for all valid tests. If the control line 'C' does not appear, the test result is to be considered invalid, even if the test line appears.

The NADAL® RSV Ag Test has one line of anti-RSV antibodies in the test line region 'T' and one line of anti-mouse IgG antibodies in the control line region 'C' When an extracted specimen is added to the specimen well, it reacts with the labeled antibodies to form complexes, the mixture then migrates along the membrane by capillary action and interacts with the coated anti-RSV antibodies in the test line region 'T'. If the specimen contains RSV antigens, a red test line will appear, indicating the presence of RSV antigens. Otherwise, the test result is to be considered negative. The test cassette also contains a control line 'C' which should turn red for all valid tests. If the control line 'C' does not appear, the test result is to be considered invalid, even if the test line appears.

4. Reagents and Materials Supplied

- 20 NADAL® SARS-CoV-2/Influenza A+B/RSV Ag test cassettes
- Additional material provided in accordance with 93/42/EEC: Due to possible supply shortages of accessory medical products, the swab manufacturer might change. Therefore, the supplied swabs are from one of the manufacturers listed below.
  a) 20 sterile swabs, CE 0197
  CITOTEST LABWARE MANUFACTURING CO., LTD No. 339 Beihai West Road, Haimen, 226100 Jiangsu, P.R. China (authorised EU representative: WellKang Ltd, Enterprise Hub, NW Business Complex, 1 Beraghmore Rd., Derry, BT48 8SE, Northern Ireland)
  b) 20 sterile swabs, CE 0197
  Hangzhou Yiguoren Biotechnology Co. Ltd., Room 402, Building 2, No. 2628, Yuhangtang Road, Cangqian Street, Yuhang District, Hangzhou, 311121 Zhejiang, China (authorised EU representative: Zoustech S.L., Paseo de la Castellana 141, 28049 Madrid, Spain)
- 20 extraction tubes containing extraction solution (approximately 600 µL each)*
- 20 dropper caps
- 1 reagent holder
- 1 package insert

*contains the following preservative: ProClin™ 300: <0.03%.

No hazard labelling for ProClin™ 300 is required according to Regulation (EC) Nº 1272/2008 CLP. Concentrations are below the exemption threshold of <0.03%.

5. Additional Materials Required

- Timer

6. Storage & Stability

Store the test kit in a cool, dry place between 2-30°C. Keep away from light. Exposure to temperatures and/or humidity outside the specified conditions may cause inaccurate results. Do not freeze. Use the test kit at temperatures between 15-30°C. Use the test kit between 10-90% humidity. Do not use the test kit beyond the expiration date (printed on the foil pouch and box).

NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (Ref. 243502N-20)

Note: All expiration dates are printed in Year-Month-Day format. 2022-06-18 indicates June 18, 2022.

7. Warnings and Precautions

- For *in-vitro* diagnostic use only.
- This package insert must be read completely before performing the test. Failure to follow the instructions provided in the package insert may lead to inaccurate test results.
- Do not open the sealed pouch unless ready to conduct the assay.
- Do not use expired tests.
- Bring all reagents to room temperature (15-30°C) before use.
- Do not use the components from any other type of test kits as a substitute for the components in this test kit.
- Wear protective clothing and disposable gloves while handling the kit reagents and clinical specimens. Wash hands thoroughly after performing the test.
- Do not smoke, drink, or eat in areas where specimens or kit reagents are being handled.
- Dispose of all specimens and materials used to perform the test as biohazardous waste.

8. Specimen Collection and Preparation

Consider any materials of human origin as infectious and handle them using standard biosafety procedures.

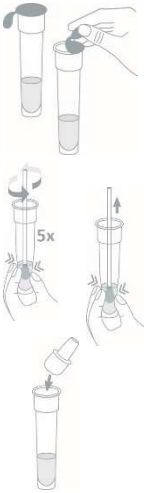
Specimen Collection:

Use the nasopharyngeal swab supplied in the test kit. It is important to obtain as much secretion as possible. Therefore, to collect a nasopharyngeal swab sample, carefully insert the sterile swab into the nostril that presents the most secretions under visual inspection. Keep the swab near the floor of the nasal septum while gently pushing it into the posterior nasopharynx. Rotate the swab several times, and then remove it from the nasopharynx.

9. Test Procedure

Bring tests and extraction solutions to room temperature (15-30°C) prior to testing.

