# STANDARD M10 Flu/RSV/SARS-CoV-2

STANDARD™ M10 Flu/RSV/SARS-CoV-2

REF M10-CVFR-01

## INSTRUCTIONS FOR USE

For use with STANDARD™ M10 system


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SD BIOSENSOR

# Contents

## 1. Intended Use

STANDARD M10 Flu/RSV/SARS-CoV-2 test is a multiplex real-time RT-PCR test intended for use with STANDARD M10 system for the qualitative detection of Influenza A, Influenza B, RSV and SARS-CoV-2 nucleic acids in human nasopharyngeal swab collected from individuals suspected of a respiratory disease by their healthcare provider. Positive results are indicative of the presence of Influenza A, Influenza B, RSV and/or SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Negative results should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information. STANDARD M10 Flu/RSV/SARS-CoV-2 test is intended to be performed by trained users in both laboratory and near-patient testing setting.

## 2. Summary and Explanation

Acute respiratory infection can be caused by a variety of viruses and bacteria, including recently introduced SARS-CoV-2. Acute respiratory infection of SARS-CoV-2 outbreak in Wuhan, China has spread across the world since 2019. Common signs of a person infected with SARS-CoV-2 include respiratory symptoms, fever, cough, shortness of breath, and dyspnea. In more severe cases, the infection causes pneumonia, acute respiratory syndrome, kidney failure, or even death.

Influenza, commonly known as the flu, is a highly contagious and acute viral infection of the respiratory tract caused by an influenza virus. Three types of influenza viruses affect people, called Type A, Type B, and Type C. Type A viruses are the most prevalent and are associated with most serious epidemics. The clinical symptoms caused by influenza A virus infection are more severe than those caused by the influenza B virus. Both type A and B viruses can circulate simultaneously, but usually one type is dominant during a given season. Influenza can take on a variety of appearances, ranging from isolated respiratory findings that resemble the common cold, to severe pneumonia that may lead to hospitalization and death.

RSV (Respiratory syncytial virus) is an enveloped, negative-sense RNA virus belonging to the *Paramyxoviridae* family. It occurs throughout the world, and in each location it tends to occur in yearly winter outbreaks. The virus infects the cells lining the respiratory system, causing swelling of this lining coupled with the production of large amounts of excess mucus. In adults, this shows up as a severe, lingering cold with thick nasal congestion and a deep, productive cough. In infants, however, the excess mucus can be enough to plug their small airways or bronchioles, resulting in a severe illness called bronchiolitis that requires hospitalization. Children under 6 months of age who have serious underlying illnesses are at the highest risk for severe disease. Therefore, rapid and accessible detection of RSV is important for efficient prevention and prompt treatment of it.

Respiratory infections caused by SARS-CoV-2, influenza A, influenza B and RSV have similar transmission routes and symptoms. Therefore, the use of assays capable of simultaneous detection and differentiation enables efficient control of viruses, appropriate treatment, and prevention of widespread outbreaks.

### Cartridge Description

STANDARD M10 Flu/RSV/SARS-CoV-2 is a molecular *in vitro* diagnostic assay that aids in the simultaneous detection and differentiation of Influenza A, Influenza B, RSV and SARS-CoV-2 virus RNA based on nucleic acid amplification technology, RT-PCR. STANDARD M10 Flu/RSV/SARS-CoV-2 cartridge contains viral RNA extraction buffers and RT-PCR reagents for the *in vitro* qualitative detection of Influenza A, Influenza B, RSV and SARS-CoV-2 virus RNA in nasopharyngeal swab specimens.

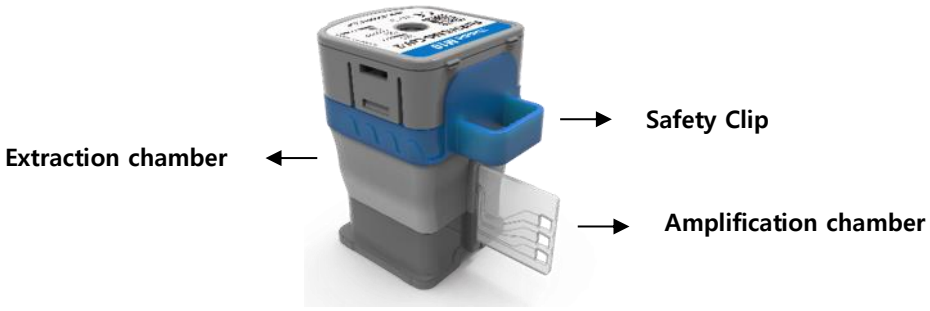


**Figure 1. Layout of STANDARD M10 Flu/RSV/SARS-CoV-2 cartridge**

## 3. Principle of the Procedure

STANDARD M10 Flu/RSV/SARS-CoV-2 test is an automated *in vitro* diagnostic test for the qualitative detection of nucleic acid from Flu A, Flu B, RSV and SARS-CoV-2. STANDARD M10 Flu/RSV/SARS-CoV-2 test is performed on STANDARD M10 system.

