RapiGEN INC. CE IVD

BIOCREDIT COVID-19 Ag

SARS-CoV 2 Antigen test

» The first commercialization Black Gold Particle technology In the world (high sensitivity and specificity)

» User friendly Dual Color System (Control line: Red, Test line: Black)

» Rapid Test Time (5~8 Min)

» Simple detection of SARS-CoV2 antigen

Core Technology Black Gold Particle

Differentiated Black Gold Conjugate Technology

Dual Color System

8 minutes is ok!

Digitally signed by Botnaru Andrei
Date: 2021.01.22 10:00:24 EET
Reason: MoldSign Signature
Location: Moldova

BIOCREDIT COVID-19 Ag rapid test kit

Intended Use	Detection of SARS-CoV2 antigen 20
Package	Tests / kit
Storage	1~40℃
Specimen Type	Nasopharynx / Nasopharyngeal
Shelf life	12 months from manufacture
Time to result	date 5~8 minute

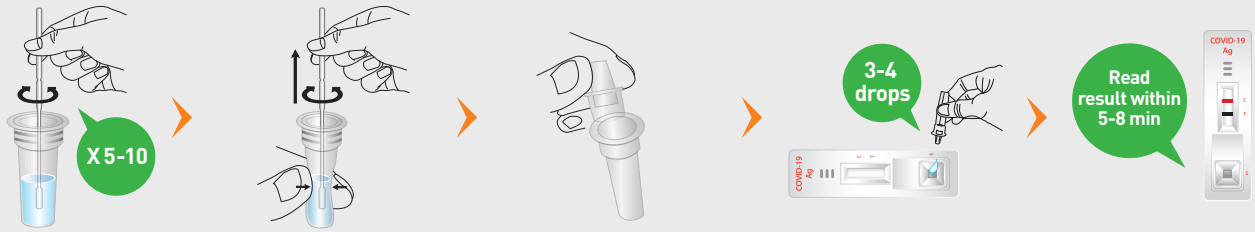
SARS-CoV 2 Antigen test ***BIOCREDIT COVID-19 Ag***

www.rapigen-inc.com

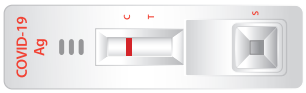
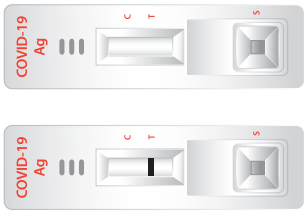
COVID-19 Rapid Diagnostic Test

PROCEDURE

Insert the swab specimen and swirl the swab 5-10 times.	Remove the swab while gently squeezing the head of the swab.	Close the assay diluent tube with a filter cap securely.	Invert the assay diluent tube and gently squeeze it to draw 3~4 drops (90~150㎕) into a sample well on the device.	Read the result within 5-8 minutes.



INTERPRETATION

NEGATIVE	POSITIVE	INVALID
		
One **red** line "C" within the result window.	Two bands, **black** To test line and **red** "C" control line within the result window.	No "C" line within the result window. It is recommended that the specimen be retested.

RapiGEN INC.

BIOCREDIT COVID-19 Ag

SARS-CoV 2 Antigen test

» Comercializarea pentru prima dată la nivel mondial a tehnologiei cu particule din aur negru (sensibilitate și specificitate ridicate)

» Sistem facil, bicolor (linie de control: Roșu, Linie de test: Negru)

» Timp scurt de efectuare a testului (5~8 Min)

» Detecția simplă a antigenului pentru SARS-CoV2

Tehnologie cu particule din aur

Tehnologie cu conjugat diferențiat din aur negru

Sistem bicolor

Rezultatul în 8 minute!

BIOCREDIT COVID-19 Ag rapid test kit

Utilizare	Detecția antigenului pentru SARS-CoV2
Pachet	20 Teste/kit
Depozitare	1~40°C
Tip probă	Nasopharynx / Nasopharyngeal
Perioadă de valabilitate	24 luni de la data producției
Timp până la rezultat	5~8 minute

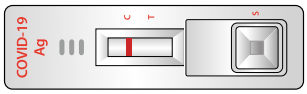
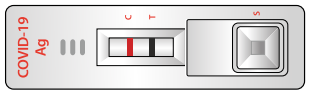
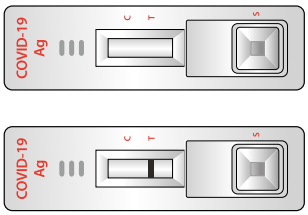
Test antigen SARS CoV-2 **BIOCREDIT COVID-19 Ag**

COVID-19 Test rapid de diagnostic

PROCEDURĂ

Introduceți tamponul și agitați de 5-10 ori.	Scoateți tamponul, scuturându-l cu grijă.	Închideți tubul de test cu capacul de filtrare.	Întoarceți tubul de test și apăsați ușor pentru a aplica 3~4 picături (90~150°) în caseta de test a dispozitivului.	Rezultatul este gata în 5-8 minute.

INTERPRETARE

NEGATIV	POZITIV	NUL
		
O bandă roșie pe linia de control “C” care apare până la final în fereastra de timp.	Două benzi: neagră, pe linia de test “T” și roșie pe linia de control “C” care apar până la final în fereastra de timp.	Nu apare banda roșie pe linia de control “C” până la final în fereastra de timp. Se recomandă repetarea testului

BIOCREDIT COVID-19 Ag

One Step SARS-CoV-2 Antigen Rapid Test

Introduction

2019 novel coronavirus (2019-nCoV) is a single-stranded RNA coronavirus. Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by the 2019-nCoV. 2019-nCoV belongs to the Beta-coronavirus Genus, which also includes Severe Acute Respiratory Syndrome coronavirus (SARS-CoV, 2003) and Middle East Respiratory Syndrome coronavirus (MERS-CoV, 2012). Coronaviruses, 2019-nCoV consist of four viral proteins named spike (S), envelope (E), membrane (M), and nucleocapsid (N).

Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

General recommendations to prevent infection spread include regular hand washing, covering mouth and nose when coughing and sneezing. Avoid close contact with anyone experiencing symptoms of respiratory illness such as coughing and sneezing.

[Principle of Test]

BIOCREDIT COVID-19 Ag is a lateral flow immunochromatographic assay that adopted dual color system. The test contains colloid gold conjugate pad and a membrane strip pre-coated with antibodies specific to SARS-CoV-2 antigen on the test lines (T). If SARS-CoV-2 antigen is present in the specimen, a visible black band appears on the test lines (T) as antibody-antigen-antibody gold conjugate complex forms. The control line (C) is used for procedural control and should always appear if the test is performed correctly.

[Intended Use]

BIOCREDIT COVID-19 Ag is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 antigen in human nasopharynx.

This test is for in-vitro professional diagnostic use and intended as an aid to early diagnosis of SARS-CoV-2 infection in patient with clinical symptoms. It provides only an initial screening test result and more specific alternative diagnosis methods should be performed in order to confirm COVID-19 infection.

