IVD REF CAN-025

CandiDia

Antibody

Instruction for Use – English

Please read this user manual carefully before using the test

INTENDED USE

CandiDia-Antibody is a non-automated rapid immunochromatographic test for the qualitative detection of IgG/IgM antibodies specific to a patented combination of *Candida sp.* antigens in plasma, serum or bronchoalveolar lavage samples from patients suspected of *Candida sp.* infection. This in vitro diagnostic test is strictly for medical professional use only and not intended for personal use or home testing. The use of the test and the interpretation of the results should be done by a trained healthcare professional. This test is an aid to diagnosis of Candida infections and the result of this test should not be the sole basis for the diagnosis; the results of other tests and confirmatory testing is required.

SUMMARY

Candida species are the leading opportunistic fungal pathogens in immuno-compromised patients and increase in non-immunocompromised, surgical and critically ill adult patients. Approximately 30-50% of all episodes of candidemia occur in ICU patients. The overall mortality attributable to candidemia is ranged from 10-47%. Blood culture remains the gold standard for diagnosis of invasive candidiasis, but the sensitivity is between 21-71%. Furthermore, it can take 2-4 days before Candida is identified and anti-fungal susceptibility data are available. Early and rapid detection is a key factor in the effective treatment and reduction of mortality.

DETECTION PRINCIPLE

The test has three pre-coated lines on a nitrocellulose membrane, one Control line (C) and two Test line (T1 and T2). The test lines are coated with anti-human IgM (T1) and anti-human IgG (T2) antibodies. The control line is coated with BSA-biotin. Specific and patented combination of Candida sp. antigens are conjugated with red-colored gold nanoparticles, used as detectors for Candida sp. antibodies. If the sample is positive, the anti-Candida antibodies in the sample react with the red-colored nanoparticles and form a complex (anti-Candida antibodies – gold nanoparticles), which was previously pre-dried on the conjugate pad. The mixture then moves upward on the membrane by capillary action. As the sample flows through the test membrane, the binding conjugate complexes migrate. The anti-Candida IgM present on the sample will be captured by the anti-human IgM antibody on the Test line (T1) as well as the anti-Candida IgG will be captured by the anti-human IgG antibody on the test line (T2) forming red lines.

If the sample is negative, there is no anti-Candida antibodies present or the antibodies may be present in a concentration lower than the detection limit. The anti-human IgM/IgG antibodies present on the membrane (Test lines) will not capture the antibody-red-colored conjugate complex (not formed), and the red line will not appear.

Whether the sample is positive or not, the nanoparticle complex continues to move across the membrane to the immobilized specific BSA-biotin placed in the control line. The BSA-biotin present on the membrane (Control line) will react with the streptavidin coated on the gold nanoparticles and capture the complex to form a red line. The presence of this red line serves as: 1) verification that sufficient volume is added, 2) that proper flow is obtained and 3) an internal control for the reagents. The control line must always appear.

KIT COMPONENTS

Components	Quantity per kit
CandiDia-Antibody rapid test in aluminum pouch (Art. CAN-001)	25
Sample treatment solution in plastic bottle (Art. CAN-002)	8.0 mL
Instructions for use (Art. CAN-004)	1

Note: The components of kits cannot be exchanged

Materials Required but Not Supplied

1. Pipettes and sterile tips
2. Timer
3. Disposable sterile micro-centrifuge tubes

STORAGE CONDITIONS AND SHELF LIFE

1. Store at 5-25°C for 24 months, store in a dry and cool place.
2. The rapid test should be used within 90 minutes after opening the aluminum pouch.
3. The date of expiration is printed on the labels.

SAMPLE PREPARATION

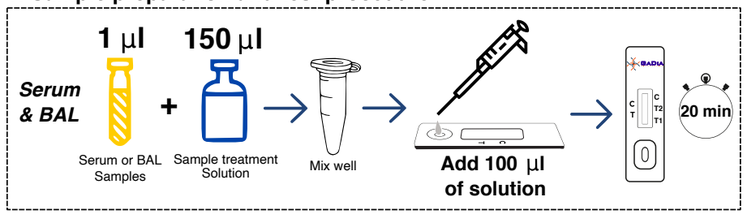
1. Sample type: Plasma, serum or Bronchoalveolar Lavage fluid (BAL)
2. Specimen collection: Collect patient sample according to the clinical collection guidelines for laboratory test samples.
3. Avoid contamination during sample collection, transportation, and preservation.
4. The sample should be stored at 2-8 °C for 24h or 4h at 25°C. If samples cannot be tested in time, store below -20°C.
5. Avoid sample contamination, deterioration and repeated freeze-thaw.
6. Grossly hemolyzed, icteric or lipidemic specimens are not recommended for testing.