STANDARD M10 system automates and integrates sample preparation, nucleic acid extraction, reverse transcription polymerase chain reaction (RT-PCR), and detection of the target sequences in various specimens using molecular diagnostic assays. The system consists of the STANDARD M10 Module and the STANDARD M10 Console with preloaded software for running tests and viewing the results. The system requires the use of single-use disposable cartridges that hold the RT-PCR reagents and host the RT-PCR

process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the STANDARD M10 system User Manual.
STANDARD M10 Flu/RSV/SARS-CoV-2 test includes reagents for the detection of RNA from Flu A, Flu B, RSV and SARS-CoV-2 in nasopharyngeal swab specimens. The cartridge is present to control for adequate processing of the sample, nucleic acid extraction and RT-PCR. The sample is first lysed under highly denaturing conditions to inactivate RNases and to ensure isolation of intact viral RNA. Buffering conditions are then adjusted to provide optimal binding of the RNA to the glass fibers. The RNA binds to the glass fibers, and contaminants are efficiently washed away several times using a wash buffer. High-quality RNA is eluted with elution buffer, ready for amplification. The purified nucleic acids are mixed with the lyophilized PCR master beads. And it is denatured under the customized temperature conditions to carry out effective multiplex real-time RT-PCR and amplified according to the PCR conditions.
An Internal Control(IC) is also included in the cartridge. The IC is present to control for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the RT-PCR reaction. The IC also ensures that the RT-PCR reaction conditions are appropriate for the amplification reaction and that the RT-PCR reagents are functional.
The table below indicates which target is designed to be detected by three channels: FAM, HEX, Cy5.

**Table 1. Fluorescent channel of each target Pathogen**

| Target Pathogen | Channel |
|---|---|
| Flu A | FAM |
| Flu B | HEX |
| Internal control | Cy5 |
| RSV | HEX |
| Internal control | Cy5 |
| SARS-CoV-2 | FAM |
| | HEX |
| Internal control | Cy5 |

## 4. Materials Provided

STANDARD M10 Flu/RSV/SARS-CoV-2 kit contains sufficient reagents to process 10 specimens or quality control samples.

**Table 2. Contents of STANDARD M10 Flu/RSV/SARS-CoV-2 kit**

| | Contents | Quantity | Usage in each reaction |
|---|---|---|---|
| 1 | Cartridge | 10 | 1ea |
| 2 | Quick Reference Instructions | 1 | - |

## 5. Storage and Handling

Store STANDARD M10 Flu/RSV/SARS-CoV-2 kit at 2 ~ 28°C (36 ~ 82°F). If the cartridge has been refrigerated, perform the test after stabilizing it for 30 minutes at room temperature (20 ~ 28°C, 68 ~ 82°F). Do not remove the Safety Clip of the cartridge and do not press the cartridge until actual use. Do not use a cartridge that has leaked or is wet. Under these conditions, cartridges can be stored until the expiration date printed on the packaging.

## 6. Materials Required but Not Provided

- STANDARD M10 system with User Manual
  At least one STANDARD M10 Console (Cat. No. 11M1011) and one STANDARD M10 Module (Cat. No. 11M1012)
- Sample collection tools
  - Noble Bio CTM (Noble Biosciences : UTNFS-3B-2)
  - COPAN eNAT (Copan : 606CS01P)
  - COPAN Universal Transport Medium (recommended 3mL of UTM-RT medium)
- Sample transfer pipettes
  - STANDARD Fixed volume dropper (300µL) (Cat. No. 90DR20)
  - Micropipette with filter tips
- PPE (Personal Protective Equipment)

## 7. Warnings and Precautions

1) This kit is only for *in vitro diagnosis.*
2) Please read the Instructions for Use carefully before testing.
3) Improper specimen collection, transfer, storage, and processing may cause erroneous test results.
4) Do not remove the Safety Clip of the cartridge before use.
5) Do not press the cartridge until actual use.
6) Do not use a cartridge that has leaked or is wet.
7) Do not use the kit after its expiration date.
8) Do not shake, tilt, or invert the cartridge especially after pressing the cartridge to punch the seal. It may yield invalid or false test results.
9) Do not use a cartridge with a damaged barcode label.
10) Do not reuse processed cartridges.
11) Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions.
12) As this test involves extraction of viral RNA and PCR amplification, care should be taken to avoid contamination. Regular monitoring of laboratory contamination is recommended.
    To avoid contamination of working areas after accidental spills/exposures, a solution of bleach or 70% alcohol should be used where effective for target organisms. A second wiping with sterile water is needed when a corrosive disinfectant, such as bleach, is used. *(ref. LABORATORY BIOSAFETY MANUAL_WHO)*
13) Clinical laboratories should be equipped with equipment and operators in strict accordance with the "Code of Practice for Clinical Gene Amplification Laboratories".
14) When using this cartridge, it should be operated strictly in accordance with the instructions.
15) Follow your institution's environmental waste procedures for proper disposal of used cartridges.

## 8. Specimen Collection, Transport, and Storage

Proper sample collection, transportation, and storage are critical to the performance of the test. Improper sample collection, inappropriate sample handling and/or transportation can lead to false results.
Refer to the WHO Laboratory Biosafety Guidance Related to the Coronavirus Disease 2019 (COVID-19).
https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-(covid-19)

### Nasopharyngeal swab collection procedure

1) Gently and slowly insert the nasopharyngeal swab through the nostril parallel to the back of the nasopharynx.
2) Rotate it several times to obtain secretions.
3) Remove the swab from the nasopharynx and place it into the specimen collection tube, and discard the tail.
4) Cap the specimen collection tube tightly.
5) The swab specimens in the collection tube can be stored for 1 day at room temperature (19 ~ 25°C, 66 ~ 77°F), 4 days at 2 ~ 8°C (36 ~ 46°F), and 6 months storage below -70°C (-94°F).

