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Report of two clinical performance studies of KaiBiLi COVID-19 Antigen Pro in comparison with real-time RT-PCR methods

1. Information about the trial

Trial site:		Trial I	Novamedik Bioresearch laboratory, Novamedik Bioresearch BV, Zeewinde 3-119738AM Groningen, Netherlands.
		Trial II	Locus Medicus Medical SA 246 Mesogeion Ave.155 61 Holargos, Athens, Greece
Lead Investigator, Responsible Person of the investigation:			Reuben Weng Hangzhou Genesis Biodetection & Biocontrol Co., LTD
Period of Testing:	Trial I	Start date	01/03/2021
		End date	15/03/2021
	Trial II	Start date	14/12/2021
		End date	08/01/2022
Product evaluated	Trial I	Product name	KaiBiLi COVID-19 Antigen Pro
		Representative product	Production unit N° batch : GP210101P
	Trial II	Product name	KaiBiLi COVID-19 Antigen Pro
		Representative product	Production unit N° batch : LB21110202
Comparator(s) Method(s)	Trial I	Brief description of the comparison method (s)	Roche LC 480II RT-PCR test Covid-19 Tellgen™ (Shanghai Tellgen Corporation) Cartridge RT-PCR system were used as double control.
	Trial II	Brief description of the comparison method(s)	Sacace™ SARS-CoV-2 Real-TM (REF：V435-100FRT) baring the CE mark, manufactured by Sacace Biotechnologies Srl.

Statistic design

Statistical analysis	Comparison method is the reference one used in the criteria comparison	**Specificity** gives information on the degree of interference due to external events during the analysis. **Sensitivity** gives a degree of agreement between the methods taking into account the number of discordant negative results with the product evaluated.

		Positive predictive value (PPV) gives a degree of agreement between both methods on the positive results obtained with repeated tests. **Negative predictive value (NPV)** gives a degree of agreement between both methods on the negative results obtained with repeated tests. It is the probability that subjects with a negative test truly do not have the disease. **Accuracy** gives an indication on the equivalency/closeness of both methods.
Acceptance criteria	KaiBiLi COVID-19 Antigen Pro will be qualified if the test result can reach 98% for specificity, accuracy, NPV and PPV comparing to RT-PCR results. The statistics is calculated from Mc Nemar's test or Cohen-Kappa. In independent evaluations of unselected subjects, assays should have a sensitivity of 90% or greater for subjects with a Ct < 25.	
Purpose of the study:	Comparative analysis of the performance of the test KaiBiLi COVID-19 Antigen Pro with a molecular approach (real-time RT-PCR)	

2. Sample type tested and collection method

Study Population	Trial I	Comparative test 1: 30 confirmed as PCR positive and 15 confirmed as PCR negative specimens (45 in total) were applied for the comparative test. Comparative test 2: 170 freshly collected specimens from non-symptomatic passengers from several countries and has connecting flight at Amsterdam Airport Schiphol.
	Trial II	483 clinical specimens were collected from individual symptomatic outpatients who have respiratory symptom onset within 7 days in the Locus Medicus Medical SA, Greece. Participants will be prospectively enrolled and tested sequentially and blindly. Both nasal and nasopharyngeal swabs will be collected from each participant by medical professionals. The nasal swab will be tested directly with COVID-19 Antigen Pro rapid test, and the nasopharyngeal swab will be tested with RT-PCR assay for detection of SARS-CoV-2.

Number of samples	Trial I	45+170 (RT-PCR positive：30+70)
	Trial II	483
Collection method	Trial I	Brand of swab：type A-04 of HanHeng. Procedure followed: • Insert sterilized swab into nostril parallel to the palate and leave in place for a few second to absorb secretions. • Immerse the swab in the buffer and rotate the swab 7-10 times, while squeezing the outer walls of the tube against the swab to mix well. • Wipe it out by pressing it on the tube wall to extract all the contents of the swab and insert tightly the dropper on the tube • Invert vertically the test tube and dispense 2 drops of diluted sample into the sample well of the cassette. • Allow reacting **for 15 min** before reading the results in the test cassette and disregard the new ones after 30 minutes. Operators performed the tests without extra training, i.e. a test operator with limited or no training or hands-on experience in conducting laboratory testing.
	Trial II	Brand of swab：type A-01 of HanHeng. Procedure followed: (1) Peel off the foil seal from the prefilled extraction tube. (2) Tear open the swab packaging and gently take out the swab. (3) Nasal Swabbing：Insert nasal swab into one nostril, and the tip should be inserted up to 2.5 cm from the edge of the nostril. Gently rotate the swab 5 times or more against the nasal wall for collecting cells and mucus. Using the same swab, repeat sample collection in the other nostril. (4) Sample Extraction：Insert swab with collected sample into extraction tube containing 0.5 ml of sample extraction buffer. Squeeze the swab several times by compressing the outside walls of the tube end against the swab to mix well. Finally squeeze the swab to make most of the solution stays in the extraction tube and remove the swab. Use extraction solution as test sample.

		(5) Remove test device from sealed foil pouch prior to testing and lay flat on workbench. (6) Insert filtered nozzle into the extraction tube with test sample. (7) Invert the extraction tube and add 2 drops of test sample into sample well by gently squeezing the extraction tube. (8) Read results at 15 minutes and disregard after 30 minutes. A positive result may be visible at 3 minutes. However, the complete reaction time of 15 minutes is required to confirm a negative result.

