FIND Evaluation of Hangzhou Biotest Biotech Co., Ltd. RightSign COVID-19 Rapid Test Cassette External Report

Version 2.0, [28 July 2022]

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Evaluation process – private sector engagement

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For the COVID-19 response, FIND has commissioned independent evaluations of in vitro diagnostics following an Expression of Interest (EOI) process available on FIND's website by which all test submissions were scored according to their regulatory status and time to market; the manufacturing and distribution capacity of the supplier; and the supplier-reported clinical and analytical performance.

Document history

Document version	Date	Comment
1.0	10 February 2022	First release
1.1	03 June 2022	Omicron results added

2.0	28 July 2022	Data from Switzerland added

1 Product Info:

Manufacturer name	Hangzhou Biotest Biotech Co., Ltd.
Test name	RightSign COVID-19 Rapid Test Cassette
Product code(s)	ICOVN-C81
Pack size(s)	25 tests/kit
Contents of kit	Test cassettes, extraction buffer, sample collection vials, sterile nasal swabs, workstation, package insert
Equipment and consumables required, but not provided	Equipment: Timer, pipette Consumables: Gloves/PPE
Product storage (temperature range)	2-30 °C.
Shelf-life (months)	24 months
Manufacturing site (country)	China

2 Study details:

Study design:	Prospective diagnostic evaluation studies across multiple, independent sites to determine the accuracy of COVID-19 antigen RDTs, using consecutive enrolment. Interim analyses are performed at 25% and 50% enrolment, and the evaluation is stopped if tests do not meet 95% specificity. Presence of symptoms, date of symptom onset and hospitalization status is collected for all enrolled participants.
Index assays:	Novel lateral flow format tests that detect recombinant SARS-CoV-2 antigens.
Reference method:	Results of the index test are compared to the routine, diagnostic RT-PCR result, which is used for clinical management
Limit of detection:	Analytical sensitivity, i.e. Limit of detection, was performed at the Liverpool School of Tropical Medicine in which standardized serial dilutions of cultured viral isolate were prepared. Proprietary swab provided in the kit was soaked in viral dilution series. Dilutions were tested in triplicate and the LOD was defined as the last dilution where all repeats were interpreted as positive.

Clinical performance:	Sensitivity was calculated as the proportion of true positive results detected by RightSign COVID-19 RDT among all positives by the reference method, and reported as a percentage Specificity was calculated as the proportion of true negative specimens, identified as negative by RightSign COVID-19 RDT among all negatives by the reference method and reported as a percentage. The 95% confidence intervals were calculated to assess the level of uncertainty introduced by sample size, using the Wilson's score method.

3 Evaluation details:

Country of collaborator	South Africa	Switzerland
Location of clinical site(s) (city, town)	Hilcrest and Durban central	University Hospital of Geneva
Health care level of site(s)	Drive-through testing centers	Community Testing Clinic
Study period (date to date)	15 September to 8 December 2021	18 May to 8 July 2022
Study cohort inclusion/exclusion	Prospective, cohort with consecutive enrolment Inclusion criteria Residents of the selected communities falling under any of the following criteria: tested COVID-19 positive <7 days; presence of COVID-19 symptoms <7 days; Exposed to COVID-19 5-10 days ago; Heath care worker; Doctor referral for testing; Exclusion criteria: Anyone in the selected communities not willing to participate or unable to provide consent to participate.	Individuals (age 18+) in community meeting Departement of Public Health definition of a suspected COVID-19 case and being tested for SARS-CoV-2 part of routine medical care. Provided informed consent
Sample type, antigen test	Nasal swabs	Nasal swabs
Reference PCR method	Abbott RealTime SARS-CoV-2 (Abbott Molecular, Inc)	Roche cobas SARS-CoV-2 (Roche Diagnostics)

	Ct values adjusted to account for unread cycles (n=10) by the Abbott platform.	
Sample type, PCR test	Nasopharyngeal swab	Nasopharyngeal swab

