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# Premarket Registration Full Evaluation Route
# Summary Assessment Report for
# *Roffe International BUZUD COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette (Swab)*

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|---|---|
| **Listing number** | MDPR250827H0002 |
| **Date of approval** | 27-Aug-2025 |
| **Product owner** | Roffe International Holdings Pte Ltd |
| **Registrant** | Roffe International Holdings Pte Ltd |
| **Risk Class** | Class D |
| **Intended use / Indications of use** | The COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette (Swab) is an in vitro immunochromatographic assay for the qualitative and differential detection of SARS-CoV-2, influenza A, influenza B, Respiratory Syncytial Virus (RSV) and Adenovirus (ADV) antigens in nasal swab specimens directly from individuals within the first seven days of symptom onset. It is intended to aid in the rapid diagnosis of SARS-CoV-2, influenza A, influenza B, RSV and Adenovirus infections. This test provides only a preliminary test result. Therefore, any reactive specimen with the COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette (Swab) must be confirmed with alternative testing method(s) and clinical findings. It is for in vitro diagnosis use only. It is not automated. It is intended for Self-testing use and not for near patient use. |

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## 1. Device description

The BUZUD COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette is an immunochromatographic lateral flow immunoassay for self-testing use. The device features a dual-strip design within a single cassette: one strip detects COVID-19, Flu A and Flu B, while the other detects RSV and Adenovirus. Each test kit includes the test cassette, extraction tube with buffer and tip, sterile swab, waste bag, and workstation. The device is available in 1, 5, and 20 test configurations.

The principle of operation is based on immunochromatographic technology using specific monoclonal antibodies to detect viral antigens. Users collect nasal swab specimens, mix with extraction buffer, and apply the solution to both sample wells of the test cassette. Results are read visually after 15 minutes, with control lines indicating test validity and test lines indicating positive results for specific pathogens.

Each test strip comprises a sample pad, reagent pad containing colloidal-gold conjugated detector antibodies, nitrocellulose membrane with immobilised capture antibodies, and absorbing pad, all housed within a plastic cassette. When sample is applied, the conjugates migrate through the membrane with the sample. Target antigens, if present, form complexes with their respective conjugated antibodies and are captured by specific monoclonal antibodies immobilised in designated test regions (CoV for SARS-CoV-2, A for Influenza A, B for Influenza B, RSV for respiratory syncytial virus, ADV for adenovirus). A control line always appears in the control region to confirm proper sample flow and adequate sample volume.

The device provides qualitative results and is manually operated. It is intended for symptomatic individuals within the first seven days of symptom onset. Adults over 18 years old can perform this test independently, while adolescents between 12-17 years old should perform the test under adult supervision. Children between 3-11 years old should be tested by an adult.

Limitations of the device include the inability to differentiate between SARS-CoV and SARS-CoV-2 in positive COVID-19 results. Additional warnings and precautions can be found in the labelling.

## 2. List of Standards applied

| Standards | Title |
|---|---|
| EN ISO 14971 | Medical devices — Application of risk management to medical devices |
| ISO 20916 | In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice |
| EN ISO 23640 | In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents |
| IEC 62366-1 | Medical devices — Part 1: Application of usability engineering to medical devices |
| EN 13612 | Performance evaluation of in vitro diagnostic medical devices |
| EN 13641 | Elimination or reduction of risk of infection related to in vitro diagnostic reagents |

## 3. Pre-clinical assessment

**(i) Stability**:

Studies provided support for a shelf life of 24 months at 2-30°C and open pouch stability of 1 hour at 15-30°C with RH≤60%. Real-time stability studies were completed on three lots up to 30 months for shelf life and 2 hours for open pouch stability. A transport stability study was conducted on three lots of test kits under various transportation conditions: 45±3°C, 2-8°C, 25±5°C, and -20±10°C, each for 7 days, along with drop simulations. The results demonstrated that the test kits maintained stability when exposed to both temperature fluctuations and severe turbulence during transportation.

