BIOMEX

Clinical Performance Study Report - CPSR 2021_58

AESKU.RAPID SARS-CoV-2 Rapid Test

REF: 840001E, 840003E, 840005E

Analytical/diagnostic specificity

Diagnostic sensitivity

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Content

1 Purpose of the Study

The objective of this performance study is to establish the sensitivity and specificity of the Aesku SARS-CoV-2 Antigen Rapid Test and to provide data to demonstrate the product is safe and effective for its intended use. The data obtained will be used in the application for certification.

2 Sponsor – investigation – study coordination

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3 Scope

3.1 Objectives

The objective of this performance study was to establish the diagnostic sensitivity and diagnostic and analytical specificity of the AESKU.RAPID SARS-CoV-2 Rapid Test Kit in order to meet the Medical Device Coordination Group Document MDCG 2021-21 "Guidance on performance evaluation of SARS-CoV-2 *in vitro* diagnostic medical devices " of the Medical Device Coordination Group dated August 2021.

Samples included:

- 157 persons with COVID-19 symptoms within seven days after onset of symptoms.
  The collection of the swabs was carried out in Germany with European subjects, usually the samples have been collected in the patients' home environment. No samples have been collected in hospitals.
  For this study nasal swabs have been used. A dry frozen swab was extracted in extraction buffer of the antigen test, the antigen test was performed and with the remaining volume of the extraction the PCR was performed. This method ensures that the antigen-test and the PCR could be carried out of exactly the same sample.
  The initial diagnosis of each patient was performed with a nasopharyngeal or oropharyngeal swab.
- Among the positive samples, genetic variants shall be considered. A total of five genetic variants will be evaluated in the study (Wuhan (wild type), alpha, beta, gamma and delta genetic variants). For each genetic variant 3 different samples will be tested.
- Establishment of a limit of detection, according to CLSI EP17-A2, 3 dilution series of 6 dilutions have been prepared, each dilution was tested in triplicate over 3 days.
- 300 asymptomatic persons without a concrete risk of exposure in the rapid SARS-CoV2 antigen test. The collection of the swabs was carried out in Germany with European subjects.
- 100 negative specimens from hospitalized patients.
- 50 negative specimens of potentially interfering and cross-reactive samples; including virus-positive samples of endemic human coronaviruses 229E, OC43, NL63, influenza A, B, RSV, and other pathogens of respiratory diseases, eligible for differential diagnosis including bacteria present in the sampling area.

3.2 Study Design Type

This retrospective study on frozen dry swab samples from COVID-19 infected and healthy donors is an observational study which aims to establish the analytical/diagnostic specificity and sensitivity of the AESKU.RAPID SARS-CoV-2 Rapid Test Kit (REF: 840001E, 840003E, 840005E).
The swabs for the positive samples have been collected during the infectious phase of COVID-19 infected patients, the swabs of the negative samples have been collected from healthy donors. The swabs for the hospitalized samples have been collected from hospitalized patients in the St. Josephskrankenhaus in Heidelberg (station 3S and 3N, internal medicine).
After collection all swabs (dry swabs) have been immediately stored at ≤-20°C.
As reference method all samples were tested with a RT-PCR system.

3.3 Current state of the art

The following "minimum" acceptance criteria are defined by the MDCG 2021-21 Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices:

Diagnostic sensitivity: >80% (rapid tests);

Diagnostic specificity >98% (rapid tests);

Analytical specificity: no acceptance criteria are applied. However, potential limitations for specificity should be determined.

3.4 Reference Test

An analysis should be performed of the correlation between the antigen -positive/PCR-positive and the antigen-negative/PCR-negative samples with the Ct values of the PCR. The detection rate of the antigen test (e.g. detection rate >90%) should be observed in relation to the ct value. However, it should be noted that the Ct values vary between PCR tests in the case of a given concentration of the target RNA.

3.5 Expected Risk & benefits

There is no risk attributed to the patient since the evaluation is done retrospectively on frozen samples. The results obtained in this study will not be used for patient care decisions.

The risks related to the user have been reduced as far as possible by providing detailed instructions for use with the kits, including warning and precautions for the users and known limitations of the device. Furthermore, the study will be performed by professionals who are qualified and trained for conducting the clinical performance study.