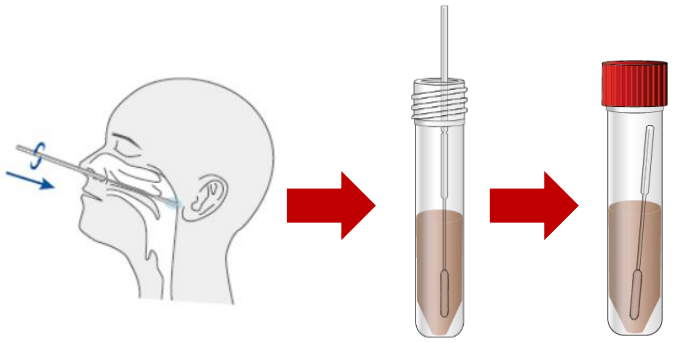

**Figure 2**. Nasopharyngeal swab collection

# 9. Procedure

## 9.1 Starting the STANDARD M10 system

| | |
|---|---|
| **Note** | For the detailed instructions, refer to the STANDARD M10 system User Manual.<br>If you have scanned the cartridge barcode in the STANDARD M10 and the software version is not compatible, a 'Not Supported Device' error message appears. Update the software before proceeding with the test. |

1) Turn on the STANDARD M10 system.
2) Check the STANDARD M10 Console and the STANDARD M10 Module are connected and functional.


**Figure 3. Power connection**

3) Enter the User ID and Password on the Log In screen of the STANDARD M10 Console and click the Log In button.
4) Touch the STANDARD M10 Module to run on the Home screen.
(The door of the selected STANDARD M10 Module will automatically open for cartridge loading.)

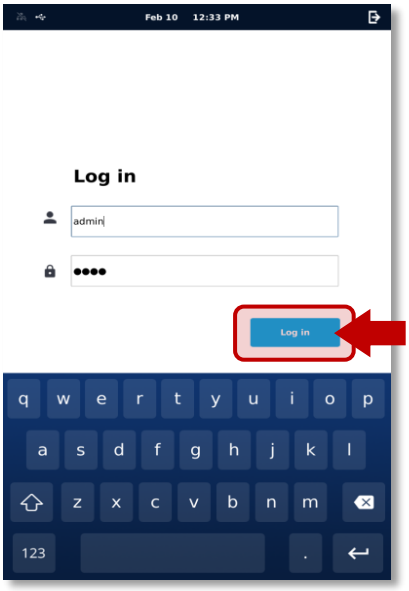


**Figure 4. Log In screen**


**Figure 5. Home screen, Status of M10 module**

5) Enter a Patient ID by scanning the barcode or using virtual keyboard on the M10 Console screen.
(Patient ID is optional. You can turn off the Patient ID option from the 'Settings'.)
6) Enter a Sample ID by scanning the barcode fo the specimen or using virtual keyboard on the M10 Console screen.
Make sure that the specimen tube cap is firmly closed when scan the ID barcode printed on the specimen tube.
(For quality control test, tick the QC check box.)

**Figure 6. Entering Sample ID**

**Figure 7. Scanning a cartridge**

7) Scan STANDARD M10 Flu/RSV/SARS-CoV-2 cartridge to be used. The STANDARD M10 Console automatically recognizes the assay to be run based on the cartridge barcode.

| | |
|---|---|
| **Note** | If you have scanned the cartridge barcode in the STANDARD M10 and the expiration date has expired, An 'Expired Device' error message appears. Check validity period and test with unexpired cartridges. |

## 9.2 Loading a sample into STANDARD M10 Flu/RSV/SARS-CoV-2 cartridge

| | |
|---|---|
| **Caution** | If the cartridge has been refrigerated, perform the test after stabilizing it for 30 minutes at room temperature (20 ~ 28°C, 68 ~ 82°F).<br>Once the sample has been loaded into the cartridge, start the test as soon as possible. (within 30 minutes) |
| **Note** | False negative results may occur if insufficient sample is added into the cartridge. |

**1)** Remove the Safety Clip located underneath the lid of the cartridge.
**2)** Press down the cartridge to pierce the seal until fully engaged into the cartridge groove.
**3)** Open the lid and check that the seal is completely punctured before loading a sample.
**4)** Mix sample by rapidly inverting the specimen or external control tube 5 times. Carefully open the cap of the specimen tube or external control.
**5)** Dispense 300µL of the sample into the hole in the lower right corner of the cartridge using a 300 µL of fixed volume dropper or a micro pipette.
**6)** After a few seconds, Sample Guide screen will automatically change to the Insert Cartridge screen. Touch the Sample Guide screen if you want to skip the guide.
**7)** Close the lid.

