# SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test Package Insert

CE IVD

**REF ISIR-535**

**English**

*SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 Nucleocapsid protein, Influenza A, Influenza B and Respiratory Syncytial Virus (RSV) antigens present in human nasopharyngeal swab specimen or nasal swab specimen.*
*For professional in vitro diagnostic use only.*

**INTENDED USE**

The SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test is a rapid chromatographic immunoassay for the qualitative detection of SARS-CoV-2 Nucleocapsid protein, Influenza A, Influenza B and Respiratory Syncytial Virus (RSV) antigens in human nasopharyngeal or nasal swab specimens from individuals with suspected SARS-CoV-2/Influenza/RSV infection in conjunction with clinical presentation and the results of other laboratory tests.

Results are for the detection of SARS-CoV-2 Nucleocapsid protein, Influenza A+B and RSV Antigens. An antigen is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out other bacterial/viral infection. The agent detected may not be the definite cause of disease.

Negative results do not preclude SARS-CoV-2/Influenza A+B/RSV infection and should not be used as the sole basis for treatment or patient management decisions. Negative results should be treated as presumptive and confirmed with a molecular assay, if necessary for patient management. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with SARS-CoV-2, Influenza A+B and RSV.

**SUMMARY**

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases.[1]

Influenza (commonly known as 'flu') is a highly contagious, acute viral infection of the respiratory tract. It is a communicable disease easily transmitted through the coughing and sneezing of aerosolized droplets containing live virus. Laboratory identification of human influenza virus infections is commonly performed using direct antigen detection, virus isolation in cell culture, or detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT-PCR). Rapid tests for influenza A and B virus infections, which can provide results within 30 minutes. [2]

Respiratory Syncytial Virus (RSV), which causes infection of the lungs and breathing passages, is a major cause of respiratory illness in young children. In adults, it may only produce symptoms of a common cold, such as a stuffy or runny nose, sore throat, mild headache, cough, fever, and a general feeling of being ill.Most children with RSV infection, both those who were hospitalized and those who were treated as outpatients, had no coexisting medical conditions or characteristics that significantly identified them as being at greater risk for severe RSV disease, except for being under 2 years of age. [3]

**PRINCIPLE**

The SARS-CoV-2 Antigen Rapid Test is a qualitative membrane-based immunoassay for the detection of SARS-CoV-2 Nucleocapsid protein in human swab specimen. SARS-CoV-2 antibody is coated in test line region. During testing, the specimen reacts with SARS-CoV-2 antibody-coated particles in the test. The mixture then migrates upward on the membrane by capillary action and reacts with the SARS-CoV-2 antibody in test line region. If the specimen contains SARS-CoV-2 Nucleocapsid protein, a colored line will appear in test line region as a result of this. If the specimen does not contain antigens to SARS-CoV-2, no colored line will appear in the test line region, indicating a negative result. To serve as a procedural control, a colored line will always appear in the control line region, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

The Influenza A+B Rapid Test is a qualitative, lateral flow immunoassay for the detection of Influenza A and Influenza B nucleoproteins in human swab specimen. In this test, antibody specific to the Influenza A and Influenza B nucleoproteins is separately coated on the test line regions of the test. During testing, the extracted specimen reacts with the antibody to Influenza A and/or Influenza B that are coated onto particles. The mixture migrates up the membrane to react with the antibody to Influenza A and/or Influenza B on the membrane and generate one or two colored lines in the test regions. The presence of this colored line in either or both of the test regions indicates a positive result. To serve as a procedural control, a colored line will always appear in the control region if the test has performed properly.

The RSV Rapid Test is a qualitative, lateral flow immunoassay for the detection of Respiratory Syncytial Virus nucleoproteins in human swab specimen. In this test, antibody specific to the Respiratory Syncytial Virus nucleoproteins is coated on the test line region of the test. During testing, the extracted specimen reacts with the antibody to Respiratory Syncytial Virus that is coated onto particles. The mixture migrates up the membrane to react with the antibody to Respiratory Syncytial Virus on the membrane and generate one colored line in the test region. The presence of this colored line in the test region indicates a positive result. To serve as a procedural control, a colored line will always appear in the control region if the test has performed properly.

**REAGENTS**

The test contains anti-SARS-CoV-2, anti-Influenza A, anti-Influenza B and anti-RSV as the capture reagent, anti-SARS-CoV-2, anti-Influenza A, anti-Influenza B and anti-RSV as the detection reagent.