Kit Components

- Each test device sealed in a foil pouch with a desiccant -
Assay diluent tube
- Filter cap
- Sterilized swab for nasopharynx specimen collection
- Instructions for use

Specimen Collection and Storage

1. Specimen should be handled carefully as an infectious agent and should be collected by trained personnel.
2. As improper collection of the sample affects the test result significantly, handle with care.
3. More accurate results can be obtained if samples are collected from several parts.
4. Specimen should be tested as soon as possible upon collection. If the sample has to be stored, store the swab sample at room temperature for up to 1 hours or 2~8℃ for up to 4 hours prior to testing.

[Nasopharyngeal swab specimen]

To collect nasopharyngeal swab specimen, tilt the patient's head slightly backwards. Insert a nasopharyngeal swab horizontally into the nasal cavity until resistance is met at the level of the turbinate. Rotate the swab gently against the nasopharyngeal mucosa for 10 – 15 seconds. Remove the swab while making sure that the tip of the swab is wet.

* When collect the specimens, follow the Instruction for use thoroughly.

Assay Procedure

[PREPARATION]

1. Equilibrate kit components and specimen to room temperature before testing.
2. Do not break the seal of the foil pouch until ready to perform the test.

[TESTING]

1. Remove the aluminum seal from the assay diluent tube. Immerse nasopharyngeal swab in the assay diluent and swirl the swabs 5~10 times while pressing the head against the bottom and side of the collection tube.
2. Withdraw the swab while pinching and squeezing against the tube. Dispose it with biosafety.
3. Close the assay diluent tube with a filter cap securely.
4. Remove the device from the foil pouch and place it on a flat and dry surface.
5. Invert the assay diluent tube and gently squeeze it to draw 3~4 drops (90~150㎕) into a sample well(S) of the device.

*** Please ensure that an appropriate amount of specimen and assay diluent is used for testing. Too much or too little amount of specimen and/or assay diluent may lead to deviation of results.**

6. Read the result between 5~8 minutes.
☞Do not interpret the result after 8 minutes.

Interpretation of Results

[Negative]

The presence of only one red band at the control line (C) within the result window indicates a negative result.

[Positive]

Two bands appear; one red control line(C) and one black test line(T).

[Invalid]

If the control line fails to appear within the result window, the result is considered invalid. The directions may not have been followed correctly or the test may have deteriorated. It is recommended that the specimen be retested.

Note: There is no meaning attributed to line color intensity or width.

Performance Characteristics

1. Sensitivity and Specificity:

BIOCREDIT COVID-19 Ag has been evaluated comparing to PCR as reference at 3 different countries. The results are summarized in the following table:

Europe		PCR (after symptoms occur)		Sensitivity	Specificity
		Positive	Negative		
BIOCREDIT COVID-19 Ag	Positive	24	0	96.0%	100.0%
	Negative	1	25		
Total		25	25		

South America		PCR (after symptoms occur)		Sensitivity	Specificity
		Positive	Negative		
BIOCREDIT COVID-19 Ag	Positive	10	0	90.9%	100.0%
	Negative	1	109		
Total		11	109		

KOREA		PCR (after symptoms occur)		Sensitivity	Specificity
		Positive	Negative		
BIOCREDIT COVID-19 Ag	Positive	12	0	80.0%	100.0%
	Negative	3	2		
Total		15	2		

Total		PCR (after symptoms occur)		Sensitivity	Specificity
		Positive	Negative		
BIOCREDIT COVID-19 Ag	Positive	46	0	90.2%	100.0%
	Negative	5	136		
Total		51	136		

2. Precision

Within-run and between run precision has been determined in triplicates of three lots using the following specimen panel: negative, low positive, medium positive and strong positive. All specimens are correctly identified 100% of the time.

3. Cross reactivity

BIOCREDIT COVID-19 Ag has been tested with 20 potentially cross reacting microorganisms and viruses. The results showed that BIOCREDIT COVID-19 Ag had no cross-reaction with microorganisms and viruses except very weak cross reacting with SARS-coronavirus.

4. Interference

BIOCREDIT COVID-19 Ag has been tested with 14 potentially interfering endogenous or exogenous substances. The results showed that BIOCREDIT COVID-19 Ag had no interference with endogenous or exogenous substances.

Limitations

1. A negative result can occur if the quantity of coronavirus present in the specimen is below the detection limits of the assay or if a poor quality specimen is tested.
2. A negative test result cannot exclude a recent infection.

Precautions

1. For *in vitro* diagnostic use only.
2. The test device is sensitive to humidity as well as heat. Perform the test immediately after removing the test device from the foil pouch.
3. Do not use the test kit if the pouch is damaged or the seal is broken.
4. Decontaminate and dispose of all specimens, reaction kit and potentially contaminated materials, as if they were infectious waste, in a biohazard container with biosafety.
5. Wear protective clothing, gloves and eye protection while handling specimens. Wash hands afterwards.
6. Repeated freeze-thawing specimen can cause false positive or false negative results.
7. Discard the solid waste by autoclaving at 121℃ for 1 hour.
8. The assay diluent contains less than 0.1% of sodium azide. In case of dermal or eye exposure, wash out thoroughly with running water and seek medical attention if necessary.
9. Do not use it beyond the expiration date.
10. Do not reuse.
11. Do not interchange or mix reagents of different lots.
12. A clinical decision should be made by physician after all clinical and laboratory findings have been evaluated.
13. Do not use the nasopharnygeal specimen in transport media.

Package

Refer to the outer packaging

Storage Condition

Store at 2~30℃.

Notification

This assay has received Provisional Authorization from the Health Sciences Authority in Singapore

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I-H073A-E06(2020.08.13)

BIOCREDIT

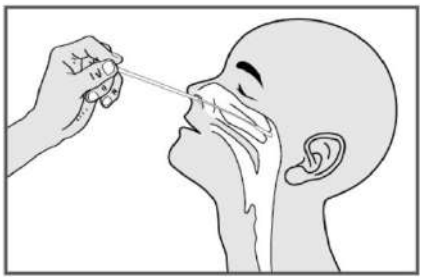
COVID-19 Ag

Cat.No. G61RHA20

One Step SARS-CoV-2 Antigen Rapid Test

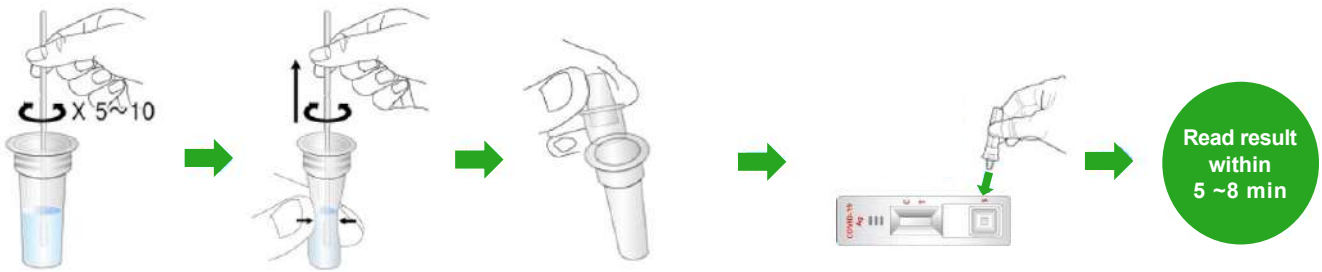
■Specimen Collection

Nasopharyngeal Swab



① Tilt the patient's head slightly backwards.
② Insert a nasopharyngeal swab horizontally into the nasal cavity until resistance is met at the level of the turbinate.
③ Rotate the swab gently against the nasopharyngeal mucosa for 10 – 15 seconds.
④ Remove the swab while making sure thatthe tip of the swab is wet.