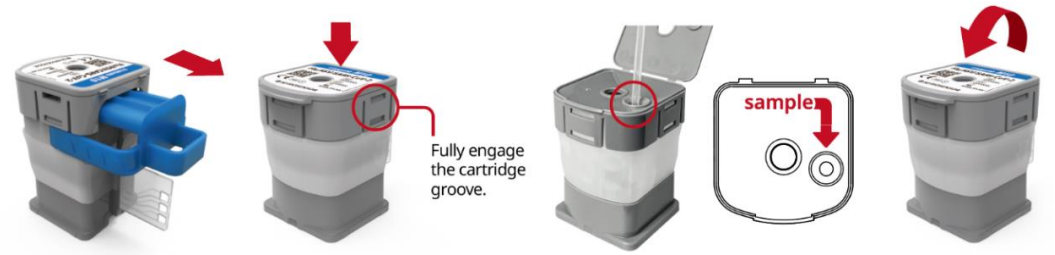


**Figure 8. Loading a sample**


**Figure 9. Sample Guide screen**

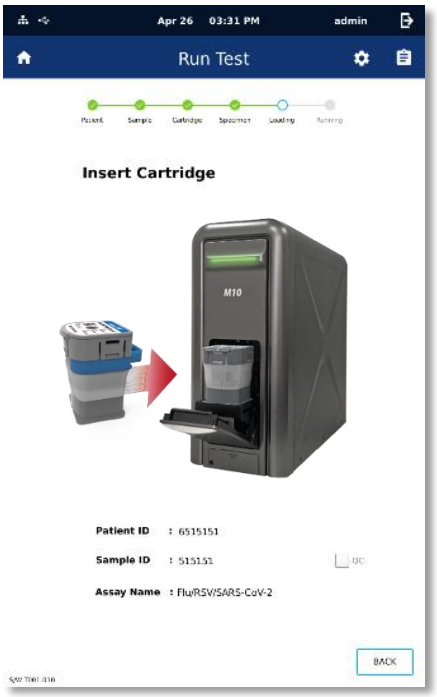


**Figure 10. Insert Cartridge screen**

## 9.3 Running a test

**1)** Load the cartridge on the selected STANDARD M10 Module with the Amplification chamber facing the inside of the module. (The status indicator of the selected module will blink green.)
**2)** Close the door completely.
**3)** After confirming the sample and cartridge information, touch the OK button on the screen. (Touch the Reset button to re-input the information.)
**4)** Assay starts automatically, and remaining time will appear on the screen.

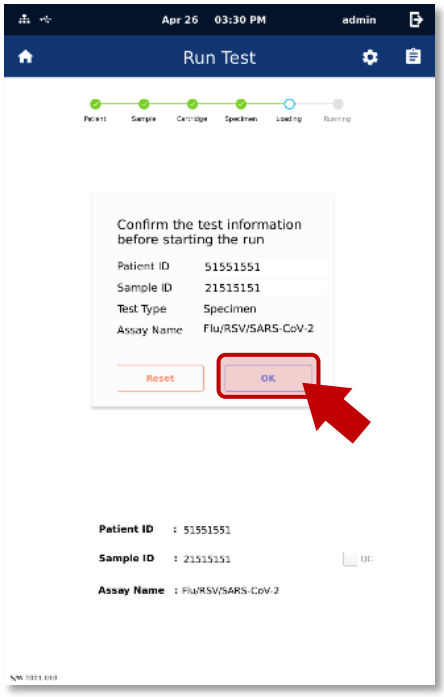


**Figure 11. Confirm the test screen**

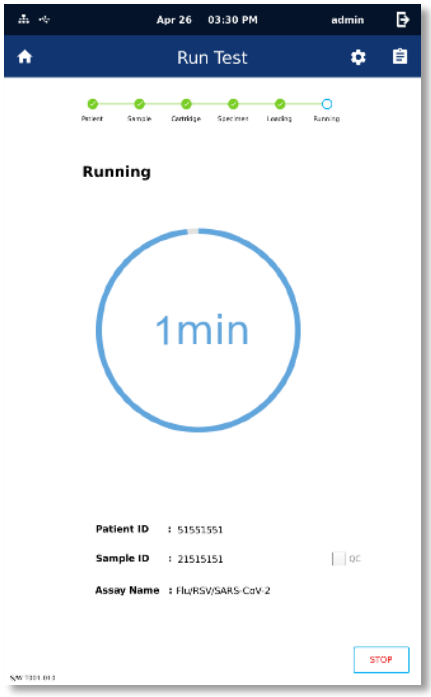


**Figure 12. Running screen**

**5)** If the signal from the target reaches a certain threshold before the full process have been completed, an Early Detection Call function is initiated and it will provide earlier time to results.

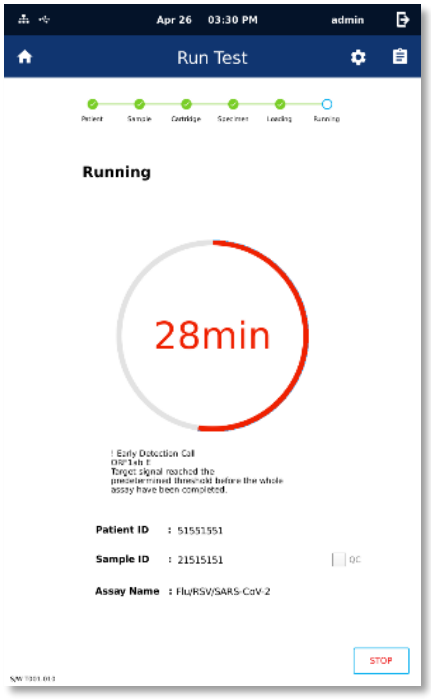


**Figure 13. Early Detection Call function**

**6)** When the run is finished, it switches to the Review screen and the result is displayed.
**7)** Dispose of used cartridges in the appropriate biohazard waste container according to your institution's standard practices.
**8)** To run another test, touch the Home icon and repeat the process. (If another STANDARD M10 Module connected to the STANDARD M10 Console is available, you can start a new test while another test is running.)

## 10. Interpretation of Results

The results are interpreted automatically by STANDARD M10 Console and are clearly shown in the Review screen. STANDARD M10 Flu/RSV/SARS-CoV-2 test provides test results based on the detection of respective gene targets according to the algorithms shown in Table 3.