1. Open the extraction solution (in the sealed tube).
2. Collect a specimen as outlined in the section 'Specimen Collection and Preparation'.
3. Insert the swab with the collected specimen into the extraction tube filled with extraction solution. Roll the swab 5 times while pressing the tip against the bottom and wall of the extraction tube.
4. Remove the swab while squeezing the wall of the tube to extract the liquid from the swab. Try to expunge as much liquid as possible. Dispose of the used swab as biohazardous waste.
5. Attach a dropper cap to the extraction tube.



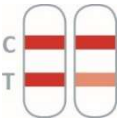
6. Take out a test cassette from its sealed foil pouch and put it on a clean and level surface.
7. Apply 3 drops of the extracted specimen into each specimen well. Please avoid bubbles forming during application.
8. Read the test result after 15 minutes. Do not read results after more than 20 minutes.

10. Result Interpretation

For SARS-CoV-2:

Positive result:

Both the control line 'C'and the test line 'T' appear.



Negative result:

Only the control line 'C' appears, no line appears in the test line region 'T'.

Invalid result:

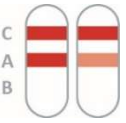
The control line 'C' fails to appear, indicating the test is invalid no matter whether the test line 'T' appears or not. Collect a new specimen and perform another test with a new test cassette.

For Influenza A+B:

Positive results:

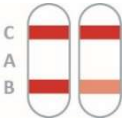
Positive for influenza A antigens:

Both the control line 'C' and the influenza A test line 'A' appear, while the influenza B test line 'B' does not appear.



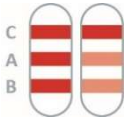
Positive for influenza B antigens:

Both the control line 'C' and the influenza B test line 'B' appear, while the influenza A test line 'A' does not appear.



Positive for influenza A and B antigens:

All 3 lines appear, including the control line 'C' as well as the influenza A and influenza B test lines 'A' and 'B'.



Negative result:

Only the control line 'C' appears, no lines appear in the influenza A and influenza B test line regions 'A' and 'B'. This indicates the test result is negative for both influenza A and influenza B antigens.

Invalid results:

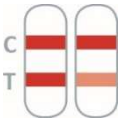
The control line 'C' fails to appear, indicating that the test is invalid, no matter whether the influenza A or influenza B test line appears or not.

Collect a new specimen and perform another test using a new test cassette.

For RSV:

Positive result:

Both the control line 'C' and the test line 'T' appear.



Negative result:

Only the control line 'C' appears, no line appears in the test line region 'T'.

Invalid result:

The control line 'C' fails to appear, indicating that the test is invalid, no matter whether the test line 'T' appears or not. Collect a new specimen and perform another test with a new test cassette.

11. Quality Control

Internal procedural controls are included in the test. A coloured line appearing in the control region 'C' is an internal procedural control. This procedural control line indicates that sufficient flow has occurred, and the functional integrity of the test cassette has been maintained. Control standards are not supplied with this test kit; however, it is recommended that positive and negative controls be tested as good laboratory practice to confirm the test procedure and to verify proper test performance.

12. Limitations

- The NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test is for *in-vitro* diagnostic use only and should not be re-used.
- The used test should be treated as potentially infectious material and be disposed of properly.
- The test kit should be kept away from direct sunlight, moisture and heat.
- Please check whether the test kit has any damage and check the expiry date before use.
- The sample volume may affect the accuracy of the test result. Inaccurate sample volume may cause a false positive or negative result.
- Test results must be evaluated in conjunction with other clinical data available to the physician.
- Positive test results do not rule out co-infections with other pathogens.
- Positive and negative predictive values are highly dependent on prevalence. The local prevalence should be taken into consideration when interpreting diagnostic test results.
- Please be very careful when collecting nasopharyngeal swab specimens from children.
- Components from different batches are not to be used in combination.

13. Performance Characteristics

Clinical performance

Diagnostic sensitivity and specificity

A total of 362 specimens were tested using the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test. These specimens were obtained by collecting nasopharyngeal swabs from symptomatic patients. The performance of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test was compared to a commercialised molecular assay.

Table 1: SARS-CoV-2 performance of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test as compared to a PCR Test.

		PCR		
NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (for SARS-CoV-2)		Positive	Negative	Total
	Positive	102	1	103
	Negative	4	255	259
	Total	106	256	362

Diagnostic sensitivity: 96.23% (102/106, 95%CI, 90.70% - 98.52%)
Diagnostic specificity: 99.61% (255/256, 95%CI, 97.82% - 99.93%)
Overall agreement: 98.62% (357/362, 95%CI, 96.81% - 99.41%)

Table 2: Influenza A performance of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test as compared to a PCR Test.

