abionic IVD CAPSULE COVID-19-NP User Manual

Contents

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abionic IVD CAPSULE COVID-19-NP

Intended use

The IVD CAPSULE COVID-19-NP is a single use, rapid in vitro diagnostic test intended for the qualitative detection of SARS-CoV-2 viral nucleocapsid antigens in nasopharyngeal specimens from individuals suspected of

SARS-CoV-2 infection. The IVD CAPSULE COVID-19-NP is intended to be used in conjunction with the abioSCOPE 2.0 in vitro diagnostic test system for professional use in near-patient/point of care (PoC) locations. In conjunction with accessory REF P04.00019 (saliva swab) saliva specimens can be collected and analyzed instead of nasopharyngeal specimens.

Summary

COVID-19 is the infectious disease caused by the recently discovered SARS-CoV-2. The virus is spread by human-to-human transmission through droplets of saliva or discharge from the nose when an infected person coughs or sneezes.1 The most common symptoms of COVID-19 are fever, dry cough, tiredness, headache, shortness of breath, sore throat, aches and pains.1 However, some people are infected but do not develop any symptoms and do not feel unwell.2 Older people and those with underlying medical problems like cardiovascular disease, chronic respiratory disease, diabetes, and cancer are more likely to require hospitalization. Current epidemiological findings show that the incubation period can be up to 14 days while it is most often within 4 to 7 days1,2.

Test principle

The nasopharyngeal (or saliva) sample is first collected from the nasopharynx (or the mouth) using a swab, and then mixed with a solution composed of a fluorescently labeled antibody reactive to SARS-CoV-2 nucleocapsid antigen. The collected sample, now containing the complex of SARS-CoV-2 antigen and antibodies, is loaded onto the capsule of the kit. Patient material is drawn through the capsule by capillary action and passes through a built-in separator that excludes particles from the measurement area. After passing through the separator, the SARS-CoV-2-antibody complex is bound by antibodies immobilized on the capsule's read-out area. In the case where sufficiently high concentrations of SARS-CoV-2 antigen are present in the sample, a fluorescence signal above the limit of detection is generated by the fluorophore conjugated to the signal antibody. The abioSCOPE (REF P01.00007) reader will detect this signal, process it and display. a message whether the patient is SARS-CoV-2 infected ("positive") or not ("negative"), or "failed" in case of an invalid procedure.

Reagents

Each assay contains one squeeze tube with a drop-dispensing cap containing 150l of the abioMIX reagent. The abioMIX reagent is composed of the fluorescently labeled anti-nucleocapsid antibody, dissolved in a viral lysis buffer. The abioMIX reagent also contains a preservative.

Ingredient	Conc.
Fluorescently labelled anti-nucleocapsid antibody	1.4 µg/ml
Tris-HCl	150 mM
Sodium Chloride	450 mM
Deoxycholic Acid	0.75%
NP-40	3%
EDTA	3 mM
ProClin300 (CAS number 55965-84-9)	0.04% (v/v)

Table 1| Composition of the **abioMIX** reagent.

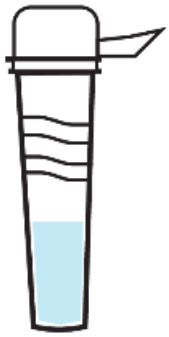
Materials included

- 1x COVID-19 capsule
- 1x squeeze tube of abioMIX reagent including a drop-dispensing cap
- 1x CE-marked swab for nasopharyngeal sample collection (provided separately outside of the blister package).
- 1x desiccant bag
- 1 x printed Instructions for Use (IFU)

Not included in the kit: 1x swab for saliva (accessory to be ordered separately, REF P04.00019).

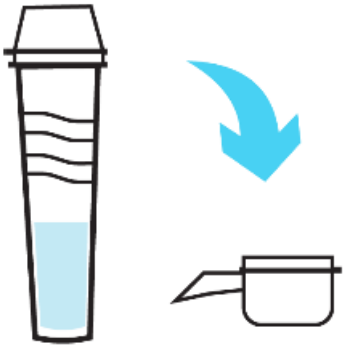
Test procedure

1. Allow the abioMIX reagent to warm up to room temperature (about 10 min) before opening and use immediately after.
2. The test subject shall not eat, drink or smoke for 30 min before the test.
3. It is recommended to put on protective gloves before starting the procedure.
4. Initiate the abioSCOPE analyser
    - Make sure that the abioSCOPE is switched on and ready to measure.
5. To start using the IVD Capsule COVID-19-NP kit, open the blister package, and keep it within reach in your working space. The reagent tube can already be removed from the package if required but it should not be opened yet.

