VAN OOSTVEEN MEDICAL B.V.
MEDICAL DISPOSABLES

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CLINICAL RESULTS

– ROMED CORONAVIRUS AG RAPID TEST CASSETTE (SWAB)

This document is an overview of the clinical test results obtained with the Romed COVID-19 Ag Rapid Tests.

Overall the specificity of our Antigen Rapid test is very high. Out of the 4 studies, 3 showed a specificity of 100%, and 1 showed a specificity of 99.22%.

The sensitivity depends on the viral load that is present in the samples. Based on the results of the studies described below we recommend that the tests should be used on samples collected in the first 10 days following symptom onset, or on samples with a Ct-value <30.

One of the 4 studies included information on the number of days since symptom onset for the positive samples. The sensitivity determined on samples collected in the first 4 days from symptom onset was 100%. After the first 4 days there is a possibility of false negative results compared to the PCR.

The last sections of this document include information on the limit of detection, cross reactivity and interference from substances which might be present in the nasal cavity or nasopharynx.

1. CLINICAL PERFORMANCE STUDY - US

Test method:
The Clinical Performance of the Coronavirus Ag Rapid Test (Swab) was evaluated by being involved in 7 non-laboratory sites within the US, where patients were enrolled and tested. Testing was performed by 24 non laboratorian Health Care Workers that were not familiar with the testing procedure. A total of 317 fresh nasopharyngeal swab samples were collected and tested, which includes 61 positive samples and 256 negative samples. The Coronavirus Ag Rapid Test (Swab) results were compared to results of Emergency Use Authorized RT-PCR assays for SARS-CoV-2 from nasopharyngeal swab specimen.

The COVID-19 Ag Rapid Test vs PCR

Method		PCR		Total Results
COVID-19 Ag Rapid Test Cassette	Results	Positive	Negative	
	Positive	59	2	61
	Negative	2	254	256
Total Results		61	256	317

Relative Sensitivity: 96.72% (95%CI*: 88.65%-99.60%)
Relative Specificity: 99.22% (95%CI*: 97.21%-99.91%)
Accuracy: 98.74 (95%CI*: 96.80%-99.66%)
*Confidence Intervals

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2. SECOND CLINICAL PERFORMANCE STUDY

Test method:
203 patients exhibiting pneumonia or respiratory symptoms were sequentially enrolled and nasopharyngeal (NP) swab samples were collected for testing. Two nasopharyngeal swab samples were collected at the same time from each person, one swab sample for the COVID-19 Ag Rapid Test, the other swab sample for commercial PCR assay testing. The test results obtained with the two testing methods have been compared.

The COVID-19 Ag Rapid Test vs PCR

Method		PCR		Total Results
COVID-19 Ag Rapid Test Cassette	Results	Positive	Negative	
	Positive	71	0	71
	Negative	2	130	132
Total Results		73	130	203

Relative Sensitivity: 97.3% (71/73)
Relative Specificity: 100% (130/130)
Accuracy: 99.0% (201/203)

Positive results broken down by days since symptom onset

Days Since Symptom Onset	Cumulative PCR Positive(+)	Cumulative COVID-19 Ag Rapid Test Cassette Positive(+)	PPA
1	7	7	100%
2	18	18	100%
3	30	30	100%
4	44	44	100%
5	59	58	98.3%
6	62	60	96.8%
7	70	68	97.1%
8	71	69	97.2%
9	72	70	97.2%
10	73	71	97.3%

COVID-19 Ag Performance against the Comparator Method – by Cycle Threshold Counts

COVID-19 Ag Rapid Test Cassette	PCR Results (Ct) of nucleoprotein(N) gene	
	Positive (Ct<30)	Positive (Ct ≥30)
Positive	62	9
Negative	0	2
Total	62	11

COVID-19 Ag Rapid Test Cassette	PCR Results (Ct) of open reading frame(ORF) gene	
	Positive (Ct<30)	Positive (Ct ≥30)
Positive	40	31
Negative	0	2
Total	40	33

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3. INITIAL FACTORY CLINICAL PERFORMANCE STUDY

The initial results obtained by the factory before the tests have been placed on the market have been included in the first versions of the IFU.

The COVID-19 Ag Rapid Test vs PCR

Method		PCR		Total Results
COVID-19 Ag Rapid Test Cassette	Results	Positive	Negative	
	Positive	39	0	39
	Negative	6	116	122
Total Results		45	116	161

Relative Sensitivity: 86.7% (95%CI*: 73.2%-95.0%)
Relative Specificity: 100% (95%CI*: 96.9%-100%)
Accuracy: 96.3% (95%CI*: 92.1%-98.6%)
*Confidence Intervals

4. DUTCH CLINICAL PERFORMANCE STUDY (ONGOING)

The RIVM (Dutch National Institute for Public Health and the Environment) is working in cooperation with the GGD (Dutch Municipal Health Services) to evaluate the tests that are currently on the market. This evaluation is organized by the Landelijk Coördinatieteam Diagnostische Keten (LCDK).

We have obtained a set of preliminary test results. Our tests have been simultaneously compared to 2 other antigen tests that are currently on the market. We have not been informed of the names of the other 2 manufacturers.