**PRECAUTIONS**

1. This package insert must be read completely before performing the test. Failure to follow directions in package insert may yield inaccurate test results.
2. For professional *in vitro* diagnostic use only. Do not use after the expiration date.
3. Do not eat, drink or smoke in the area where the specimens or kits are handled.
4. Do not use test if pouch is damaged.
5. Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the collection, handling, storage, and disposal of samples and used kit contents.
6. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
7. Viral Transport Media (VTM) may affect the test result, do not store specimens in viral transport media; extracted specimens for PCR tests cannot be used for the test.
8. Wash hands thoroughly after handling.
9. Please ensure that an appropriate amount of samples are used for testing. Too much or too little sample size may lead to deviation of results.
10. The used test should be discarded according to local regulations.
11. Humidity and temperature may adversely affect results.

**STORAGE AND STABILITY**

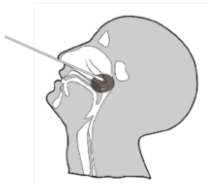
Store as packaged in the sealed pouch at room temperature or refrigerated (2-30 °C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

**SPECIMEN COLLECTION, TRANSPORT AND STORAGE**

- **Specimen Collection**

**Nasopharyngeal Swab Specimen**

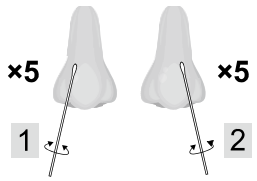
1. Insert a sterile swab into the nostril of the patient, reaching the surface of the posterior nasopharynx.
2. Swab over the surface of the posterior nasopharynx.
3. Withdraw the sterile swab from the nasal cavity.



Caution: If the swab stick breaks during specimen collection, repeat specimen collection with a new swab.

**Nasal Swab Specimen**

1. Insert a sterile swab into one nostril until slight resistance is met (Approx. 2cm up the nose). Slowly twist the swab, rubbing it along the inside of the nostril for 5-10 times against the nasal wall.
2. Gently remove the swab.
3. Using the same swab, repeat step 1 with the other nostril.
4. Withdraw the swab.




Caution: If the swab stick breaks during specimen collection, repeat specimen collection with a new swab.

- **Specimen transport and storage**

Specimens should be tested as soon as possible after collection.

If swabs are not been processed immediately, it is highly recommended the swab sample is placed into a dry, sterile, and tightly sealed plastic tube for storage. The swab specimen in dry and sterile condition is stable for up to 24 hours at 2-8°C.

**SPECIMEN PREPARATION**

*Only the extraction buffer and tubes provided in the kit are to be used for swab specimen preparation.*
*Please refer to the Procedure card for detailed information of Specimen Extraction.*

1. Place the swab specimen in the extraction tube with extraction buffer. Rotate the swab for approximately 10 seconds while pressing the head against the inside of the tube to release the antigen in the swab.
2. Remove the swab while squeezing the swab head against the inside of the extraction tube as you remove it to expel as much liquid as possible from the swab. Discard the swab in accordance with your biohazard waste disposal protocol.

***NOTE**: The storage of the specimen after extraction is stable for 2 hours at room temperature or 24 hours at 2-8 °C.

**MATERIALS**

**Materials provided**

- Test cassettes
- Extraction buffer
- Procedure card
- Package insert
- Extraction tubes and tips (Optional)
- Sterile swabs
- Workstation

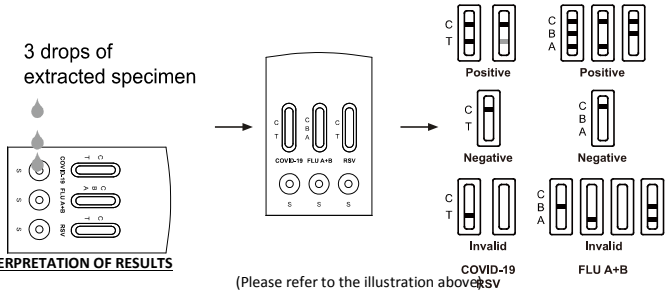
**Materials required but not provided**

- Timer

**DIRECTIONS FOR USE**

**Allow the test, extracted specimen and/or controls to equilibrate to room temperature (15-30 °C) prior to testing.**

1. Remove the test cassette from the sealed foil pouch and use it within one hour. Best results will be obtained if the test is performed immediately after opening the foil pouch.
2. Invert the specimen collection tube and add **3 drops of extracted specimen** to each of the specimen well (S) respectively and then start the timer.
3. Wait for the colored line(s) to appear. **Read the result at 15 minutes**. Do not interpret the result after 20 minutes.