4 Description Device

4.1 Identification

AESKU.RAPID SARS-CoV-2

4.2 Manufacturer if different from the sponsor

Not applicable.

4.3 Intended purpose

The AESKU.RAPID SARS-CoV-2 rapid test is an immunochromatographic sandwich method with two specific antibodies for the qualitative detection of the N-protein antigen in human nasal swab samples. The point-of- care test is designed to detect SARS-CoV-2 N-protein antigens detectable during the acute phase of infection.

4.4 Specimen Type

Nasal swab specimen swab

4.5 Technical and Functional Features

The AESKU.RAPID SARS-CoV-2 rapid test is based on immunochromatographic polymer technology combined with the sandwich principle for the qualitative detection of the nucleocapsid protein antigen in human nasal swab samples. The sample is mixed with colored polymer-labeled SARS-CoV-2 monoclonal antibody 1 in the test device's sample well and chromatographed along the nitrocellulose membrane. If SARS-CoV-2 antigens are present in the sample, they will bind to SARS-CoV-2 antibody 1, and the mixture will bind to immobilized SARS-CoV-2 antibody 2 on the nitrocellulose membrane. The resulting complex of antibody 1, antigen, and antibody 2 forms the colored test line. The test device's control line is coated with secondary antibodies, resulting in a colored result during a standard test procedure.

5 Study Design

5.1 Parameters of clinical performance to be determined

This retrospective study is designed according to the MDCG 2021-21 Guidance on performance evaluation of SARS-CoV-2.

The study focuses on the assessment of the diagnostic sensitivity and diagnostic/analytical specificity of the AESKU.RAPID SARS-CoV-2 for the detection of SARS-CoV-2 antigens when compared to the original diagnostic/known status of the sample and verified using and R-Biopharm RIDA Gene SARS-CoV-2 real-time PCR and Applied Biosystems TaqPath COVID-19 CE-IVD RT-PCR reference results

5.2 Materials Supplied by the manufacturer.

5.2.1 Test Kits and Instructions for Use

Sufficient kits of the AESKU.RAPID SARS-CoV-2 Rapid Test together with the Instructions for Use have been supplied free of charge to carry out the entire evaluation.
AESKU.RAPID SARS-CoV-2 Rapid Test:

Lot number:	**Expiry date:**
P202010005	04/2020
P202011003	05/2020
P202104001	09/2022

5.2.2 Instrument

Not applicable.

5.3 Materials Supplied by the Investigator

5.3.1 Standard laboratory reagents and disposables.

These are supplied by the Investigator and must meet the specifications required to correctly carry out the test procedure.

5.3.2 Equipment/Instrumentation

Nucleic acid extraction was performed with the R-Biopharm RIDA Xtract (REF: PGZ001) and analyzed with the R-Biopharm RIDA Gene SARS-CoV-2 real-time PCR kit (REF: PG6815), with the CFX96 Touch Real-Time PCR Detection System from Bio-Rad Laboratories (Hercules, USA).

R-Biopharm RIDA Xtract Kit used:
Lot number: QL200056 Expiry date: 2022-05

R-Biopharm RIDA Gene SARS-CoV-2 real-time PCR kit used:
Lot number: 26081Z Expiry date: 2023-02

In addition nucleic acid extraction was performed with the MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit (REF: A42352; lots: 01066648; expiraton dates: 17.03.2022) and analyzed with the TaqPath™ COVID-19 CE-IVD RT-PCR Kit (REF: A48067; lot: 2107176; expiration date: 02.07.2022), with the KingFisher Flex instrument and the Quant Studio 5 (ThermoFisher) analyzer.

5.3.3 Samples

The samples used have been collected as dry swabs and are stored at -20°C.

5.4 Study population

According to the MDCG 2021-21 Guidance on performance evaluation of SARS-CoV-2 the following sample numbers must be tested:

Diagnostic sensitivity (positive Specimen):

- 100 NAT positive samples from early infection within the first 7 days after symptom onset; samples should represent naturally occurring viral loads; consideration of genetic variants; consideration of variations in specimen collection and/or specimen handling. Parallel examination of diagnostic PCR tests and antigen tests in at least 100 persons with COVID-19 symptoms within seven days after onset of symptoms

Acceptance criteria: Detection of >80% (rapid tests); relative to SARS-CoV-2-NAT.