Test method:
Swab from throat and nasopharynx swab is incorporated into Virus Transport Medium and then vortexed for approximately 10 seconds. After this, 350 microliters were mixed with the recommended amount of buffer supplied for each antigen test. The antigen test was then carried out with this liquid as described in the package insert.

The COVID-19 Ag Rapid Test vs PCR, sensitivity based on Cycle Threshold Counts

	Number of PCR-tested samples		**Specificity (%) Ct-value < 40**	**Sensitivity (%) Ct-value < 40**	**Sensitivity (%) Ct-value < 35**	**Sensitivity (%) Ct-value < 30**
	Positive	**Negative**				
Romed Ag test 1	37	40	100	73.0	79.4	92.9
COVID Ag test 2	37	40	87.5	62.2	67.6	82.1
COVID Ag test 3	37	40	97.5	54.1	58.8	71.4

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LIMIT OF DETECTION (LOD)

LOD studies determine the lowest detectable concentration of SARS-CoV-2 at which approximately 95% of all (true positive) replicates test positive. Heat inactivated SARS-CoV-2 virus, with a stock concentration of 4.6×10^5 $TCID_{50}$ / mL, was spiked into negative specimen and serially diluted. Each dilution was ran in triplicate on the Coronavirus Ag test. The Limit of Detection of the Coronavirus Ag Rapid Test Cassette (Swab) is 1.15×10^2 $TCID_{50}$ / mL **(Table 2).**

Concentration	No. Positive/Total	Positive Agreement
1.15×10^2 $TCID_{50}$ / mL	180/180	100%

HIGH DOSE HOOK EFFECT

No high dose hook effect was observed when testing up to a concentration of 4.6×10^5 $TCID_{50}$ / mL of heat inactivated SARS-CoV-2 virus.

CROSS REACTIVITY

Cross reactivity with the following organisms has been studied. Samples positive for the following organisms were found negative when tested with the Coronavirus Ag Rapid Test Cassette (Swab).

Pathogens	Concentration
Respiratory syncytial virus Type A	5.5×10^7 PFU/mL
Respiratory syncytial virus Type B	2.8×10^5 TCID50/mL
Novel influenza A H1N1 virus (2019)	1×10^6 PFU/mL
Seasonal influenza A H1N1 virus	1×10^5 PFU/mL
Influenza A H3N2 virus	1×10^6 PFU/mL
Influenza A H5N1 virus	1×10^6 PFU/mL
Influenza B Yamagata	1×10^5 PFU/mL
Influenza B Victoria	1×10^6 PFU/mL
Rhinovirus	1×10^6 PFU/mL
Adenovirus 3	$5\times10^{7.5}$ TCID50/mL
Adenovirus 7	2.8×10^6 TCID50/mL
EV-A71	1×10^5 PFU/mL
Mycobacterium tuberculosis	1×10^3 bacteria/mL
Mumps virus	1×10^5 PFU/mL
Human coronavirus 229E	1×10^5 PFU/mL
Human coronavirus OC43	1×10^5 PFU/mL
Human coronavirus NL63	1×10^6 PFU/mL
Human coronavirus HKU1	1×10^6 PFU/mL
Parainfluenza virus 1	7.3×10^6 PFU/mL
Parainfluenza virus 2	1×10^6 PFU/mL
Parainfluenza virus 3	5.8×10^6 PFU/mL
Parainfluenza virus 4	2.6×10^6 PFU/mL
Haemophilus influenzae	5.2×10^6 CFU/mL
Streptococcus pyogenes	3.6×10^6 CFU/mL

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Streptococcus pneumoniae	4.2×10^6 CFU/mL
Candida albicans	1×10^7 CFU/mL
Bordetella pertussis	1×10^4 bacteria/mL
Mycoplasma pneumoniae	1.2×10^6 CFU/mL
Chlamydia pneumoniae	2.3×10^6 IFU/mL
Legionella pneumophila	1×10^4 bacteria/mL

INTERFERING SUBSTANCE

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated with the Romed Coronavirus Ag Rapid Test Cassette (Swab) at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Human blood (EDTA anticoagulated)	20% (v/v)
Mucin	5 mg/mL
Oseltamivir phosphate	5 mg/mL
Ribavirin	5 mg/mL
Levofloxacin	5 mg/mL
Azithromycin	5 mg/mL
Meropenem	5 mg/mL
Tobramycin	2 mg/mL
Phenylephrine	20% (v/v)
Oxymetazoline	20% (v/v)
0.9% sodium chloride	20% (v/v)
A natural soothing ALKALOL	20% (v/v)
Beclomethasone	20% (v/v)
Hexadecadrol	20% (v/v)
Flunisolide	20% (v/v)
Triamcinolone	20% (v/v)
Budesonide	20% (v/v)
Mometasone	20% (v/v)
Fluticasone	20% (v/v)
Fluticasone propionate	20% (v/v)

Wilnis, 4 November 2020
For: VAN OOSTVEEN MEDICAL B.V. – ROMED – HOLLAND

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