**(ii) IVD specific studies**:

- Analytical sensitivity

Studies provided supported the following limit of detection (LoD) values for the different pathogens:

| Virus Strains | LoD |
|---|---|
| SARS CoV-2 | $1.15 \times 10^2$ $TCID_{50}$/ml |
| 1st WHO International Standard for SARS-CoV-2 antigen | 50 IU/ml |
| Influenza A (H1N1) | $3.0 \times 10^5$ $TCID_{50}$/ml |
| Influenza B (Yamagata lineage) | $3.0 \times 10^6$ $TCID_{50}$/ml |
| RSV type A (A2) | $2.1 \times 10^4$ PFU/ml |
| RSV type B (B WV-14617-85) | $2.2 \times 10^2$ $TCID_{50}$/ml |
| Adenovirus 3 | $2.0 \times 10^{4.5}$ $TCID_{50}$/ml |
| Adenovirus 7 | $1.1 \times 10^3$ $TCID_{50}$/ml |

- Inclusivity

Studies demonstrated detection of COVID-19 variants (Alpha, Delta, Omicron), Flu A subtypes (H1N1, H2N2, H3N2, H5N1, H5N3, H7N3, H7N8, H9N2, H10N4), Flu B lineages (Yamagata, Victoria), RSV Types A & B, and Adenovirus Types 1, 2, 4, 5, 6, 8, 11, 18, 19, 37, 41, 42.

- Analytical specificity

The analytical specificity of the test was evaluated by testing various related microorganisms, those potentially encountered in nasal swab specimens, and diseases with similar clinical manifestations. Viruses were tested at concentrations of $\geq 10^5$ $TCID_{50}$/mL (PFU/mL), while bacteria and fungi were tested at concentrations of $\geq 10^6$ CFU/mL. None of the organisms tested showed cross-reactivity, except for SARS-CoV-1 with the COVID-19 line.

| | |
|---|---|
| EV-A71 | MERS-coronavirus |
| EV-B69 | Legionella pneumophila |
| EV-C95 | Mycobacterium tuberculosis |
| EV-D70 | Mycoplasma pneumoniae |
| Human Metapneumovirus (hMPV) | Parainfluenza virus 1 |
| Rhinovirus | Parainfluenza virus 2 |
| Mumps virus | Parainfluenza virus 3 |
| Varicella zoster virus | Parainfluenza virus 4 |
| Bordetella pertussis | Streptococcus pyogenes |
| Candida albicans | Streptococcus agalactiae |
| Chlamydia pneumoniae | Streptococcus pneumoniae |
| Haemophilus influenzae | Staphylococcus aureus |
| Human coronavirus 229E | Staphylococcus epidermidis |
| Human coronavirus OC43 | Pooled human nasal wash |
| Human coronavirus NL63 | Measles virus |
| Human coronavirus HKU1 | |

Interference studies demonstrated no impact from endogenous and exogenous substances, including mucin, whole blood, and pharmaceutical substances, in the absence and presence of the subject analytes.

| Substances (Active Ingredient) | Concentration Tested | Substances (Active Ingredient) | Concentration Tested |
|---|---|---|---|
| Human blood (EDTA anticoagulated) | 20% (v/v) | Phenylephrine | 0.5 mg/mL |
| Mucin | 5 mg/mL | Oxymetazoline | 0.1 mg/mL |
| Oseltamivir phosphate | 5 mg/mL | 0.9% sodium chloride | 20% (v/v) |
| Ribavirin | 5 mg/mL | A natural soothing ALKALOL | 20% (v/v) |
| Levofloxacin | 5 mg/mL | Beclomethasone | 0.2 mg/mL |
| Azithromycin | 5 mg/mL | Hexadecadrol | 20% (v/v) |
| Meropenem | 5 mg/mL | Flunisolide | 20% (v/v) |
| Tobramycin | 2 mg/mL | Triamcinolone | 0.22 mg/mL |
| 4-Acetamidophenol | 10 mg/mL | Budesonide | 0.256 mg/mL |
| Acetylsalicylic Acid | 20 mg/mL | Mometasone | 0.2 mg/mL |
| Chlorpheniramine | 5 mg/mL | Fluticasone | 0.1 ug/mL |
| Dextromethorphan | 10 mg/mL | Fluticasone propionate | 0.2 mg/mL |
| Diphenhydramine | 5 mg/mL | Interferon | 10 U/mL |
| Ephedrine | 20 mg/mL | Zanamivir | 0.5 mg/mL |
| Guaiacol glyceryl ether | 20 mg/mL | Lopinavir | 1 ug/mL |
| Phenylpropanolamine | 20 mg/mL | | |

Competitive inhibition studies confirmed the detection capability of pathogens at low concentrations in the presence of other pathogens at higher concentrations in co-infection scenarios.

- Precision
  Studies showed acceptable repeatability (within-run) and reproducibility (between-lot, between-day, between-operator and between-site) with no significant variance reported. The agreement of obtained results with expected results was 100% across all runs, lots, days, operators, and sites.

