BZ COVID-19 Ag Test

BioZentech

Company Profile

2015-2016

Y2015

- Established BioZentech Co, LTD.

Y2016

- Medical Equipment Manufacturer approved
- Microscanner ver1.0 approved by KFDA
- Grant from Korea University Guro Hospital IVD support center
- MOU agreement with Korea University Guro Hospital IVD support center to develop IVD equipment
- Designated Industry-Academy Cooperation technique development project of Small and Medium Business Administration

2017-2018

Y2017

- Technology transfer agreement with Korea Univ.(Control of Micro & Nano particles)
- CSF Counter approved by Korea FDA
- CSF Stain Solution approved by Korea FDA
- Join in Research support project with Korea Medical center.
- MOU with R-Biopharm for Europe market

Y2018

- Annex research institute approved
- Selection of government project by Small and Medium Business Administration, Grant total US$400K

2019-2020

Y2019

- President's Commendation at 12th Korean Medical Device Day
- MOU contract with Korea University Industry-Academy Cooperation (TB/NTM diagnosis)

Y2020

- BZ QPCR COVID-19 kit approved by Korea FDA and CE-IVD certificate diagnostic kit (April)
- Attract investment – Korea Technology Finance Corporation, Kibo) (June)
- BZ COVID-19 IgM/IgG approved by Korea FDA (July)
- BZ COVID -19 IgM/IgG approved by CE- IVD certificate (August)
- BZ IsoMDx COVID-19 kit approved by Korea FDA and CE-IVD Certificate(August)

R&D Oriented Company OK

Innovative R&D and Technology

- R&D members accounts 75%
- Detection technology for Super-low cell concentration & Pathogen
- Best-In-Class of On-site quantitative testing system
- Fully automated all-in-one molecular isothermal amplification technology, 1st in Korea
- Patent registration (4)

