IVD

Ver. 3.0 of November 2018

Please read this package insert carefully before use.

Capilia™ hMPV

INTENDED USE

To detect human metapneumovirus antigens in nasal swab, nasal aspirate or pharyngeal swab (to assist in the diagnosis of human metapneumovirus infection)

SUMMARY AND EXPLANATION OF THE TEST

Human metapneumovirus (hMPV), first identified in the Netherlands in 2001, is an RNA virus that belongs to the Metapneumovirus genus within the Pneumovirinae subfamily of the Paramyxoviridae family.

hMPV is a virus that can cause respiratory infection.

hMPV infection is a typical respiratory infection in infants. It is similar to respiratory syncytial (RS) virus infection and differentiation from each other is difficult. hMPV infection is an important factor for inducing bronchiolitis.

The majority experience primary hMPV infection during infancy, and re-infection occurs frequently. As hMPV infection may become prevalent in infants and the elderly and increase in severity, early detection is important.

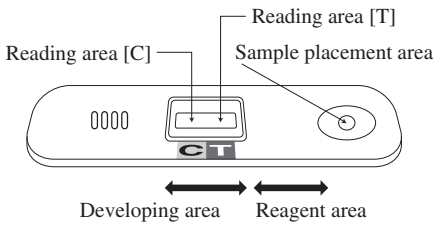
Conventionally, genetic testing is used for the detection of hMPV, but it has some disadvantages, for instance, requiring complicated manipulation, special equipment and instruments, and a certain period of time to obtain the test results.

Compared to genetic testing, this product allows rapid detection of hMPV, without requiring special skills or instruments.

PRINCIPLE OF THE TEST

Measurement using this product is based on an immunochromatography assay using a monoclonal antibody that recognizes human metapneumovirus antigens. This product comprises a test plate with a carrier strip containing a sample placement area, a reagent area including a colloidal platinum-gold labeled anti-human metapneumovirus monoclonal antibody (mouse) (hereinafter referred to as "colloidal platinum-gold labeled anti-human metapneumovirus antibody"), and a developing area that fixes an anti-human metapneumovirus monoclonal antibody (mouse) (hereinafter referred to as "anti-human metapneumovirus antibody") and an anti-mouse immunoglobulin polyclonal antibody (rabbit) (hereinafter referred to as "anti-mouse immunoglobulin antibody").

Names of each area of the test plate



When a sample is placed on the sample placement area of the test plate, the colloidal platinum-gold labeled anti-human metapneumovirus antibody dissolves and forms an immune complex with human metapneumovirus antigens in the sample. This immune complex migrates through the developing area by capillary action, is captured by the anti-human metapneumovirus antibody fixed in the developing area, and forms a black line of colloidal platinum-gold in the reading area [T]. The black line visually displays the existence of human metapneumovirus antigens in the sample.

Regardless of the existence of human metapneumovirus antigens in the sample, excess colloidal platinum-gold labeled anti-human metapneumovirus antibodies further migrate through the developing area, are captured by anti-mouse immunoglobulin antibodies fixed in the developing area, and form a black line of colloidal platinum-gold in the reading area [C]. This means the colloidal platinum-gold labeled anti-human metapneumovirus antibodies have migrated normally.

REAGENTS AND MATERIALS PROVIDED

REF CAHM1670 Capilia hMPV (20 Tests)

Test plates

・Components

Colloidal platinum-gold labeled anti-human metapneumovirus monoclonal antibody (mouse)

Anti-human metapneumovirus monoclonal antibody (mouse)

Extraction Buffer (to be used equally with the four products.) Note

・Components

Buffer, detergent, sodium azide (0.09%)

Note The extraction buffer is able to be used equally with the four products below:

- Capilia Flu Neo (rapid test for detecting influenza virus antigen)
- Capilia Adeno Neo (rapid test for detecting Adenovirus antigen)
- Capilia RSV Neo (rapid test for detecting RS virus antigen)
- Capilia hMPV (rapid test for detecting human metapneumovirus antigen)