**Table 3. Description of results**

| Outcome (Home screen) | Result (Review screen) | Description |
|---|---|---|
| Positive |  | At least one pathogen/target gene is positive. |
| Negative |  | No pathogen was detected. |
| Invalid |  | IC signal does not have a Ct within the valid range. |
| Error |  | The test failed because either an error occurred or the test was canceled by the user. |

**Table 4. Description of IC results**

| Outcome (Summary screen) | Result (Summary screen) | Description |
|---|---|---|
| IC Valid |  | IC has a Ct within the valid range.<br>The test was completed. Report positive/negative results of target according to the interpretation shown in table 5.<br>(If the target is positive, it is displayed as IC Valid regardless of the IC Ct value.) |
| IC Invalid |  | All pathogens are not detected and IC signal does not have a Ct value within the valid range. |
| IC Error |  | The test failed because either an error occurred or the test was canceled by the user. Repeat the test. |

**Table 5. Interpretation of results**

| Result | Interpretation |
|---|---|
| Flu A Positive | The Flu A target RNA is detected.<br>• The Flu A signal has a Ct within the valid range.<br>• IC: N/A (not applicable); IC may be inhibited and delayed Ct value when Flu A is positive at high concentration. |
| Flu B Positive | The Flu B target RNA is detected.<br>• The Flu B signal has a Ct within the valid range.<br>• IC: N/A (not applicable); IC may be inhibited and delayed Ct value when Flu B is positive at high concentration. |
| RSV Positive | The RSV target RNA is detected.<br>• The RSV signal has a Ct within the valid range.<br>• IC: N/A (not applicable); IC may be inhibited and delayed Ct value when RSV is positive at high concentration. |
| SARS-CoV-2 Positive | The SARS-CoV-2 target RNA is detected.<br>• The SARS-CoV-2 signal has a Ct within the valid range.<br>• IC: N/A (not applicable); IC may be inhibited and delayed Ct value when SARS-CoV-2 is positive at high concentration. |
| Flu A Positive,<br>Flu B Positive,<br>RSV Positive,<br>SARS-CoV-2 Positive | • Flu A, Flu B, RSV or/and SARS-CoV-2 target RNAs are detected.<br>• IC: N/A (not applicable); IC may be inhibited and delayed Ct value when Flu A, Flu B, RSV, and SARS-CoV-2 are positive at high concentration. |
| Flu A Negative,<br>Flu B Negative,<br>RSV Negative,<br>SARS-CoV-2 Negative | • Flu A, Flu B, RSV and SARS-CoV-2 target RNAs are not detected.<br>• IC: Valid; IC has a Ct within the valid range. |
| Invalid | IC does not meet acceptance criteria and all targets are not detected. Repeat test.<br>• IC: Invalid; IC and Flu A, Flu B, RSV and SARS-CoV-2 signals do not have a Ct within valid range. |
| Error | The test failed because either an error occurred or the test was canceled by the user. Presence or absence of target nucleic acids cannot be determined. Repeat the test. |

| | |
|---|---|
| **Note** | - Co-infection can occur with these targets: Flu A, Flu B, RSV, SARS-CoV-2.<br>- If the IC is negative and the results for any of the targets are positive, the results for all targets are considered valid. A high copy number of target-specific gene can lead to reduced or absent IC.<br>- When either the result of IC or target shows negative, it means that the sample was not properly processed. Please conduct a re-test. |

# 11. Quality Control

Quality Control procedures are intended to monitor cartridge and assay performance. If the controls are not valid, the patient results cannot be interpreted.
Internal control(IC): Ensures a proper sample has been applied, reagents in the cartridge are well functioning, there were no other interfering factors in the sample, and the procedure was performed correctly. In clinical samples showing positive signal for target pathogens, the IC is reluctant and is ignored. If the IC fails where no target pathogens are detected. The result is invalid.
External controls should be performed in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's standard quality control procedures.
For external controls, it is recommended to use the list below. Please comply with the information stated on the user manual.
- STANDARD™ M10 Flu/RSV/SARS-CoV-2 Quality Control Kit (SD Biosensor,Inc, Cat. no.11COVC20N)
-AccuPlex ™ SARS-CoV-2, Flu A/B and RSV Molecular Controls Kit (SeraCare, 0505-0260)
Products other than the mentioned substance can be used after being evaluated and validated for efficacy by each country or hospital independently.

# 12. Performance

## 12.1 Limit of Detection Test

The analytical sensitivity of the STANDARD M10 Flu/RSV/SARS-CoV-2 test was assessed with two lots of cartridges and 7 standard materials (Influenza A H1N1pdm, Influenza A H1, Influenza A H3, Influenza B, Respiratory Syncytial Virus Type A, Respiratory Syncytial Virus Type B, SARS-CoV-2) diluted into pooled negative clinical nasopharyngeal swab matrix.
For the LoD test, each positive standard was diluted 2-fold, and the test product of 2 lots was repeated 24 times for each concentration. Based on the test results, LoD were set through probit analysis(CLSI EP17-A2; Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition).
The verified LoD values for the tested viruses are summarized in Table 6.

**Table 6. Summary of the LoD test results**

| Target | | Source (Cat.no.) | Strain | LoD (copy/mL) |
|---|---|---|---|---|
| Flu A H1N1 | | Zeptometrix (NATFLUAH1-STQ) | A/Singapore/63/04 | 631 |
| Flu A H1N1 pdm | | Zeptometrix (NATFLUAH1(2009)-STQ) | A/NY/02/09 | 399 |
| Flu A H3N2 | | Zeptometrix (NATFLUAH3-STQ) | A/Brisbane/10/07 | 525 |
| Flu B | | Zeptometrix (NATFLUB-STQ) | B/Florida/02/06 | 399 |
| RSV A | | Zeptometrix (NATRSVA-STQ) | - | 795 |
| RSV B | | Zeptometrix (NATRSVB-STQ) | 3H93(18)-18 | 2631 |
| SARS-CoV-2 | ORF1ab gene | Zeptometrix (NATSARS(COV2)-ST) | USA-WA1/2020 | 813 |
| | N gene | | | 795 |

## 12.2 Cross-Reactivity

The following 39 cross-reacting organisms were tested 3 times per sample in the dedicated analyzer as 1 lot. As a result, no cross-reactivity was observed for 35 substances.
For the remaining four cross-reacting substances (Flu A, Flu B, RSV A, RSV B), detection was confirmed for each target.