Certificate

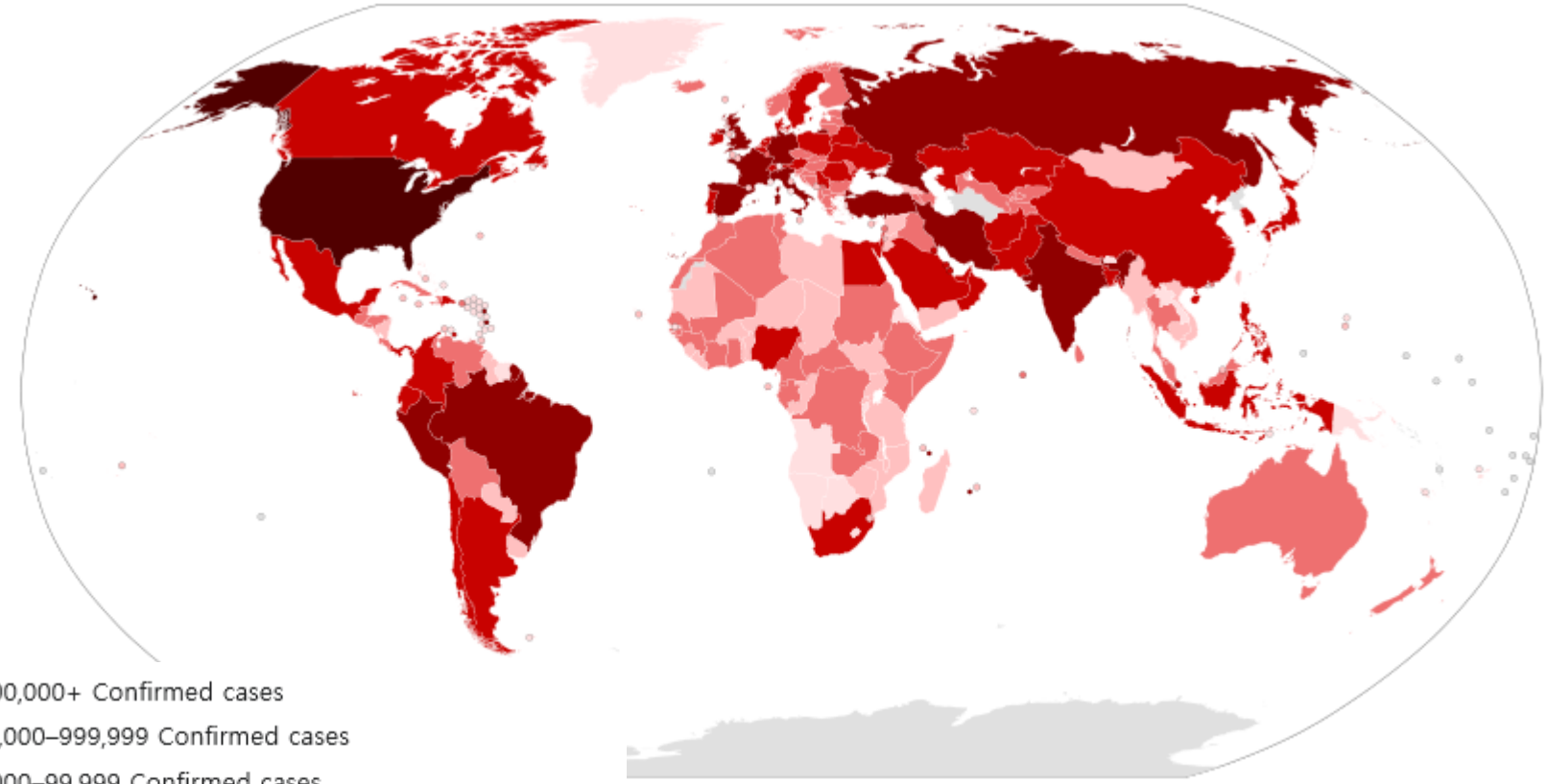
Manufacturing
under KGMP and ISO13485

Coronavirus, what is COVID-19 ?

- **Enveloped viruses with positive single-stranded RNA with a nucleocapsid of helical symmetry**
- **Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is the name given to the 2019 novel coronavirus COVID-19**
- **SARS-CoV-2 is a new strain of coronavirus that has not been previously identified in humans**
- **Genetically distinct from**
  - SARS-CoV-1 (Severe Acute Respiratory Syndrome Coronavirus-1), sequence homology apprx. 77.5%
  - MERS-CoV (Middle East Respiratory Syndrome coronavirus), sequence homology apprx. 50%
- **The first case of COVID-19 was reported in Wuhan city, Hubei Province, China in December 2019**
- **Symptom : Fever, dry cough, tiredness, muscular pain, difficulty breathing, severe pneumonia**
- **Incubation period : 2 – 14 days**
- **No vaccines or treatments up to date**

COVID-19 case map (based on 30th May 2020)

Over 6M of COVID-19 infection cases in world-wide have been reported in 215 countries, and expected that the pandemic would continue for a year or more.



BZ COVID-19 Ag Test

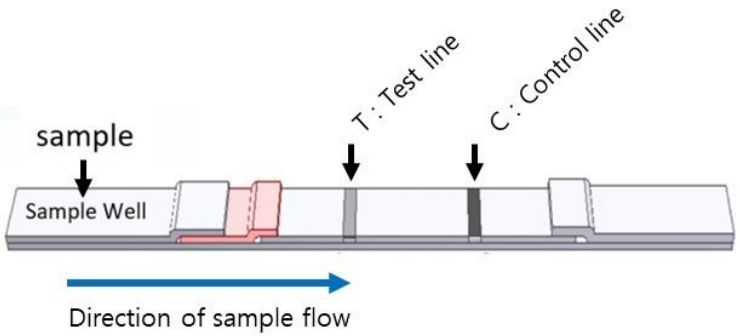
BZ COVID-19 Ag Test is a rapid, qualitative and convenient immunochromatographic in vitro assay for the differential detection of SARS-CoV-2 virus antigen in human nasal swab, nasopharyngeal swab samples.