■Assay Procedure



1 Insert the swab specimen and swirl the swab 5~10 times.

2 Remove the swab while gently squeezing the head of the swab.

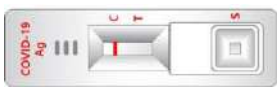
3 Close the assay diluent tube with a filter cap securely.

4 Invert the assay diluent tube and gently squeeze it to draw 3~4 drops (90~150㎕) into a sample well on the device.

5 Read the result within 5~8 minutes.

■Interpretation of Results

Negative

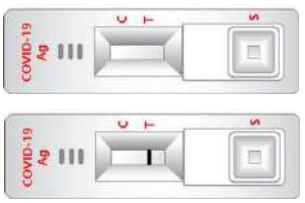


One **red** line "C" within the result window.

Positive

Two bands ; **black** "T" test line and **red** "C" control line within the result window.

Invalid



No "C" line within the result window. It is recommended that the specimen be retested.

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I-H073A-E06(2020.08.13)

BIOCREDIT

COVID-19 Ag

Test rapid cu antigen pentru SARS-CoV-2 într-o singură etapă

Introducere

Noul coronavirus 2019 (2019-nCoV) este un coronavirus cu genom ARN monocatenar. Boala Coronavirus 2019 (COVID-19) este o afecțiune respiratorie cauzată de 2019-nCoV. 2019-nCoV face parte din Genul betacoronavirus, care, de asemenea, include coronavirusul Sindromului Respirator Acut Sever (SARS-CoV, 2003) și coronavirusul Sindromului Respirator din Orientul Mijlociu (MERS-CoV, 2012). Coronavirusul 2019-nCoV este alcătuit din patru proteine virale: proteina în formă de spiculi (S) (S, de la engl. spike), proteina din înveliș (E, de la engl. envelope), proteina membranară (M) și nucleocapsida (N). Între simptomele comune în cazul infectării se numără cele respiratorii, febră, tuse, dispnee și dificultăți de respirație. În cele mai grave cazuri, se poate ajunge la pneumonie, sindromul respirator acut sever, insuficiență hepatică și chiar deces. Între recomandările standard pentru a preveni răspândirea infectării se numără spălarea regulată a mâinilor, acoperirea gurii și a nasului atunci când persoana strănută sau tușește. A se evita contactul direct cu persoanele care prezintă simptome ale unei boli respiratorii cum ar fi tuse ori strănut.

[Principiul de testare]

BIOCREDIT COVID-19 Ag este un test rapid imunocromatografic cu flux lateral care adoptă sistemul cu două culori. Testul conține un suport conjugat de aur coloidal și o bandă de membrană pre-acoperită cu anticorpi specifici pentru antigenul SARS-CoV-2 pe liniile de testare (T). Dacă antigenul SARS-CoV-2 este prezent în probă, o linie neagră vizibilă va apărea pe liniile de testare (T) ca urmare a unui complex conjugat anticorp-anticorp- antigen-particulă de aur. Linia de control (C) este folosită pentru controlul procedurii și trebuie să apară întotdeauna dacă testul este efectuat în mod corect.

[Domeniul de utilizare]

BIOCREDIT COVID-19 Ag este test imunologic cromatografic rapid pentru detectarea calitativă a antigenului SARS-CoV-2 în nazofaringele uman. Acest test este pentru a fi utilizat in diagnosticări profesioniste in-vitro și conceput ca un instrument ajutător în diagnosticul timpuriu al infecției SARS-CoV-2 la pacienții cu simptome clinice. Oferă doar rezultate de testare preliminare și se vor efectua metode alternative de testare mai specifice pentru a confirma infectarea cu COVID-19.

Componentele kitului

- Casetă de testare sigilată în mod individual în folie protectoare cu sicativ -
Recipient cu solvent pentru probă
- Capac filtru
- Tampon sterilizat pentru colectarea probei din nazofaringe - Instrucțiuni de utilizare

Prelevarea și depozitarea probei

1. Proba va fi manipulată cu grijă ca și cum ați manipula un agent infecțios și va fi prelevată de către personal instruit
2. Deoarece o prelevare necorespunzătoare a probei afecteaza semnificativ rezultatele de testare, manipulați proba cu grijă
3. Se pot obține rezultate mai precise dacă probele sunt colectate din mai multe părți
4. Proba va fi testată cât mai curand posibil după prelevare. Dacă proba trebuie depozitată, depozitați proba cu tampon la 2-8°C timp de maxim 4 ore înainte de testare.

[Proba cu tampon nazofaringeal]

Pentru a preleva proba cu tampon nazofaringeal, înclinați ușor capul pacientului în spate. Introduceți orizontal un tampon nazofaringeal în cavitatea nazală până când întâmpinați rezistență la nivelul cornetelor nazale. Rotiți ușor tamponul de mucoasa nazofaringeală timp de 10-15 secunde. Scoateți tamponul în timp ce vă asigurați că vârful acestuia este ud.
*Atunci când colectați probele, respectați cu strictețe instrucțiunile de utilizare.

Procedura de testare

[PREGĂTIREA]

1. Asigurați-vă că toate componentele kitului și proba sunt la temperatura camerei înainte de testare
2. Nu rupeți etanșarea foliei protectoare până ce nu sunteți gata să efectuați testul

[TESTAREA]

1. Înlăturați etanșarea de aluminiu de la tubul cu solvent de testare. Scufundați tamponul nazofaringeal în solventul de testare și învârtiți tamponul de 5-10 ori în timp ce apăsați capul de partea de jos și partea laterală a tubului de colectare
2. Scoateți tamponul în timp ce apăsați de tub. Debarasați-vă de tampon respectând procedurile de siguranță biologică
3. Închideți securizat tubul de solvent de testare cu un capac de filtru
4. Scoateți caseta de testare din folia protectoare și puneți-o pe o suprafață uscată și plană
5. Luați tubul de solvent de testare și apăsați-l ușor pentru a extrage 3-4 picături (90-150µl) în orificiul absorbant (S) al casetei de testare
*Asigurați-vă că utilizați o cantitate suficientă de probă și solvent de testare pentru testare. O cantitate prea mare sau prea mică de probă și/sau solvent de testare poate duce la abateri.
6. Citiți rezultatele după 5-8 minute

**Nu interpretați rezultatele după 8 minute

Interpretarea rezultatelor

Negativ

Prezența exclusivă a unei linii roșii (linia de control C) pe afișaj indică un rezultat negativ.

