WHO Emergency Use Assessment SARS-CoV-2 IVDs PUBLIC REPORT

Product: BIOCREDIT COVID-19 Ag

Manufacturer: RapiGEN, Inc.

EUL Number: EUL 0650-160-00

Outcome: Accepted

The EUL process is intended to expedite the availability of in vitro diagnostics needed in public health emergency situations and to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products in the context of a Public Health Emergency of International Concern (PHEIC), based on an essential set of available quality, safety, and performance data. The EUL procedure includes the following:

- Quality Management Systems Review and Plan for Post-Market Surveillance: desktop review of the manufacturer's Quality Management System documentation and specific manufacturing documents.
- Product Dossier Review: assessment of the documentary evidence of safety and performance.

BIOCREDIT COVID-19 Ag, with product codes G61RHA20 and G61RHA20C, CE marked regulatory version, manufactured by RapiGEN, Inc., 161 Saneop-ro 115 bon-gil, Gwonseon-gu Suwon-si, Geonggi-do 14119 Republic of Korea, was listed on 6 February 2023.

Intended use:

According to the claim of intended use from RapiGEN, Inc., *"BIOCREDIT COVID-19 Ag is a rapid chromatographic immunoassay for qualitative detection of SARS-CoV-2 nucleocapsid antigen in human nasopharyngeal swab specimen collected by trained users in laboratory or point-of-care settings from patients suspected of COVID-19 within the first 7 days of symptom onset. This assay is intended to aid in diagnosing SARS-CoV-2 infection, and it is for in-vitro professional use."*

Specimen type that was validated:

Nasopharyngeal swab specimens.

Test kit contents:

Component	20 tests (product code G61RHA20)	20 tests (product code G61RHA20C)
Test device (individually in a foil pouch with desiccant)	20	20
Assay diluent tube (in a foil pouch) (0.4ml/tube)	20	20
Filter cap	20	20
Extraction tube caps	25	25
Plastic tube rack	2	2
Sterilized nasopharyngeal swab	20	20
Positive Control Swab	/	1
Negative Control Swab	/	1
Instructions for use	1	1

Items required but not provided

- Personal Protective Equipment per local recommendations (i.e. gown/lab coat, face mask, face shield/eye goggles and gloves)
- Timer
- Biohazard container

Storage:

2-30°C.

Shelf-life upon manufacture:

24 months (real-time stability studies are ongoing).

Warnings/limitations:

Refer to the instructions for use (IFU).

Product dossier assessment

RapiGEN, Inc. submitted a product dossier for the BIOCREDIT COVID-19 Ag for detecting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as per the *"Instructions for Submission Requirements: In vitro diagnostics (IVDs) Detecting SARS-CoV-2 Nucleic Acid and rapid diagnostics tests detecting SARS-CoV-2 antigens (PQDx_0347)"*. The information (data

and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

Post listing Commitments for EUL:

As commitments to listing, RapiGEN, Inc. committed to:

1. Assess the traceability of the materials used to validate the product (including estimation of LoD) with the WHO International Standard when available.
2. Partaking in an independent performance evaluation conducted by a laboratory commissioned by WHO. Any such performance evaluation testing will be performed using the protocol and technical criteria established by WHO.
3. Provide a supplementary clinical specificity study including at least 30 negative clinical specimens. The submitted information is under review.
4. Provide the full shelf-life study report by 28 February 2024. If results at any of the testing time points are outside the acceptance criteria, or the planned shelf-life changes, the WHO is required to be notified.

Risk-benefit assessment conclusion is acceptable.

Quality Management Systems Review

To establish eligibility for WHO procurement, RapiGEN, Inc. was asked to provide up-to-date information about the status of its quality management system.

Based on the review of the submitted quality management system documentation by WHO staff, it was established that sufficient information was provided by RapiGEN, Inc. to fulfil the requirements described in the "*Instructions for Submission Requirements: In vitro diagnostics (IVDs) Detecting SARS-CoV-2 Nucleic Acid and rapid diagnostics tests detecting SARS-CoV-2 antigens (PQDx_347)*".

Quality management documentation assessment is acceptable.

Plan for Post-Market Surveillance

Post-market surveillance, including monitoring all customer feedback, detecting and acting on adverse events, product problems, non-conforming goods and processes is critical component of minimizing potential harm of an IVD listed for emergency use.

The following post-EUL activities are required to maintain the EUL listing status:
1. Notification to WHO of any planned changes to a EUL product, in accordance with "*WHO procedure for changes to a WHO prequalified in vitro diagnostic" (document number PQDx_121*); and
2. Post-market surveillance activities, in accordance with "*Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics"* (ISBN 978-92-4-001531-9).

RapiGEN, Inc. is also required to submit an annual report that details sales data and all categories of complaints in a summarized form. There are certain categories of complaints and changes to the product that must be notified immediately to WHO, as per the above-mentioned documents.

The manufacturer has committed to ensuring that post-emergency use listing safety, quality and performance monitoring activities are in place in accordance with WHO guidance "*Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics*" (ISBN 978-92-4-001531-9).[1]

Scope and duration of procurement eligibility

RapiGEN, Inc., with product codes G61RHA20 and G61RHA20C, manufactured by RapiGEN, Inc., is eligible for WHO procurement 12 months from the day of listing[2]. The assay may be used for the detection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigens. This listing does not infer that the product meets WHO prequalification requirements and does not mean that the product is listed as WHO-prequalified.

As part of the ongoing requirements for listing as eligible for WHO procurement, RapiGEN, Inc. must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality, and performance requirements. RapiGEN, Inc. is required to notify WHO of any complaints, including adverse events related to the use of the product, within 7 days and any changes to the product.

WHO reserves the right to rescind eligibility for WHO procurement if additional information on the safety, quality, and performance during post-market surveillance activities and if new data becomes available to WHO that changes the risk-benefit balance.

[1] Available on the web page https://www.who.int/publications/i/item/guidance-for-post-market-surveillance-and-market-surveillance-of-medical-devices-including-in-vitro-diagnostics.

[2] EUL renewal assessment is ongoing.