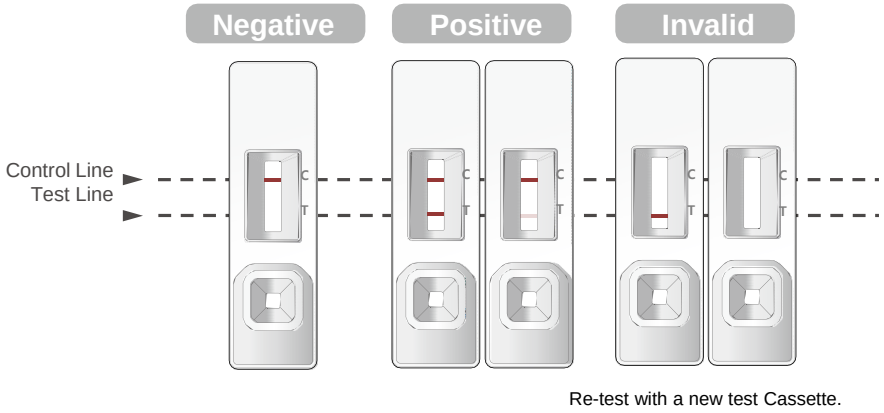
- Immunochromatographic method using antibodies of SARS-CoV-2
- Detection Antigen : SARS-CoV-2 virus antigen
- Limit of Detection : 1.6 x 10^3 $TCID_{50}$/mL
- Reaction Time : 20 mins

Components (50 T/Kit)	Amount
Test Cassette with Desiccant	50 EA
Reagent Solution	20 mL
Reagent Tube	50 EA
Sterilized Nasal swab	50 EA
Instruction for Use	

BZ COVID-19 Ag Test

- Detection of SARS-CoV-2 virus using immunochromatographic method
- Superior detection performance with a reaction time shorter than 20mins
- No specific equipment needed





Re-test with a new test Cassette.

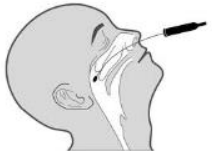
BZ
COVID-19
Ag Test

Work Procedure

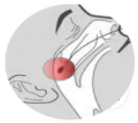
Reaction time shorter than 20mins improving laboratory efficiency

SPECIMEN COLLECTION

1. Insert a sterile swab into the nostril of the patient, reaching the surface of the posterior nasopharynx.



2. Swab over the surface Of the posterior nasopharynx.



3. Withdraw the sterile swab from the nasal cavity.

TEST PROCEDURE

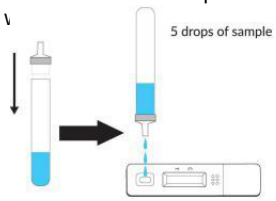
1. Add 300ul reagent solution (approximately 9 drops) into the reagent tube.

2. Add Nasal/Nasopharyngeal swab to the tube with reagent solution.

3. Vigorously rotate and twist the swab against the side of the tube at least 10 times.

4. Squeeze the sides of the tube to obtain as much liquid as possible. Dispose of swab properly.

5. Apply the cap to the tubes with specimen, and hold the tube vertically, add 5 drops (about 120 μL) of the specimen without air bubbles into the sample



Performance Data: Sensitivity

- BZ COVID-19 Ag Test demonstrated high **sensitivity** in a comparative study by a clinical research institute
- Evaluation Criteria(Simplified Signal Intensity Description)

Description	Result	Reactivity Level
Negative, Trace	Negative	None
VW+, W	Positive	Low
1+, 2+ and 3+	Positive	Medium
4+ and 5+	Positive	High

Determination of LoD Test (10-fold serial dilution at Stock conc.)

Strain name	Stock concentration	Diluted concentration			
SARS-Related Coronavirus 2, Isolate USA-USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)	1.6×10^5 $TCID_{50}$/mL	1.6×10^4 $TCID_{50}$/mL	1.6×10^3 $TCID_{50}$/mL	1.6×10^2 $TCID_{50}$/mL	1.6×10 $TCID_{50}$/mL
Dilution ratio (Stock : diluted sample)		1 : 10	1 : 100	1 : 1,000	1 : 10,000

Confirmation of LoD Test (2-fold dilution and 20 repeats test at BEI resources LOD conc.)