TEST PROCEDURE

1. Sample preparation and test procedure

- Take 150 μl of sample treatment solution into a centrifuge tube, add 1 μl of sample and mix well (dilution 1/150).
- Take out the test from aluminum foil bag and place it on the clean horizontal bench.
- Add 50 μl of supernatant to the sample well (S) of the test device.
- Incubate for 20 minutes and read the result. Do not interpret the test result after 30 minutes.

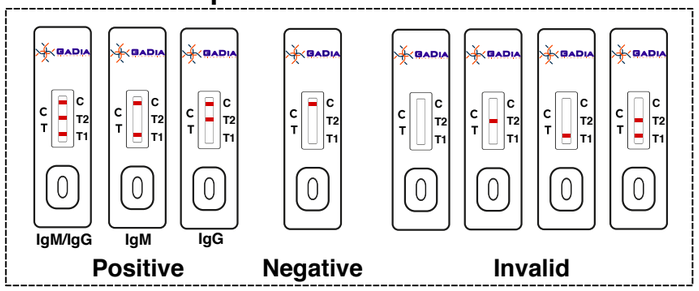
1. Sample preparation and test procedure



RESULTS INTERPRETATION

The presence of 1 or 2 lines in T1 or T2, regardless of the intensity of the test line, indicates a positive result. If the control line (line C) does not appear, the result is invalid and the test should be repeated.

2. Results interpretation



1. Negative results cannot exclude Candida infection, and it is possible that the sample is collected before the appearance of Candida antibody, the production of antibody is reduced due to physiological conditions, or the concentration is below the limit of detection (LOD).
2. The color intensity of the test results cannot be used as the basis for determining the total content of Candida antibody.
3. Positive test results do not rule out co-infections with other pathogens

LIMITATIONS

1. The test procedure, precautions and interpretation of results for this test must be followed strictly when testing.
2. The test is for professional use only and not for home-testing or near-patient testing.
3. The product is only used for the detection of Candida antibody in serum, plasma and BAL samples.
4. The test results of this kit are for reference only and should not be used as the only basis for clinical diagnosis and treatment. The clinical management of patients should be comprehensively considered in conjunction with their symptoms, medical history, other laboratory tests and treatment responses.
5. The sample treatment solution must be clear and without turbidity.

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PERFORMANCES CHARACTERISTICS

1. CLINICAL PERFORMANCE

A total of 90 samples were analyzed with CandiDia rapid diagnostic test and with the reference CE-IVD Candida IgG ELISA (DRG Diagnostics, Marburg, Germany). Rapid test results were interpreted with Qiagen LFA reader and naked eyes. The diagnostic performances were calculated using VassarStats Online Software for clinical research Calculator.

		Candida IgG ELISA	
		+	-
CandiDia RDT	+	30	10
	-	3	47

		CI 95%
Sensitivity	**90,9%**	(74.5-97.6%)
Specificity	**82,5%**	(69.2-90.7%)
PPV	**75,0%**	(58.5-86.8%)
NPV	**93,9%**	(82.1-98.4%)
Accuracy	**85,4%**	

2. CROSS-REACTIVITY

Disease states	Candida positive (ELISA)	Candida negative (ELISA)	Cross-reactivity
Celiac disease positive	0	3/4	1/4 (false positive)
Bacterial Sepsis	4/4	3/5	2/5 (false positive)
Lactose intolerance	0	1/2	1/2 (false positive)
COVID-19 positive	2/2	1/1	NO
HBsAg	1/1	4/4	NO
H.pylori IgG	1/1	2/2	NO
Anti-CCP	3/3	0	NO
F.rhumatoides IgG	1/1	2/2	NO
Anti-ANA antibody	0	3/3	NO
ANA positive	0	2/2	NO

3. INTERFERRING SUBSTANCES

Interferring Substances	Concentration	Positive sample	Negative sample
Mannan from *Saccharomyces cerevisiae*	50 ug/ml	POS (3/3)	NEG (3/3)
Beta Glucan from *Saccharomyces cerevisiae*	7 ug/ml	POS (3/3)	NEG (3/3)
Aspergillus Galactomannan	8.3 ng/ml	POS (3/3)	NEG (3/3)
Hemoglobin Human	500 mg/dl	POS (3/3)	NEG (3/3)
Cholesterol	700 mg/dl	POS (3/3)	NEG (3/3)
Bilirubin Conjugate Ditaurate Disodium Salt	7.5 mg/dl	POS (3/3)	NEG (3/3)
Acetylsalicylic acid (ASA)	100 ug/ml	POS (3/3)	NEG (3/3)
Ethanol	1%	POS (3/3)	NEG (3/3)

4. LIMIT OF DETECTION

High concentrated samples were diluted and the limit of detection was determined at 10 AU (ELISA Value), corresponding to the ELISA Assay cut-off value.

5. HOOK EFFECT

No Hook Effect has been observed with high concentrated samples (ELISA Value: 39.506). The sample was tested in triplicates and signal intensity was within a CV of 5%.