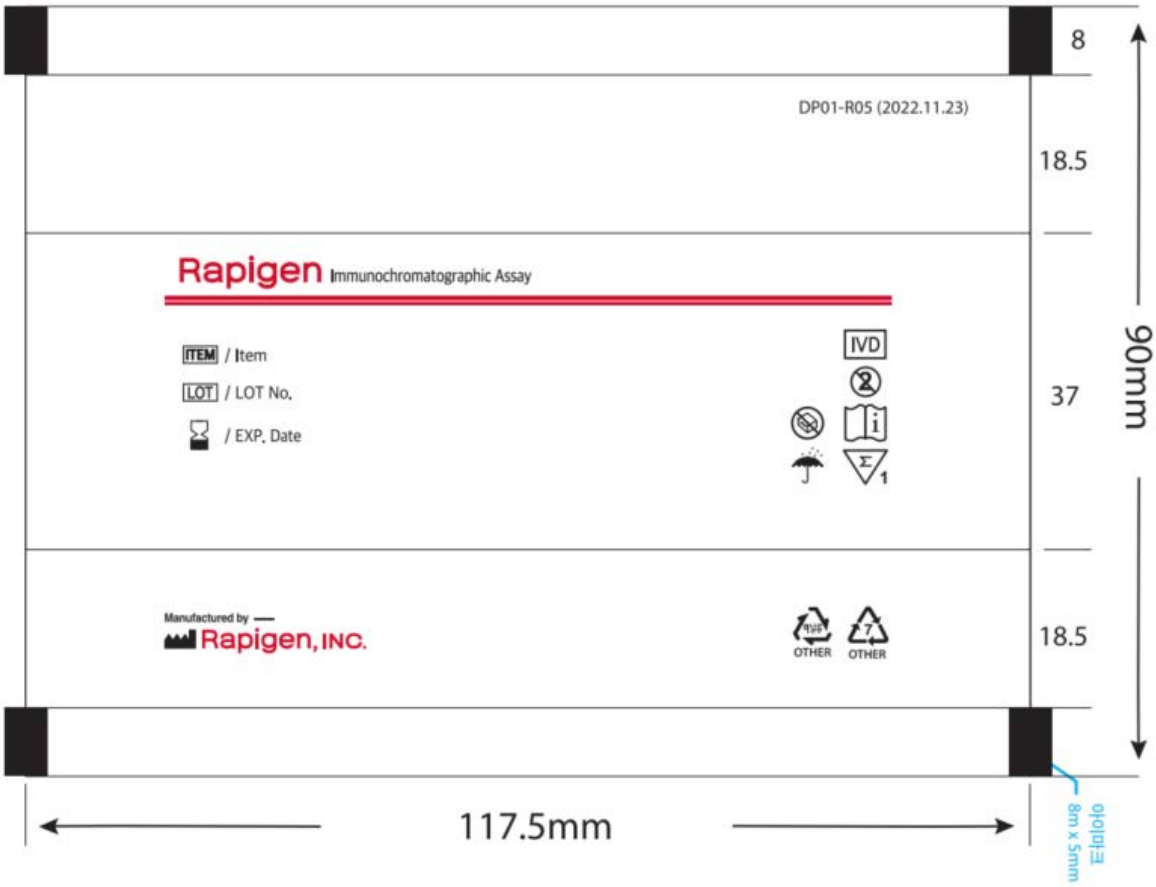
Labelling

1.0 Labels

2.0 Instructions for Use (IFU)

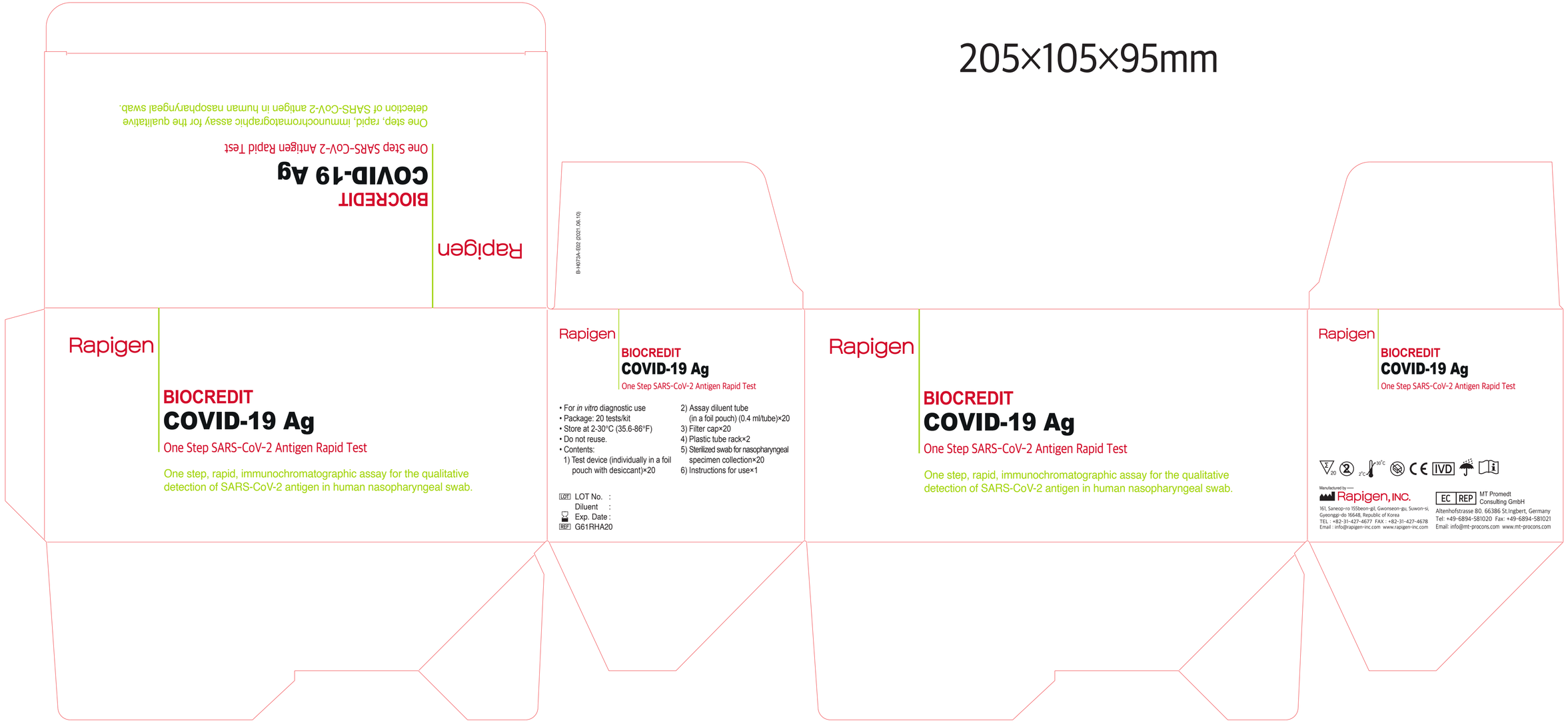
1.0 Product labels

1.1 Primary packaging



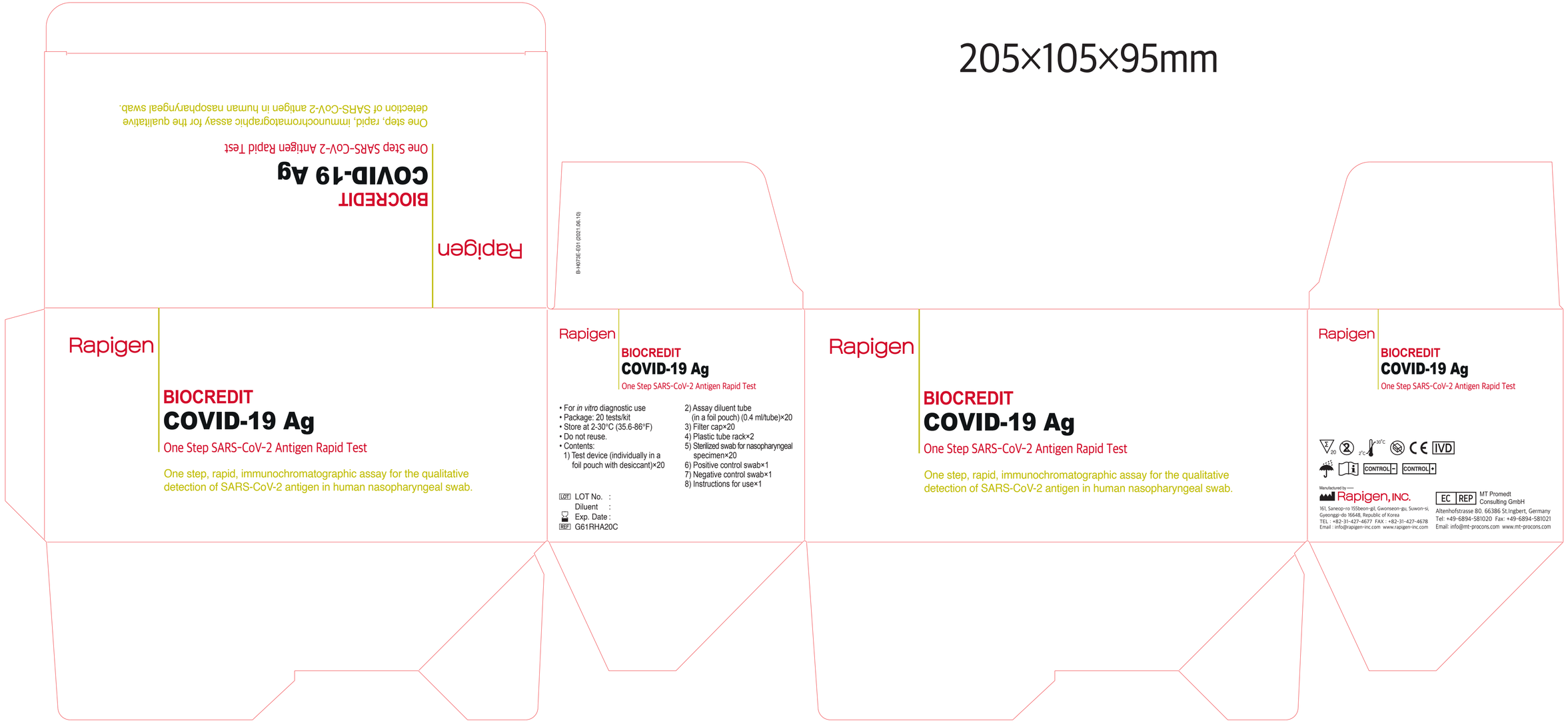
1.2 Secondary Packaging Product code G61RHA20

205×105×95mm

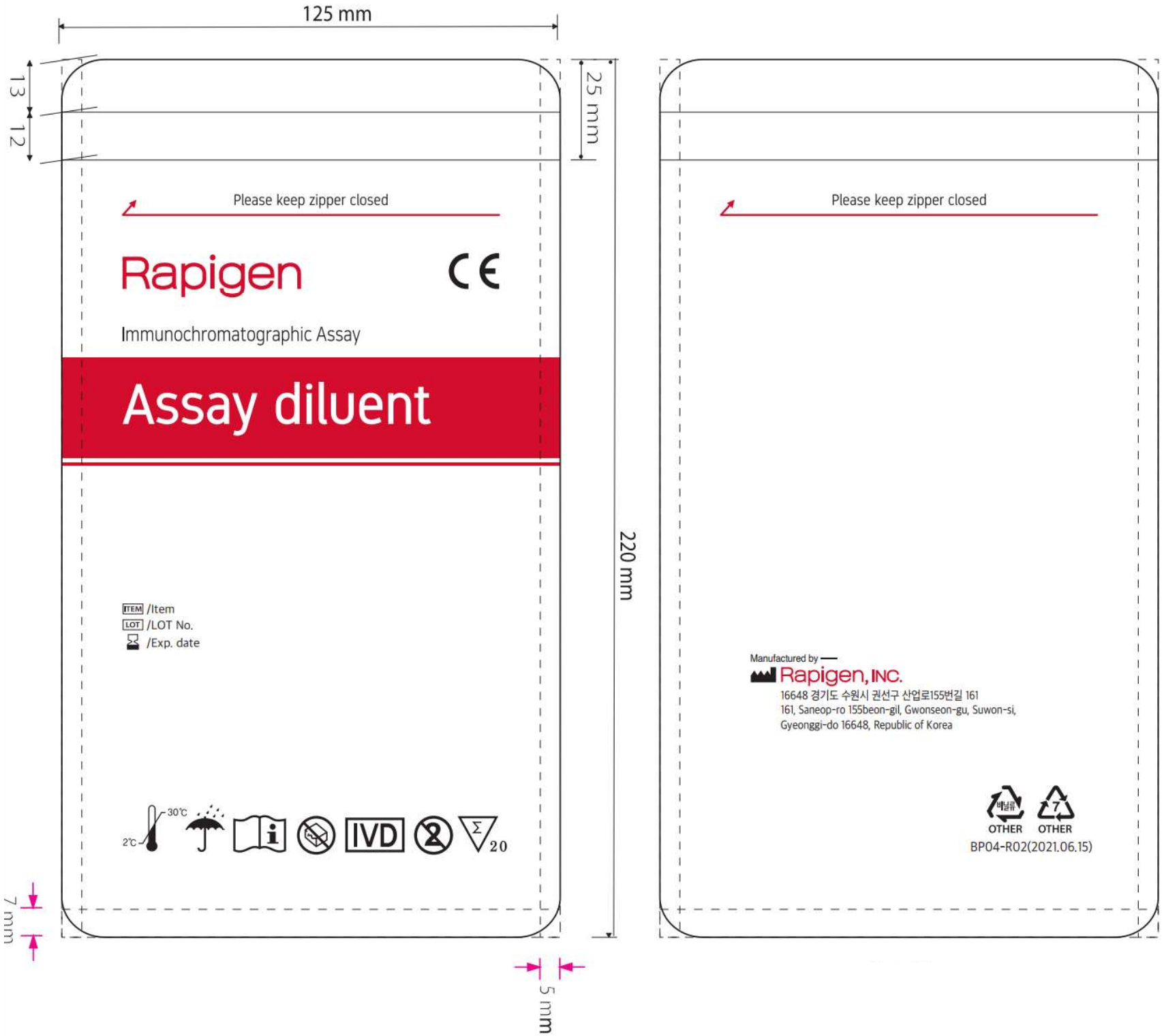

Rapigen
BIOCREDIT
COVID-19 Ag
One Step SARS-CoV-2 Antigen Rapid Test
One step, rapid, immunochromatographic assay for the qualitative detection of SARS-CoV-2 antigen in human nasopharyngeal swab.
B-H0723A-EI02 (2021.06.10)
• For in vitro diagnostic use
• Package: 20 tests/kit
• Store at 2-30°C (35.6-86°F)
• Do not reuse.
• Contents:
1) Test device (individually in a foil pouch with desiccant)×20
2) Assay diluent tube (in a foil pouch) (0.4 ml/tube)×20
3) Filter cap×20
4) Plastic tube rack×2
5) Sterilized swab for nasopharyngeal specimen collection×20
6) Instructions for use×1
LOT LOT No. :
Diluent :
Exp. Date :
REF G61RHA20
IVD
Manufactured by
Rapigen, INC.
161, Saneop-ro 155beon-gil, Gwonseon-gu, Suwon-si, Gyeonggi-do 16648, Republic of Korea
TEL : +82-31-427-4677 FAX : +82-31-427-4678
Email : info@rapigen-inc.com www.rapigen-inc.com
EC REP
MT Promedt Consulting GmbH
Altenhofstrasse 80, 66386 St.Ingbert, Germany
Tel: +49-6894-581020 Fax: +49-6894-581021
Email: info@mt-procons.com www.mt-procons.com