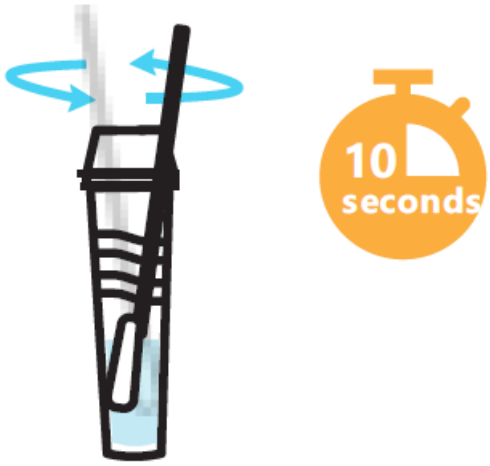


For nasopharyngeal specimen collection, take the included nasopharyngeal swab, and insert it through the nostril along the nasal septum to the nasopharynx, until resistance is felt. Gently roll the swab for several seconds to collect the specimen and then slowly withdraw the swab while rotating it.
For saliva specimen collection, take the saliva swab (accessory REF P04.00019), insert it into the mouth, and place it under the tongue. Let the saliva passively pool under the tongue and between the tongue and cheek for approximately 15 seconds. Soak the swab with the pooled saliva by rolling and moving the swab under the tongue from side-to-side 5 times and then withdraw the swab from the mouth.

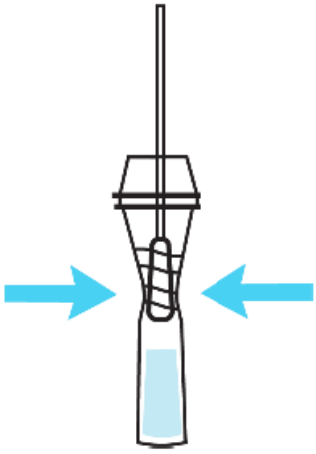
6. The sample should be processed immediately using the IVD CAPSULE COVID-19-NP kit, and the whole procedure should be executed within 5 min.
7. Take the extraction reagent tube and flick the tube in a downwards motion to move all the reagent to the bottom of the tube. Subsequently, remove and discard the cap from the tube.



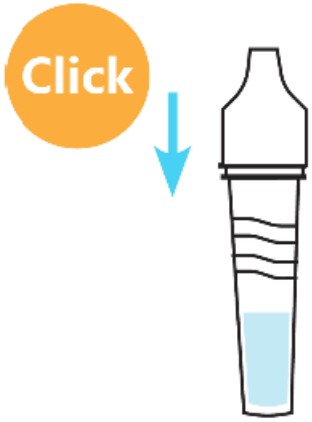
8. Carefully insert the swab into the extraction buffer in the tube and stir the swab in the fluid against the tube wall for a minimum of 10 seconds, taking care not to splash contents out of the tube.



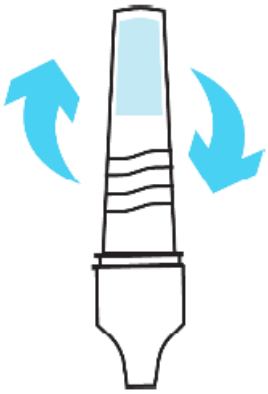
9. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab.



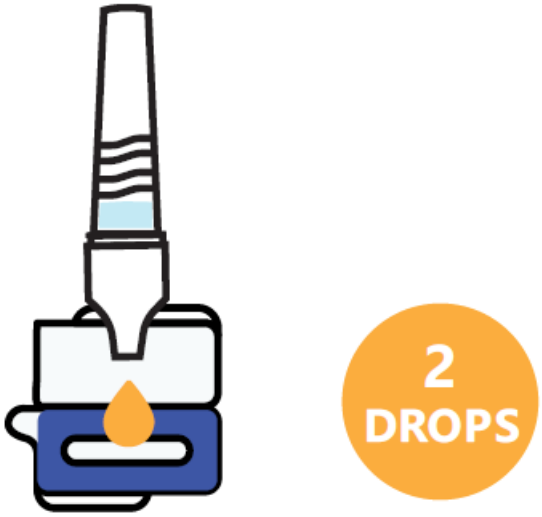
10. Press the dropper tip firmly onto the extraction reagent tube containing the processed sample (twisting is not required).



