FIND Evaluation of Hotgen Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold6 External Report

Version 2.1, [6 May 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
2.1	6 May 2022	First release
2.0	15 Sept 2021	Data for UK added

2.1	5 May 2022	Adding the LOD results for other VOCs

1 Product Info:

Manufacturer name	Beijing Hotgen BioTech Co. Ltd.
Test name	Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold)
Product code(s)	HGCG134A0140
Pack size(s)	40 tests per kit
Contents of kit	Antigen Test Cassette, Sample extraction buffer, Disposable virus sampling swab
Equipment and consumables required, but not provided	Timer, PPE
Product storage (temperature range)	4-30°C
Shelf-life (months)	18 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 Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold)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 Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) 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	**Brazil**	**United Kingdom**
Location of clinical site(s) (city, town)	Rio de Janeiro and Guapimirim, state of Rio de Janeiro	Liverpool John Lennon Airport, United Kingdom
Health care level of site(s)	Community testing clinic	Drive through testing centre
Study period (date to date)	11 June – 28 June 2021	13 May – 2 July 2021
Study cohort inclusion/exclusion	Adults in community meeting national suspect definition Provided informed consent	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
Sample type, antigen test	Nasal swabs	Nasopharyngeal swab
Reference PCR method	Lab-developed assay based on the US CDC protocol, which targets two regions (N1 and N2) of the nucleocapsid (N)	TaqPath™ COVID-19 CE-IVD RT-PCR Kit (ThermoFisher Scientific)

	gene of SARS-CoV-2 (https://www.fda.gov/media/134922/download)	
Sample type, PCR test	Nasopharyngeal (NP) swab	Combined Nasal (anterior nares) and oropharyngeal swabs

4 Results:

4.1 Study cohort

Country	**Brazil**	**UK**
Total N (valid PCR results)	453	248
Age [mean (min-max), N]	39.4 (18-100), 453	40.5 (18-76), 248
Gender [%F, (n/N)]	40.1%, (272/454)	57.5%, (142/247)
Symptoms present [%Yes, (n/N)]	97.4%, (442/454)	100%, (248/248)
Hospitalized (n, % Yes)	Not applicable	Not applicable
Days from symptom onset [median (Q1-Q3); N]	3 (3-5), 442	2 (1-3), 245
Days < 0-3 (n, %)	231, 52%	199, 81%
Days 4-7 (n, %)	195, 44%	33, 13%
Days 8+ (n, %)	16, 4%	13, 5%
Positivity [%, (n/N)]	23%, (106/454)	27%, (68/248)
PCR Ct [median (Q1-Q3); N]	20.4 (17.7-23.8), 106	21.2 (18.5-24.1), 68
Ct > 33 (n, %)	1, 1%	1, 1%
Ct > 30 (n, %)	7, 7%	1, 1%
Ct > 25 (n, %)	17, 16%	10, 15%

4.2 Estimation of Clinical Performance

Country	Brazil	UK
Clinical Sensitivity (95% CI), N	88.7% (81.2, 93.4), 106	80.9% (70, 88.5), 68
Sensitivity days ≤7, N	90.1% (82.7, 94.5), 101	84.4% (73.6, 91.3), 64
Sensitivity Ct ≤ 33, N	89.5% (82.2, 94), 105	80.6% (69.6, 88.3), 67
Sensitivity Ct ≤ 25, N	95.5% (89, 98.2), 89	82.8% (71.1, 90.4), 58
Clinical Specificity (95% CI), N	100% (98.9, 100), 348	99.4% (96.9, 99.9), 180
Invalid rate (%, n/N)	0% (0/454)	0% (0/248)

4.3 Estimation of analytical performance

- Supplier-reported LOD = 2.5 x $10^{2.2}$ $TCID_{50}$/ml ~ 5.59 x 10^2 $TCID_{50}$/ml ~ 2.81 x 10^2 pfu/ml (isolate BetaCoV/Beijing/IME-BJ01/2020-01)

- Verified LOD

Variant (lineage)	Lowest dilution detected	Verified LOD concentration	Viral Copy equivalent
UK wild type (B1)	**5.0 x10^2 pfu/ml ~** 7.05 x 10^2 $TCID_{50}$/ml	**5.0 x10^2 pfu/ml**	**1.18x10^6 genome copies/ml** applied to test
Alpha (B.1.1.7)	**1.0 x10^3 pfu/ml** ~ 1.41 x 10^3 $TCID_{50}$/ml	**1.0 x10^3 pfu/ml**	**2.1 x10^4 genome copies/ml** applied to test
Gamma (P1)	**2.5 x10^3pfu/ml** ~ 3.525 x 10^3 $TCID_{50}$/ml	**2.5 x10^3 pfu/ml**	**1.73 x10^6 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**	**9.90 x10^5 genome copies/ml** applied to test
Omicron (BA.1)	**5.0 x10^3 pfu/ml** ~ 7.05 x 10^3 $TCID_{50}$/ml	**5.0 x10^3 pfu/ml**	**8.83 x10^5 genome copies/ml** applied to test

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