Strain name	Stock concentration	Diluted concentration			
SARS-Related Coronavirus 2, Isolate USA-USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)	1.6×10^5 $TCID_{50}$/mL	3.2×10^3 $TCID_{50}$/mL	1.6×10^3 $TCID_{50}$/mL	8×10^2 $TCID_{50}$/mL	4×10^2 $TCID_{50}$/mL
Dilution ratio (Stock : diluted sample)		1 : 50	1 : 100	1 : 200	1 : 400

Performance Data: Sensitivity with specimen

Result

The ten-fold serial dilution test results with three replicates for inactivated SARS-CoV-2 strain diluted sample matrix were presented in the table below:

Strain name	Sample matrix	Virus Serial dilution concentration($TCID_{50}$/mL) (No. of positive /No of replicate)			
		1.6×10^4	1.6×10^3	1.6×10^2	1.6 x 10
SARS-Related Coronavirus 2, Isolate Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)	Negative nasopharyngeal swab	3/3	3/3	1/3	0/3
	Negative Nasal swab	3/3	3/3	1/3	0/3

The two-fold serial dilution test results with 20 replicates at expected LOD conc. for inactivated SARS-CoV-2 strain diluted sample matrix were presented in the table below:

Strain name	Sample matrix	Virus Serial dilution concentration($TCID_{50}$/mL) (No. of positive /No of replicate)			
		3.2×10^3	1.6×10^3	8×10^2	4×10^2
SARS-Related Coronavirus 2, Isolate Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)	Negative nasopharyngeal swab	20/20	20/20	11/20	2/20
	Negative Nasal swab	20/20	20/20	13/20	3/20

Conclusion

SARS-CoV-2 virus panel was tested with BZ COVID-19 Ag Test. The LoD concentration of the virus strain was determined by 3 replicates of serial dilution test. The determined LoD concentration of the virus strain was verified with 20 additional replicates. In this study, LoD of the BZ COVID-19 Ag Test was determined as **1.6×10^3 $TCID_{50}$/mL**.

Performance Data: Cross Reactivity

- **No Cross reactivity is observed for the pathogens showing the similar symptoms**

Panel information (Virus)	Lot #1		Lot #2		Lot #3	
	Antigen : 3x LoD		Antigen : 3x LoD		Antigen : 3x LoD	
	Positive	Negative	Positive	Negative	Positive	Negative
Adenovirus1	3/3	0/3	3/3	0/3	3/3	0/3
Adenovirus7	3/3	0/3	3/3	0/3	3/3	0/3
Enterovirus 71, Tainan/4643/1998	3/3	0/3	3/3	0/3	3/3	0/3
Human coronavirus (OC43)	3/3	0/3	3/3	0/3	3/3	0/3
Human coronavirus (229E)	3/3	0/3	3/3	0/3	3/3	0/3
Human coronavirus (NL63)	3/3	0/3	3/3	0/3	3/3	0/3
Human metapneumovirus (hMPV)	3/3	0/3	3/3	0/3	3/3	0/3
Influenza A/Michigan/45/2015	3/3	0/3	3/3	0/3	3/3	0/3
Influenza B/Wisconsin/01/2010	3/3	0/3	3/3	0/3	3/3	0/3
MERS-Coronavirus, Irradiated Lysate	3/3	0/3	3/3	0/3	3/3	0/3
Parainfluenza virus type 1	3/3	0/3	3/3	0/3	3/3	0/3
Parainfluenza virus type 2	3/3	0/3	3/3	0/3	3/3	0/3
Parainfluenza virus type 3	3/3	0/3	3/3	0/3	3/3	0/3
Parainfluenza virus type 4	3/3	0/3	3/3	0/3	3/3	0/3
Respiratory syncytial virus Type B	3/3	0/3	3/3	0/3	3/3	0/3
Rhinovirus	3/3	0/3	3/3	0/3	3/3	0/3
SARS-Coronavirus	3/3	0/3	3/3	0/3	3/3	0/3
Pooled human nasal wash	3/3	0/3	3/3	0/3	3/3	0/3

Performance Data: Cross Reactivity

- **No Cross reactivity is observed for the pathogens showing the similar symptoms**