**Table 7. Substances tested in cross-reactivity**

| No. | Strain | Concentration |
|---|---|---|
| 1 | SARS-CoV | $1x10^5$ PFU/mL |
| 2 | MERS-CoV | $1x10^5$ $TCID_{50}$/mL |
| 3 | HCoV-OC43 | $1x10^5$ $TCID_{50}$/mL |
| 4 | HCoV-NL63 | $1x10^5$ $TCID_{50}$/mL |
| 5 | HCoV-229E | $1x10^5$ $TCID_{50}$/mL |
| 6 | Adenovirus Type03 (Species B) | $1x10^5$ $TCID_{50}$/mL |
| 7 | Adenovirus Type01 (Species C) | $1x10^6$ $TCID_{50}$/mL |
| 8 | Human Metapneumovirus (hMPV) 16 Type A1 | $1x10^5$ $TCID_{50}$/mL |
| 9 | Human Metapneumovirus (hMPV) 3 Type B1 | $1x10^5$ $TCID_{50}$/mL |
| 10 | Parainfluenza Virus Type 1 | $1x10^5$ $TCID_{50}$/mL |

| No. | Strain | Concentration |
|---|---|---|
| 11 | Parainfluenza Virus Type 2 | $1x10^5$ $TCID_{50}$/mL |
| 12 | Parainfluenza Virus Type 3 | $1x10^5$ $TCID_{50}$/mL |
| 13 | Parainfluenza Virus Type 4A | $1x10^5$ $TCID_{50}$/mL |
| 14 | Parainfluenza Virus Type 4B | $1x10^5$ $TCID_{50}$/mL |
| 15 | Influenza A H1N1pdm (NY/02/09) | $1x10^5$ $TCID_{50}$/mL |
| 16 | Influenza B (Massachusetts/2/12) | $1x10^5$ $TCID_{50}$/mL |
| 17 | Enterovirus Type 68 | $1x10^5$ $TCID_{50}$/mL |
| 18 | Human respiratory syncytial virus A (RSV_A) | $1x10^5$ PFU/mL |
| 19 | Human respiratory syncytial virus B (RSV_B) | $1x10^5$ $TCID_{50}$/mL |
| 20 | Rhinovirus A16 | $1x10^5$ $TCID_{50}$/mL |
| 21 | Rhinovirus B | $1x10^5$ PFU/mL |
| 22 | Chlamydia pneumoniae | $1x10^6$ IFU/mL |
| 23 | Haemonphilus influenzae Type B | $1x10^6$ CFU/mL |
| 24 | Streptococcus pneumoniae Type 1 | $1x10^6$ CFU/mL |
| 25 | Streptococcus pneumoniae Type 2 | $1x10^6$ CFU/mL |
| 26 | Streptococcus pneumoniae Type 3 | $1x10^6$ CFU/mL |
| 27 | Streptococcus pneumonia | $1x10^6$ CFU/mL |
| 28 | Streptococcus pyogenes | $1x10^6$ CFU/mL |
| 29 | Bordetella pertussis | $1x10^6$ CFU/mL |
| 30 | Mycoplasma pneumoniae | $1x10^6$ CFU/mL |
| 31 | Pseudomonas aeruginosa | $1x10^6$ CFU/mL |
| 32 | Staphylococcus epidermis | $1x10^6$ CFU/mL |
| 33 | Streptococcus salivarius | $1x10^6$ CFU/mL |
| 34 | Moraxella catarrhalis | $1x10^7$ CFU/mL |
| 35 | Cytomegalovirus (CMV) | $1x10^5$ $TCID_{50}$/mL |
| 36 | Measles virus | $1x10^5$ $TCID_{50}$/mL |
| 37 | Mumps virus | $1x10^5$ $TCID_{50}$/mL |
| 38 | Epstein Barr virus | $1x10^7$ Copies/mL |
| 39 | Candida albicans | $1x10^6$ CFU/mL |

## 12.3 Interference

We confirmed no interference reaction for the following 17 interfering substances as following: tested with one lot for negative and positive standard materials, both with or without interfering substances, in three repeated tests.

**Table 8. Substances tested in interference**

| No. | Interfering Substance | Concentration |
|---|---|---|
| 1 | Human whole Blood | 5% |
| 2 | Human genomic DNA | 15 μg/mL |
| 3 | Hemoglobin | 0.2 g/mL |
| 4 | Mucin | 2.5 mg/mL |
| 5 | Albumin | 0.24 mg/mL |
| 6 | Biotin | 200 μg/mL |
| 7 | Dexamethasone | 6 mg/mL |
| 8 | LISTERINE | 5% |
| 9 | Oseltamivir | 25 mg/mL |
| 10 | Oxymetazoline (Nasal Spray) | 15% |
| 11 | Ribavirin | 800 mg/mL |

| No. | Interfering Substance | Concentration |
|---|---|---|
| 12 | Chloraseptic Spray (Phenol/Glycerin) | 15% |
| 13 | Sore throat and cough lozenges | 3 mg/mL |
| 14 | Tobacco | 0.03 mg/mL |
| 15 | Tobramycin | 512 μg/mL |
| 16 | Toothpaste | 0.5% |
| 17 | Zanamivir | 3.3 mg/mL |

## 12.4 Competitive interference

Competitive interference reaction test among the analytes was evaluated to verify whether there is mutual interference or inhibition caused by co-infections with respect to the performance of this product. Four target strains were mixed with a low concentration of 3X LoD and a high concentration of 100X LoD; a single lot was used to conduct three repeated tests to confirm no mutual interference or inhibition.
As a result, 100% detection was confirmed under all conditions, and it was verified that there was no mutual interference and inhibition.