6. REPEATABILITY AND REPRODUCIBILITY

Reproducibility and reproducibility of the test have been evaluated internally with three different lots and a coefficient of variation (CV) of less than 10% was observed.

WARNING AND PRECAUTIONS

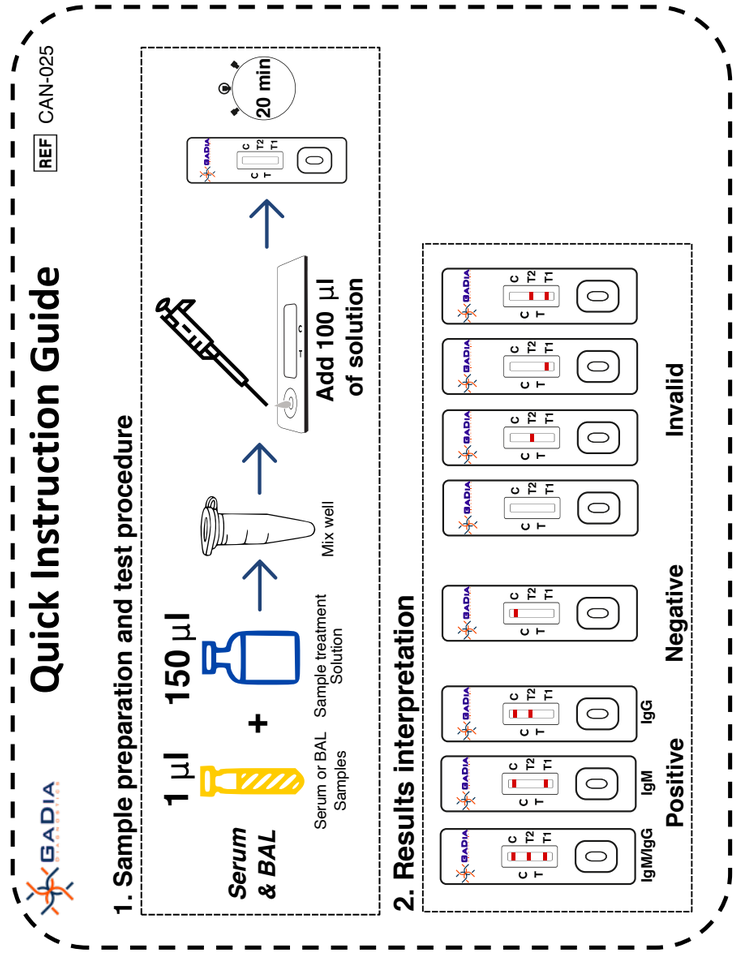
1. This product is used for in vitro diagnosis, professional use only.
2. Do not reuse the test kit or accessories.
3. Do not use the test after expiry date
4. Do not use the test kit if the pouch is damaged or the seal is broken.
5. Please read the test results within the specific time to avoid wrong interpretation.
6. Do not use the components from different batches or different types of reagents.
7. Properly dispose the specimen and used materials following the local biohazardous disposal regulation.
8. Use protective equipment when using the test and handling samples as they may contain infectious agents, human or animal components.
9. Sodium azide is used as preservative in the sample treatment solution. Dispose material according to relevant local regulations and avoid contact with eyes and skin.
10. Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

REFERENCES

1. Pappas et al., Invasive Candidiasis, Nature Reviews Disease Primers, 2018 ; 4, 18026
2. Calandra et al., Diagnosis and management of invasive candidiasis in the ICU: an updated approach to an old enemy, Critical Care (2016) 20:125
3. Eggimann & Pittet, Candida colonization index and subsequent infection in critically ill surgical patients: 20 years later, Intensive Care Med (2014) 40:1429–1448
4. He et al., Development of a Lateral Flow Immunoassay for the Rapid Diagnosis of Invasive Candidiasis. Front Microbiol. 2016; 7:1451
5. Patch et al., Impact of rapid, culture-independent diagnosis of candidaemia and invasive candidiasis in a community health system, J Antimicrob Chemother 2018; 73 Suppl 4: iv27–iv30
6. Pfaller & Diekema, Epidemiology of Invasive Candidiasis: a Persistent Public Health Problem, Clinical Microbiology Reviews, Jan. 2007, p. 133–163
7. Safavieh et al., Advances in Candida detection platforms for clinical and point- of-care applications, Crit Rev Biotechnol. 2017 June; 37(4): 441–458

SYMBOLS

	Manufacturer		Expiry Date
	Do not reuse	LOT	Lot Number
	Manufacturing date	EC REP	European Authorized Representative
	Consult instructions for use	IVD	In vitro diagnostic medical device
	Temperature limitation	REF	Catalog number
	Sufficient for <n> Test	CE	CE-Marking
	Not for near patient testing (IVDR only)		Not for self-testing (IVDR only)



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SWISS QUALITY

CE IVD

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