- High-dose hook effect
  High-dose hook effect was not observed when tested with high concentrations of all pathogens up to $4.6 \times 10^5$ $TCID_{50}$/mL for SARS-CoV-2, $3 \times 10^8$ $TCID_{50}$/mL for Influenza A, $3 \times 10^8$ $TCID_{50}$/mL for Influenza B, $5.5 \times 10^7$ PFU/mL for RSV Type A, $2.8 \times 10^5$ $TCID_{50}$/mL for RSV Type B, $5.0 \times 10^{7.5}$ $TCID_{50}$/mL for Adenovirus Type 3, and $2.8 \times 10^6$ $TCID_{50}$/mL for Adenovirus Type 7.

- Specimen stability
  Studies validated claims for sample stability in buffer for up to 30 minutes at room temperature (15-30°C) and nasal swab stability prior to being placed in the sample buffer for up to 1 hour at 2-30°C.

- Robustness/Flex study
  Flex studies demonstrated acceptable performance on all major aspects of the test procedure, including reading time flexibility from 10 to 25 minutes, supporting IFU claim of reading at 15 minutes with warning not to read after 20 minutes, and sample volume variability showing acceptable results with 3-6 drops per well, supporting IFU claim of 4 drops per well.

## 4. Clinical assessment

### (i) Evaluation of Clinical Investigations

**IVD Specific Requirements**

Clinical performance

The clinical performance of the BUZUD COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette (Swab) was established based on the evaluation of clinical samples prospectively collected from three independent clinical sites between October 2022 and July 2024. A clinical evaluation was conducted comparing the test results to PCR tests performed by healthcare professionals. Symptomatic individuals with respiratory tract infection symptoms within 7 days post symptom onset were recruited, including children between 3-11 years old, adolescents between 12-17 years old, and adults over 18 years old. Samples with unclear collection time or information, obviously contaminated samples (bacteria contamination or nosebleed), samples that underwent freeze-thaw cycles, and invalid rapid test or PCR results were excluded from the studies.

Clinical studies demonstrated the following performance when compared against the method comparator:

| Pathogens | Sample size | Sensitivity | Specificity |
|---|---|---|---|
| SARS-CoV-2 | 1,067 | 89.36% (95% CI: 83.06-93.92%) | 99.57 (95% CI: (98.90-9.88%) |
| Influenza A | 662 | 88.73% (95% CI: 82.35-93.42%) | 99.04% (95% CI: 97.77-99.69%) |
| Influenza B | 662 | 87.32% (95% CI: 80.71-92.31%) | 98.65% (95% CI: 97.25-99.46%) |
| RSV | 360 | 88.16% (95% CI: 82.06-92.38%) | 99.52% (95% CI: 97.33-99.92%) |
| Adenovirus | 360 | 85.88% (95% CI: 79.85-90.33%) | 99.47% (95% CI: 97.08-99.91%) |

Self-testing

Usability studies were conducted to assess the lay user's ability to understand the instructions for use and to adequately execute the test workflow accordingly. A total of 217 subjects comprising various educational levels were enrolled in the study and observed during testing.

- Label comprehension: majority of participants found IFU easy to understand
- Result interpretation: >97% correct interpretation of predetermined results
- Diagnostic performance: 100% positive and negative agreement between self-test and professional results for COVID-19, Flu A, Flu B, and RSV. For ADV, positive agreement was 97.56% and negative agreement was 99.14%.

## 5. Assessment of device quality

Device is manufactured in China at Zhejiang Orient Gene Biotech Co., Ltd. The manufacturing site conforms to ISO 13485 quality management system. Comprehensive batch release testing protocol is in place including positive and negative controls for all five pathogens to ensure consistent identification of relevant antigens across all batches.

## 6. Conclusion

The BUZUD COVID-19/Flu A&B/RSV/Adeno Ag Combo Rapid Test Cassette demonstrates acceptable safety and performance for its intended use as a self-testing device for the qualitative detection of five respiratory pathogens. The benefits of this device outweigh its risks as it provides lay users with the ability to simultaneously test for five respiratory pathogens when experiencing upper respiratory tract infection symptoms, offering clinical benefit not currently available in approved self-testing devices. All foreseeable risks have been identified and reasonably mitigated through appropriate design controls, labelling, and user instructions. The comprehensive pre-clinical and clinical validation data supports the device's safety and effectiveness for the intended population and use environment.