1.3 Secondary packaging Product Code G61RHA20C

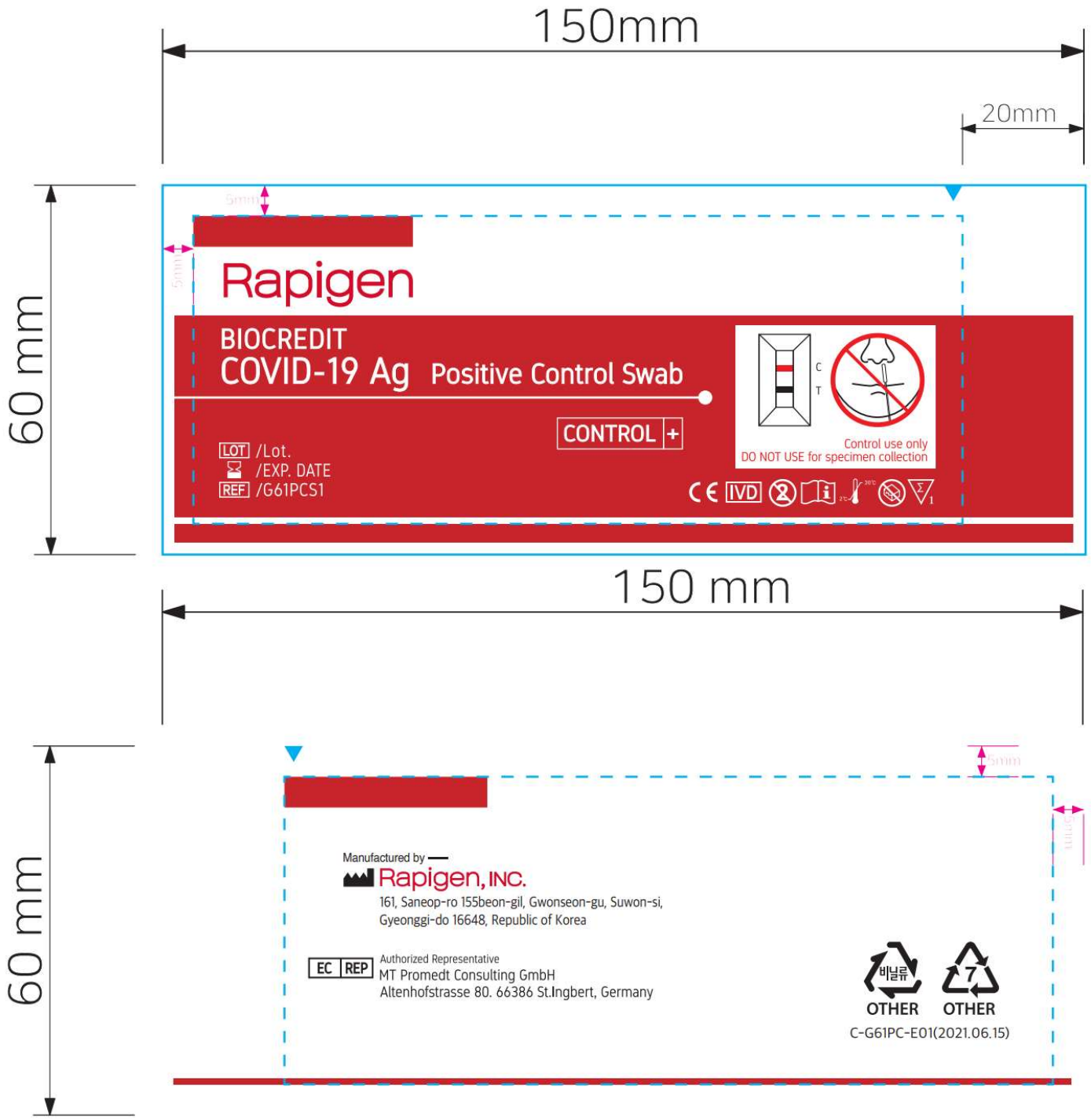
205×105×95mm


Rapigen
BIOCREDIT
COVID-19 Ag
One Step SARS-CoV-2 Antigen Rapid Test
One step, rapid, immunochromatographic assay for the qualitative detection of SARS-CoV-2 antigen in human nasopharyngeal swab.
B-H072E-E01 (2021.06.16)
• For in vitro diagnostic use
• Package: 20 tests/kit
• Store at 2-30°C (35.6-86°F)
• Do not reuse.
• Contents:
1) Test device (individually in a foil pouch with desiccant)×20
2) Assay diluent tube (in a foil pouch) (0.4 ml/tube)×20
3) Filter cap×20
4) Plastic tube rack×2
5) Sterilized swab for nasopharyngeal specimen×20
6) Positive control swab×1
7) Negative control swab×1
8) Instructions for use×1
LOT No. :
Diluent :
Exp. Date :
REF G61RHA20C
2-30°C
IVD
CONTROL -
CONTROL +
Manufactured by
Rapigen, INC.
161, Saneop-ro 155beon-gil, Gwonseon-gu, Suwon-si, Gyeonggi-do 16648, Republic of Korea
TEL : +82-31-427-4677 FAX : +82-31-427-4678
Email : info@rapigen-inc.com www.rapigen-inc.com
EC REP
MT Promedt Consulting GmbH
Altenhofstrasse 80, 66386 St.Ingbert, Germany
Tel: +49-6894-581020 Fax: +49-6894-581021
Email: info@mt-procons.com www.mt-procons.com