Pozitiv

Vor apărea două linii: o linie de control roșie (C) și o linie de testare neagră (T).

Nevalid

Dacă linia de control nu apare pe afișaj, rezultatul este considerat a fi nevalid. Este posibil ca instrucțiunile să nu fi fost respectate sau testul să fie deteriorat. Se recomandă ca proba să fie retestată.

Notă: Nu există nici o semnificație atribuită intensității culorii sau lățimii liniei.

Caracteristici de funcționare

1. Sensibilitate și specificitate

BIOCREDIT COVID-19 Ag a fost evaluat în comparație cu PCR ca referință în 3 țări diferite. Rezultatele sunt prezentate în următorul tabel:

Europa		PCR (după aparitia simptomelor)		Sensibilitate	Specificitate
		Pozitiv	Negativ		
BIOCREDIT COVID-19 Ag	Pozitiv	24	0	96.0%	100.0%
	Negativ	1	25		
Total		25	25		

America de Sud		PCR (după aparitia simptomelor)		Sensibilitate	Specificitate
		Pozitiv	Negativ		
BIOCREDIT COVID-19 Ag	Pozitiv	10	0	90.9%	100.0%
	Negativ	1	109		
Total		11	109		

Coreea		PCR (după aparitia simptomelor)		Sensibilitate	Specificitate
		Pozitiv	Negativ		
BIOCREDIT COVID-19 Ag	Pozitiv	12	0	80.0%	100.0%
	Negativ	3	2		
Total		15	2		

Total		PCR (după aparitia simptomelor)		Sensibilitate	Specificitate
		Pozitiv	Negativ		
BIOCREDIT COVID-19 Ag	Pozitiv	46	0	90.2%	100.0%
	Negativ	5	136		
Total		51	136		

2. Precizie

Precizia în cadrul ciclului de testare și între mai multe serii de testare a fost stabilită în trei serii de loturi cu următoarele tipuri de probe: negative, slab pozitive, mediu pozitive și puternic pozitive. Toate probele au fost identificate corect în 100% din cazuri.

3. Reactivitate încrucișată

BIOCREDIT COVID-19 Ag a fost testat cu 20 de potențiale microorganisme și virusuri care reacționează încrucișat. Rezultatele au indicat că BIOCREDIT COVID-19 Ag nu a avut nici o reacție încrucișată cu microorganismele și virusurile cu excepția unei reacții încrucișate foarte slabe cu coronavirusul SARS.

4. Interferență

BIOCREDIT COVID-19 a fost testat cu 14 substanțe cu potențial de interferență endogenă și exogenă. Rezultatele au indicat că BIOCREDIT COVID-19 Ag nu a prezentat nici o interferență cu substanțele endogene sau exogene.

Limitări

1. Un rezultat negativ poate apărea dacă cantitatea de coronavirus prezentă în probă este sub limitele de detectare ale testării sau dacă s-a testat o probă de calitate slabă
2. Un rezultat negativ nu poate exclude o infecție recentă

Precauții

1. A se utiliza exclusiv pentru diagnostic *in vitro*.
2. Caseta de testare este sensibilă la umezeală și căldură. Faceți testul imediat după ce scoateți caseta din folia protectoare.
3. Nu folosiți kitul de testare în cazul în care folia protectoare este deteriorată sau desigilată.
4. Decontaminați și eliminați toate probele, kitul de reacție și materialele posibil contaminate ca și cum ar fi deșeuri infecțioase, într-un container pentru produse cu risc biologic.
5. Purtați echipament de protecție, mănuși, ochelari de protecție în timpul manevrării probelor. Ulterior, spălați-vă pe mâini.
6. Procesele repetate de congelare – decongelare a probelor pot duce la obținerea unor rezultate fals pozitive sau fals negative.
7. Eliminați deșeurile solide prin autoclavizare la 121ºC timp de 30 de minute.
8. Solventul pentru probă conține sub 0,1% azidă de sodiu. În cazul expunerii pielii sau ochilor la această substanță, spălați bine cu apă zona expusă și solicitați un control medical, dacă este cazul.
9. A nu se utiliza după data de expirare. 10. A nu se reutiliza.
11. A nu se folosi sau amesteca reactivi din loturi diferite.
12. O decizie clinică va fi luată de un medic după ce toate constatările clinice și de laborator au fost evaluate
13. Nu utilizați proba nazofaringeală în medii de transport

Ambalaj

Consultați ambalajul exterior.

Condiții de depozitare

Depozitați la 2-30°C.

Manufactured by RapiGEN. INC.
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I-H073A-E06(2020.08.13)

BIOCREDIT

COVID-19 Ag

Cat.No. G61RHA20

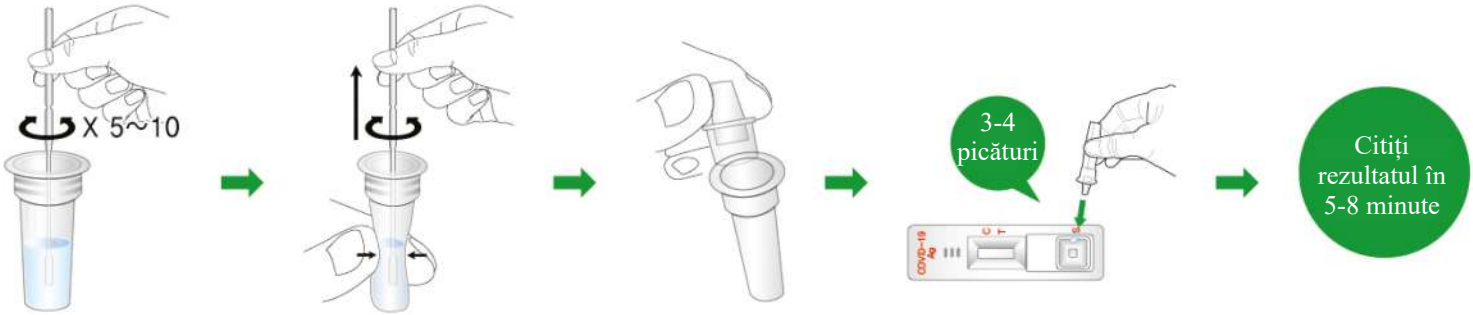
Test rapid cu antigen pentru SARS-CoV-2 într-o singură etapă