**INTERPRETATION OF RESULTS**

(Please refer to the illustration above)

**SARS-CoV-2/RSV POSITIVE:* Two colored lines appear in the COVID-19/RSV window.** One colored line should be in the control region (C) and another colored line should be in the test region (T). Positive result in the Test region indicates detection of SARS-CoV-2/RSV antigens in the sample.

**Influenza A POSITIVE: * Two colored lines appear in the FLU A+B window.** One colored line should be in the control region (C) and another colored line should be in the Influenza A region (A). Positive result in the Influenza A region indicates that Influenza A antigen was detected in the sample.

**Influenza B POSITIVE:* Two colored lines appear in the FLU A+B window.** One colored line should be in the control region (C) and another colored line should be in the Influenza B region (B). Positive result in the Influenza B region indicates that Influenza B antigen was detected in the sample.

**Influenza A and Influenza B POSITIVE:* Three colored lines appear in the FLU A+B window.** One colored line should be in the control region (C) and two colored lines should be in the Influenza A region (A) and Influenza B region (B). Positive result in the Influenza A region and Influenza B region indicates that Influenza A antigen and Influenza B antigen were detected in the sample.

***NOTE**: The intensity of the color in the test line region (T) will vary based on the amount of SARS-CoV-2 antigen, Flu A and/or B antigen, RSV antigen present in the sample. So any shade of color in the test region (T/B/A) should be considered positive.

**NEGATIVE: One colored line appears in the control region (C).** No colored line appears in the test line region (T/B/A).

**INVALID: Control line fails to appear.** Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

**QUALITY CONTROL**

**Internal Quality Control**

Internal procedural controls are included in the test. A colored line appearing in the control region (C) is an internal procedural control. It confirms sufficient specimen volume and correct procedural technique. A clear background is another internal procedural control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

**External Quality Control**

Controls are not included in this kit. However, in compliance with Good Laboratory Practice (GLP) positive/negative controls are recommended. [1]

**LIMITATIONS**

1. The DIRECTIONS FOR USE and the INTERPRETATION OF RESULTS must be followed closely when testing for the presence of SARS-CoV-2/Influenza A/Influenza B/RSV antigens in the human nasopharyngeal or nasal swab specimens from suspected individuals. For optimal test performance, proper sample collection is critical. Failure to follow the procedure may give inaccurate results.
2. The performance of the SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test was evaluated using the procedures provided in this product insert only. Modifications to these procedures may alter the performance of the test.
3. The SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test is for *in vitro* diagnostic use only. This test should be used for detection of SARS-CoV-2/Influenza A/Influenza B/RSV Antigens in human nasopharyngeal or nasal swab specimens as an aid in the diagnosis of patients with suspected SARS-CoV-2, Influenza A, Influenza B or RSV infection in conjunction with clinical presentation and the results of other laboratory tests. Neither the quantitative value nor the rate of increase in the concentration of SARS-CoV-2/Influenza A/Influenza B/RSV antigens can be determined by this qualitative test.
4. The SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test will only indicate the presence of SARS-CoV-2/Influenza A/Influenza B/RSV Antigens in the specimen and should not be used as the sole criteria for the diagnosis of SARS-CoV-2/Influenza A/Influenza B/RSV infections.
5. The results obtained with the test should be considered with other clinical findings from other laboratory tests and evaluations.
6. If the test result is negative or non-reactive and clinical symptoms persist, it is recommended to re-sample the patient a few days later and test again or test with a molecular diagnostic device to rule out infection in these individuals.

7. The test will show negative results under the following conditions:
   a) The concentration of the novel coronavirus antigens, Influenza A Influenza B or RSV virus antigens in the sample is lower than the minimum detection limit of the test.
   b) The optimal sampling time (peak virus concentration) after infection has not been verified, so collecting samples at different times for the same patient may avoid false negatives.
   c) Incorrect specimen collection and storage.
8. Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
9. A negative result for Influenza A or Influenza B or RSV obtained from this kit should be confirmed by RT-PCR/culture.
10. Positive results of SARS-CoV-2 may be due to infection with non-SARS-CoV-2 coronavirus strains or other interference factors. A positive result for influenza A and/or B, RSV does not preclude an underlying co-infection with another pathogen, therefore the possibility of an underlying bacterial infection should be considered.