Specimen	Flu	Adeno	RSV	hMPV
Nasal swab	○	○	○	○
Nasal aspirate	○	○	○	○
Nasal discharge/Nasal mucus	○	×	×	×
Pharyngeal swab	○	○	×	○
Keratoconjunctivitis swab	×	○	×	×

Nozzles

REF CAHM1671 Capilia hMPV Test Plate (10 Tests)

Test plates

・Components

Colloidal platinum-gold labeled anti-human metapneumovirus monoclonal antibody (mouse)

Anti-human metapneumovirus monoclonal antibody (mouse)

MATERIALS REQUIRED BUT NOT PROVIDED

Timer, micropipette, pipette tips suction machine, suction trap, sterile swabs (as listed here)

Recommended Swab

The following swabs are recommended for use with the kit.

For Nasal Swab

①FLOQSwabs ™ (Cat No. 534CS01, Copan Italia S.p.A, Italy)

②Sterilized Swab P156A 10 pcs (Cat No. 4124, HEIWA MEDIC. CO., LTD, Japan)

For Pharyngeal Swab

①FLOQSwabs ™ (Cat No. 502CS01, Copan Italia S.p.A, Italy)

②Sterilized Swab PL6S 10 pcs (Cat No. 4371, HEIWA MEDIC. CO., LTD, Japan)

To collect nasal aspirate, any of the above swabs may be used.

Acceptable Swab

The following swabs are acceptable for use with the kit.

・Tip material

Rayon, flocked nylon and polyester

・Standard tip size

For nasal swab

Plain dry swab:maximum diameter 3 mm, length 12 mm

Flocked swab:maximum diameter 3 mm, length 15 mm

For pharyngeal swab

Plain dry swab: maximum diameter 6 mm, length 14 mm

Flocked swab: maximum diameter 6 mm, length 16 mm

・Shaft material

Paper, plastic (PS, nylon), aluminum

Unacceptable Swab

Do not use calcium alginate swabs.

WARNING AND PRECAUTIONS

1. Precautions when handling (including hazard control)

1) Handle all the specimens as if they contain infectious agents.
2) In consideration of the risk of infection, wear protective clothes such as a mask and gloves and handle the specimens and samples carefully during the test.
3) If the extraction buffer gets into your eyes, immediately flush with a large quantity of water for 15 minutes or more. If you still feel some abnormality, see a doctor for treatment.
4) If the extraction buffer comes into contact with your hands or clothes, wash your hands and/or clothes with soap and a large quantity of water.
5) If a spill of the specimen or the sample occurs, immediately disinfect the area with sodium hypochlorite or other disinfectants.

2. Precautions when using

1) This product is a reagent kit for rapid detection of human metapneumovirus antigen. A definite diagnosis should be made by an attending physician, in combination with clinical symptoms, results of viral isolation and other test results.
2) This product should be used in accordance with the procedure stated in the package insert.
3) Avoid touching saliva when collecting pharyngeal swab.
4) In order to prevent deterioration, this product should be stored between 2°C and 30°C, avoiding high temperatures, high humidity and direct sunlight.
5) If this product has been refrigerated, it must be removed from the refrigerator at least 30 minutes before use and kept at room temperature when used for testing.
6) **The aluminum pouch containing a test plate should not be opened until the test plate is about to be used.**
7) The sample placement area and the reading area of the test plate should not be touched with the hands.
8) A precipitate may be seen in the extraction buffer, but the product can be used as it is, because the precipitate has been shown not to affect test results.
9) Do not use a swab if it is broken, bent partially whitened, or stained.
10) Avoid the following when using the swab since they may cause the breakage of the shaft. (Please read the package insert of the swab.)
    - To use the swab in a manner such that the shaft (especially the narrow part of the shaft) receives too much force, pressure or torsional load at the time of specimen collection.
    - To intentionally deform the shaft, more specifically, to bend, arch or break the shaft.
11) Particularly when collecting a pharyngeal swab from a child, collect the specimen with great caution lest he or she should act up, bite or break the swab and swallow the broken part, and by firmly retaining the upper body of the child to be tested.
12) For nasal sampling, do not keep forcibly insert the swab, when the distance to the site is clearly shorter than usual. In particular, there is the possibility of resistance being imposed on the stick when the sample is collected from an infant or a patient with a narrow nasal cavity. In such a case, do not swab hard, exerting force on the stick. Moreover, do not rotate the stick forcibly.
13) For nasal sampling, any mass of mucus on the tip of the swab should be gently removed with gauze. Do not wipe the tip too hard. Mucosal epidermal cells should remain on the tip for testing.
14) Do not use any products beyond the expiration date.
15) All specimens should be handled as potentially infectious, and special precautions should be exercised.