Prelevarea probei

Tamponul nazofaringeal

1.Înclinați ușor pe spate capul pacientului
2.Introduceți un tampon nazofaringeal orizontal în cavitatea nazală până când întâmpinați rezistență la nivelul cornetului nazal
3.Rotiți ușor tamponul de mucoasa nazofaringeală timp de 10-15 secunde
4.Scoateți tamponul în timp ce vă asigurați că vârful tamponului este ud

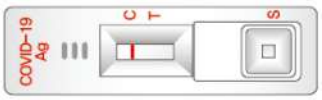
Procedura de testare



1. Introduceți tamponul cu proba și rotiți-l de 5-10 ori
2. Scoate-ți tamponul în timp ce apăsați ușor pe capacul tamponului
3. Luați capacul cu filtru de la pachet închideți securizat tubul de solvent
4. Introduceți tubul de solvent de testare și apăsați-l încet pentru a extrage 3-4 picături (90-150µl) în orificiul absorbant al dispozitivului
5. Citiți rezultatul în 5-8 minute

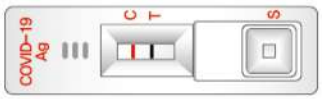
Interpretarea rezultatelor

Negativ



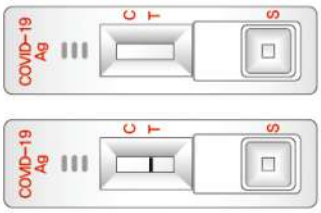
O linie roșie ”C” pe afișaj.

Pozitiv



Două linii: linia de testare ”T” **neagră** și linia de control ”C” pe afișaj

Invalid



Nici o linie ”C” pe afișaj.
Se recomandă retestarea probei.

EC REP MT Promedt Consulting GmbH
Altenhofstrasse 80.66386 St.Ingbert, Germany
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I-H073A-E06(2020.08.13)

DECLARATION OF CONFORMITY

Manufacturer: RapiGEN Inc.
3-4F, 16, LS-ro 91beon-gil, Dongan-gu, Anyang-si, Gyeonggi-do 14119,
Republic of Korea

European Representative: MT Promedt Consulting GmbH
Altenhofstrasse 80, 66386 St. Ingbert, Germany

CE

Product : BIOCREDIT COVID-19 Ag

Catalog no.: G61RHA20

Classification: Neither listed in the annex II of the IVDD, nor self-testing device
This declaration of conformity is issued under the sole responsibility of the manufacturer.
EDMA code: 15.70.90.90.00; Other Other Virology Rapid Tests

Conformity Assessment Route: Self Declaration (according to annex III of IVDD)

We herewith declare that the above mentioned products meet the provisions of the council Directive 98/79EC for in vitro diagnostic medical devices. All supporting documentation is retained under the premises of the manufacturer.

Standards applied :ISO13485:2016, EN ISO14971:2012, EN13640:2002, EN13641:2002, EN13612:2002, EN ISO 15223-1:2016, ISO17511:2003, EN13975:2003, EN ISO 18113-1:2011, EN ISO 18113-2:2011, EN 62366:2008, KGMP

This declaration of conformity is issued under the sole responsibility of the manufacturer.

Place, Date of Issue: Gyeonggi-Do, Republic of Korea, 9th September, 2020.

Signature:

Jae-Ku, Park
CEO/President
RapiGEN Inc.

DECLARAȚIE DE CONFORMITATE

Producător: RapiGEN Inc.
3-4F, 16, LS-ro 91beon-gil, Dongan-gu, Anyang-si, Gyeonggi-do 14119,
Republica Corea

Reprezentant European: MT Promedt Consulting GmbH
Altenhofstrasse 80, 66386 St. Ingbert, Germany

CE

Produs: BIOCREDIT COVID-19 Ag

Nr. Catalog: G61RHA20

Clasificare: Nu este listat nici în anexa II a IVDD, nici ca dispozitiv de auto-testare.
Această declarație de conformitate este emisă sub responsabilitatea exclusivă a producătorului.
Cod EDMA 15.70.90.90.00; Alte alte teste rapide de virologie

Traseul de evaluare a conformității: Declarație pe proprie Răspundere (conform anexei III la IVDD)

Declarăm că produsele menționate mai sus respectă prevederile Directivei Consiliului 98/79/CE pentru dispozitivele medicale de diagnostic in vitro. Toată documentația justificativă este păstrată la sediul producătorului

Standarde aplicate :ISO13485:2016, EN ISO14971:2012, EN13640:2002, EN13641:2002, EN13612:2002, EN ISO 15223-1:2016, ISO17511:2003, EN13975:2003, EN ISO 18113-1:2011, EN ISO 18113-2:2011, EN 62366:2008, KGMP

Această declarație de conformitate este emisă pe responsabilitatea exclusivă a producătorului.

Locul, Data Emiterii: Gyeonggi-Do, Republica Corea, 9 Septembrie, 2020.

Semnătură:

Jae-Ku, Park
CEO/President
RapiGEN Inc.

Clinical Performance Report

BIOCREDIT COVID-19 Ag

Authorization	Dept. & Name	Signature	Date
Prepared by	RA A. J. J. Kim		20. 8. 11
Reviwer	RA I. J. Cho		20. 8. 11
Approved by	Quality Assurance T. Y. Park		20. 8. 11

Summary Clinical study Report

BIOCREDIT COVID-19 Ag is a rapid lateral flow immunochromatographic assay for the detection of SARS-CoV-2 antigen in human nasopharynx. Nasopharyngeal swab specimen is needed to perform the assay. Reading of the results is done visually i.e. subjectively read.

Performance evaluation (Total)

Total sensitivity and specificity are in the following.

BIOCREDIT COVID-19 Ag		**RT-PCR**		**Sensitivity (%)**	**Specificity (%)**
		Positive	**Negative**		
Ag	Positive	46	0	90.2% (46/51)	100% (136/136)
	Negative	5	136		
Total		51	136		

Sensitivity: 90.2% (46/51, 95% CI, 77.81% - 96.33%)

Specificity: 100% (136/136, 95% CI, 96.57% - 100%)

Positive predictive value (PPV): 100% (46/46, 95% CI, 90.40% - 100%)

Negative predictive value (NPV): 96.45% (136/141, 95% CI, 91.49% - 98.69%)

1) Clinical Evaluation 1

a. Test site: Seoul Asan Hospital(South Korea), Eunpyung St. Mary's Hospital(South Korea)

b. Test date: April 01, 2020

c. Specimen: 15 COVID-19 positive and 2 COVID-19 negative specimens

d. Test result: Summary of performance of BIOCREDIT COVID-19 Ag compare to PCR confirmed specimens

BIOCREDIT COVID-19 Ag		**RT-PCR**		**Sensitivity (%)**	**Specificity (%)**
		Positive	**Negative**		
Ag	Positive	12	0	80 (12/15)	100 (2/2)
	Negative	3	2		
Total		15	2		