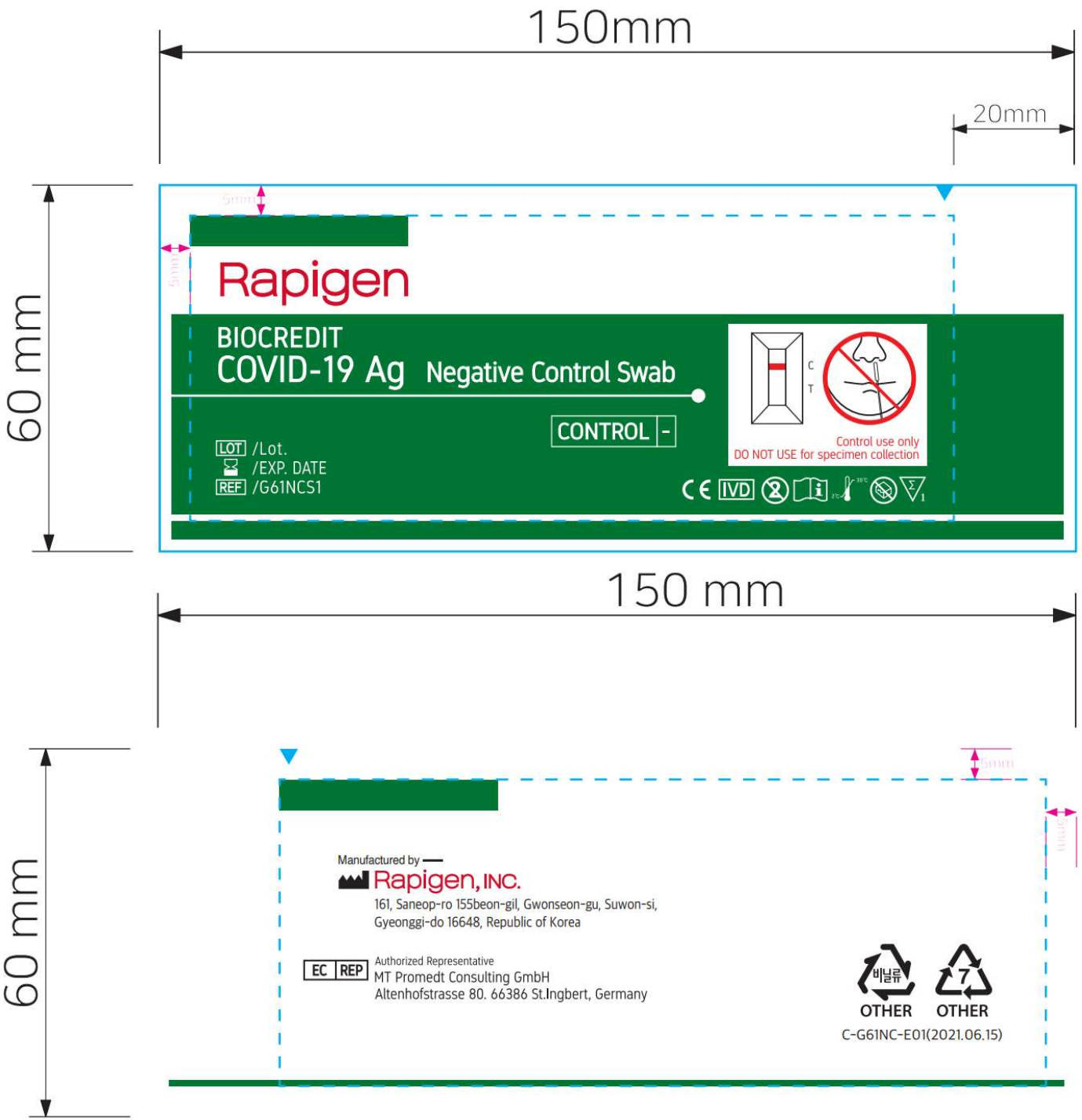
1.4 Buffer pouch


125 mm
13
12
25 mm
Please keep zipper closed
Rapigen
CE
Immunochromatographic Assay
Assay diluent
ITEM /Item
LOT /LOT No.
/Exp. date
2℃
30℃
IVD
Σ 20
220 mm
7 mm
5 mm
Please keep zipper closed
Manufactured by
Rapigen, INC.
16648 경기도 수원시 권선구 산업로155번길 161
161, Saneop-ro 155beon-gil, Gwonseon-gu, Suwon-si,
Gyeonggi-do 16648, Republic of Korea
OTHER
OTHER
BP04-R02(2021.06.15)

1.5 Sterilized nasopharyngeal swab

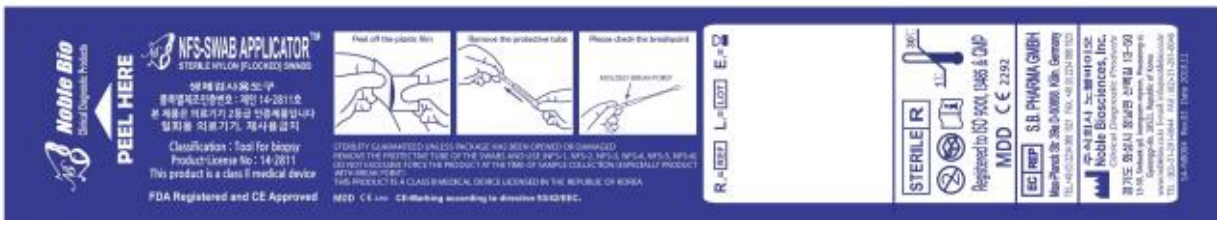

150mm
20mm
60 mm
5mm
5mm
Rapigen
BIOCREDIT
COVID-19 Ag Positive Control Swab
CONTROL +
LOT /Lot.
/EXP. DATE
REF /G61PCS1
C
T
Control use only
DO NOT USE for specimen collection
IVD
150 mm
60 mm
5mm
5mm
Manufactured by
Rapigen, INC.
161, Saneop-ro 155beon-gil, Gwonseon-gu, Suwon-si,
Gyeonggi-do 16648, Republic of Korea
EC REP
Authorized Representative
MT Promedt Consulting GmbH
Altenhofstrasse 80. 66386 St.Ingbert, Germany
비닐류
OTHER
7
OTHER
C-G61PC-E01(2021.06.15)

1.6 Negative Control Swab


150mm
20mm
60 mm
5mm
5mm
Rapigen
BIOCREDIT
COVID-19 Ag Negative Control Swab
CONTROL -
LOT /Lot.
/EXP. DATE
REF /G61NCS1
C
T
Control use only
DO NOT USE for specimen collection
IVD
150 mm
60 mm
5mm
5mm
Manufactured by
Rapigen, INC.
161, Saneop-ro 155beon-gil, Gwonseon-gu, Suwon-si,
Gyeonggi-do 16648, Republic of Korea
EC REP
Authorized Representative
MT Promedt Consulting GmbH
Altenhofstrasse 80. 66386 St.Ingbert, Germany
비닐류
OTHER
7
OTHER
C-G61NC-E01(2021.06.15)

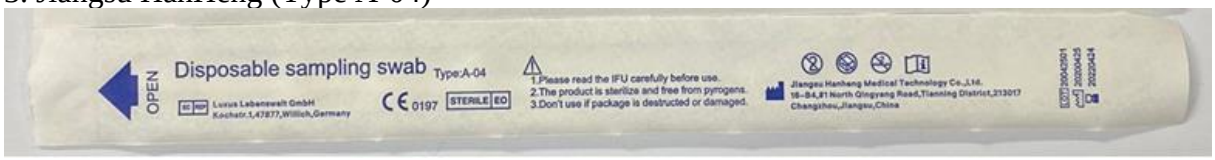
1.7 Positive Control Swab

1. Noble Bioscience (NFS-1)



2. COPAN (534CS01)

3. Jiangsu HanHeng (Type A-04)



4. Jinagsu Changfeng (JSCF-ZR-3)

5. FA INC. (FANAB01)

6. Medico Technology (MFS-96000BQ)

2.0 Instructions for use[3]

[3] English version of the IFU was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

Rapigen

REF G61RHA20/G61RHA20C

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 [1]. 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 nucleocapsid protein antigen on the test lines (T). If SARS-CoV-2 nucleocapsid protein 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 qualitative detection of SARS-CoV-2 nucleocapsid protein antigen in human nasopharyngeal swab specimen collected by trained users in laboratory or point-of-care settings from the patients suspected of COVID-19 within the first 7 days of symptom onset. This assay is intended to aid in diagnosing SARS-CoV-2 infection, and it is for in-vitro professional diagnostic use.

