SUMMARY OF SAFETY AND PERFORMANCE (SSP) CandiDia-Antibody

1. Introduction

The Summary of Safety and Performance (SSP) is one of the requirements of the new Regulation (IVDR 2017/746), specific for class C and D devices, to enhance transparency and adequate access to information. It intends to provide public access to summarised data on the safety and performance of class C and class D IVD devices to all intended users – professionals and lay persons. GaDia is also providing this information for class B devices.

2. Summary of Safety and Performance (SSP)

Requirements based on IVDR Article 29	Potential regulatory sources
Device identification and general information	
Name or trade name including any model number or version	CandiDia-Antibody Rapid Test
Manufacturer (name and address)	GaDia SA Route de l'Ile-au-Bois 1A 1870 Monthey Switzerland
Manufacturers single registration number (SRN), if available	CH-MF-000031123
Basic UDI-DI	7649990065CANL5
Intended purpose of the device	
Intended purpose and indications	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 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.
Target populations	Patients with signs of acute and systemic fungal infections or fever or other suspicious symptoms. Patients following an

	anti-fungal treatment to follow-up the treatment efficacy. Patient in the triage setting, suspected of sepsis infections with unknown etiology and classical sepsis symptoms or medical indications.
Contraindications (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.
Device description	
Device description	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.
Reference to previous generation(s) or variants of the device (as applicable) and a description of the differences	N/A
Description of accessories intended to be used in combination with the device (as applicable)	N/A
Description of other devices and products intended to be used in combination with the device (as applicable)	Materials Required but Not Supplied 1. Pipettes and sterile tips 2. Timer 3. Disposable sterile micro-centrifuge tubes
Standards Reference	
Harmonised standards and Common Specifications (CS) applied	IVDD 98/79/EC EN ISO 13485:2016 EN ISO 15223-1:2021

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	EN ISO 17511:2021 ISO 14971:2019 ISO 18113-1:2009 ISO 18113-2:2009 ISO 20417:2021 ISO 13975:2003 ISO 13612:2002 ISO 23640:2011 ISO 20916:2019 IEC 62366-1:2015+A1:2020

Summary of the Performance Evaluation

A total of 90 anonymized leftover of serum and plasma samples, supplied by AbBaltis Ltd (UK), Discovery Life Sciences Inc., Augurix SA and INO Specimens Biobanks ISB, were used in this study. 33 samples (prevalence of 37%) were classified as positive with the CE-IVD ELISA Candida IgG reference method (DRG Instruments GmbH, Marburg, Germany) and 55 were negative. The primary end point was to assess the diagnostic performance of CandiDia Rapid test (GaDia SA, Monthey, Switzerland) in serum and plasma against the ELISA reference method, within a cohort of 34 ELISA positive samples and 55 control samples. The secondary end point is to evaluate the specificity of the device using typical cross-reactive samples. Vassarstats online tool (www.vassarstats.net) was used to calculate sensitivity (SE), specificity (SP), positive and negative predictive values (PPV, NPV), 95% confidence intervals, median, and Interquartile range (IQR); while significance (p-values) was calculated using student t test for independent samples with equal variances and Mann-Whitney U test. Statistical significance was defined as $p < 0.05$.

The demographic characteristics of patients' samples were as follows: the 21 ELISA positive samples were from patients with similar age (median = 34 years old, IQR 32–44) compared to the healthy patients group (n = 31) (median = 34 years old, IQR 28–51). The proportion of females was 29 % in both positive and healthy control groups. The diagnostic specificity of CandiDia Rapid test was assessed on ELISA negative control group (n = 57). In this group, cross-reactive samples, negative with ELISA, were also evaluated to determine the cross-reactivity of CandiDia rapid test on common cross-reactive samples, including Celiac disease positive (n=4), Bacterial sepsis (Procalcitonin positive) (n=9), lactose intolerance (n=2), COVID-19 positive (n=3), HBsAg positive (n=5), Helicobacter pylori IgG positive (n=3), Anti-CCP positive (n=3), Factor rheumatoid positive (n=3), Anti-ANA antibody positive (n=3) and ANA positive (n=2) samples.

The results of specificity and cross-reaction are shown in Tables 1 and 2.

A total of 10 discordant results showed a positive CandiDia results while negative with ELISA reference method (false positive results). The overall specificity (SP) of the CandiDia test for the detection of Candida specific antibodies was therefore 83 % (47/57) (95 % CI: 70 − 91 %).

		Candida IgG ELISA	
		Positive	Negative
CandiDia RDT	Positive	30	10
	Negative	3	47

		CI 95%
SE	91%	75 - 98%
SP	83%	70 - 91%
PPV	75%	59 - 87%
NPV	94%	82 - 98%
Accuracy	86%	

Table 1: Diagnostic performance of CandiDia-Antibody rapid test compared to ELISA

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

Table 2: Cross-reactive samples tested with CandiDia-Antibody rapid test

Four false positive results out of the total of 10 were obtained with common cross-reactive diseases. One celiac sample, 1 lactose intolerance sample and 2 Bacterial sepsis samples were positive with the test while negative with ELISA method. The table 2 indicates the possible cross-reactivity.

The diagnostic sensitivity of CandiDia was assessed using 33 samples positive for Candida antibody with ELISA. The results are shown in Table 1. Both methods revealed similar results in 91 % (30/33) of the samples (95 %CI: 75 − 98 %). Three discordant results showed a negative result with the rapid test while being positive with ELISA method. The overall sensitivity of CandiDia rapid test is 91% (30/33) (95 %CI: 75 − 98 %), while the positive predictive value (PPV; using a prevalence of 33/90 = 37 %) was 75 % (30/40) (95 % CI: 59 – 87 %) and the negative predictive value (NPV) 94 % (47/50) (95 % CI: 82 – 98 %). The overall concordance of results was 86 % (77/90).

Summary of the Post-Market Performance Follow-Up	
No Post-Market Performance Follow-Up (PMPF) study was conducted with this device.	
Metrological traceability	
Metrological traceability of assigned values	N/A
Users	
User Profile	The tests can be performed in laboratories by health care workers or laboratory

	technicians with appropriate training in sample collection, biosafety and in the use of rapid tests.
User Training	Appropriate training in sample collection, biosafety and in the use of rapid tests.
Device Risks Information	
Residual risks and undesirable effects	- Contamination of the user by infected samples - Wrong interpretation of the test results - False negative - Interference - Cross-reactivity
Warnings 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.