## PERFORMANCE CHARACTERISTICS

### Sensitivity, Specificity and Accuracy

The SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test has been evaluated with specimens obtained from the patients. RT-PCR is used as the reference method for the SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test. Specimens were considered positive if RT-PCR indicated a positive result. Specimens were considered negative if RT-PCR indicated a negative result.

**Nasopharyngeal Swab Specimen**

SARS-CoV-2 Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| SARS-CoV-2 Antigen | Positive | 97 | 1 | 98 |
| | Negative | 3 | 99 | 102 |
| Total | | 100 | 100 | 200 |
| Relative Sensitivity | | 97.0% (95%CI*: 91.5%~99.4%) | | |
| Relative Specificity | | 99.0% (95%CI*: 94.6%~100%) | | |
| Accuracy | | 98.0% (95%CI*: 95.0%~99.5%) | | |

Influenza A+B Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | Type A | | | Type B | | |
|---|---|---|---|---|---|---|---|
| | | RT-PCR | | Total | RT-PCR | | Total |
| | | Positive | Negative | | Positive | Negative | |
| Flu A+B | Positive | 38 | 2 | 40 | 39 | 2 | 41 |
| | Negative | 2 | 215 | 217 | 3 | 213 | 216 |
| Total | | 40 | 217 | 257 | 42 | 215 | 257 |
| Relative Sensitivity | | 95.0% (95%CI*: 83.1%-99.4%) | | | 92.9% (95%CI*: 80.5%-98.5%) | | |
| Relative Specificity | | 99.1% (95%CI*: 96.7%-99.9%) | | | 99.1% (95%CI*: 96.7%-99.9%) | | |
| Accuracy | | 98.4% (95%CI*: 96.1%-99.6%) | | | 98.1% (95%CI*: 95.5%-99.4%) | | |

RSV Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| RSV Antigen | Positive | 33 | 9 | 42 |
| | Negative | 2 | 225 | 227 |
| Total | | 35 | 234 | 269 |
| Relative Sensitivity | | 94.3% (95%CI*:80.8%-99.3%) | | |
| Relative Specificity | | 96.2% (95%CI*:92.8%-98.2%) | | |
| Accuracy | | 95.9% (95%CI*:92.8%-97.9%) | | |

*Confidence Intervals

**Nasal Swab Specimen**

SARS-CoV-2 Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| SARS-CoV-2 Antigen | Positive | 161 | 2 | 163 |
| | Negative | 5 | 482 | 487 |
| Total | | 166 | 484 | 650 |
| Relative Sensitivity | | 97.0% (95%CI*: 93.1%~99.0%) | | |
| Relative Specificity | | 99.6% (95%CI*: 98.5%~100%) | | |
| Accuracy | | 98.9% (95%CI*: 97.8%~99.6%) | | |

Influenza A+B Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | Type A | | | Type B | | |
|---|---|---|---|---|---|---|---|
| | | RT-PCR | | Total | RT-PCR | | Total |
| | | Positive | Negative | | Positive | Negative | |
| Flu A+B | Positive | 68 | 2 | 70 | 48 | 3 | 51 |
| | Negative | 3 | 485 | 488 | 3 | 504 | 507 |
| Total | | 71 | 487 | 558 | 51 | 507 | 558 |
| Relative Sensitivity | | 95.8% (95%CI*: 88.1%~99.1%) | | | 94.1% (95%CI*: 83.8%~98.8%) | | |
| Relative Specificity | | 99.6% (95%CI*: 98.5%~100%) | | | 99.4% (95%CI*: 98.3%~99.9%) | | |
| Accuracy | | 99.1% (95%CI*: 97.9%-99.7%) | | | 98.9% (95%CI*: 97.7%-99.6%) | | |

RSV Test:

| SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test | | RT-PCR | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| RSV Antigen | Positive | 52 | 1 | 53 |
| | Negative | 2 | 297 | 299 |
| Total | | 54 | 298 | 352 |
| Relative Sensitivity | | 96.3% (95%CI*:87.3%-99.6%) | | |
| Relative Specificity | | 99.7% (95%CI*:98.1%-100%) | | |
| Accuracy | | 99.2% (95%CI*:97.5%-99.8%) | | |