11. Adding drops to the test device
    - Invert the extraction reagent tube and hold it vertically (approximately half a centimetre above the sample port).

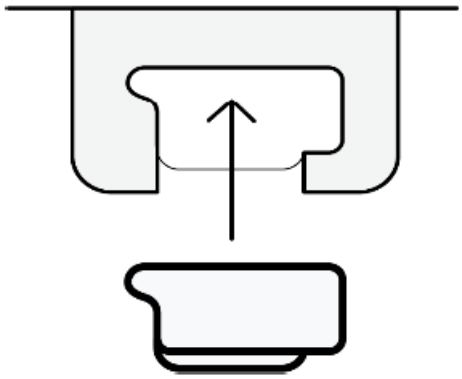


- Gently squeeze the ridged body of the tube, dispensing two (2) drops of the processed specimen into the middle of the sample port, as displayed in the image below.



- Fold the lid over to close the capsule. Hold the capsule only by the edges. Be careful not to touch the bottom side of the capsule.
- Excess volume that remains in the tube can be used for retesting if necessary.
- Immediately (within 30 seconds) measure the capsule in the abioSCOPE.

12. Measurement in the abioSCOPE analyser
    - Press the measurement button on the screen. The tray of the abioSCOPE will automatically open.
    - Place the capsule inside and press the close tray button.



    - Add the patient information in the following fields. After confirmation (push next step) the measurement is automatically initiated.
13. After the measurement process (within 2 minutes) the result of the test is directly displayed on the screen (in a coded form if required) and stored in abioSCOPE's internal memory.
14. Dispose the used device (abioMIX tube, capsule and swab) according to your local regulations and biohazard waste disposal protocol.

Interpretation of results of the test
A positive result indicates that the patient (very probably) has contracted COVID-19 and that he/she should contact a medical doctor for further information and instructions.
In case of a negative result the patient is (probably) not infected. It is still advised to closely follow the protection and hygiene measures. In case that an invalid/failed result is displayed, a retest should be done with a new capsule.

Storage and stability
To be stored at 2-8 °C up to the expiration date printed on the label. The abioMIX reagent is ready-to-use. Allow the abioMIX reagent to warm up to room temperature (about 10 min.) before opening and use immediately after. The maximum stay at room temperature after opening must not exceed 3 hours. After removal from refrigerated storage, the unopened kit must be used within 3 days. The nasopharyngeal (or saliva) sample mixed with the abioMIX reagent should be immediately loaded onto the COVID-19 capsule. The filled capsule should be immediately measured.

Traceability and calibration
Each lot of IVD CAPSULE COVID-19-NP is calibrated by the manufacturer using a purified preparation of recombinant 2019nCoV antigen nucleocapsid protein (N protein) based on the mass (concentration) of the analyte present in an artificial matrix simulating nasopharyngeal secretion and saliva in order to guarantee the diagnostic performance.

Quality control
The abioSCOPE evaluates internal controls at power-on and after insertion of the capsule. If controls fail the abioSCOPE displays a specific error message.
For external positive control material, it is recommended to use SARS-CoV-2 Culture Fluid (UV Inactivated Hong Kong/VM20001061/2020, 0810590UV) from ZeptoMetrix Corporation mixed into a negative SARS-CoV-2 saliva pool or artificial nasopharyngeal matrix. Contact the manufacturer for assistance and follow the applicable local regulations and guidelines. The control intervals should be adapted to individual requirements. The negative sample shall report a negative test result. The positive sample shall report a positive test result.

Warnings and precautions

- For in vitro diagnostic use.
- The IVD CAPSULE COVID-19-NP must be kept refrigerated until use.
- Do not freeze.
- Make sure that all packaging is intact. Do not use the test if the bister packaging is visibly damaged.
- Allow the abioMIX reagent tube to reach room temperature before use.
- Use only the swabs specifically provided with/for the kit.
- This product requires the handling of human specimens. It is recommended that all human-sourced material should be considered potentially infectious. Appropriate precautions should be used for handling and disposal of materials during and after testing.
- Do not use reagents after the expiration date printed on the box.
- Incubation of the specimen in the abioMIX for more than 5 minutes may impact test results.
- This product is intended for use with nasopharyngeal and saliva samples only.
- Clean the abioSCOPE surfaces regularly with alcohol (at least before switching it on and after switching it off, as well as in-between consecutive tests when appropriate).

Reagent deterioration
The following observations indicate reagent deterioration:

- Presence of turbidity in the abioMIX vial.