Sensitivity: 80% (12/15, 95% CI, 51.37% - 94.69%)

Specificity: 100% (2/2, 95% CI, 19.79% - 100%)

2) Clinical Evaluation 2

a. Test site: Fundação Oswaldo Cruz, Brazil

b. Test date: June 18, 2020

c. Specimen: 11 COVID-19 positive and 109 COVID-19 negative specimens

d. Test result: Summary of performance of BIOCREDIT COVID-19 Ag compare to PCR confirmed specimens

BIOCREDIT COVID-19 Ag		RT-PCR		Sensitivity (%)	Specificity (%)
		Positive	Negative		
Ag	Positive	10	0	90.9% (10/11)	100% (109/109)
	Negative	1	109		
Total		11	109		

Sensitivity: 90.9% (10/11, 95% CI, 57.18% - 99.52%)

Specificity: 100% (109/109, 95% CI, 95.76% - 100%)

3) Clinical Evaluation 3

a. Test site: Infectious Clinical Hospital No. 2 of the Moscow City Health Department, Russia
(Web site: https://www.ikb2.ru/english)

b. Test date: June 15~18, 2020

c. Specimen: 25 COVID-19 positive and 25 COVID-19 negative specimens

d. Test result: Summary of performance of BIOCREDIT COVID-19 Ag compare to PCR confirmed specimens

BIOCREDIT COVID-19 Ag		RT-PCR		Sensitivity (%)	Specificity (%)
		Positive	Negative		
Ag	Positive	24	0	96 (24/25)	100 (25/25)
	Negative	1	25		
Total		25	25		

Sensitivity: 96% (24/25, 95% CI, 77.68% - 99.79%)

Specificity: 100% (25/25, 95% CI, 83.42% - 100%)

Table of CONTENTS

No	Clinical Site	Test date
1	Catholic University, Eunpyung St. Mary's Hospital, South Korea	Apr 1, 2020
	Seoul Asan Hospital, South Korea	Apr 9, 2020

Retrospective clinical trial to evaluate clinical performance of BIOCREDIT COVID-19 Ag using clinical specimens of nasopharyngeal swap obtained from symptomatic patients confirmed by RT-PCR

Catholic University, Eunpyung St. Mary's Hospital, South Korea

Seoul Asan Hospital, South Korea

Clinical Performance Report

BIOCREDIT COVID-19 Ag

List of Abbreviations

- COVID-19: Novel Coronavirus (SARS-CoV-2)
- WHO: World Health Organization
- SARS: Severe Acute Respiratory Syndrome
- MERS: Middle East Respiratory Syndrome
- RT-PCR: Real Time Polymerase Chain Reaction
- NP: Nasopharyngeal
- uL: microliter

1 Introduction

1.1 Background

The World Health Organization (WHO) has been declared pandemic, since the outbreak of the novel coronavirus (COVID-19) in Wuhan, China, the disease has spread rapidly to the world. While COVID-19 reports low-fatality rate compare to previous SARS or MERS, cases of significant respiratory failure requiring cases of significant respiratory failures requiring mechanical ventilation have been reported.

Person-to-person spread is thought to occur mainly via respiratory droplets, and even asymptomatic carriers can spread the virus, posing challenges in containing widespread of the disease. Non-severe symptoms of COVID-19, which includes fever, cough, malaise, may overlap with symptoms of common cold and influenza infection.

Real Time Reverse-Transcription Polymerase Chain Reaction (qRT-PCR) is the current standard for COVID-19 diagnosis. Nasopharygeal swab (and/or from oropharyngeal/mid turbinate) samples are analyzed using qRT-PCR. These qRT-PCR tests, however, are expensive and requires dedicated laboratory and specimen handling capability, with turnaround time in hours if not days. This delay in diagnosis leads to increased resource utilization in some cases and cross-contamination in others. Furthermore, qRT-PCR analysis heavily relies on the presence of viral genome in sufficient quantities at the sample collection site that can be amplified.

There have been efforts to produce accurate yet faster results via less invasive sampling measures. Also, Immunochromatographic Assay, which detects presence of COVID-19 viral antigen, has been developed. These Assays are inexpensive, do not require laboratory or special equipment and have turnaround time of under 10 minutes. These kits have potential benefit of large-scale testing without the significant resource burden on healthcare. This is crucial because hospitals are overwhelmed with increased resource utilization, limited medical equipment including personal protection equipment (PPE), and rapid diagnosis providing appropriate resource triage.

Here we aim validate the sensitivity and specificity of these point of care immunochromatographic COVID-19 antigen test kits by comparing its result against standard RT-PCR.

1.1 Objectives

The goal of the study is to validate the sensitivity and specificity of BIOCREDIT COVID-19 Ag kits compared to standard of care (RT-PCR) in patients infected with COVID-19 virus. The results from this study will be used to verify that antigen test kits can accurately identify patients with COVID-19 infections.

2 Device Description

2.1 BIOCREDIT COVID-19 Ag Kit

BIOCREDIT COVID-19 Ag kit is a point-of-care (POC) in vitro diagnostic test based on immunochromatographic assay. It is designed for qualitative detection of serum Novel Coronavirus (COVID-19) antigens (nucleocapside proteins), which are markers of novel coronavirus infection. It is a small sized standalone single use kit.

Operation of the device is fully automated and requires minimal sample handling. After sample has been collected (either via nasopharyngeal swab or saliva specimen), samples are mixed with assay diluent and 3-4 drops (90- 150 uL) of this mixture is added to device sample well. Device will then produce result within 8 minutes. Photographic evidence of result can be obtained for study, and once the test is complete, the single use device can be discarded in a biosafety Sharps Container.

2.2 BIOCREDIT COVID-19 Ag Kit Mechanism

BIOCREDIT COVID-19 Ag kit mechanism is based on lateral flow immunochromatographic assay. The nitrocellulose membrane strip within the device contains test line pre-coated with anti-SARS-CoV-nucleocapside protein (NP) for capture of SARS-CoV-2. The captured SARS-CoV is also detected by mouse anti-SARS-CoV·NP-gold conjugate for visualization. When sample is added to device sample pad, it moves through the nitrocellulose membrane by capillary action and contact the immobilized antibody coated test region. Should the sample contain specific COVID-19 antigen, immunocomplex will form revealing visible colored conjugate. Control region contains colored conjugate regardless of test specimen composition.