**Table 9. Summary of the competitive interference test results**

| Target Pathogen | Interference | Detection Rate |
|---|---|---|
| Flu A 3X LoD | Flu B 100X LoD, RSV 100X LoD, SARS-CoV-2 100X LoD | 3/3 (100%) |
| Flu B 3X LoD | Flu A 100X LoD, RSV 100X LoD, SARS-CoV-2 100X LoD | 3/3 (100%) |
| RSV 3X LoD | Flu A 100X LoD, Flu B 100X LoD, SARS-CoV-2 100X LoD | 3/3 (100%) |
| SARS-CoV-2 3X LoD | Flu A 100X LoD, Flu B 100X LoD, RSV 100X LoD | 3/3 (100%) |
| Flu A 3X LoD, Flu B 3X LoD, RSV 3X LoD, SARS-CoV-2 3X LoD | | 3/3 (100%) |

## 12.5 Precision Test

**1. Repeatability**
Three concentrations of each of the four standard materials (Influenza A virus, Influenza B virus, RSV, SARS-CoV-2) were repeated twice a day using one lot for 5 days.
As a result, within-Run, Between-Run, Between-Day, and Within-Laboratory satisfy the acceptance criteria with SD < 2.0 Ct, confirming repeatability.

**Table 10. Summary of the repeatability test results**

1) Influenza A virus

| Concentration | Within-Run (Sr) | Between-Run (Srr) | Between-Day (Sdd) | Within-laboratory (ST) |
|---|---|---|---|---|
| 3X LoD | 0.70 | 0.46 | 0.51 | 0.98 |
| 1X LoD | 0.69 | 0.38 | 0.45 | 0.91 |
| 0.1X LoD | - | - | - | - |

2) Influenza B virus

| Concentration | Within-Run (Sr) | Between-Run (Srr) | Between-Day (Sdd) | Within-laboratory (ST) |
|---|---|---|---|---|
| 3X LoD | 0.47 | 0.07 | 0.26 | 0.54 |
| 1X LoD | 0.73 | 0.43 | 0.35 | 0.92 |
| 0.1X LoD | - | - | - | - |

3) Respiratory Syncytial Virus

| Concentration | Within-Run (Sr) | Between-Run (Srr) | Between-Day (Sdd) | Within-laboratory (ST) |
|---|---|---|---|---|
| 3X LoD | 0.72 | 0.32 | 0.27 | 0.83 |
| 1X LoD | 0.68 | 0.31 | 0.39 | 0.84 |
| 0.1X LoD | - | - | - | - |

4) SARS-CoV-2 (ORF1ab)

| Concentration | Within-Run (Sr) | Between-Run (Srr) | Between-Day (Sdd) | Within-laboratory (ST) |
|---|---|---|---|---|
| 3X LoD | 0.49 | 0.20 | 0.18 | 0.56 |
| 1X LoD | 0.62 | 0.22 | 0.32 | 0.73 |
| 0.1X LoD | 0.11 | 0.48 | 0.75 | 0.90 |

5) SARS-CoV-2 (N gene)

| Concentration | Within-Run (Sr) | Between-Run (Srr) | Between-Day (Sdd) | Within-laboratory (ST) |
|---|---|---|---|---|
| 3X LoD | 0.55 | 0.26 | 0.04 | 0.61 |
| 1X LoD | 1.17 | 0.80 | 0.8 | 1.63 |
| 0.1X LoD | - | - | - | - |

**2. Reproducibility**

Reproducibility was confirmed by repeating the test twice a day, for 5 days, by two operators at two sites with two lots using the same test concentration.

As a result, it was confirmed that there was reproducibility by satisfying the acceptance criteria with SD < 2.0 Ct and CV < 5% in the evaluation between the following: operators and lots, sites and the instrument.

**Table 11. Summary of the reproducibility test results**

1) Influenza A virus

| Concentration (copies/mL) | Between-site & instrument(%CV) | Between-Operator & lot(%CV) |
|---|---|---|
| 3X LoD | 2.47 | 2.95 |
| 1X LoD | 1.89 | 2.39 |
| 0.1X LoD | 1.10 | 1.28 |

2) Influenza B virus

| Concentration (copies/mL) | Between-site & instrument(%CV) | Between-Operator & lot(%CV) |
|---|---|---|
| 3X LoD | 1.90 | 1.52 |
| 1X LoD | 2.02 | 2.37 |
| 0.1X LoD | 0.78 | 3.67 |

3) Respiratory Syncytial Virus

| Concentration (copies/mL) | Between-site & instrument(%CV) | Between-Operator & lot(%CV) |
|---|---|---|
| 3X LoD | 3.26 | 3.62 |
| 1X LoD | 2.85 | 3.02 |
| 0.1X LoD | 2.74 | 1.93 |