Diagnostic specificity (negative Specimen):

- 300 from non-infected individuals

Acceptance criteria: Specificity >98% (rapid tests).

- 100 from hospitalized patients

Required patient information:

- Collection date of swab
- Age, sex
- Date of onset of symptoms (if present)/time of infection
- Severity of symptoms (if known)
- Date of initial PCR testing (when patient was tested for the first time)
- Initial PCR result (i.e. positive or negative)

Analytical specificity

- *Potentially cross-reactive markers:*
  50 potentially interfering and cross-reactive samples: including virus-positive samples of endemic human coronaviruses 229E, OC43, NL63, HKU1; influenza A, B, RSV, and other pathogens of respiratory diseases, eligible for differential diagnosis; including bacteria present in the sampling area
- cross-reactive samples (samples of related human coronaviruses)
  - *human coronavirus 229E*
  - *human coronavirus OC43*
  - *human coronavirus NL63*
  - *MERS coronavirus*
- Potentially interfering substances (pathogen-positive samples in which the pathogen can cause analogous symptoms or could interfere with the test principle):
  - *Adenovirus Type 01 (Species C)*
  - *Adenovirus Type 02 (Species C)*
  - *Adenovirus Type 11 (Species B)*
  - *Enterovirus Type 68 (2014 Isolate)*
  - *Human Metapneumovirus (hMPV) 16 Type A1*
  - *Parainfluenza Virus Type 1*
  - *Parainfluenza Virus Type 2*
  - *Parainfluenza Virus Type 2*
  - *Parainfluenza Virus Type 3*
  - *Parainfluenza Virus Type 4B*
  - *Respiratory Syncytial Virus Type A (Isolate: 2006)*
  - *Influenza A H3N2 (HK/8/68)*
  - *Influenza A H1N1 (Brisbane/59/07)*
  - *Influenza A H1N1pdm (Canada/6294/09)*
  - *Influenza B Virus (Strain: Washington/02/19)*
  - *Influenza B (Texas/6/11)*
  - *Influenza B (Alabama/2/17)*
  - *Staphylococcus epidermidis*

- *Staphylococcus epidermidis*
- *Staphylococcus epidermidis*
- *Bordetella pertussis*
- *Bordetella pertussis*
- *Legionalle pneumophila*
- *Legionalle pneumophila*
- *Streptococcus pyogenes*
- *Streptococcus pyogenes*
- *Streptococcus pyogenes*
- *Haemophilus influenzae*
- *Haemophilus influenzae*
- *Haemophilus influenzae*
- *Mycobacterium tuberculosis*
- *Streptococcus pneumoniae*
- *Streptococcus pneumoniae*
- *Streptococcus pneumoniae*
- *Mycoplasma pneumoniae*
- *Mycoplasma pneumoniae*
- *Candida albicans*
- *Candida albicans*
- *Candida albicans*
- *Pseudomonas aeruginosa*
- *Pseudomonas aeruginosa*
- *Pseudomonas aeruginosa*
- *Streptococcus salivarius*
- *Streptococcus salivarius*

Analytical sensitivity

Establishment of a limit of detection according to CLSI EP17-A2:

- Positive SARS-CoV-2 cell culture supernatant.
- Three independent 3-fold dilution series of the cell culture supernatant have been prepared in the assay's sample buffer.
- Each dilution series (3 series) was tested in parallel with the AESKU.RAPID SARS-CoV-2 Rapid Test Kit and the comparative method [RT-PCR] for 3 days with 3 replicates per day to obtain 27 replicates per dilution in total on each assay.

Acceptance criteria:

For each dilution tested, the proportion of positive test results on the total number of replicates and corresponding hit rate ratios will be defined. LoD will be reported as the dilution for which the assay is positive in 95% of the cases.

An analysis should be performed of the correlation between the antigen -positive/PCR-positive and the antigen-negative/PCR-negative samples with the Ct values of the PCR. In addition, the PCR protocol should be described. The mean Ct value should be determined for the antigen-positive samples. In another evaluation, the detection rate of the antigen test (e.g. detection rate >90%) should be observed in relation to the ct value. However, it should again be noted that the Ct values vary between PCR tests in the case of a given concentration of the target RNA.

