FIND Evaluation of Rapigen BIOCREDIT COVID-19 Ag External Report

Version 2.0, [26 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	25 May 2022	First release
2.0	26 July 2022	Data for Brazil added

1 Product Info:

Manufacturer name	Rapigen Inc.
Test name	BIOCREDIT COVID-19 Ag
Product code(s)	Nasopharyngeal: G61RHA20 Nasal: G69RHA20
Pack size(s)	20 tests/kit
Contents of kit	Test device sealed in foil pouch with a desiccant, assay diluent tube, filter cap, sterilized swab, instructions for use
Equipment and consumables required, but not provided	PPE, timer
Product storage (temperature range)	2-30°C
Shelf-life (months)	24
Manufacturing site (country)	Republic of Korea

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 Rapigen BIOCREDIT COVID-19 Ag 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 Rapigen BIOCREDIT COVID-19 Ag 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	United Kingdom	Brazil
Location of clinical site(s) (city, town)	Liverpool John Lennon Airport, United Kingdom	1. Rio de Jenairo 2. Guapimirim
Health care level of site(s)	Drive through testing centre	1. Tertiary hospitals 2. Community testing clinics
Study period (date to date)	6 December 2021 – 18 March 2022	20-22 June 2022
Study cohort inclusion/exclusion	Inclusion: • 18 years or older, who are undergoing testing for COVID-19 • Symptomatic for COVID-19 • Provided informed consent Exclusion: • Asymptomatic • Younger than 18 years	Adults in the community meeting the national suspect definition Provided informed consent or assent
Sample type, antigen test	Nasopharyngeal and nasal swab	Nasopharyngeal and nasal swab
Reference PCR method	TaqPath™ COVID-19 CE-IVD RT-PCR Kit (ThermoFisher Scientific)	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the

		nucleocapsid (N) gene of SARSCoV-2 (https://www.fda.gov/media/134922/download)
Sample type, PCR test	Nasopharyngeal swab	Nasopharyngeal swab

4 Results:

4.1 Study cohort

Country	**United Kingdom**	**Brazil**
Total N (valid PCR results)	224	329
Age [mean (min-max), N]	42.8 (18-78), 224	37.7 (18-80), 329
Gender [%F, (n/N)]	58.5%, 131/224	61.7%, 203/329
Symptoms present [%Yes, (n/N)]	100%, 224/224	98.8%, 325/329
Hospitalized (n, % Yes)	Not applicable	Not applicable
Days from symptom onset [median (Q1-Q3); N]	2 (1-3), 224	4 (2-6), 325
Days < 0-3 (n, %)	179, 80%	156, 48%
Days 4-7 (n, %)	41, 18%	137, 42%
Days 8+ (n, %)	4, 2%	32, 10%
Positivity [%, (n/N)]	53%, 118/224	40%, 131/329
PCR Ct [median (Q1-Q3); N]	19.7 (17.0-24.7), 118	20 (16.3-24.4), 131
Ct > 33 (n, %)	5, 4%	5, 4%
Ct > 30 (n, %)	11, 9%	15, 11%
Ct > 25 (n, %)	28, 24%	31, 24%

4.2 Estimation of Clinical Performance

Country	United Kingdom		Brazil	
	Nasopharyngeal	**Nasal**	**Nasopharyngeal**	**Nasal**
Clinical Sensitivity (95% CI), N	82.2% (74.3, 88.1), 118	82.2% (74.3, 88.1), 118	82.4% (75, 88), 131	78.6% (70.8, 84.4), 131
Sensitivity days ≤7, N	82.1% (74.1, 88), 117	82.1% (74.1, 88), 117	85.3% (77.8, 90.6), 116	81% (73, 87.1), 116+
Sensitivity Ct ≤ 33, N	85.8% (78.2, 91.1), 113	85.8% (78.2, 91.1), 113	84.9% (77.6, 90.1), 126	81.7% (74.1, 87.5), 126
Sensitivity Ct ≤ 25, N	92.2% (84.8, 96.2), 90	95.6% (89.1, 98.3), 90	100% (96.3, 100), 100	95% (88.8, 97.8), 100
Clinical Specificity (95% CI), N	98.1% (93.4, 99.5), 106	100% (96.5, 100), 106	100% (98.1, 100), 198	100% (98.1, 100) 198
Invalid rate (%, n/N)	0% (0/224)	0% (0/224)	0% (0/329)	0% (0/329)
Positive percent agreement – nasal/NP (95% CI), N	89.9% (82.4, 94.4), 99	NA	94.4% (88.4, 97.4)	NA
Negative percent agreement – nasal/NP	93.6% (87.9, 96.7), 125	NA	223/224	99.6% (97.5, 99.9)

***Important note**: There was a 1h to 3h delay between Ag RDT sample collection and Ag RDT testing which may have degraded the overall performance results of the test.*

4.2.1 Estimation of analytical performance

- Supplier-reported LOD

Limit of Detection	Specimen type	Name	Cat. No.	Source of strain
8.03 x 10^2 $TCID_{50}$/ml ~ 5.62 x 10^2 PFU/ml	Cell culture-derived virus	SARS-CoV-2 (S clade) (BetaCoV/Korea/KCDC03 /2020)	43326 SARS-CoV-2	NCCP
5.35x10^2 $TCID_{50}$/ml ~ 3.74x10^2 PFU/ml	SARS-CoV-2 Inactivated virus (Heat inactivation)	Heat Inactivated 2019 Novel Coronavirus (USA-WA1/2020)	VR-1986HK™	ATCC

- Verified LOD

Variant (lineage)	Lowest dilution detected	Verified LOD concentration	Viral Copy equivalent
UK wild type (B1)	**5.0 x10^3 pfu/ml ~** 7.05 x 10^3 $TCID_{50}$/ml	**5.0 x10^3 pfu/ml**	**9.8x10^6 genome copies/ml** applied to test
Alpha (B.1.1.7)	**5.0 x10^4 pfu/ml** ~ 7.05 x 10^4 $TCID_{50}$/ml	**5.0 x10^3 pfu/ml**	**4.7 x10^6 genome copies/ml** applied to test
Gamma (P1)	**1.0 x10^3pfu/ml** ~ 1.41 x 10^3 $TCID_{50}$/ml	**1.0 x10^3 pfu/ml**	**5.60 x10^5 genome copies/ml** applied to test
Delta (B.1617.2)	**1.0 x10^2 pfu/ml** 1.41 x 10^2 $TCID_{50}$/ml	**1.0 x10^2 pfu/ml**	**1.64 x10^5 genome copies/ml** applied to test
Omicron (BA.1)	**2.5 x10^2 pfu/ml** ~ 3.525 10^2 $TCID_{50}$/ml	**2.5 x10^2 pfu/ml**	**8.80 x10^4 genome copies/ml** applied to test

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