3. Precautions for disposal

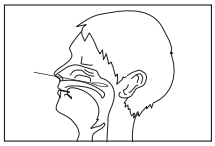
1) Because used test plates, swabs, tubes and nozzles after use, remaining samples, etc. may cause infections, they should be autoclaved (121°C, 20 min) or soaked in 0.1% sodium hypochlorite for more than one hour. When remaining reagents or their accessories are disposed of, they should be treated in accordance with the laws and regulations concerning medical waste disposal and water pollution control.
2) In the extraction buffer, 0.09% of sodium azide is included as a preservative. When solutions containing sodium azide continue to be discarded over a long period of time, explosive metallic azide may be produced if a drain is made of metal. Therefore, they should be discarded with a large quantity of water.

STORAGE CONDITIONS

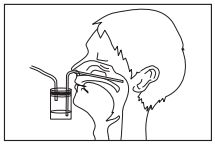
Storage : Store at 2°C to 30°C **DO NOT FREEZE.**
Keep away from direct sunlight.
Do not use test plate or extraction buffer after expiration date.

SPECIMEN COLLECTION AND PREPARATION

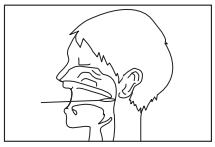
1. Methods of specimen collection



1) Sampling of nasal swab
Firmly insert a nasal swab into the nasal cavity and collect mucosal epithelium by swabbing the nasal turbinate several times.



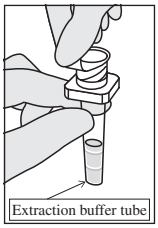
2) Sampling of nasal aspirate
Firmly insert one tube of a suction trap into the suction pump, and the other tube into a nasal cavity through an external nostril. Collect the nasal discharge aspirate in the suction trap by operating the suction pump. Soak the swab in the nasal aspirate collected by the trap, and let the swab absorb the nasal aspirate well. When nasal aspirate is taken using a micropipette or other instruments, dilute the nasal aspirate twofold with physiological saline and sample 200 µL of this dilution.



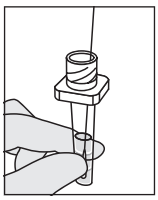
3) Sampling of pharyngeal swab
Firmly insert a pharyngeal swab into the pharynx through the oral cavity, and collect the mucosal epithelium by swabbing the posterior wall of the pharynx and the palatine tonsil several times, centering around the rubefacient portion. **Avoid touching saliva.** If the specimen is mixed with saliva, the test result lines may become fainter on the test plate.

With a collected specimen, prepare the sample according to the procedure specified in the following "Sample preparation" section and perform the test as quickly as possible.

2. Sample preparation



Remove the aluminum sealing cap from the extraction buffer tube, while taking care not to spill the liquid.

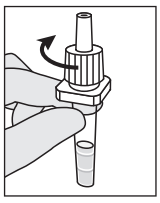


Soak the swab that collected the specimen in the extraction buffer, and stir.
Then, pinch the tip of the swab firmly with the soft wall of the extraction buffer tube with your fingers and squeeze out the swab. Use this squeezed-out liquid as the sample.
When using a nasal aspirate specimen diluted twofold with physiological saline, add 200 µL of the specimen to the extraction buffer in the tube, and mix well. Use this mixture as the sample.