- Consistently positive or negative values from assay kits from the same batch.

Limitations

- Eating, drinking, or smoking within 30 min before the test may adversely affect the test performance.
- Failure to correctly follow the test procedure may adversely affect the test performance and/or invalidate the test result.
- A false-negative test result may occur if the level of viral antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly; therefore, a negative test result does not eliminate the possibility of SARS-CoV-2 infection.
- Positive test results do not rule out co-infections with other pathogens.
- Negative test results are not intended to rule out other viral or bacterial infections.
- Negative results should be treated as presumptive and confirmed with a molecular test if COVID-19 disease is suspected.
- The collected specimens should be tested as quickly as possible after collection.
- All assay materials are single-use and cannot be re-used.
- Clinical performance was evaluated with frozen samples, and test performance may be different with fresh samples.
- The amount of antigen in a sample may decrease as the duration of the illness increases. Specimens collected after day 5 of illness are more likely to be negative compared to an RT-PCR assay.
- Monoclonal antibodies may fail to detect or detect with less sensitivity, SARS-CoV-2 viruses that have undergone minor amino acid changes in the target epitope region.

The user shall report any serious incident that has occurred in relation to the device to the manufacturer and the relevant national competent authority.

Performance characteristics

Analytical sensitivity
LoD was determined by spiking SARS-CoV-2 Culture Fluid UV Inactivated Hong Kong/VM20001061/2020 (0810590UV, batch 326734, ZeptoMetrix Corporation) into a negative SARS-CoV-2 saliva pool or artificial nasopharyngeal matrix. In the first phase, a 10-fold dilution series, starting from a target concentration of 105 TCID50/ml was performed. Each dilution was tested in 3 replicates on bioscope 2.0. The lowest concentration to give 3 positive results was selected to measure a 2-fold dilution series where each dilution is tested in 3 replicates on the bioscope 2.0. The lowest concentration to give 3 positive results was 755 TCID50/mL. When tested in 20 replicates this dose gave 20 out of 20 results. The limit of detection (LoD) within a 95% confidence interval for IVD CAPSULE COVID-19-NP is 755 TCID50/mL.

Microbial interferences
The IVD CAPSULE COVID-19 assay was tested for cross-reactivity and interference using bacteria and viruses that are reasonably likely to be encountered in respiratory clinical specimens, and no cross-reactions nor interferences were observed at the concentrations as listed below:

Cross-reactant	Conc.
Adenovirus Type 5 (Hexon protein)	1 µg/mL
Candida albicans (antigen, Purified lysate)	1 µg/mL
Enterovirus (antigen, Recombinant antigen)	1 µg/mL
Human Coronavirus 229E (Purified viral Lysate)	1 µg/mL
Human Coronavirus NL63 (Purified viral Lysate)	1 µg/mL
Human Coronavirus OC43 (Purified viral Lysate)	1 µg/mL
Human Metapneumovirus 9 (Type A1, Lysate)	1 µg/mL
Human Parainfluenza Virus (Type 1, Lysate)	1 µg/mL
Human Parainfluenza Virus (Type 2, Lysate)	1 µg/mL
Human Parainfluenza Virus (Type 3, Lysate)	1 µg/mL
Human Parainfluenza Virus (Type 4A, Lysate)	1 µg/mL
Human Parainfluenza Virus (Type 4B, Lysate)	1 µg/mL
Influenza A (A/Brisbane/10/2007 (H3N2), Lysate)	1 µg/mL
Influenza A (A/New Caledonia/20/1999 (H1N1), Lysate)	1 µg/mL
Influenza B (B/Brisbane/33/08 Lysate)	1 µg/mL
Coronavirus Spike Glycoprotein (MERS, S1, Camel Fc-Tag (HEK293), Recombinant protein)	1 µg/mL
Mycoplasma pneumoniae (Purified lysate)	1 µg/mL
Respiratory Syncytial Virus A (Type A, Lysate)	0.1 µg/mL
Respiratory Syncytial Virus B (Type B, Lysate)	1µg/mL
Rhinovirus (Type 1A, Lysate)	1 µg/mL
Coronavirus HKU1 (Recombinant nucleoprotein)	1 µg/mL
Coronavirus HKU1 (Recombinant spike protein)	1 µg/mL
SARS-CoV (SARS-CoV-1, Recombinant nucleoprotein)	0.1 µg/mL
Bordetella pertussis (Lysate)	1 µg/mL
Bordetella pertussis toxin (Toxin)	1 µg/mL
Chlamydophila pneumoniae Antigen (CWL-029, Native extract)	1 µg/mL
Nasal Irrigation/Wash - Normal (Pooled human donors)	N/A

