FIND Evaluation of RapiGEN Inc.

BIOCREDIT COVID-19 Ag

External Report

Version 2.2, 8 June 2021

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Evaluation process – private sector engagement

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More information on our policy and guidelines for working with private sector partners can be found here: https://www.finddx.org/policies/

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	16 October 2020	Interim version
2.0	3 November 2020	Data for Germany added
2.1	10 December 2020	LOD methodology updated; EoU data added

2.2	8 June 2021	Note on product version added

1 Product info:

Manufacturer name	RapiGEN Inc.
Test name	BIOCREDIT COVID-19 Ag
Product code(s)	G61RHA20 (**Please note:** this product is no longer distributed; a new product is currently distributed)
Pack size(s)	20
Contents of kit	Test device sealed in a foil pouch with a desiccant, assay diluent tube, filter cap, sterilized swab, IFU
Equipment and consumables required, but not provided	Equipment: Timer, refrigerator (optional, for storage of specimens prior to testing, if applicable) Consumables: PPE
Product Storage (temperature range)	1-40°C
Shelf-life (months)	24 months
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.
Ease of use	A System usability survey and ease of use questionnaire assessing the quality of the test, test preparation, ease of test execution, procedure time, ease of result interpretation, storage conditions and perceived settings of use was completed by operators and a final score out of 100 was calculated.

3 Evaluation Details:

Country of collaborator	Brazil	Germany
Location of clinical site(s) (city, town)	Marica, state of Rio de Janeiro	1. Heidelberg 2. Berlin
Health care level of site(s)	Community testing clinic	1. Heidelberg: Drive-in testing Center 2. Berlin: Ambulatory testing clinic of Charité – University Hospital
Study period (date to date)	27 July – 16 September 2020	1. Heidelberg: 4 May – 3 Sept 2020 2. Berlin: 4 May – 18 Aug 2020
Study cohort inclusion/exclusion	Adults in community meeting national suspect definition Provided informed consent	Adults able to ambulate and meeting suspect definition of the Department of public health Provided informed consent
Sample type, antigen test	Nasopharyngeal swab	1. HD: Nasopharyngeal swabs 2. Berlin: Combined naso-/oropharyngeal swab
Reference PCR method	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N)	• Cobas SARS-CoV-2 (Roche Diagnostics Inc) ○ N = 344

	gene of SARS-CoV-2 (https://www.fda.gov/media/134922/download)	• Abbott *RealTime* SARS-CoV-2 (Abbott Molecular, Inc) ○ N = 114 • Allplex 2019-nCov Assay (Seegene Inc) ○ N = 571 • LightMix® Modular SARS-CoV (COVID19) E-gene (Tib Molbiol) ○ N = 132 • RealStar® SARS-CoV-2 RT-PCR Kit (Altona Diagnostics) ○ N = 80
Sample type, PCR test	Nasopharyngeal (NP) swab	Nasopharyngeal (NP, n=843), Naso/oropharyngeal (NP/OP, n=276), or oropharyngeal (OP, n=131) swabs

4 Results:

4.1 Study cohort

Country	**Brazil**	**Germany**
Total N (valid PCR results)	476	1239
Age [mean (min-max), N]	44.8 (0-106), 473	39.5 (1759.2), 1239
Gender [%F, (n/N)]	46.7%, (221/473)	50.2%, (612/1219)
Symptoms present [%Yes, (n/N)]	98.7%, (470/476)	59.9%, (733/1223)
Hospitalized (n, % Yes)	Not available	Not available
Days from symptom onset [median (Q1-Q3); N]	5 (4-7); 470	3 (2-4); 701
Days < 0-3 (n, %)	95, 20%	472, 67.3%
Days 4-7 (n, %)	296, 63%	161, 23%
Days 8+ (n, %)	79, 17%	68, 9.7%
Positivity [%, (n/N)]	25%, (117/476)	2%, (25/1239)
PCR Ct [median (Q1-Q3); N]	25.6 (20.4-31.1); 117	23.9 (19.6-28); 25
Ct > 33 (n, %)	20, 17%	4, 4%
Ct > 30 (n, %)	34, 29%	6, 24%

Ct > 25 (n, %)	62, 53%	10, 40%

4.2 Estimation of clinical performance

Country	**Brazil**	**Germany**
Clinical Sensitivity (95% CI), N	74.4% (65.8, 81.4), 117	52% (33.5, 70), 25[§]
Sensitivity days ≤7, N	77.6% (68.3, 84.7), 98	76.9 (49.7, 91.8), 13
Sensitivity Ct ≤ 33, N	82.5% (73.7, 88.8), 97	61.9 (40.9, 79.2), 21
Sensitivity Ct ≤ 25, N	90.9% (80.5, 96.1), 55	80 (54.8, 93), 15
Clinical Specificity (95% CI), N	98.95 (97.2, 99.6), 359	100% (99.7, 100), 1214
Invalid rate (%, n/N)	0% (0/476)	0% (0/1239)
Analytical Sensitivity (pfu/ml)	5 x 10^4 pfu/ml ~ 7.14 x 10^4 $TCID_{50}$/ml (LSTM)[1]	

Note: *We found the verified LOD to be 20-35 times lower than the supplier reported LOD of $10^{3.54}$ – $10^{3.56}$ $TCID_{50}$/ml, which is the equivalent of 1.4-2.5x10^3 pfu/ml, using a different viral strain.*

[§] Of the positive samples: 1/25 were tested by Abbott, 4/25 by altona, 8/25 by Roche Cobas, 11/25 by Seegene Allpex and 1/25 by TibMolbiol; 15/25 PCR positives were from NP swabs, 8/25 by NP/OP combined swabs, and 2/25 were from OP swabs. All Ag testing was performed using the same sample type as the PCR.

4.2.1 Estimation of analytical performance

	Lowest dilution detected	Verified LOD concentration	Viral Copy equivalent	Supplier-reported LOD
Analytical Sensitivity	**5 x 10^4 pfu/ml** ~ [XX] x 10^3 $TCID_{50}$/ml	**6.8 x 10^3** pfu/ml	**8.64 x 10^6 copies/ml**	1 x $10^{3.54}$ – $10^{3.56}$ $TCID_{50}$/ml ~ **1.43 – 2.54 x 10^3 pfu/ml**

Note: verified concentration accounts for volume of dilution that is absorbed onto the swab and then diluted into the proprietary extraction buffer.

4.3 Ease of use

RapiGEN, Inc.	90 out of 100	6 operators, Germany 2 operators, Brazil