3. Trials findings summary (at the end of study)

3.1 Trial 1 analysis of the results

3.1.1 Comparative Test 1：

		RT-PCR		
		Positive	Negative	Total
COVID-19 Antigen Pro	Positive	28	0	28
	Negative	2	15	17
	Total	30	15	45

Statistics	Numerical ratio	Percentage (95% C.I.)
Sensitivity（Positive Percent Agreement）	28/30	93.33% (77.93% ~ 99.18%)
Specificity（Negative Percent Agreement）	15/15	100.00% (78.20%～100.00%)
Positive Predictive Value	28/28	100.00% (87.66%～100.00%)
Negative Predictive Value	15/17	88.24% (63.56% ~ 98.54%)
Accuracy（Overall Percent Agreement）	43/45	95.56% (84.85% ~ 99.46%)
Kappa value: 0.903, p<0.05		

Among the specimens diagnosed by RT-PCR positive result, 30 were tested with a Ct value less than 28, and COVID-19 Antigen Pro detected 28 out of the 30 specimens (93.3%).

3.1.2 Comparative Test 2：

		RT-PCR		
		Positive	Negative	Total
COVID-19 Antigen Pro	Positive	69	2	71
	Negative	1	98	99
	Total	70	100	170

Statistics	Numerical ratio	Percentage (95% C.I.)[1]
Sensitivity （Positive Percent Agreement）	69/70	98.57% (92.30% ~ 99.96%)
Specificity （Negative Percent Agreement）	98/100	98.00% (92.96% ~ 99.76%)
Positive Predictive Value	69/71	97.18% (90.19% ~ 99.66%)
Negative Predictive Value	98/99	98.99% (94.50% ~ 99.97%)
Accuracy （Overall Percent Agreement）	167/170	98.24% (94.93% ~ 99.63%)
Kappa value: 0.964, $p<0.05$		

Among the specimens diagnosed by RT-PCR positive result, 70 were tested with a Ct value less than 30, and COVID-19 Antigen Pro detected 69 out of the 70 specimens (98.6%).

3.1.3 Overall results：

		RT-PCR		
		Positive	Negative	Total
COVID-19 Antigen Pro	Positive	97	2	99
	Negative	3	113	116
	Total	100	115	215

Statistics	Numerical ratio	Percentage (95% C.I.)[1]
Sensitivity （Positive Percent Agreement）	97/100	97.00% (91.48% ~ 99.38%)
Specificity （Negative Percent Agreement）	113/115	98.26% (93.86% ~ 99.79%)
Positive Predictive Value	97/99	97.98% (92.89% ~ 99.75%)

Negative Predictive Value	113/116	97.41% (92.63% ~ 99.46%)
Accuracy （Overall Percent Agreement）	210/215	97.67% (94.66% ~ 99.24%)

Kappa value: 0.953, p<0.05

3.2 Trial 2 analysis of the results

		RT-PCR		
		Positive	Negative	Total
COVID-19 Antigen Pro	Positive	118	0	118
	Negative	5	360	365
	Total	123	360	483

Statistics	Numerical ratio	Percentage (95% C.I.)
Sensitivity (Positive Percent Agreement)	118/123	95.93% (90.77% ~ 98.67%)
Specificity (Negative Percent Agreement)	360/360	100.00% (98.98% ~ 100.00%)
Positive Predictive Value	118/118	100.00% (96.92% ~ 100.00%)
Negative Predictive Value	360/365	98.63% (96.83% ~ 99.55%)
Accuracy (Overall Percent Agreement)	478/483	98.96% (97.60% ~ 99.66%)

Kappa value: 0.9724, p<0.05

Among the specimens diagnosed by RT-PCR positive result, 110 were tested with a Ct value less than 30, and COVID-19 Antigen Pro demonstrate positive result for all 110 specimens (100%).

4. Conclusions

Trial I	According to the result of the evaluation performed in Netherlands, KaiBiLi™ COVID-19 Antigen Pro demonstrated 97.0% positive agreement and 98.26% negative agreement compared to ROCH COVID-19 RT-PCR detection kit. Applying the test result of ROCH LC 480II COVID-19 RT-PCR as the reference, the KaiBiLi™ COVID-19 Antigen Pro manufactured by Hangzhou Genesis Biodetection& Biocontrol Co., Ltd demonstrated 97.0% positive percent agreement, 98.26% negative percent agreement, 97.98% positive predictive value, 97.41% negative predictive value, and overall percent agreement of 97.67% for nasopharyngeal swabbing specimen. For the criteria that unselected participants assays should have a sensitivity of 90% or greater for subjects with a Ct value 25, KaiBiLi™ COVID-19 Antigen Pro shows great performance as the sensitivity of 93.3% for specimens with PCR Ct value under 28 in comparative test 1, and 98.6% for specimens with PCR Ct value under 30 in comparative test 2.
Trial II	The 483 clinical specimens were collected from individual symptomatic patients in the Locus Medicus Medical SA, Greece. Among the 483 specimens, 123 were confirmed positive with SacaceTM SARS-CoV-2 RT-PCR, and COVID-19 Antigen Pro detected 118 out of the 123 specimens. The diagnostic sensitivity of COVID-19 Antigen Pro is 95.9%. COVID-19 Antigen Pro revealed parallel negative result to RT-PCR testing for the remaining 360 clinical specimens and demonstrated 100% in diagnostic specificity. Accuracy：98.96%；Kappa value：0.97. Indicates good consistency. For subjects with a Ct value 25 in this trial, KaiBiLi™ COVID-19 Antigen Pro reached 100% sensitivity (110/110). The KaiBiLi™ COVID-19 Antigen Pro manufactured by Hangzhou Genesis Biodetection& Biocontrol Co., Ltd revealed good and consistent result comparing to the reference RT-PCR methodology.