■ Contents
Contents provided

Cat. No. G61RHA20	Cat. No. G61RHA20C
- Test device (individually in a foil pouch with desiccant)×20 - Assay diluent tube (in a foil pouch) (0.4 ml/tube)×20 - Filter cap×20 - Plastic tube rack×2 - Sterilized nasopharyngeal swab×20 - Instructions for use×1	- Test device (individually in a foil pouch with desiccant)×20 - Assay diluent tube (in a foil pouch) (0.4 ml/tube)×20 - Filter cap×20 - Plastic tube rack×2 - Sterilized nasopharyngeal swab×20 - Positive control swab×1 - Negative control swab×1 - Instructions for use×1

Contents required but not provided

● Personal protective Equipment per local recommendations (i.e. gown/lab coat, face mask, face shield/eye goggles and gloves) ● Timer ● Biohazard container (for potentially infectious waste)

■ Nasopharyngeal swab Specimen Collection
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. Specimen should be tested immediately after collection. If the sample has to be stored, close the filter cap with swab removed and store the collected sample in the assay diluent at room temperature (15 - 25°C) up to 2 hours, at 2 - 8°C up to 4 hours prior to testing.
4. To collect nasopharyngeal swab specimen, tilt the patient's head back 70 degrees. Insert a nasopharyngeal swab horizontally into the nasal cavity until resistance is met at the level of the turbinate, reaching the surface of the posterior nasopharynx. The distance is equivalent to that from the nostril to the ear of the patient, indicating contact with the nasopharynx. Gently rub and rotate the swab against the nasopharyngeal mucosa for 10 - 15 seconds to absorb secretion. Do not remove the swab until the tip of the swab is wet.
   * When collect the specimens, follow the Instructions for use thoroughly.
5. Specimen must only be collected using the swabs provided with the product.

■ 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. Do not eat or smoke while handling specimens.
6. Wear protective clothing, gloves and eye protection while handling specimens. Wash hands afterwards.
7. Repeated freeze-thawing specimen can cause false positive or false negative results.
8. Discard the solid waste by autoclaving at 121°C for 1 hour.
9. 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. It should be discarded with copious amounts of water when drained down the drainage system.
10. Do not use the kit beyond the expiration date.
11. Do not reuse the test device and kit components.
12. Do not interchange or mix reagents of different lots.
13. A clinical decision should be made by physician after all clinical and laboratory findings have been evaluated.
14. Specimen must only be collected using the swab provided with the product.
15. Immediately use the swab after opening it and put it into assay diluent tube right after specimen collection.

■ Assay Procedure
【PREPARATION】
1. Equilibrate kit components and specimen to room temperature (15 - 25°C) before testing.
2. Do not open 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. Place the assay diluent tube in the plastic tube rack.
5. Remove the device from the foil pouch and place it on a flat and dry surface.
6. Invert the assay diluent tube and gently squeeze it to dispense 4 drops (120 - 150 µℓ) into a sample well (S) of the device.

Note: 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.

Note: The reagent should be dropped on the site marked with sample well (S). The test can lead to erroneous or invalid results, if the reagent is dropped in the results window.

7. Read the result within 10 - 15 minutes. ► Do not interpret the result after 30 minutes.
8. Dispose of the used device according to your local, state and national regulations and biohazard waste disposal protocol.

■ 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 using a new test device.

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

■ Performance Characteristics
1. Limit of Detection (LoD)

BIOCREDIT COVID-19 Ag was confirmed to 5.35×10^2 $TCID_{50}$/ml (3.55×10^1 copies/µl) of SARS-CoV-2 inactivated virus (SARS-CoV-2 (2019-nCoV) VR-1986HK™ from ATCC (American Type Culture Collection))

BIOCREDIT COVID-19 Ag was confirmed to 5.62×10^2 PFU/ml (8.03×10^2 $TCID_{50}$/ml) of SARS-CoV-2 Cell culture derived live virus (SARS-CoV-2 (2019-nCoV) NCCP 43326 from KCDC pathogen bank)

2. Hook Effect

There was no hook effect up to 2.76×10^5 $TCID_{50}$/ml (1.80×10^4 copies/µl) of SARS-CoV-2 inactivated virus (SARS-CoV-2 (2019-nCoV) VR-1986HK™ from ATCC (American Type Culture Collection))

There was no hook effect up to 9×10^5 PFU/ml (≈ 1.28×10^6 $TCID_{50}$/ml) of cell culture virus (SARS-CoV-2(2019-nCoV) NCCP 43326 from KCDC pathogen bank)

3. Clinical performance

365 nasopharyngeal samples were identified positive with WHO EUL RT-PCR reference method with a total number of enrolled individuals of 1076 to evaluate the clinical performance of BIOCREDIT COVID-19 Ag in Uganda, United Kingdom and Brazil. It was determined by testing 365 positive and 711 negative specimens for SARS-CoV-2 nucleocapsid protein antigen (Ag) to have a sensitivity of 80.8% (295/365, 95% CI 76.3% - 84.7%) and specificity of 98.7% (702/711, 95% CI 97.5% - 99.4%). Stratification of the positive samples post onset of symptoms between 0 - 3 days has a sensitivity of 84.8% (173/204, 95% CI 79.0% - 89.3%) and within 7days has a sensitivity of 82.5% (269/326, 95% CI 77.9% - 86.4%). Positivie samples with Ct value≤33 has a higher sensitivity of 87.1% (291/334, 95% CI 82.9% - 90.4%).

Country	Uganda (QARAD)	United Kingdom (FIND)	Brazil (FIND)	Overall
Sensitivity (Ct≤25)	100% (44/44, 95% CI 92.0% - 100%)	92.2% (83/90, 95% CI 84.8% - 96.2%)	100% (100/100, 95% CI 96.3% - 100%)	97% (227/234, 95% CI 93.7% - 98.7%)
Sensitivity (Ct≤33)	91.6% (87/95, 95% CI 83.6% - 96.0%)	85.8% (97/113, 95% CI 78.2% - 91.1%)	84.9% (107/126, 95% CI 77.6% - 90.1%)	87.1% (291/334, 95% CI 82.9% - 90.4%)
Sensitivity (0≤ Days post onset of symptoms ≤3)	80.4% (37/46, 95% CI 66.8% - 89.3%)	81.8% (81/99, 95% CI 72.5% - 88.6%)	93.2% (55/59, 95% CI 82.7% - 97.8%)	84.8% (173/204, 95% CI 79.0% - 89.3%)
Sensitivity (Days post onset of symptoms ≤7)	79.6% (74/93, 95% CI 70.3% - 86.5%)	82.1% (96/117, 95% CI 74.1% - 88.0%)	85.3% (99/116, 95% CI 77.8% - 90.6%)	82.5% (269/326, 95% CI 77.9% - 86.4%)
Clinical Sensitivity	77.6% (90/116, 95% CI 69.2% - 84.2%)	82.2% (97/118, 95% CI 74.3% - 88.1%)	82.4% (108/131, 95% CI 75% - 88%)	80.8% (295/365, 95% CI 76.3% - 84.7%)
Clinical Specificity	98.3% (400/407, 95% CI 96.5% - 99.2%)	98.1% (104/106, 95% CI 93.4% - 99.5%)	100% (198/198, 95% CI 98.1% - 100%)	98.7% (702/711, 95% CI 97.5% - 99.4%)

4. Precision

Within-run, between-run, between day, between lot and between site precision has been determined in quintuplicate using the following specimen: negative, low positive, medium positive and strong positive. All specimens are correctly identified 100% of the time.