5.5 Test procedure

Throughout the evaluation, all sample swabs were extracted in the AESKU.RAPID SARS-CoV-2 Rapid Test extraction buffer as described in the IFU of the rapid test. 3- drops of the specimen (approximately 145 µL) were added to the sample well of the test cassette. Results obtained with the rapid test device were visually read-out by two operators between 15 and 20 minutes after the

sample had been applied onto the test cassette. Digital images were taken from used rapid test cassettes after visual read-out.

The RNA was extracted from 300 µl of the remaining liquid with the r-biopharm RIDA Xtract (REF:PGZ001) lot QL2000033, expiry date April 2022 and analyzed with the r-biopharm RIDA Gene SARS-CoV-2 RUO real-time PCR kit (REF:PG6815 RUO) lot 24110N, expiry date March 2022. The instruction of the PCR kit manufacturer was followed with the exception that 300 µl instead of 400 µl of the solution was used for the extraction due to the limited volume in the specimen processing tube.

The PCR analysis was performed in duplicate for all samples that were collected from infected donors. The PCR result was interpreted as positive if both replicates were positive. Real-time RT-PCR analysis was performed in singlicate analysis for all samples that were collected from healthy donors.

6 Data management

Data management entails the planning for the creation, identification, verification, storage, transfer and archiving of data pertinent to the study, by means of the format of the study records, as well as associated responsibilities.

6.1 Data and results recording

The sample information and reference results of the samples are recorded in the Study Record Forms (SRFs) in excel.
SRF completion:

- Each item on the SRF must be completed
- No blanks can be left
- If an item is missing or not available, the entry shall be completed with 'NA'

Upon completion of the SRF, the study coordinator reviewed the recorded data for completeness, accuracy and legibility.
To protect the subject or patient's privacy, no personal data shall appear anywhere on the SRF.

The data obtained with the AESKU.RAPID SARS-CoV-2 Rapid Test are recorded on a sample sheet and as digital images taken within the prescribed time frame. The results are transferred to the SRF.

The completed SRF with sample information and reference results will be made available upon finalization of the testing.

All data will be filed both as a hard copy and in electronic files by Biomex. Data will be stored for a time period as defined in the lab's QMS procedures but at least 5 years. All laboratory results are strictly confidential.

The AESKU.RAPID SARS-CoV-2 Rapid Test results are for performance evaluation only and must not be used for diagnostic purposes.

6.2 Data analysis

The following analyses have been performed:

The diagnostic sensitivity of the AESKU.RAPID SARS-CoV-2 Rapid Test was calculated as the number of identified positive samples compared to the total number of positive samples tested in parallel on the reference RT-PCR-assay in correlation to the Ct-value.

The diagnostic specificity of the AESKU.RAPID SARS-CoV-2 Rapid Test was calculated as the number of negative samples on the total number of negative samples tested with the RT-PCR-test.

The diagnostic sensitivities and specificities are reported together with a 2-sided 95% confidence interval.

7 Results

7.1 Definitions

True positive sample: sample that was determined positive both using the AESKU.RAPID SARS-CoV-2 Rapid Test and by RT-PCR.

False positive sample: sample that was determined positive using the AESKU.RAPID SARS-CoV-2 Rapid Test, but negative by RT-PCR.

True negative sample: sample that was determined negative both using the AESKU.RAPID SARS-CoV-2 Rapid Test and by RT-PCR.

False negative sample: sample that was determined negative using the AESKU.RAPID SARS-CoV-2 Rapid Test but positive by RT-PCR.

Specificity (%): # true negative samples/(# true negative samples + # false positive samples) x 100

Sensitivity (%): # true positive samples/(# true positive samples + # false negative samples) x 100

7.2 Diagnostic sensitivity

In total 148 anterior nasal swabs and 19 throat swabs from donors with known SARS-CoV-2 infection were tested with the AESKU.RAPID SARS-CoV-2 Rapid Test.

Sex, age and symptoms of the donors as well as date of onset of symptoms were known. The date of infection was presumed from indications by the donor. Date of swab collections were documented (see annex "SRF Main Evaluation AESKU.RAPID SARS-CoV-2 Rapid Test").