*Confidence Intervals

**Specificity Testing with Various Viral Strains**

The SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test was tested with the following viral strains. No discernible line at either of the test-line regions was observed at the concentrations listed:

| Description | Concentration |
|---|---|
| Adenovirus type 3 | $3.16 \times 10^4$ $TCID_{50}$/mL |
| Adenovirus type 7 | $1.58 \times 10^5$ $TCID_{50}$/mL |
| Human coronavirus OC43 | $1 \times 10^6$ $TCID_{50}$/mL |
| Human coronavirus 229E | $5 \times 10^5$ $TCID_{50}$/mL |
| Human coronavirus NL63 | $1 \times 10^6$ $TCID_{50}$/mL |
| Human coronavirus HKU1 | $1 \times 10^6$ $TCID_{50}$/mL |
| MERS COV Florida | $1.17 \times 10^4$ $TCID_{50}$/mL |
| Human Rhinovirus 2 | $2.81 \times 10^4$ $TCID_{50}$/mL |
| Human Rhinovirus 14 | $1.58 \times 10^6$ $TCID_{50}$/mL |
| Human Rhinovirus 16 | $8.89 \times 10^6$ $TCID_{50}$/mL |
| Measles | $1.58 \times 10^4$ $TCID_{50}$/mL |
| Mumps | $1.58 \times 10^4$ $TCID_{50}$/mL |
| Parainfluenza virus 2 | $1.58 \times 10^7$ $TCID_{50}$/mL |
| Parainfluenza virus 3 | $1.58 \times 10^8$ $TCID_{50}$/mL |

**$TCID_{50}$** = Tissue Culture Infectious Dose is the dilution of virus that under the conditions of the assay can be expected to infect 50% of the culture vessels inoculated.

### Precision

**Intra-Assay & Inter-Assay**

Within-run and Between-run precision has been determined by using below standard controls: Negative specimen, SARS-COV-2 Antigen Weak and Strong positive specimen, Influenza A Weak and Strong positive specimen, Influenza B Weak and Strong positive specimen, RSV Weak and Strong positive specimen. Three different lots of SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test have been tested. Ten replicates were tested with each standard control each day, and the test was conducted for 3 consecutive days. The specimens were correctly identified >99% of the time.

### Cross-reactivity

The following organisms were tested at $1.0 \times 10^8$ org/mL and all found to be negative when tested with the SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test:

| | |
|---|---|
| *Arcanobacterium* | *Pseudomonas aeruginosa* |
| *Candida albicans* | *Staphylococcus aureus subspaureus* |
| *Corynebacterium* | *Staphylococcus epidermidis* |
| *Escherichia coli* | *Streptococcus pneumoniae* |
| *Moraxella catarrhalis* | *Streptococcus pyogenes* |
| *Neisseria lactamica* | *Streptococcus salivarius* |
| *Neisseria subflava* | *Streptococcus sp group F* |

### Interfering Substances

The interfering substances below were spiked with negative, SARS-COV-2 Antigen weak positive, Influenza A weak positive, Influenza B Weak positive and RSV Weak positive. No substances showed any interference with the SARS-CoV-2/Influenza A+B/RSV Antigen Combo Rapid Test.

| Substance | Concentration |
|---|---|
| Whole Blood | 20 µL/mL |
| Mucin | 50 µg/mL |
| Budesonide Nasal Spray | 200 µL/mL |
| Dexamethasone | 0.8 mg/mL |
| Flunisolide | 6.8 ng/mL |
| Mupirocin | 12 mg/mL |
| Oxymetazoline | 0.6 mg/mL |
| Phenylephrine | 12 mg/mL |
| Rebetol | 4.5 µg/mL |
| Relenza | 282 ng/mL |
| Tamiflu | 1.1 µg/mL |
| Tobryamycin | 2.43 mg/mL |

## BIBLIOGRAPHY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2. WHO recommendations on the use of rapid testing for influenza diagnosis, July 2005.
3. Caroline Breese Hall, M.D., Geoffrey A. Weinberg, M.D., Marika K. Iwane, Ph.D.. et al. (2009). The Burden of Respiratory Syncytial Virus Infection in Young Children. N Engl J Med, 360(6): 588–598.


| | |
|---|---|
| IVD | For *in vitro* diagnostic use only |
| 30°C / 2°C | Store between 2-30°C |
| | Do not use if package is damaged |
| EC REP | Authorized representative in EU |
| REF | Catalog # |
| Σ | Tests per kit |
| | Use by |
| LOT | Lot number |
| | Manufacturer |
| 2 | Do not reuse |
| | Consult instructions for use |


Manufacturer

**Hangzhou Alltest Biotech Co., Ltd.**
#550, Yinhai Street,
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EC REP

**Lotus NL B.V.**
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