5. Cross reactivity & Microbial interference

BIOCREDIT COVID-19 Ag has been tested with 39 potentially cross reacting microorganisms and viruses. The results showed that BIOCREDIT COVID-19 Ag has no cross-reaction with microorganisms and viruses except cross reacting with SARS-coronavirus in the following substances.:

No.	Type	Analytical specificity materials	Concentration
1	Other high priority pathogens from the same virus family	Human coronavirus (229E)	1.1×10^5 PFU/ml
2		Human coronavirus (OC43)	3.1×10^5 PFU/ml
3		Human coronavirus (HKU1)	0.5 µg/ml*
4		Human coronavirus (NL63)	0.9×10^5 $TCID_{50}$/ml
5		SARS-coronavirus (Tor2)	0.5 µg/ml**
6		MERS-CoV	0.05 µg/ml***
7	Other high priority organisms	Adenovirus type 1	5×10^5 $TCID_{50}$/ml
8		Adenovirus type 2	2.5×10^5 $TCID_{50}$/ml
9		Adenovirus type 3	2.5×10^5 $TCID_{50}$/ml
10		Adenovirus type 5	2.5×10^6 $TCID_{50}$/ml
11		Adenovirus type 6	2.5×10^6 $TCID_{50}$/ml
12		Adenovirus type 8	2.5×10^5 $TCID_{50}$/ml
13		Parainfluenza 1	8×10^4 PFU/ml
14		Parainfluenza 2	5×10^5 PFU/ml
15		Parainfluenza 3	2.5×10^6 PFU/ml
16		Parainfluenza 4a	1.41×10^7 $TCID_{50}$/ml
17		Influenza A-H1N1	1.5×10^5 PFU/ml
18		Influenza A-H3N2	2.5×10^6 PFU/ml
19		Influenza B	4.25×10^6 PFU/ml
20		Human enterovirus D Enterovirus 70	4.3×10^5 PFU/ml
21		Respiratory syncytial virus-virus A	1.2×10^6 PFU/ml
22		Respiratory syncytial virus-virus B	2.3×10^5 PFU/ml
23		Human Rhinovirus 14(B)	6×10^4 PFU/ml
24		Human Rhinovirus 21(A)	1.2×10^5 PFU/ml
25		Human metapneumovirus	8×10^5 $TCID_{50}$/ml
26	Others	Pooled human nasal wash - to represent diverse microbial flora in the human respiratory tract	N/A
27	Microbial organisms related to upper respiratory infection similar to COVID-19	*Legionella pneumophila*	5×10^5 CFU/ml
28		*Streptococcus pneumoniae*	5×10^5 CFU/ml
29		*Streptococcus pyogenes*	5×10^5 CFU/ml
30		*Bordetella pertussis*	5×10^5 CFU/ml
31		*Mycoplasma pneumonia*	2.25×10^8 CFU/ml
32		*Klebsiella pneumonia*	5×10^5 CFU/ml
33		*Candida albicans*	5×10^5 CFU/ml
34		*Staphylococcus aureus*	5×10^5 CFU/ml
35		*Staphylococcus epidermidis*	5×10^5 CFU/ml
36		*Chlamydia pneumoniae*	7×10^5 CFU/ml
37		*Haemophilus influenzae*	5×10^5 CFU/ml
38		*Mycobacterium tuberculosis* (*In- silico (protein blast)*)	-
39		*Pneumocystis jirovecii (PJP)* (*In- silico (protein blast)*)	-

* Human coronavirus (HKU1) has been tested with recombinant nucleocapsid protein in the absence of SARS-CoV-2 and cross-reaction was not happened. The % identity of the protein sequence of recombinant nucleocapsid protein for HKU1 with the NP protein sequence of SARS-CoV-2 was 37.6% which was considered as low homology.

** Cross-reactivity test of SARS-CoV (Tor2) has been performed with recombinant SARS-CoV (Tor2) nucleoprotein in the absence of SARS-CoV-2 and cross-reaction was happened. The % identity of the protein sequence of recombinant SARS-CoV (Tor2) nucleoprotein in the absence of SARS-CoV-2 was 90.3% which was considered as high homology.

*** Cross-reactivity test of MERS-CoV has been performed with recombinant nucleocapsid protein of MERS-CoV in the absence of SARS-CoV-2 and cross-reaction was not happened. The % identity of the protein sequence of recombinant nucleocapsid protein for MERS-CoV with the NP protein sequence of SARS-CoV-2 is 48.2% which is considered as low homology.

**** Mycobacterium tuberculosis was BSL 3 microorganism, so it was performed in BLAST. BLAST test result was not confirmed homology (0%) with SARS-CoV-2 nucleocapsid phosphoprotein and Mycobacterium tuberculosis.

***** Pneumocystis jirovecii was performed in BLAST. BLAST test result was not confirmed homology (0%) with SARS-CoV-2 nucleocapsid phosphoprotein sequence and Pneumocystis jirovecii.

6. Interference

BIOCREDIT COVID-19 Ag has been tested with 40 potentially interfering endogenous or exogenous substances. None of 40 substances tested showed an interference effect:

1) Endogenous factors

No.	Type	Interfering Substances	Concentration
1	Serum protein	HAMA Serum, Type I (Occurring in healthy donors)	63 ng/ml
2		HAMA Serum, Type II (Occurring after treatment with monoclonal antibodies)	63 ng/ml
3		Rheumatoid factor	20 U/ml
4		Bilirubin	200 µg/ml
5		Bilirubin Conjugate	290 µg/ml
6		Hemoglobin	200 µg/ml
7		Cholesterol	2.2 mg/ml
8	-	Whole blood	4%

2) Exogenous factors

No.	Type	Interfering substances	Concentration
1	Anticoagulants	EDTA-2Na	5 mg/ml
2		Heparin	20 mg/L
3		Sodium citrate	10 mg/ml
4	Hypoglycemia medication	Glucose	10 mg/ml
5	Anti-inflammatory medication	Acetaminophen	200 µM
6		Acetylsalicylic acid	3.7 mM
7	Antihistamine	Diphenhydramine hydrochloride	456 mg/ml
8	Nasal sprays, gels or drops	Nasal spray	15% (v/v)
9		Saline nasal gel	5% (v/v)
10		Rhinocort (Nasal corticosteroids Budesonide)	256 µg
11		Fluticasone Propionate	5% (v/v)
12		Afrin (Oxymetazoline)	15% (v/v)
13		Naso Gel (GelMed)	5% (v/v)
14		Homeopathic (Alkalol)	10% (v/v)
15		CVS Nasal Drops (Phenyleprine)	15% (v/v)
16		CVS Nasal Spray (Cromolyn)	15% (v/v)
17	Sore throat sprays, betadine, or medicine	Sore Throat Phenol Spray	15% (v/v)
18		Betadine sore throat	5% (w/v)
19		Chloraseptic (Menthol/Benzocaine)	1.5 mg/ml
20	Anti-viral drugs	Zanamivir	5% (w/v, 1 mg/ml)
21		Favipiravir	5% (w/v, 1 mg/ml)
22		Tamiflu (Oseltamivir Phosphate)	5 mg/ml
23	Antibiotic	Mupirocin	10 mg/ml
24		Ciprofloxacin (antibiotic)	5% (w/v, 250 mg/ml)
25		Tobramycin	4 µg/ml
26	Cold remedy	Zicam	5% (v/v)
27	Others	Biotin	1.2 µg/ml
28		Mucin:bovine submaxillary gland, type I-S	100 µg/ml
29	Hand sanitizer gel	PURELL® Advanced Hand Sanitizer Gel	5% (v/v)
30		Germ-X Original	5% (v/v)
31	Hand lotions	Neutrogena – Norwegian Formula Hand Cream	5% (v/v)
32	Soap	GOJO® Mild Foam Hand Wash Fragrance Free	5% (v/v)

7. Viral variants

To evaluate the potential impact of viral mutations on the performance of BIOCREDIT COVID-19 Ag, Rapigen has conducted tests using the variants in circulation. Results are tabulated below.:

Variants (WHO Label)	Detection	Specimen type used
Wild type	v	Cell cultured virus
B.1.1.7 (Alpha)	v	Cell cultured virus
B.1.351 (Beta)	v	Cell cultured virus
P.1 (Gamma)	v	Cell cultured virus
B.1.617.2 (Delta)	v	Cell cultured virus
AY.1 (Delta plus)	v	Cell cultured virus
P.2 (Zeta)	v	Cell cultured virus
B.1.621 (Mu)	v	Cell cultured virus
BA.1 (Omicron)	v	Cell cultured virus

* Rapigen will continue to monitor the performance of BIOCREDIT COVID-19 Ag with future viral variants as they become available to us and will provide additional updated results for future new variants upon request.