Analytical Results with correlation to Ct-values of the positive samples:

Ct value	Number of Samples	Number of true positive Rapid Test Samples	Number of false negative Rapid Test Samples	Sensitivity of AESKU.RAPID SARS-CoV-2 Rapid Test (CI)
≤ 30	109	109	0	100 % (96.60 - 100)
≤ 32	140	136	4	97.14 % (92.88 - 98.88)
≤ 34	179	165	14	92.18 % (87.30 - 95.28)
≤ 36	204	179	25	87.75 % (82.54 – 91.56)

The correlation between the Ct-values of the analyzed samples and the sensitivity reveals a sensitivity of 97.14 % for samples with a Ct-value of up to 32. Even samples with a higher Ct value up to 36 in the real-time RT-PCR and consequently less viral RNA copies as well as viral antigen in the samples are in compliance with the MDCG guideline with 87.75 %.

At least 22 positive samples out of the 204 have been from patients with the Delta variant of SARS-CoV-2 (lineage B.1.617.2). All 22 samples have been detected positive with the AESKU.RAPID SARS-CoV-2 Rapid Tes, indicating that the Delta variant is detected by this test with a high sensitivity.

33 positive samples out of the 204 have been from patients with the Omicron variant (lineage B.1.1.529). All 3 samples have been detected positive with the AESKU.RAPID SARS-CoV-2 Rapid Tes, so that one can conclude that this variant is also detected by this test with a very high sensitivity.

7.3 Diagnostic specificity

7.3.1 Swabs from healthy donors

325 nasal swabs from healthy donors: Sex, age and date of sample collection were known (see annex "SRF Main Evaluation AESKU.RAPID SARS-CoV-2 Rapid Test").

Analytical Results with correlation to Ct-values of the negative samples:

Number of Samples	Number of true neg. Rapid Test Samples	Number of false positive Rapid Test Samples	Sensitivity of AESKU.RAPID SARS-CoV-2 Rapid Test (CI)
325	323	2	99,38 % (97,78 – 99.83)

Diagnostic Specificity of AESKU.RAPID SARS-CoV-2 Rapid Test: 99,38 % (323/325), Wilson 95% CI: 97,78 – 99.83 %

Analytical Results (Total Accuracy) for all samples with PCR result either negative or positive with a Ct value of ≤ 32 in this study:

		RT-PCR		
		positive	negative	Total
AESKU.RAPID SARS-CoV-2 Rapid Test	positive	136	2	138
	negative	4	323	327
	total	140	325	465

Total accuracy of AESKU.RAPID SARS-CoV-2 Rapid Test: 98.71 % (459/465), CI: 97.21-99,41%

Sensitivity of AESKU.RAPID SARS-CoV-2 Rapid Test (Ct ≤32): 97.14 % (136/140), CI: 92.88 - 98.88 %

Specificity of AESKU.RAPID SARS-CoV-2 Rapid Test: 99,38 % (323/325), Wilson 95% CI: 97,78 – 99.83

7.3.2 Swabs from hospitalized patients

100 nasal swabs from hospitalized patients: Sex, age and date of sample collection were known (see annex "SRF Main Evaluation AESKU.RAPID SARS-CoV-2 Rapid Test").

Number of Samples	Number of true neg. Rapid Test Samples	Number of false positive Rapid Test Samples	Sensitivity of AESKU.RAPID SARS-CoV-2 Rapid Test (CI)
100	100	0	100 % (96.30- 100)

7.4 Analytical specificity

7.4.1 Establishment of a limit of detection:

Three independent 6-fold dilution series of the cell culture supernatant have been prepared in the assay's sample buffer.

Each dilution series (3 series) of 6 different dilutions was tested in parallel with the AESKU.RAPID SARS-CoV-2 Rapid Test Kit and the comparative method [RT-PCR] for 3 days with 3 replicates per day to obtain 27 replicates per dilution in total on each assay.