3. Precautions for sample preparation

For a highly viscous sample that can cause filter clogging, dilute the sample twofold with physiological saline before use.

TEST PROCEDURE



1) Firmly attach the nozzle (with a filter) provided in the kit to the top of the extraction buffer tube.
2) Hold the middle of the tube with the fingers and dispense **3 drops of the sample (80–120 µL)** onto the sample placement area of the test plate. Hold the tube perpendicularly and take care not to let the tip of the nozzle touch the sample placement area.
3) Observe the reading area of the test plate after **3 to 5 minutes** and interpret the result according to the "READING TEST RESULTS."

Precautions for sample placement

If an excessive amount of the sample is dispensed, the reaction time may be prolonged due to the dilution of the colloidal platinum-gold labeled antibody based on the principle of the test, and no line may be seen at [C] and/or [T] in the reading area within the judgment time or the line is faint (false negative).

READING TEST RESULTS

1. Reading the result

Allow the samples to react according to the procedure and read the black lines that appear in the reading area.

Positive

When black lines are seen at both [T] and [C] in the reading area (two lines), the result is read as positive. When a very faint black line is seen in the reading area [T], the result is also interpreted as positive.

Negative

When no black line is seen at [T] in the reading area but a black line is seen only at [C] in the reading area (one line), the result is read as negative.
When a black line at [C] in the reading area is faint but visually recognizable, chromatographic development has occurred normally.

Retesting

When no black line is seen at [C] in the reading area, there may be some problem with the test procedure or the reagent quality. The test should be performed again, using another test plate.

A line that appears anywhere within the sections of the reading area, which are separated by color, is considered valid.

(Note)

1. When black lines are seen at both [T] and [C] in the reading area 3 to 5 minutes after dispensing the sample, the result is read as positive. No black line at [T] in the reading area even 5 minutes after dispensing the sample indicates a negative result.
2. Do not use the test plate for reading a result beyond the judgment time as the result may change due to drying, etc.
   If the amount of antigen in the sample is very low and close to the detection limit of this product, a black line may appear at [T] in the reading area after 5 minutes or more of the judgment time, due to the feature of immunochromatography. In addition, due to a non-specific reaction caused by specimen-derived components, a black line may appear at [T] in the reading area after 5 minutes or more of the judgment time in rare cases.
   A definite diagnosis should be made comprehensively, not only based on the test result of this product but also taking other test results and clinical symptoms into account.
3. A black line may not appear at [C] in the reading area due to problems with the test procedure or the reagent quality. In this case, the test should be performed again, using another test plate. If the same result is obtained in the re-test, try the test once more using the sample diluted twofold with saline as the black line may not appear at [C] in the reading area due to a factor in the specimen or the effect of saliva.
4. If the amount of antigen is very high, a very thick line may be seen at [T] in the reading area and no black line may be seen at [C] in the reading area. In that case, dilute the sample with more extraction buffer and perform the test again.
   Example) Method for dilution of sample : Dispense 3 drops of the sample to a new extraction buffer tube, mix throughly and use the solution as the test sample.
5. The line is valid even if there is unevenness in depth and there are breaks in the line.

LIMITATIONS

1. This product is a reagent kit for rapid detection of human metapneumovirus antigen.
   A definite diagnosis should be made by an attending physician, in combination with the clinical symptoms, the result of virus isolation culture test and other test results.
2. The test plate should be used immediately after opening the packaging. When it absorbs moisture, the quality deteriorates and an accurate result cannot be obtained.
3. This product should be used for in vitro diagnosis only and should not be used for any other purposes.
4. Please use this product following the operational method described in this package insert. We cannot guarantee results obtained from any other operations and for any other purposes that are not described in the package insert.
5. The extraction buffer contains sodium azide. If the solution comes into contact with eye or mouth or adheres to the skin by mistake, take emergency measures such as thorough washing with water and seek medical treatment, if necessary.

