Rapid Response®

HMPV Test Cassette
(Nasal/Nasopharyngeal Swab)

REF HMPV-19CT, HMPV-19CTPC20 Product Insert

For professional laboratory *in vitro* diagnostic use only.

Intended Use

The Rapid Response® HMPV Test Cassette is a rapid visual immunoassay for the qualitative presumptive detection of human metapneumovirus from human nasal/nasopharyngeal swab samples. This kit is intended to be used as an aid in the diagnosis of human metapneumovirus infection.

Introduction

Human metapneumovirus (HMPV) is a respiratory virus from the *Pneumoviridae* family[1], this virus has a single-stranded (ss), negative-sense, and non-segmented RNA genome that is approximately 13.3 kb in size, and it represents one of the leading causes of acute respiratory tract infections (ARTI) in children[2], immunosuppressed patients, and the elderly. This pathogen is also considered a primary cause of death in infants under five years old. Studies have shown that HMPV represents a significant economic burden on health care systems worldwide, affecting up to 86% of the global population of infants under five years old[3].

Clinical signs and symptoms associated with HMPV are mainly respiratory problems ranging from coughing, wheezing, and fever to more severe complications, such as bronchiolitis and pneumonia. HMPV mainly infects and affects the lower respiratory tract (LRT), with the requirement for mechanical ventilation in the most severe cases. Infection with HMPV has also been associated with the manifestation of neural-related symptoms, such as encephalitis and febrile seizures[4]. Regarding its epidemiology, HMPV begins circulating among the general population during winter and lasts until the end of spring[5].

For diagnosis of HMPV, the traditional basis is isolation and identification of viruses, PCR can be used to diagnose HMPV. Rapid immunoassay of HMPV has become more important due to the availability of effective antiviral therapy. The Rapid Response® HMPV Test Cassette offers a simple, qualitative diagnosis of HMPV infection.

Principle

The Rapid Response® HMPV Test Cassette has been designed to detect human metapneumovirus through visual interpretation of colour development on the internal test strip. Anti-HMPV virus antibodies are immobilized on the test region of the nitrocellulose membrane. During test procedure, the extracted antigens, if present, will bind to antibodies conjugated with coloured particles on the label pad. As the specimen migrates along the strip by capillary action and interacts with reagents on the membrane, the complex will be captured by the antibodies immobilized at the test region (T). Excess coloured particles are captured at the internal control zone.

The presence of coloured line on the test region (T) indicates a positive result, while its absence indicates a negative result. A red line at the control region (C) of each test serves as a procedural control, indicating that the proper volume of specimen has been added and membrane wicking is working.

Precautions

- For professional laboratory *in vitro* diagnostic use only.
- Do not use after expiration date indicated on the package. Do not use the test if its foil pouch is damaged. Do not reuse tests.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled with the usual safety precautions (do not ingest or inhale).
- Avoid cross-contamination of specimens by using a new specimen collection container for each specimen obtained.
- Read the entire procedure carefully prior to performing any tests.
- Do not eat, drink or smoke in the area where the specimens and kits are handled. Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- Extraction buffer contains sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of buffered saline or extracted samples, always flush with copious quantities of water to prevent azide building up.
- Do not interchange or mix reagents from different lots.
- Humidity and temperature can adversely affect results.
- Used testing materials should be discarded in accordance with local, state and/or federal regulations.

Materials

Materials provided

- Individually packed test devices
- Swabs
- Product insert
- Extraction buffer tubes
- Tube Stand

Materials required but not provided

- Centrifuge
- Specimen collection container
- Timer

Storage and Stability

- The kit should be stored at 2-30°C (35.6-86°F) until the expiry date printed on the sealed pouch.
- The test must remain in the sealed pouch until use.
- **DO NOT FREEZE.**
- Care should be taken to protect the components of the kit from contamination. Do not use if there is evidence of microbial contamination or precipitation. Biological contamination of dispensing equipment, containers or reagents can lead to false results.

Collection and Storage of Specimens

Specimen Collection

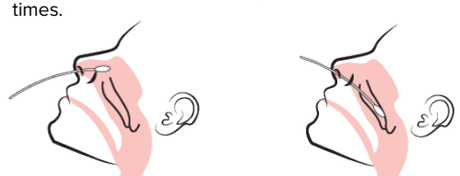
Acceptable specimens for testing with the Rapid Response® HMPV Test Cassette include samples from nasal/nasopharyngeal swabs. Do not use specimens that are obviously contaminated with blood, as it may interfere with the flow of the samples with the interpretation of test results. Use freshly collected specimens for best test performance. Rapid tests will have more reliable clinical performance when performed early in the course of infection. To ensure optimal performance, use the swabs supplied in the kit.

Nasal Swab

a) Insert the swab into the nostril that exhibits the most visible drainage, if secretion is not visible, into the nostril that is most congested. Gently push the swab until resistance is met at the level of turbinates (less than one inch into the nostril), rotate the swab a few times against nasal wall. Slowly withdraw the swab while continuing with a rotating motion.

Nasopharyngeal (NP) Swab

b) Insert the swab carefully into the nostril that presents the most secretion under visual inspection. Keep the swab near the septum floor of the nose while gently pushing the swab into the posterior nasopharynx. Rotate the swab several times.