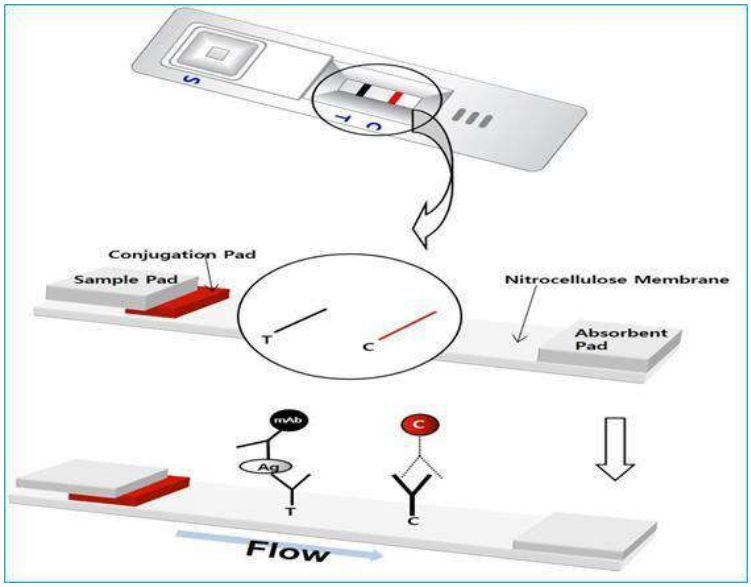

Figure 1. BIOCREDIT COVID-19 Ag kit mechanism

Interpretation of result is shown in Figure 2.

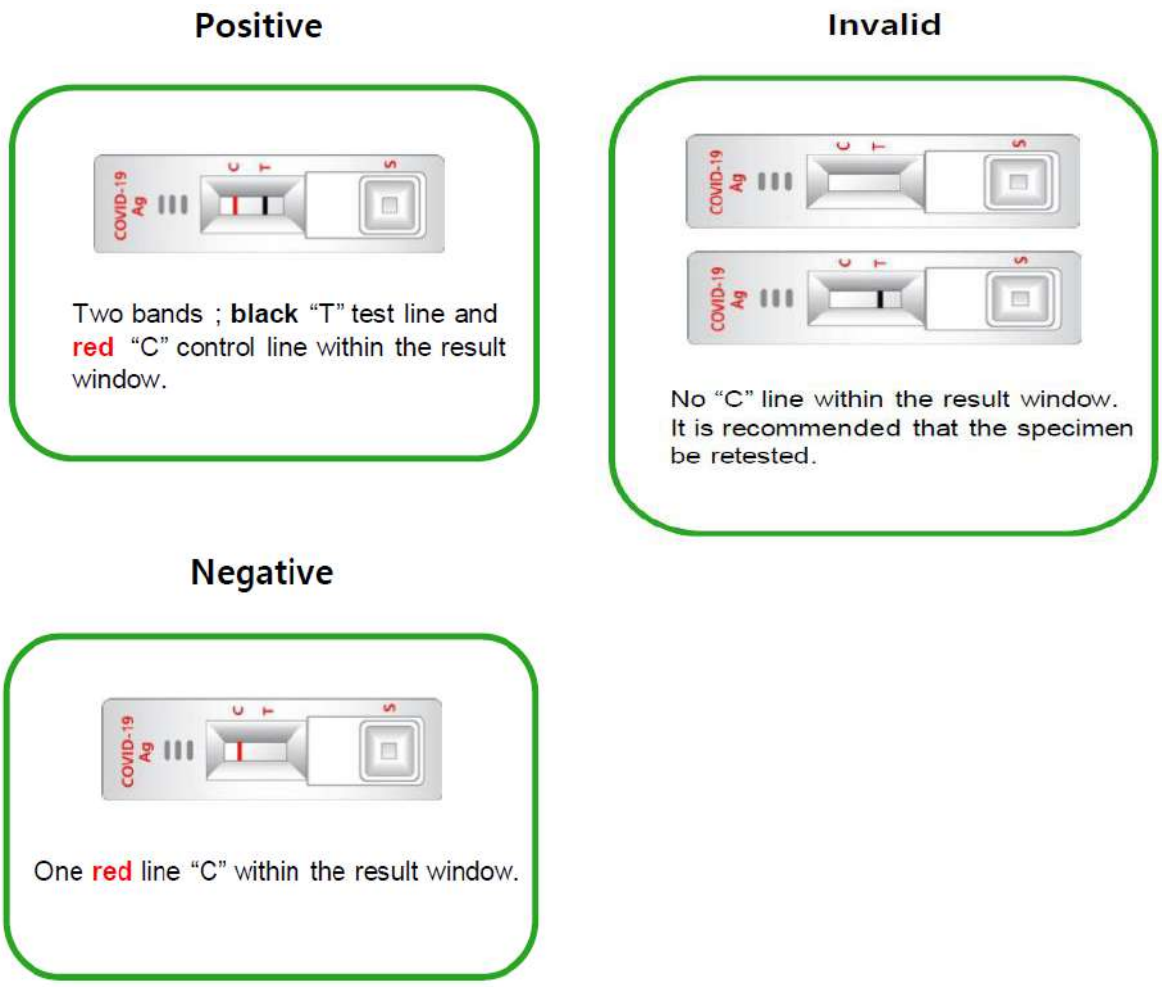

Figure 2. BIOCREDIT COVID-19 Ag kit's interpretation of results.

3 Clinical Performance Design

This is multiple site, single-blind, and retrospective study to validate the sensitivity and specificity of the BIOCREDIT COVID-19 Ag kits versus the RT-PCR in patients with COVID -19 infection. The hospitals were selected because it is currently admitting and actively testing for patients with COVID-19 infection or those who are suspected to have COVID-19 infection.

Patients who present to hospitals, signs and symptoms that are concerning for COVID-19 infection undergo nasopharyngeal swab for PCR test. Using BIOCREDIT COVID-19 Ag kit, we will compare the device results with diagnosis of COVID-19 using standard method (RT-PCR) from these patients.

3.1 Sample types

Patients with suspicion of COVID-19 infection undergo RT-PCR as a standard of care. Patients who are PCR positive case participants.

Collect nasopharyngeal swab for use on BIOCREDIT COVID-19 Ag.

Clinical Centers	Type of Specimen	Number of specimens	Comments
Catholic University of Korea, Eunpyung St. Mary's Hospital	UTM (nasopharyngeal collection)	Positive: 3 Negative: 2	RT-PCR confirmed for positive specimens
Seoul Asan Hospital	UTM (nasopharyngeal collection)	Positive: 12 Negative: 0	

3.2 Inclusion Criteria

The inclusion criteria for the test are:

- Subject has undergone RT-PCR test for COVID-19 diagnosis.

3.3 Exclusion Criteria

The exclusion criteria for the test are:

- Subject is unable to provide informed consent prior to performing any test related procedures.
- Subject is affected by conditions that, in the opinion of the clinical team, may pose additional risks. These include patients who are known to be coagulopathic or have history of significant nosebleed that would pose increased risk for nasopharyngeal swab.

3.4 Sample Exclusion Criteria

Samples will be excluded from the analysis data set if any of the test requirements or manufactural guidelines were not fulfilled. Manufacturer guideline states that collected specimen should be in room temperature.

4 Procedure

4.1 BIOCREDIT COVID-19 Ag Kit Training

Prior to subject enrollment, training will be provided to ensure that the designed instrument operators are proficient with the use of the BIOCREDIT COVID-19 Ag kit. Proficiency will be demonstrated by reproducing test kits without invalid results (control line is visible).