Analytical selectivity

No positive interference was observed with the following substances tested at the indicated concentrations into SARS-CoV-2 negative sample:

Interfering substance	Conc.
Whole Blood	4%
Mucin	2.5% w/v
Chloraseptic (Menthol/Benzocaine)	1.5 mg/mL
Naso GEL (NeilMed)	5% v/v
CVS Nasal Drops (Phenylephrine)	15% v/v
Afrin (Oxymetazoline)	15% v/v
CVS Nasal Spray (Cromolyn)	15% v/v
Zicam	5% w/v
Homeopathic (Alkalol)	1:10 dilution
Sore Throat Phenol Spray	15% v/v
Tobramycin	4 µg/mL
Mupirocin	10 mg/mL
Fluticasone Propionate	5% v/v
Tamiflu (Oseltamivir Phosphate)	5 mg/mL

Table 3| List of substances tested for interference

No negative interference was observed with the substances in Table 3 tested at the indicated concentrations into SARS-CoV-2 positive samples at 3xLoD.

High-dose effect

High dose hook effect was investigated by testing SARS-CoV-2 Culture Fluid UV Inactivated Hong Kong/VM20001061/2020 (0810590UV, batch 326734, ZeptoMetrix Corporation) spiked into a negative SARS-CoV-2 saliva pool. No high dose hook effect was observed up to a level of 2.12×107 TCID50/mL.

Diagnostic sensitivity and specificity:

For nasopharyngeal specimen:

Compared with the novel coronavirus (SARS-CoV-2) real-time RT-PCR kit executed on the nasopharyngeal samples, the positive coincidence rate (sensitivity), negative coincidence rate (Specificity), total coincidence/agreement of the IVD CAPSULE COVID-19-NP test kit is presented in the table below:

Test Specimen confirmed by RT-PCR		IVD CAPSULE COVID-19-NP test kit	
Type of specimen	Number of samples	Positive Result	Negative Result
Positive	108	90	18
Negative	301	2	299
Total results	409	92	317

The IVD CAPSULE COVID-19-NP test kit showed the following sensitivities/specificity in nasopharyngeal samples compared to the reference method RT-PCR:

- Clinical sensitivity: 83.3% (CI95: 74.9% – 89.8%),
- Clinical specificity: 99.3% (CI95: 97.6% – 99.9%),
- Total agreement rate: 95.1% (CI95: 92.6% – 97.0%).
    - **Sensitivity in reference to Ct intervals:**
- 100.0% (CI95: 85.8% -100.0%) for Ct <25,
- 91.6% (CI95: 83.4% – 96.5%) for Ct<30,

  86.5% (CI95: 78.5% – 92.4%) for Ct<35

For saliva specimen:
Compared with the novel coronavirus (SARS-CoV-2) real-time RT-PCR kit executed on the saliva samples, the positive coincidence rate (sensitivity), negative coincidence rate (Specificity), total coincidence/agreement of the IVD CAPSULE COVID-19-NP test kit is presented in the table below:

Test Specimen confirmed by RT-PCR		IVD CAPSULE COVID-19-NP test kit	
Type of specimen	Number of samples	Positive Result	Negative Result
Positive	115	75	40
Negative	309	0	309
Total results	424	75	349

Table 5| Overview of tested samples used in the validation study.

The IVD CAPSULE COVID-19-NP test kit showed the following sensitivities in saliva samples compared to the reference method RT-PCR:

- Clinical sensitivity: 69.2% (CI95: 59.5% – 77.7%),
- Clinical specificity: 100.0% (CI95: 98.8% – 100.0%),
- Total agreement rate: 90.6% (CI95: 87.4% – 93.2%).
    - Sensitivity in reference to Ct intervals:
- 100.0% (CI95: 73.5% – 100.0%) for Ct <25,
- 85.1% (CI95: 75.0% – 92.3%) for Ct<30,
- 69.2% (CI95: 59.5% – 77.7%) for Ct<35.

References

1. https://www.who.int/health-topics/coronavirus
2. https://www.bag.admin.ch

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Documents / Resources

	**abionic IVD CAPSULE COVID-19-NP** [pdf] User Manual IVD CAPSULE COVID-19-NP

References

- **Coronavirus**