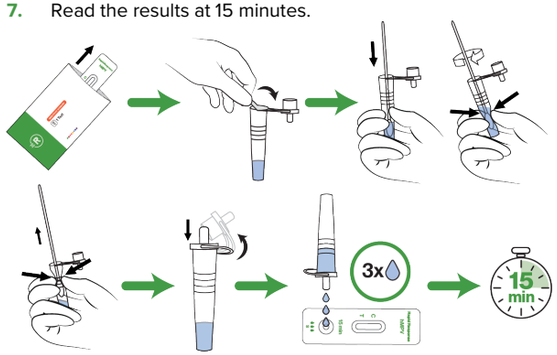


a) Nasal swab **b) Nasopharyngeal swab**

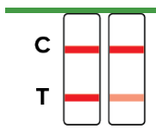
Test Procedure

Bring devices, reagents and specimens and/or controls to room temperature (59~86°F; 15~30°C) before use.

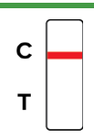
1. For each specimen swab, open the foil pouch just before testing and remove the test device, and put it on a clean, level surface. Label the tube with the patient identification. For the best results, the assay should be performed within one hour.
2. Peel off the aluminum foil cover of the extraction buffer tube.
3. Insert the swab into the extraction tube. Mix well and squeeze the swab several times by compressing the walls of the tube against the swab.
4. Roll the swab head against the inside of the tube as you remove it. Try to release as much liquid as possible. Dispose of the used swab in accordance with your biohazard waste disposal protocol.
5. Insert the filtered nozzle into the sample extraction tube.
6. Invert the tube and add 3 drops specimen into the sample well (S) by gently squeezing the tube.
7. Read the results at 15 minutes.



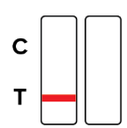
Results Interpretation



POSITIVE: Two coloured lines appear on the membrane. One line appears in the control region (C) and another line appears in the test region (T).



NEGATIVE: Only one coloured line appears in the control region (C). No apparent coloured line appears in the test region (T).



INVALID: Control line fails to appear, whether test line is present or not. Results from any test which has not produced a control line at the specified read time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.

NOTE:

1. The intensity of colour in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of colour in the test region

should be considered positive. Note that this is a qualitative test only and cannot determine the concentration of analytes in the specimen.

2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control line failure.

Quality Control

- Internal procedural controls are included in the test. A coloured line appearing in the control region (C) is considered an internal positive procedural control, confirming sufficient specimen volume and correct procedural technique.
- External controls are not supplied with this kit. It is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

Limitations

1. The Rapid Response® HMPV Test Cassette is for professional laboratory *in vitro* diagnostic use, and should be used for the qualitative detection of human metapneumovirus only.
2. Following certain antibiotic treatments, the concentration of human metapneumovirus antigens may decrease to the concentration below the minimum detection level of the test.
3. Failure to follow the TEST PROCEDURE and RESULTS INTERPRETATION may adversely affect test performance and/or invalidate the test result.
4. A high dose "hook effect" may occur where the colour intensity of test line decreases as the concentration of antigen increases. If a "hook effect" is suspected, dilution of specimens may increase colour intensity of the test line.
5. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

Performance Characteristics

Clinical Evaluation:

154 nasopharyngeal swabs were tested on the device and confirmed by RT-PCR. 50 samples presented positive results and 104 samples presented negative results by the device. In addition, 52 samples presented positive results and 102 samples presented negative results by RT-PCR.

Table 6: Rapid Response® HMPV Test Cassette vs. PCR

		RT-PCR		Total
		Positive	Negative	
Rapid Response® HMPV Test Cassette	Positive	50	0	50
	Negative	2	102	104
	Total	52	102	154

Relative Sensitivity: 96.2 % (87.0%~98.9%) *
Relative Specificity: 100.0 % (96.4%~100.0%)*
Overall Agreement: 98.7 % (95.4%~99.6 %)*

*95% Confidence Interval

Bibliography

1. Van Den Hoogen, B.G.; De Jong, J.C.; Groen, J.; Kuiken, T.; De Groot, R.; Fouchier, R.A.M.; Osterhaus, A.D.M.E. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. *Nat. Med.* 2001, *7*, 719–724.
2. Jagusic, M.; Slovic, A.; Ivancic-Jelecki, J.; Ljubin-Sternak, S.; Vilibić-Čavlek, T.; Tabain, I.; Forcic, D. Molecular epidemiology of human respiratory syncytial virus and human metapneumovirus in hospitalized children with acute respiratory infections in Croatia, 2014–2017. *Infect. Genet. Evol.* 2019, 76, 104039.
3. Divarathna, M.V.M.; Rafeek, R.A.M.; Noordeen, F. A review on epidemiology and impact of human metapneumovirus infections in children using TIAB search strategy on PubMed and PubMed Central articles. *Rev. Med. Virol.* 2019, 30, e2090.
4. Van den Hoogen, B.G.; van Doornum, G.J.J.; Fockens, J.C.; Cornelissen, J.J.; Beyer, W.E.P.; de Groot, R.; Osterhaus, A.D.M.E.; Fouchier, R.A.M. Prevalence and Clinical Symptoms of Human Metapneumovirus Infection in Hospitalized Patients. *J. Infect. Dis.* 2003, 188, 1571–1577.
5. Haynes, A.K.; Fowlkes, A.L.; Schneider, E.; Mutuc, J.D.; Armstrong, G.L.; Gerber, S.I. Human metapneumovirus circulation in the United States, 2008 to 2014. *Pediatrics* 2016, 137, e20152927.

Glossary of Symbols

Consult instructions for use
Tests per Kit
Do Not Reuse
Store between 2°C to 30°C (35.6°F to 86°F)
Use by
REF Catalogue #
LOT Lot Number
IVD For *in vitro* diagnostic use only
Manufacturer

BTNX Inc.
722 Rosebank Road,
Pickering, ON L1W 4B2
Canada
Technical Support: 1-888-339-9964