-- CONFIDENTIAL --

Report on the evaluation of the CLINITEST® Rapid COVID-19 Antigen Test in mild symptomatic population.

Population/setting	Mild symptomatic population attending GGD/hospital testlanes for COVID-19 testing
Method	Chromatographic immunoassay
Assay	CLINITEST® Rapid COVID-19 Antigen Test
Company	Healgen, distributor Siemens Healthineers
Evaluation type	Clinical prospective field- and technical lab evaluation
Evaluation period	26-10-2020 through 28-12-2020
Test locations	Delft, RH-MDC Maastricht, MUMC Groningen, UMCG and GGD Groningen Urmond, MUMC and GGD Zuid Limburg
Date	07-01-2021
Authors	5.1.2e 5.1.2e | RH-MDC 5.1.2e 5.1.2e | UMCG 5.1.2e 5.1.2e 5.1.2e | MUMC 5.1.2e | MUMC 5.1.2e 5.1.2e | RIVM 5.1.2e | RIVM 5.1.2e 5.1.2e | RIVM

Introduction

The CLINITEST® Rapid COVID-19 Antigen Test is CE marked. The assay is a chromatographic immunoassay aimed at qualitative detection of specifically the SARS-CoV-2 antigen in the nasopharynx. The test can be read by eye, but an optional reader (iPeak, MedIUL) is available. The Ministry of Health Welfare and Sport (VWS) requests a validation of SARS-CoV-2 rapid antigen tests before procurement.

Method

The antigen test was clinically evaluated in a population consisting of mainly mild symptomatic cases attending testlocations in Delft, Groningen, Maastricht and Urmond, the Netherlands. Participants were informed of the evaluation on site. Informed consent was requested for a second nasopharyngeal (NP) swab or combined NP and oropharyngeal (NP+OP) swab for the antigen test (as indicated in Tabel 1). The swabs for the antigen test was analyzed on site according to the IFU of the assay, with read-out by eye. Technicians worked in standard personal protection equipment. The swabs for RT-PCR were analyzed for regular PCR testing.

The antigen test was technically evaluated by diluting SARS-CoV-2 stock provided by Erasmus MC in 10-fold series (10^{-1} to 10^{-8}) viral transport medium (Mediaproducts B.V., Groningen, The Netherlands) with an end volume of 9 ml. The 10-fold series are vortex for 1 minute at room temperature. For each SARS-CoV-2 Rapid-Ag test, 350 µl from each dilution is added to the buffer supplied by the manufacture (n=3). After adding the dilution the procedure is follow as described in the prescription supplied by the manufacture.

Clinical prospective field evaluation

Sensitivity and specificity

The sensitivity of the assay with PCR as reference was 84.6%, 90.0%, 85.7% and 75.7% at the Delft, Maastricht, Groningen and Urmond testlocations, respectively (Table 1). The assay had an overall sensitivity of 80.6% (Figure 1). The sensitivity was correlated to viral load (indicated in this report by Ct values, Table 1). The assay had an overall specificity of 99.7% (Figure 2).

Table 1. *Sensitivity and specificity of assay with PCR as reference test in different testlocations*

Location	Studypopulation	Sensitivity with PCR as reference (95%-BI)	Specificity with PCR as reference (95%-BI)	Total n
RH-MDC	mild symptomatic (NP)	84.6 % (56.4 – 95.7%)	100 % (89.0 – 100%)	45 (13 PCR+)
MUMC	mild symptomatic (NP+OP VTM)	90.0 % (69.3 – 97.2%)	97,3 % (90.6 – 99.3%)	94 (20 PCR+)
UMCG	mild symptomatic (NP+OP)	85.7 % (64.7 - 95.0%)	100 % (98.3 – 100%)	240 (21 PCR+)
MUMC	mild symptomatic (NP)	75.7 % (64.3 – 84.2%) Ct <30: 85.2%	100 % (98.9 – 100%)	417 (70 PCR+)