4.2 Sample Source and handling

Per discussion with manufacturer, source of samples for this study will be from nasopharyngeal swab.

Sample Source	Collection Method	Handling
Nasopharynx	Gently insert a nasopharyngeal swab into the nasal cavity until the resistance is met at the level of turbinate. Rotate softly and withdraw the swab. Make sure the tip of the swab is wet. Insert the specimen swab into manufacturer provided assay diluent tube.	Perform test immediately after collection or can be stored at 2~8℃ up to 1 2 hours or at -20℃ or below up to 24 hours.

4.3 Sample Analysis

Each sample from above sources will be analyzed on the BIOCREDIT COVID-19 Ag kit as follows:

- Tests should be performed immediately after collection. However, if the collected specimens were stored in refrigerated condition, leave the samples in room temperature for 15 to 30 minutes prior to use.
- Open the sealed pouch and place the device on a clean, dry, and level surface.
- Invert the assay diluent tube and gently squeeze it to draw 3~4 drops (90~150㎕) into a sample well.
- Read the result at 8 minutes. Do not read results after 8 minutes.
- Properly discard device and diluent tube in a biohazard container.

5 Materials

The following materials are required for the performance of the study described in this document. The study sites will be responsible for ensuring the materials are handled per the manufacturer's recommended instructions for use.

5.1 materials included in purchases from RapiGEN

- the BIOCREDIT COVID-19 Ag Test Device
- Assay Diluent kits
- Nasopharyngeal swabs
- Instruction for Use

5.2 Materials to be Provided by Sites

- Biohazard container for disposing device/diluent tubes after running the test

6 Results

1) Clinical Evaluation 1

a. Test site: Eunpyeong St. Mary's Hospital, Seoul, Korea

b. Test date: Apr 1, 2020

c. Specimen: 3 COVID-19 positive and 2 COVID-19 negative specimens

d. Conditions of RT-PCR; PowerCheckTM 2019-nCoV Real-time PCR Kit (Kogenebiotech Inc., Korea); Cut-off value was determined as the detection of both target RNAs 35.0 Cycles of Threshold (CT) (CT > 35: Negative)

e. Test result: Summary of performance of BIOCREDIT COVID-19 Ag compare to PCR confirmed specimens

Catholic University of Korea, Eunpyung St. Mary's Hospital					**PCR data**		**BIOCREDIT COVID-19 Ag**	
Patient No.	Date of Symptom onset	Date of specimen collection	Specimen type	Day after onset	CT value	Results	Ag	Results
1	No data	No data	UTM	No data	E:16.76, R:17.20	Pos.	±	Pos.
2	No data	No data	UTM	No data	E:15.36, R:15.58	Pos.	+	Pos.
3	No data	No data	UTM	No data	E:18.18, R:18.55	Pos.	+	Pos.
4	No data	No data	UTM	No data	>40	Neg.	-	Neg.
5	No data	No data	UTM	No data	>40	Neg.	-	Neg.

2) Clinical Evaluation 2

a. Test site: Asan Medical Center, Seoul, Korea

b. Test date: Apr 9, 2020

c. Specimen: 12 COVID-19 positive

d. Conditions of RT-PCR; Allplex 2019-nCoV Kit (Seegene Inc., Korea); Cut-off value was determined as the detection of both target RNAs under 40.0 Cycles of Threshold (CT) (CT > 40: Negative)

e. Test result: Summary of performance of BIOCREDIT COVID-19 Ag compare to PCR confirmed specimens

Seoul Asan Hospital					**PCR data**		**BIOCREDIT COVID-19 Ag**	
Patient No.	Date of symptom onset	Date of Specimen collection	Specimen type	Day after onset	CT value	Results	Ag	Results
A001	No data	27 Feb. 2020	UTM	1	E:22.61, R:24.88 N:25.18	Pos.	w+	Pos.
	No data	29 Feb. 2020	UTM	3	E:32.5, R:33.09 N:35.24	Pos.	w+	Pos.
	No data	02 Mar. 2020	UTM	5	E:31.95, R:34.49 N:35.95	Pos.	-	Neg.
A002	No data	08 Mar. 2020	UTM	1	E:19.94, R:21.93 N:35.95	Pos.	w+	Pos.
	No data	10 Mar. 2020	UTM	3	E:22.57, R:24.53 N:26.79	Pos.	w+	Pos.
	No data	14 Mar. 2020	UTM	7	E:32.6, R:34.83 N:36.59	Pos.	-	Neg.
A003	No data	13 Mar. 2020	UTM	1	E:21.07, R:22.96 N:24.29	Pos.	-	Neg.
	No data	16 Mar. 2020	UTM	4	E:9.63, R:12.81 N:13.51	Pos.	+	Pos.

	No data	17 Mar. 2020	UTM	5	E:18.46, R:19.95 N:23.36	Pos.	w+	Pos.
A004	No data	28 Mar. 2020	UTM	1	E:20.35, R:21.93 N:23.99	Pos.	w+	Pos.
	No data	30 Mar. 2020	UTM	3	E:27.95, R:29.81 N:30.99	Pos.	w+	Pos.
	No data	03 Apr. 2020	UTM	7	E:29.99, R:31.69 N:32.26	Pos	w+	Pos.

7. Conclusion

1) 15 positive specimens which were confirmed by RT-PCR are tested with BIOCREDIT COVID-19 Ag kit, and all the specimens are identified as positive as well.
Relative Sensitivity (%) = 100 x (No. of specimens with positive results / No. of positive
specimen tested by RT-PCR)

2) 2 negative specimens collected by hospital are tested with BIOCREDIT COVID-19 Ag kit, and all the specimens are identified as negative as well.
Relative Specificity (%) = 100 x (No. of specimens with negative results/ No. of negative specimens)

Total sensitivity and specificity are in the following.

BIOCREDIT COVID-19 Ag		**RT-PCR**		**Sensitivity (%)**	**Specificity (%)**
		Positive	**Negative**		
Ag	Positive	12	0	80 (12/15)	100 (2/2)
	Negative	3	2		
Total		15	2		

8. Reference

- Gitlin N., Hepatitis B: Diagnosis, prevention and treatment. Clinical Chemistry, 1997,43:1500 - 1506

-Wang Y, Kang H, Liu X, Tong Z. Combination of RT-qPCR testing and clinical features for diagnosis of COVID-19 facilitates management of SARS-CoV-2 outbreak. J Med Virol. March 2020:jmv.25721. doi:10.1002/jmv.25721

-Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579(7798):265-269. doi:10.1038/s41586-020-2008-3

- Korean Diagnostic Examination Medical Association, Laboratory Medicine Volume5, 2014, 68-91

- Ministry of Food and Drug Safety, High-risk virus diagnostic reagent (For immunological testing) Permission* screening guidelines, 2015