4 Results:

4.1 Study cohort

Country	South Africa	Switzerland
Total N (valid PCR results)	540	170
Age [mean (min-max), N]	37.2 (2-89), 540	43.6 (18-80), 170
Gender [%F, (n/N)]	51.7%, (279/540)	57.6%, (98/170)
Symptoms present [%Yes, (n/N)]	70.6%, (381/540)	100%, (91/91)[1]
Hospitalized (n, % Yes)	Not applicable	Not applicable
Days from symptom onset [median (Q1-Q3); N]	3 (2-4), 381	2 (1-4), 90[2]
Days < 0-3 (n, %)	243, 64%	66, 73%
Days 4-7 (n, %)	111, 29%	17, 19%
Days 8+ (n, %)	27, 7%	7, 8%
Positivity [%, (n/N)]	13.3% (72/540)	54%, (92/170)
PCR Ct [median (Q1-Q3); N]	25.2 (21.6-33.7), 70	21.8 (19.2-24.9), 92
Ct > 33 (n, %)	20, 29%	4, 4%
Ct > 30 (n, %)	24, 34%	11, 12%
Ct > 25 (n, %)	36, 51%	22, 24%

[1] Symptom data only collected for PCR positive participants, symptom data missing for one participant

[2] Symptom onset date missing for 2 participants

4.2 Estimation of Clinical Performance

Country	South Africa	Switzerland
Clinical Sensitivity (95% CI), N	63.9% (52.4, 74), 72	93.3% (86.2, 96.9), 90

Sensitivity days ≤7, N	71.2% (57.7, 81.7), 52	93.8% (86.2, 97.3), 80
Sensitivity Ct ≤ 33, N	82% (69.2, 90.2), 50	96.5% (90.2, 92.8), 86
Sensitivity Ct ≤ 25, N	91.2% (77, 97), 34	100% (94.7, 100), 68
Clinical Specificity (95% CI), N	100% (99.2, 100), 468	98.7% (93, 99.8), 77
Invalid rate (%, n/N)	0% (0/540)	1.7% (3/170)

***Important note**: The clinical sensitivity estimate from South Africa may have been impacted by the high proportion of samples with low viral loads (high Ct Values).*

4.2.1 Estimation of analytical performance

- Supplier-reported LOD = 1.0 x 10^3TCID50/ml ~ 7.0 x 10^2 pfu/ml (isolate USA-WA1/2020)

- Verified LOD

Variant (lineage)	Lowest dilution detected	Verified LOD concentration	Viral Copy equivalent
UK wild type (B1)	**1.0 x10^3 pfu/ml ~** 1.41 x 10^3 $TCID_{50}$/ml	**1.0 x10^3 pfu/ml**	**2.1 x10^5 genome copies/ml** applied to test
Alpha (B.1.1.7)	**2.5 x10^1 pfu/ml** ~ 3.525 x 10^1 $TCID_{50}$/ml	**2.5 x10^1 pfu/ml**	**9.5 x10^3 genome copies/ml** applied to test
Gamma (P1)	**2.5 x10^1 pfu/ml** ~ 3.525 x 10^1 $TCID_{50}$/ml	**2.5 x10^1 pfu/ml**	**1.1 x10^4 genome copies/ml** applied to test
Delta (B.1617.2)	**2.5 x10^2 pfu/ml** ~ 3.525 x 10^2 $TCID_{50}$/ml	**2.5 x10^2 pfu/ml**	**4.1 x10^5 genome copies/ml** applied to test
Omicron (BA.1)	**2.5 x10^2 pfu/ml** ~ 3.525 x 10^2 $TCID_{50}$/ml	**2.5 x10^2 pfu/ml**	**4.4 x10^4 genome copies/ml** applied to test

***Note**: viral dilution was applied directly to the test cassette, not to the provided swab*