Figure 1. *Overall sensitivity and specificity of assay with PCR as reference test*

		Reference test (PCR)		
		+	-	
Test validation (Ag)	+	100	2	102
	-	24	669	693
		124	671	795

Sens	Spec
80.6	99.7

Technical lab evaluation

Limit of detection

The assay has a lower limit of detection at dilution 10^{-5}, corresponding with TCID50/ml of 3.16E+00 and 4.98E+02 E-gene Copies/ml (Table 2). The technical lab evaluation shows 4 levels of sensitivity, based on lower limit of detection and the signal strength of the test result (weak signals are indicated by ^). The sensitivity of the CLINITEST® Rapid COVID-19 Antigen Test was good (sensitivity level 1) compared to other SARS-CoV-2 Rapid antigen tests.

Table 2. *Results of the diluted SARS-CoV-2 stock read out. The dilution is done in triplicate in each SARS-CoV-2 Rapid-Ag test. Colored boxes show the categorization of the SARS-CoV-2 Rapid-Ag test in sensitivity levels.*

Dilution	10^{1}	10^{2}	10^{3}	10^{4}	10^{5}	10^{6}	10^{7}	10^{8}	Sensitivity level:
TCID50/ml	3.16E+04	3.16E+03	3.16E+02	3.16E+01	3.16E+00	3.16E-01	3.16E-02	3.16E-03	
E-gene Copies/ml	4.98E+06	4.98E+05	4.98E+04	4.98E+03	4.98E+02	4.98E+01	4.98E+00	4.98E-01	
Ct-value E-gene qRT-PCR	10.86	14.43	17.77	20.97	24.02	27.34	30.18	34.29	
Test A	(3/3)	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	
Test B	(3/3)	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	
CLINITEST® Rapid COVID-19 Antigen Test	(3/3)	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	1
Test D	(3/3)	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	
Test E	(3/3)	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	
Test F	(3/3)	(3/3)	(3/3)	(3/3)	(0/3)	(0/3)	(0/3)	(0/3)	
Test G	(3/3)	(3/3)	(3/3)	(3/3)	(0/3)	(0/3)	(0/3)	(0/3)	2
Test H	(3/3)	(3/3)	(3/3)	(1/3)	(0/3)	(0/3)	(0/3)	(0/3)	
Test I	(3/3)	(3/3)	(3/3)	(3/3) ^	(0/3)	(0/3)	(0/3)	(0/3)	3
Test J	(3/3)	(3/3)	(3/3)	(0/3)	(0/3)	(0/3)	(0/3)	(0/3)	
Test K	(3/3)	(3/3)	(3/3)	(0/3)	(0/3)	(0/3)	(0/3)	(0/3)	4

^ *These SARS-CoV-2 Rapid-Ag tests have a weak signal.*

Ease of use

The assay has, compared to other SARS-CoV-2 rapid antigen test, some disadvantages concerning ease of use. The buffer is not pre-filled per tube. The tubes are relatively small in comparison to the swab, causing poor fit and need to remove the swab (with biosafety and contamination risks). The quality of the extraction tube and nozzle is not very good. The test does not contain a positive control (swab). The test is less suitable to perform high volumes of tests, as is the case for large testlanes.

The optional reader, iPeak, has a barcode scanner and accurately detects (weak) bands. In general, the use of a reader is more time consuming. The benefit of the reader, in addition to read-out by eye, should be considered per testsetting.

Conclusion

Based on the data presented the assay is in agreement with the criteria proposed by WHO (*1*); sensitivity ≥80% and specificity ≥97% for detection of SARS-CoV-2 infected cases with RT-PCR as a reference. The technical lab evaluation confirms the good sensitivity of the assay compared to other SARS-CoV-2 Rapid antigen tests. The CLINITEST® Rapid COVID-19 Antigen Test can be procured by the Ministry of Health Welfare and Sport (VWS).

Reference

1. https://www.who.int/publications/i/item/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19-scientific-brief