		PCR		
NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (for influenza A)		Positive	Negative	Total
	Positive	55	4	59
	Negative	3	300	303
	Total	58	304	362

Diagnostic sensitivity: 94.83% (55/58, 95%CI, 85.86% - 98.23%)
Diagnostic specificity: 98.68% (300/304, 95%CI, 96.67% - 99.49%)
Overall agreement: 98.07% (355/362, 95%CI, 96.06% - 99.06%)

Table 3: Influenza B performance of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test as compared to a PCR Test.

		PCR		
NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (for Influenza B)		Positive	Negative	Total
	Positive	32	5	37
	Negative	1	324	325
	Total	33	329	362

Diagnostic sensitivity: 96.97% (32/33, 95%CI, 84.68% - 99.46%)
Diagnostic specificity: 98.48% (324/329, 95%CI, 96.49% - 99.35%)
Overall agreement: 98.34% (356/362, 95%CI, 96.43% - 99.24%)

Table 4: RSV performance of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test as compared to a PCR Test.

		PCR		
NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test (for RSV)		Positive	Negative	Total
	Positive	111	2	113
	Negative	2	247	249
	Total	113	249	362

Diagnostic sensitivity: 98.23% (111/113, 95%CI, 93.78% - 99.51%)
Diagnostic specificity: 99.20% (247/249, 95%CI, 97.12% - 99.78%)
Overall agreement: 98.90% (358/362, 95%CI, 97.19% - 99.57%)

Analytical performance

Detection limit

Virus type/ subtype	Concentration
SARS-CoV-2	75.5 $TCID_{50}$/mL
Influenza A (H1N1)	1320 $TCID_{50}$/mL
Influenza A (H3N2)	568 $TCID_{50}$/mL
Influenza B (Victoria lineage)	1540 $TCID_{50}$/mL
Influenza B (Yamagata lineage)	2180 $TCID_{50}$/mL
RSV	93.6 $TCID_{50}$/mL

Measuring range

No prozone effect was observed when testing SARS-CoV-2 (up to 1.51×10^5 $TCID_{50}$/mL), influenza A (up to 5.68×10^7 $TCID_{50}$/mL), influenza B (up to 4.36×10^7 $TCID_{50}$/mL) and RSV (up to 1.17×10^5 $TCID_{50}$/mL).

Cross-reactivity

No cross-reactivity was observed with the following, potentially cross-reactive pathogens when tested using the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test: Influenza A, influenza B, adenovirus, respiratory syncytial virus, coronavirus, MERS-Coronavirus, parainfluenza virus, rhinovirus A16, *Legionella pneumophila, Mycobacterium tuberculosis, Streptococcus pneumoniae, Streptococcus pyogenes, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Staphylococcus aureus, human metapneumovirus,* enterovirus, *Haemophilus influenza, Candida albicans, Bordetella pertussis, Staphylococcus epidermidis, Pneumocystis jirovecii,* pooled human nasal wash.

The NADAL® SARS-CoV-2 Ag Test may cross-react with SARS-CoV-1 which caused the 2002-2004 SARS outbreak.

Interfering substances

The following substances showed no interference with the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test:

Antiviral drugs: Zanamivir, Oseltamivir, Artemether/ Lumefantrine, Doxycycline hyclate, Quinine, Lamivudine, Ribavirin, Daclatasvir.

Respiratory specimens: Mucin from bovine submaxillary glands, type I-S; EDTA-anticoagulated human blood; Biotin.

Nasal sprays or drops: Neosynephrin® (phenylephrine), Afrin® Nasal Spray (oxymetazoline), Saline nasal spray.

Homeopathic allergy relief medicine: homeopathic Zicam® Allergy Relief Nasal Gel, sodium cromoglycate, olopatadine hydrochloride.

Anti-inflammatory medication: Paracetamol (Acetaminophen), acetylsalicylic acid, ibuprofen.

Antibiotics: Mupirocin, tobramycin, erythromycin, ciprofloxacin.

Precision

Repeatability

Repeatability was established by testing 20 replicates of specimens using 3 lots of the NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test. The NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test demonstrated acceptable repeatability.

Reproducibility

Reproducibility was established by testing 5 replicates of specimens. Testing was performed by 5 operators using 3 NADAL® SARS-CoV-2/Influenza A+B/RSV Ag test lots at 3 different sites on 5 days. The NADAL® SARS-CoV-2/Influenza A+B/RSV Ag Test demonstrated acceptable reproducibility.

14. References

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