4) SARS-CoV-2 (ORF1ab)

| Concentration (copies/mL) | Between-instrument(%CV) | Between-Operator(%CV) |
|---|---|---|
| 3X LoD | 2.73 | 2.14 |
| 1X LoD | 2.39 | 2.90 |
| 0.1X LoD | 4.24 | 3.43 |

5) SARS-CoV-2 (N gene)

| Concentration (copies/mL) | Between-instrument(%CV) | Between-Operator(%CV) |
|---|---|---|
| 3X LoD | 2.63 | 2.68 |
| 1X LoD | 2.57 | 3.22 |
| 0.1X LoD | 0.33 | 1.80 |

## 12.6 Clinical Trial

The clinical test results of the STANDAR M10 Flu/RSV/SARS-CoV-2 were compared with the confirmed results of positive samples and negative samples.
The study was conducted using residual specimen stored in nasopharyngeal swab universal transport medium (UTM) after testing, and stored at ≤ -70℃ with storage duration < 12 months. Base on this, calculated the clinical sensitivity and specificity of the medical device for clinical performance test relative to the results of MFDS authorized SARS-CoV-2/Flu A/Flu B/RSV RT-PCR test in a randomized and blinded fashion.

**Table 12. Summary of the clinical sensitivity and specificity test results**

1) Influenza A virus
- Clinical sensitivity: 98.18% (108/110) [95% CI: 93.59% - 99.78%]
- Clinical specificity: 100.00% (535/535) [95% CI: 99.31% - 100.00%]

| | | Confirmed result | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| STANDARD M10 Flu/RSV/SARS-CoV-2 | Positive | 108 | 0 | 108 |
| | Negative | 2 | 535 | 537 |
| | Total | 110 | 535 | 645 |

2) Influenza B virus
- Clinical sensitivity: 98.91% (91/92) [95% CI: 94.09% - 99.97%]
- Clinical specificity: 99.82% (552/553) [95% CI: 99.00% - 100.00%]

| | | Confirmed result | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| STANDARD M10 Flu/RSV/SARS-CoV-2 | Positive | 91 | 1 | 92 |
| | Negative | 1 | 552 | 553 |
| | Total | 92 | 553 | 645 |

3) Respiratory Syncytial virus
- Clinical sensitivity: 98.78% (81/82) [95% CI: 94.09% - 99.97%]
- Clinical specificity: 100.00% (563/563) [95% CI: 99.00% - 100.00%]

| | | Confirmed result | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| STANDARD M10 Flu/RSV/SARS-CoV-2 | Positive | 81 | 0 | 81 |
| | Negative | 1 | 563 | 564 |
| | Total | 82 | 563 | 645 |

4) SARS-CoV-2
- Clinical sensitivity: 99.42% (170/171) [95% CI: 96.78% - 99.99%]
- Clinical specificity: 98.73% (468/474) [95% CI: 97.72% - 99.53%]

| | | Confirmed result | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| STANDARD M10 Flu/RSV/SARS-CoV-2 | Positive | 170 | 6 | 176 |
| | Negative | 1 | 468 | 469 |
| | Total | 171 | 474 | 645 |

# 13. Limitation

**1)** ,False negative results may occur from several causes.
- Sample concentrations is near or below the limit of detection of the test.
- A specimen is improperly collected, transported or handled.
- Inadequate respiratory tract organisms are present in the specimen.
- Cartridges are exposed to improper environmental factors (temperature / humidity).

**2)** Modifications to the procedures provided in the QRI(Quick Reference Instructions) within the package may alter the performance of the test.
**3)** False positive results may occur from cross-contamination between patient samples, specimen mix-up and/or RNA contamination during product handling.
**4)** Qualitative detection of positive results in this cartridge does not indicate the presence of infectious virus.
**5)** This cartridge only classifies and identifies the Flu A, Flu B, RSV or SARS-CoV-2. The test results are for clinical reference only, and it should not be used as the only evidence for clinical diagnosis and treatment.
**6)** Mutations within the target regions of the M10 Flu/RSV/SARS-CoV-2 test could affect primer and/or probe binding resulting in failure to detect the presence of virus or the virus being detected less predictably.

## 14. References


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## 15. Symbols

| | | | |
|---|---|---|---|
| REF | Reference number | LOT | Batch code |
| IVD | *In vitro* diagnostics medical device | CE | CE marking - European Conformity |
| | Consult Instructions for Use | | Manufacturer |
| Σ | Contains Sufficient for <n> Tests | | Date of manufacture |
| | Caution | EC REP | Authorized representative in the European Community |
| | Note | | Keep dry |
| | Do not re-use. | | Keep away from sunlight |
| | Temperature limit | | Do not use if packaging is damaged |
| | Use-by date | | |

For further information on

# STANDARD M10
# Flu/RSV/SARS-CoV-2

Please contact your
SD BIOSENSOR representative


Manufacturer
**SD Biosensor, Inc.**
**Head office :** C-4th&5th, 16, Deogyeong-daero 1556beon-gil, Yeongtong-gu, Suwon-si, Gyeonggi-do, 16690, REPUBLIC OF KOREA
**Manufacturing site :** 14, Jeungpyeongsandan-ro, Jeungpyeong-eup, Jeungpyeong-gun, Chungcheongbuk-do, 27915, REPUBLIC OF KOREA

EC REP **Authorized Representative**
MT Promedt Consulting GmbH
Ernst-Heckel-Straße 7 66386 St. Ingbert Germany
Phone: +49 6894591020, Fax: +49 6894 581021


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Any inquiries regarding instructions provided should be addressed to: ts@sdbiosensor.com
or you can also contact us through www.sdbiosensor.com

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