FIND Evaluation of Acon Biotech (Hangzhou) Co. Ltd Flowflex SARS-CoV-2 Antigen Rapid Test External Report

Version 2.0, 26 January 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	9 June 2021	Initial release
2.0	26 January 2022	Data for Peru and South Africa added

1 Product info:

Manufacturer name	Acon Biotech (Hangzhou) Co. Ltd.
Test name	Flowflex SARS-CoV-2 Antigen Rapid Test
Product code(s)	L031-11815
Pack size(s)	25 tests per kit
Contents of kit	Test cassettes, positive control swab, negative control swab, disposable swabs, specimen collection guide, extraction buffer tubes, package insert.
Equipment and consumables required, but not provided	PPE, timer
Product storage (temperature range)	2-30°C
Shelf-life (months)	24 months
Manufacturing site (country)	China

2 Study details: (NOTE: will be the same for all reports)

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:	Verification of 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 Flowflex SARS-CoV-2 Antigen Rapid Test 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 Flowflex SARS-CoV-2 Antigen Rapid Test

	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 (NOTE: if multiple sites, info per site)

Country of collaborator	Switzerland	Peru	South Africa
Location of clinical site(s) (city, town)	University Hospital of Geneva	Universidad Peruana Cayetano Heredia	Groote Schuur Hospital
Health care level of site(s)	Community Testing Clinic	University Hospital	Community Testing Centre
Study period (date to date)	19 April 2021 – 1 June 2021	29 Sept 2021 - 11 Jan 2022	20 Aug – 6 Dec 2021
Study cohort inclusion/exclusion	Individuals (age 16+) in community meeting Department 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	Inclusion: Adults with acute respiratory illness who meets WHO case definition of a COVID-19 suspected case presenting to temporary testing locations around clinical sites Voluntarily given written consent and the willing to participate in this study. Exclusion: Hemodynamic instability as determined by the treating physician Patient unable to cooperate with respiratory sample collection Patient unable to give informed consent Recent history of excessive nose bleeds	Inclusion: Adults (>18 years) presenting with symptoms compatible with COVID-19 Exclusion: Hemodynamic instability as determined by the treating physician. Patient unable to cooperate with respiratory sample collection. Patient unable to give informed consent. Recent history of excessive nose bleeds.

Sample type, antigen test	Nasal swab	Nasal swab	Mid-turbinate
Reference PCR method	Cobas SARS-CoV-2 (Roche Diagnostics Inc)	Norgen RT-PCR kit (Norgen Biotek)	Seegene Allplex™ 2019-nCoV Assay (Seegene) (n=367) Abbott RealTime SARS-CoV-2 Assay (Abbott) (n=10
Sample type, PCR test	Nasopharyngeal swab	Nasopharyngeal swab	Mid-turbinate

4 Results

4.1 Study cohort (NOTE: if multiple sites, one column per site/country)

Country	Switzerland	Peru	South Africa
Total N (valid PCR results)	279	173	377
Age [mean (min-max), N]	34.4 (16-77), 279	35.5 (18-79), 173	30.7 (18-72), 377
Gender [%F, (n/N)]	55.2%, (154/279)	53.2%, (92/173)	54.1% (204/377)
Symptoms present [%Yes, (n/N)]	95.3%, (61/64) [1]	100%, (173/173)	96.3% (363/377)
Hospitalized (n, % Yes)	Not applicable	Not applicable	Not applicable
Days from symptom onset [median (Q1-Q3); N]	2 (1-2), 52[2]	4 (3-5), 173	3 (2-4), 363
Days < 0-3 (n, %)	45, 87%	80, 46%	224, 62%
Days 4-7 (n, %)	6, 12%	90, 52%	121, 33%
Days 8+ (n, %)	1, 2%	3, 2%	18, 5%
Positivity [%, (n/N)]	23%, (63/279)	37%, (64/173)	16%, (59/377)
PCR Ct [median (Q1-Q3); N]	21 (19.2-24.8), 63	23.3 (20.1-29.7), 64	27.5 (24.5-31.4), 58
Ct > 33 (n, %)	5, 8%	8, 12%	11, 19%
Ct > 30 (n, %)	6, 10%	16, 25%	22, 38%
Ct > 25 (n, %)	15, 24%	27, 42%	41, 71%

[1] Note: data on symptom onset only available for individuals who tested PCR positive, or false positive by antigen RDT.

[2] symptom onset date missing for 12 samples.

4.2 Estimation of clinical performance

Country	Switzerland	Peru	South Africa
Clinical Sensitivity (95% CI), N	92.1% (82.7, 96.6); 63	79.7% (68.3, 87.7), 64	81.4% (69.6, 89.3), 59
Sensitivity days ≤7, N	92.2% (81.5, 96.9); 51	79% (67.4, 87.3), 62	81% (69.1, 89.1), 58
Sensitivity Ct ≤ 33, N	98.3% (90.9, 99.7); 58	85.7% (74.3, 92.6), 56	87.2% (74.8, 94), 47
Sensitivity Ct ≤ 25, N	100% (92.6, 100); 48	100% (90.6, 100), 37	88.2% (65.7, 96.7), 17
Clinical Specificity (95% CI), N	99.5% (97.5, 99.9); 216	100 (96.6, 100), 109	99.7 (98.2, 99.9), 318
Invalid rate (%, n/N)	0% (0/216)	0% (0/173)	0% (0/377)

4.3 Estimation of analytical performance

	Lowest dilution detected	Verified LOD concentration	Viral Copy equivalent	Supplier-reported LOD
Analytical Sensitivity	**5.0 x10^1 pfu/ml** ~ 7.05 x 10^1 $TCID_{50}$/ml	5.0 x10^1 **pfu/ml**	6.8 x10^3 **copies/ml** applied to test	1.6 x10^2 $TCID_{50}$/ml ~ **1.13 x10^2 pfu/ml**

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