■ 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.
3. The test should be used for the detection of SARS-CoV-2 nucleocapsid protein antigen in human nasopharyngeal swab specimens.
4. A negative result may occur if the specimen was collected or transported improperly, therefore a negative test result does not eliminate the possibility of SARS-CoV-2 infection, and should be confirmed by viral culture or a molecular assay.
5. Positive test results do not rule out co-infections with other pathogens.
6. Reading the test results earlier than 10 minutes or later than 30 minutes may give incorrect results.
7. Positive results may occur in cases of infection with SARS-CoV.

■ External Quality Control
External control swabs can be provided as additional quality control to verify the test performance. It is recommended that positive and negative control swabs are run once with every new lot, shipment and untrained operator. The external control swabs should be treated and tested under the same method and standard as the patient specimens, as required by the test procedures stated in this instruction and in accordance with local, state and federal regulations or accreditation requirements. The positive control will produce a positive test result so a visible black test line (T) will be seen whereas the negative control will produce a negative test result. If these results are not obtained, do not perform any tests using samples from patients or read any results from the test device.

* G61RHA20C contains the external control swabs only.

* Do not insert the external control swab into the patient's nose.

■ Package 20 tests/kit

■ Storage Condition
Store at 2-30°C. Kit materials are stable until the expiration date marked on the kit box and/or the packaging of individual contents when stored as specified. Do not store the kit in the freezer.

■ Symbol Key

Symbol	Explanation	Symbol	Explanation
Σ n	Contains sufficient for <n> tests		Consult instructions for use
	Do not reuse	LOT	Lot number
	Temperature limitation	REF	Catalogue number
	Do not use if packaging is damaged		Expiration date (YYYY.MM.DD)
	European mark of conformity		Manufacturer
IVD	*In vitro* diagnostic medical device	EC REP	Authorized representative in the European Community
	Keep dry	CONTROL -	Negative control
		CONTROL +	Positive control

■ References

[1] WHO (World Health Organisation) A coordinated Global Research Roadmap. http://www.who.int/who-documents-detail/a-coordinated-global-research-roadmap,2020a (accessed 15 May 2020).

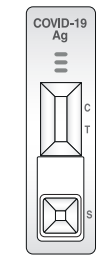
Rapigen

REF G61RHA20/G61RHA20C

BIOCREDIT
COVID-19 Ag

One Step SARS-CoV-2 Antigen Rapid Test

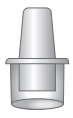
■ Description of materials provided

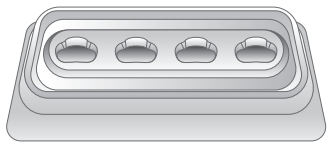


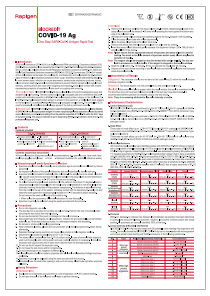
Test Device


Assay diluent tube

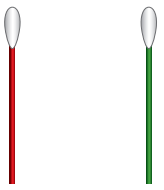
Sterilized swab


Filter cap


Plastic tube rack

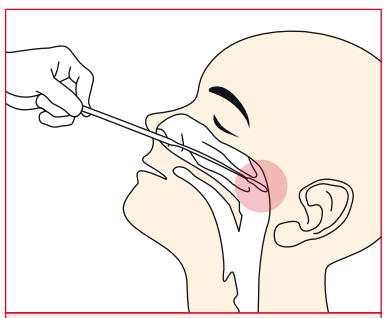

Instructions for use

External control swab
(Only for G61RHA20C)


Positive Swab

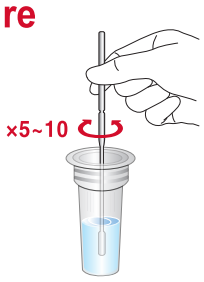
Negative Swab

■ Specimen collection

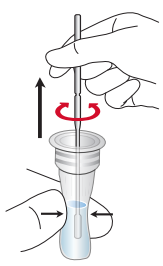

Nasopharyngeal Swab

- 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, reaching the surface of the posterior nasopharynx.
- The distance is equivalent to that from the nostril to the ear of the patient, indicating contact with the nasopharynx.
- Gently rub and rotate the swab against the nasopharyngeal mucosa for 10-15 seconds to absorb secretion.
- Do not remove the swab until the tip of the swab is wet.

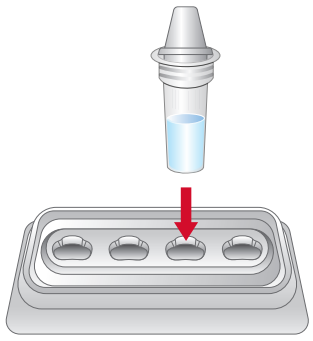
■ Assay Procedure

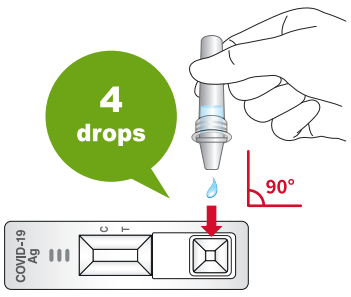


1 Insert the swab specimen and swirl the swab 5-10 times.


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


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


4 Place the assay diluent tube in the plastic tube rack. Remove the device from the foil pouch and place it on a flat and dry surface.



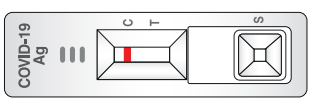
5 Invert the assay diluent tube and gently squeeze it to dispense 4 drops (120 - 150 μℓ) into a sample well on the device vertically.

Read 10~15 mins

6 Read the result within 10 - 15 minutes.
Do not interpret the result after 30 minutes.

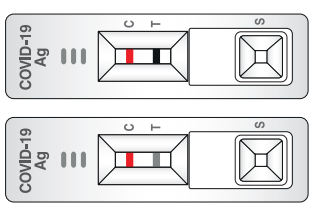
■ Interpretation of Results

Negative



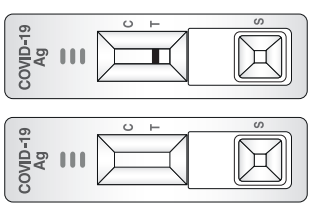
One red line "C" within the result window.

Positive



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

Invalid



No "C" line within the result window. It is recommended that the specimen be retested using a new test device.

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