PERFORMANCE CHARACTERISTICS

1. Clinical data

1) Nasal swab

① Correlation with the control product

		Control product		
		Positive	Negative	Total
This Product	Positive	72	8[note 1)]	80
	Negative	0	111	111
	Total	72	119	191

Sensitivity: 100 %
Specificity: 93.3 %
Accuracy: 95.8 %

Note 1) By the PCR method, all 8 patients tested positive.

② Correlation with the PCR method

		PCR method		
		Positive	Negative	Total
This Product	Positive	80	0	80
	Negative	7	104	111
	Total	87	104	191

Sensitivity: 92.0 %
Specificity: 100 %
Accuracy: 96.3 %

2) Nasal aspirate

① Correlation with the control product

		Control product		
		Positive	Negative	Total
This Product	Positive	96	5[note 2)]	101
	Negative	0	194	194
	Total	96	199	295

Sensitivity: 100 %
Specificity: 97.5 %
Accuracy: 98.3 %

Note 2) By the PCR method, all 5 patients tested positive.

② Correlation with the PCR method

		PCR method		
		Positive	Ngative	Total
This Product	Positive	101	0	101
	Negative	15	179	194
	Total	116	179	295

Sensitivity: 87.1 %
Specificity: 100 %
Accuracy: 94.9 %

3) Pharyngeal swab

① Correlation with the PCR method

		PCR method		
		Positive	Negative	Total
This Product	Positive	107	0	107
	Negative	10	54	64
	Total	117	54	171

Sensitivity: 91.5 %
Specificity: 100 %
Accuracy: 94.2 %

2. Information on the reference material for calibration

Using the culture fluid of human metapneumovirus as the reference material for calibration, the following procedure was established.

Virus infectivity titer determination for the standard culture fluid:

A tenfold dilution series of the human metapneumovirus culture fluid was prepared. Cells inoculated with a specified amount of each dilution were incubated for a certain period of time, cytopathic effects (CPE) were then observed and recorded, and the virus infectivity titers were calculated from the number of CPE-positive cells.

3. Sensitivity (Detection limit)

The minimum detection limit of this product is as follows.
Genotype A : 4.5×10^2 $TCID_{50}$/test
Genotype B : 3.0×10^2 $TCID_{50}$/test

4. Cross reactivity

No cross-reactivity was found in all the viruses and bacteria listed below.

1) Viruses

Adenovirus Type1	Adenovirus Type2
Adenovirus Type3	Adenovirus Type4
Adenovirus Type5	Adenovirus Type6
Adenovirus Type7	Adenovirus Type10
Adenovirus Type11	Adenovirus Type14
Adenovirus Type18	Adenovirus Type19
Adenovirus Type22	Adenovirus Type37
Adenovirus Type40	Adenovirus Type53
Adenovirus Type54	Influenzavirus A, (H1N1)
Influenzavirus A, (H1N1) pdm09	Influenzavirus A, (H3N2)
Influenzavirus B	Respiratory syncytial virus A
Respiratory syncytial virus B	