Panel information (Bacteria)	Lot #1		Lot #2		Lot #3	
	Antigen : 3x LoD		Antigen : 3x LoD		Antigen : 3x LoD	
	Positive	Negative	Positive	Negative	Positive	Negative
Bodetella pertussis	3/3	0/3	3/3	0/3	3/3	0/3
Candida albicans	3/3	0/3	3/3	0/3	3/3	0/3
Chlamydophila pneumoniae	3/3	0/3	3/3	0/3	3/3	0/3
Haemophilus influenzae	3/3	0/3	3/3	0/3	3/3	0/3
Legionella pneumophila	3/3	0/3	3/3	0/3	3/3	0/3
Mycoplasma pneumoniae	3/3	0/3	3/3	0/3	3/3	0/3
Streptococcus pneumoniae	3/3	0/3	3/3	0/3	3/3	0/3
Streptococcus pyogenes, Group A	3/3	0/3	3/3	0/3	3/3	0/3

- **Conclusion**

All cross-reaction specimens were tested with BZ COVID-19 Ag Test. No cross-reaction was observed. The results demonstrated that BZ COVID-19 Ag Test has good analytical specificity (no have cross-reactivity).

Performance Data: Interference test

- **The performance of the kit is not interfered by the substances of component of specimen and specimen storage buffer**

No.	Potential interfering substances	
1	Acetaminophen	10 mg/mL
2	Acetylsalicylic acid	15 mg/mL
3	Beclomethasone	0.5 mg/mL
4	Chlorpheniramine maleate	5 mg/mL
5	Dextromethorphan HBr	2 mg/mL
6	Diphenhydramine HCl	5 mg/mL
7	Ephedrine HCl	10 mg/mL
8	Guaialcol Glyceryl Ether	20 mg/ml
9	Histamine dihydrochloride	10 mg/mL
10	Mometasone	1 mg/mL
11	Mucin	2%
12	Throat drop (Halls)	15%

No.	Potential interfering substances	
13	Throat drop (Ricola)	15%
14	Throat drop (Zinc)	15%
15	Nasal spray (Afrin)	15%
16	Nasal spray (VicksSinex)	15%
17	Nasal spray (Zicam)	15%
18	Oxymetazoline HCl	10 mg/mL
19	Phenylephrine HCl	50 mg/mL
20	Phenylpropanolamine	20 mg/mL
21	Tobramycin	1 mg/mL
22	Triamcinolone	1 mg/mL
23	Whole blood	5%

Performance Data: Reproducibility

- **There is no bias result between experimenters in different places.**

	Panel	RUN#11(AM)			RUN#2(PM)		
Lot #1~3 DAY 1~5 Operator 1 Site 1	CoV19 Ag	**R1**	**R1**	**R2**	**R3**	**R2**	**R3**
	Positive 3*LoD	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+
	Negative Nashpharyngeal	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0
	Sample buffer	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0

	Panel	RUN#11(AM)			RUN#2(PM)		
Lot #1~3 DAY 1~5 Operator 2 Site 2	CoV19 Ag	**R1**	**R1**	**R2**	**R3**	**R2**	**R3**
	Positive 3*LoD	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+
	Negative Nashpharyngeal	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0
	Sample buffer	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0

※ Test Sample panel : SARS-Related Coronavirus 2, Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071) 3*LoD (4.8 x 10^3 $TCID_{50}$/mL)

Performance Data: Repeatability

- **The Repeatability analysis shows 100% consistent precise result by day, site, operator.**

	Panel	RUN#11(AM)			RUN#2(PM)		
Lot #1 DAY 1~20 Operator 1 Site 1	CoV19 Ag	**R1**	**R1**	**R2**	**R3**	**R2**	**R3**
	Positive 3*LoD	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+
	Negative Nashpharyngeal swab	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0
	Sample buffer	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0

	Panel	RUN#11(AM)			RUN#2(PM)		
Lot #1 DAY 1~20 Operator 2 Site 2	CoV19 Ag	**R1**	**R1**	**R2**	**R3**	**R2**	**R3**
	Positive 3*LoD	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+	4+/2+
	Negative Nashpharyngeal swab	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0
	Sample buffer	4+/0	4+/0	4+/0	4+/0	4+/0	4+/0