Sample	Percentage/Ct-value of positive samples						Total percentage/ Ct-values over all days and all replicates	
	Day 1		Day 2		Day 3			
	Ag-Test	PCR	Ag-Test	PCR	Ag-Test	PCR	Ag-Test	PCR
Dilution 1	100 %		100 %		100 %		100 %	100 %
Dilution 2	100 %		100 %		100 %		100 %	100 %
Dilution 3	100 %		100 %		100 %		100 %	100 %
Dilution 4	100 %		100 %		100 %		100 %	100 %
Dilution 5	100 %		100 %		88.8 %		100 %	96.3%
Dilution 6	0 %		33.3 %		0 %		0 %	11.1%

PCR-data to be submitted asap.

7.4.2 Croos reactants/interfering substances

The following inactivated viruses, bacteria and fungi were tested in triplicate with the AESKU.RAPID SARS-CoV-2 Rapid Test:

Cross reactant/interferant analyte	Strain	Titer ($TCID_{50}$)	Concentration tested PFU/ml "
Coronavirus	229E		1.52×10^5
Coronavirus	NL63	$4,68 \times 10^4$	$3.23\ 68 \times 10^4$
Coronavirus	OC43	3.80×10^6	1.064×10^5
MERS-CoV	Florida/USA-2_Saudi Arabia_2014	$1,17 \times 10^5$	0.8 x 105
Adenovirus Type 01 (Species C)		3.80×10^6	1.064 x 105
Adenovirus Type 02 (Species C)		1.05×10^6	1.470 x 105
Adenovirus Type 118 (Species B)		1.02×10^8	1.020 x 105
Enterovirus Type 68 (2014 Isolate)		1.05×10^6	1.470 x 105
Human Metapneumovirus (hMPV) 16 Type A1		3.80×10^6	1.064 x 105
Parainfluenza Virus Type 1		1.26×10^6	1.764 x 105
Parainfluenza Virus Type 2		1.51×10^6	1.057 x 105
Parainfluenza Virus Type 2		1.26×10^6	1.764 x 105
Parainfluenza Virus Type 3		3.39×10^7	1.187 x 105
Parainfluenza Virus Type 4B		3.80×10^6	1.064 x 105
Respiratory Syncytial Virus Type A	Isolate: 2006	1.05×10^6	1.470 x 105
Influenza A H3N2	HK/8/68	1.51×10^6	1.057 x 105
Influenza A H1N1	Brisbane/59/07	1.51×10^6	1.057 x 105
Influenza A H1N1pdm	Canada/6294/09	4.57×10^6	1.066 x 105
Influenza B Virus	Washington/02/19	1.26×10^6	1.764 x 105
Influenza B	Texas/6/11	1.26×10^6	1.764 x 105
Influenza B	Alabama/2/17	3.16×10^6	1.106 x 105
Staphylococcus epidermidis		4.90×10^{10}	3.380 x 108
Staphylococcus epidermidis		5.10×10^{10}	3.520 x 108
Staphylococcus epidermidis		6.30×10^{10}	4.350 x 108
Bordetella pertussis		2.71×10^{10}	x 108

Bordetella pertussis		2.02 x10^{10}	1.870 x 108
Legionalle pneumophila		4.50 x10^{10}	1.390 x 108
Legionalle pneumophila		1.17 x10^{10}	3.110 x 107
Streptococcus pyogenes		1.37 x10^{9}	9.450 x106
Streptococcus pyogenes		9.30 x10^{8}	6.420 x106
Streptococcus pyogenes		1.08 x10^{9}	7.450 x106
Haemophilus influenzae		7.77 x10^{8}	5.360 x106
Haemophilus influenzae		1.41 x10^{9}	9.730 x106
Haemophilus influenzae		1.23 x10^{9}	8.490 x106
Mycobacterium tuberculosis		4.69 x10^{9}	3.240 x107
Streptococcus pneumoniae		4.05 x10^{9}	2.790 x107
Streptococcus pneumoniae		3.80 x10^{8}	2.620 x107
Streptococcus pneumoniae		2.70 x10^{9}	1.860 x107
Mycoplasma pneumoniae		>10^6 cells/ml	>10^6 cells/ml
Mycoplasma pneumoniae		>10^6 cells/ml	>10^6 cells/ml
Candida albicans		6.53 x10^{9}	4.510 x107
Candida albicans		2.39 x10^{9}	1.650 x107
Candida albicans		2.55 x10^{9}	1.760 x107
Pseudomonas aeruginosa		1.90 x10^{10}	1.310 x108
Pseudomonas aeruginosa		5.70 x10^{10}	3.930 x108
Pseudomonas aeruginosa		5.17 x10^{10}	3.570 x108
Streptococcus salivarius		7.89 x10^{9}	5.440 x107
Streptococcus salivarius		7.37 x10^{9}	5.090 x107

The $TCID_{50}$ value is converted to plaque forming units by the equation 0.69 PFU = 1 $TCID_{50}$. Example: a $TCID_{50}$ value of 1,15 x 10^3 corresponds to 794 PFU.

All dilutions tested with the AESKU.RAPID SARS-CoV-2 Rapid Test were found to be negative.

8 Conclusion

The specificity and sensitivity of the AESKU.RAPID SARS-CoV-2 Antigen Rapid Test Kit was evaluated in this study with 604 samples collected as nasal or throat swabs. All samples were tested in parallel with the AESKU.RAPID SARS-CoV-2 Antigen Rapid Test Kit and a real-time RT-PCR assay. Samples with a Ct value below 32 were selected for the calculation of the sensitivity of the AESKU.RAPID SARS-CoV-2 Antigen Rapid Test Kit.

The specificity of the AESKU.RAPID SARS-CoV-2 Antigen Rapid Test Kit calculated from results of all samples was 99.38.%, the sensitivity calculated from results of samples with a Ct-value less than 32 (140 samples) was 97.14 % (95% CI: 92.88 - 98.88 %). As expected, the sensitivity decreases by including samples with higher Ct value. Thus, by including all samples with a Ct value of or below 36 (204 samples) the sensitivity is calculated as 87.75 % (95% CI: 82.54 – 91.56%), which is still a very high sensitivity.

No cross-reactivity was detected with various tested viruses in the AESKU.RAPID SARS-CoV-2 Rapid Test.

No cross-reactivity was detected with the hospitalized samples in the AESKU.RAPID SARS-CoV-2 Rapid Test.

In conclusion, the results from this study confirm that the AESKU.RAPID SARS-CoV-2 Rapid Test can be used for the qualitative detection of antigen from SARS-CoV-2 in human nasal swabs with a very high sensitivity and specificity.

9 Bibliography

- EU Regulation 2017/746 on in vitro Diagnostic Medical Devices
- Minimum criteria for Rapid SARS-CoV-2 Antigen Tests Pursuant to Section 1 para 1 Sentence 1 TestVO (Statutory Test Regulation): Rapid Antigen Tests " of the Paul-Ehrlich-Institut (PEI) dated 15.01.2021).
- Medical Device Coordination Group Document MDCG 2021-21 "Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices" of the Medical Device Coordination Group dated August 2021
- ISO 20916 in vitro Diagnostic Medical Devices – Clinical Performance Studies using specimens form human subjects – Good Study Practices
- EU Guidance on the management of clinical trials during the COVID-19 pandemic version 3. April 2020.
- European Commission, Working document of Commission services – Current performance of COVID-19 test methods and devices and proposed performance criteria, 16 April 2020

10 Annexes

Annex I	SRF Main Evaluation AESKU.RAPID SARS-CoV-2 Rapid Test
Annex II	Pictures of positive samples
Annex III	Pictures of negative samples
Annex VI	Pictures of cross reactive samples
Annex V	Pictures of hospitalized samples

11 Approval

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Approval

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Date: 15.01.2022	Signature:
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Change management

Document name	Document version	Date of creation	Change labelling	Change description
CPSR AESKU_SARS-CoV-2 Antigen Rapid Test_2021-58	V01	19.10.2021	-	-
CPSR AESKU_SARS-CoV-2 Antigen Rapid Test_2021-58 V002	V02	30.11.2021	Background of the text, grey color ~~Strikethrough~~	Updated numbers after testing additional 6 Hospitalized samples and additional 30 negative samples from healthy donors to reach MDCG Guidelines.
CPSR AESKU_SARS-CoV-2 Antigen Rapid Test_2021-58 V003	V03	14.01.2022		Updated numbers of diagnostic sensitivity after testing additional 15 Delta-variant and 33 Omicron-variant positive samples