※ Test Sample panel : SARS-Related Coronavirus 2, Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071) 3*LoD (4.8 x 10^3 $TCID_{50}$/mL)

Performance Data: Stability (Acceleration test)

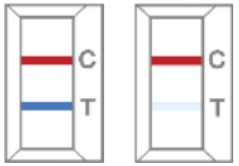
- **The accelerated stability testing during 7 weeks showed the same performance across all samples, We confirmed that the shelf life was 12 months. The acceleration test is ongoing and the stability can Be extended according to subsequent test results.**
- **Result (Stability at 60°C (Lot #1~3))**

Storage condition	Storage duration	Replicate	Test results : C/T	
			Negative	SARS-CoV-2 Positive (3XLoD, 4.8 x 10^3TCID$_{50}$/mL)
			Nasopharyngeal matrix	Nasopharyngeal matrix
60℃	0 week (Initial test)	1st, 2nd, 3rd	4+/0	4+/2+
	1 week	1st, 2nd, 3rd	4+/0	4+/2+
	2 week	1st, 2nd, 3rd	4+/0	4+/2+
	3 week	1st, 2nd, 3rd	4+/0	4+/2+
	4 week	1st, 2nd, 3rd	4+/0	4+/2+
	5 week	1st, 2nd, 3rd	4+/0	4+/2+
	6 week	1st, 2nd, 3rd	4+/0	4+/2+
	7 week	1st, 2nd, 3rd	4+/0	4+/2+

Clinical Evaluation

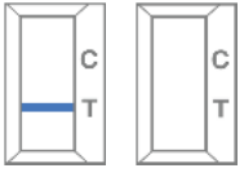
Study design & Materials

- Test device : BZ COVID-19 Ag Test (Biozentech Co., Ltd.)
- Reference device : Allplex 2019-nCoV Assay; approved Emergency Use Authorization from Korea Centers for Disease Control
- Specimens : Nasopharyngeal swab, Sputum, Nasal swab
  - ➢ Sixty positive positive nasopharyngeal samples
  - ➢ One hundred thirty eight negative nasopharyngeal samples
  - ➢ Thirty eight positive sputum samples
  - ➢ Ten negative sputum samples
  - ➢ Two positive nasal samples
  - ➢ Two negative nasal samples
- Data Analysis
  - ➢ Positive : Two distinct lines appear
    - ● One red-colored line next to "C" and one blue-colored line next to "T" indicates COVID-19 positive result.



  - ➢ Negative
    - ● One red-colored line only next to "C" indicates a negative result.

  - ➢ Invalid
    - ● If the red-colored line in the control region "C" is not visible, the result is invalid. Re-run the test one time using the remaining specimen in the extraction vial if an invalid result is obtained during initial testing



Clinical Evaluation

1-1. Summary(Nasopharyngeal swab, sputum, nasal swab test)

Method		Comparator Method (Allplex™ 2019-nCoV Assay)	
		Positive	Negative
BZ COVID-19 Ag Test	Positive	97	1
	Negative	3	149
Total		100	150
PPA(Positive Percent Agreement)		97/100*100=97.0%	
NPA(Negative Percent Agreement)		149/150*100=99.3%	

Conclusion

Based on section 3-1, clinical sensitivity was 97.0% (97/100) and clinical specificity was 99.3% (149/150) comparing Allplex™ 2019-nCoV Assay in nasopharyngeal swab, sputum and nasal swab sample. In conclusion, BZ COVID-19 Ag Test proved effective diagnosis for SARS-CoV-2 infection.

Ordering Information

Cat#: RCOV-2050

Components (50 tests/Kit)	Amount	Storage
Test Cassette with Desiccant	50 EA	2°C~30°C
Reagent Solution	20 mL	2°C~30°C
Reagent Tube	50 EA	
Sterilized Nasal swab	50 EA	
Instruction for Use		

- **A caution for Ordering**

  Ordering q'ty is not less than 16Kit (800tests)

- **Lead-Time**

  The priority of supply is for Korea CDC and governmental sites, so lead-time will be fixed in an order confirmation but could be delayed depending on raw materials' shortage

- **Shipment & storage condition**

  Shipping and storage at room temperature.