2) Bacteria

Acinetobacter baumannii	*Aspergillus niger*
Bordetella pertussis	*Burkholderia cepacia*
Candida albicans	*Candida glabrata*
Chlamydia trachomatis	*Chlamydophila pneumoniae*
Enterococcus faecalis	*Enterococcus gallinarum*
Escherichia coli	*Haemophilus aphrophilus*
Haemophilus influenzae	*Haemophilus parainfluenzae*
Haemophilus paraphrophilus	*Kingella kingae*
Klebsiella pneumoniae	*Legionella anisa*
Legionella bozemanii	*Legionella dumoffii*
Legionella gornmanii	*Legionella jordanis*
Legionella longbeachae	*Legionella micdadei*
Legionella pneumophila SG-1	*Legionella pneumophila* SG-2
Legionella pneumophila SG-3	*Legionella pneumophila* SG-4
Legionella pneumophila SG-5	*Legionella pneumophila* SG-6
Legionella pneumophila SG-7	*Legionella pneumophila* SG-8
Legionella pneumophila SG-9	*Legionella pneumophila* SG-10
Legionella pneumophila SG-11	*Legionella pneumophila* SG-12
Legionella pneumophila SG-13	*Legionella pneumophila* SG-14
Legionella pneumophila SG-15	*Listeria monocytogens*
Moraxella catarrhalis	*Mycobacterium kansasii*
Mycobacterium marinum	*Mycoplasma pneumoniae*
Proteus mirabilis	*Proteus vulgaris*
Pseudomonas aeruginosa	*Serratia marcescens*
Staphylococcus aureus	*Staphylococcus epidermidis*
Streptococcus agalactiae	*Streptococcus bovis*
Streptococcus dysgalactiae	*Streptococcus mitis*
Streptococcus mutans	*Streptococcus pneumoniae*
Streptococcus pneumoniae Type 1	*Streptococcus pneumoniae* Type 3
Streptococcus pneumoniae Type 5	*Streptococcus pneumoniae* Type 19F1
Streptococcus porcinus	*Streptococcus pyogenes*
Streptococcus sanguinis	*Streptococcus sp.* Group C
Streptococcus sp. Group D	*Streptococcus sp.* Group F
Streptococcus sp. Group G	

INTERFERING SUBSTANCES OR DRUGS

The following over-the-counter drugs and prescription drugs were found to have no effect on the results at the concentrations indicated.
commercially available cold remedy (1 mg/mL); commercially available cough drop (40 mg/mL); 2 types of commercially available eye drops (0.25 mL/mL); 2 types of commercially available nose drops (0.025 mL/mL); commercially available gargle (0.1 mL/mL); commercially available mouthwash (0.25 mL/mL); acetylsalicylic acid (2 mg/mL); amantadine hydrochloride (5 mg/mL); oxymetazoline hydrochloride (1 µg/mL); powdered Platycodon root (0.1 mg/mL); erythromycin (1 mg/mL); zanamivir (1 µg/mL); diphenhydramine hydrochloride (1 mg/mL); minocycline hydrochloride (0.1 mg/mL); dextromethorphan hydrobromide monohydrate (1 mg/mL); clarithromycin (2 mg/mL); (R)-(-)-phenylephrine hydrochloride (1 mg/mL); caffeine (2 mg/mL).

REFERENCES

1. Kikuta H, Sakata C, Gamo R, Ishizaka A, Koga Y, Konno M, Ogasawara Y, Sawada H, Taguchi Y, Takahashi Y, Yasuda K, Ishiguro N, Hayashi A, Ishiko H, Kobayashi K. Comparison of a lateral-flow immunochromatography assay with real-time reverse transcription-PCR for detection of human metapneumovirus. *J Clin Microbiol.* 2008;46(3):928-932.
2. Kaida A, Iritani N, K ubo H, Shiomi M, Kohdera U, Murakami T. Seasonal distribution and phylogenetic analysis of human metapneumovirus among children in Osaka City, Japan. *J Clin Virol.* 2006;35(4):394-399.
3. Montes M, Vicente D, Esnal O, Cilla G, Pérez-Trallero E. A PCR–restriction fragment length polymorphism assay to genotype human metapneumovirus. *Clin Microbiol Infect.* 2008;14(1):91-93.

INQUIRES

TAUNS Laboratories, Inc.
761-1, Kamishima, Izunokuni,
Shizuoka, 410-2325 Japan

FAX : +81-558-76-0022

EC REP Emergo Europe
Prinsessegracht 20
2514 AP The Hague
The Netherlands

GLOSSARY OF SYMBOLS

CE	CE Marking (European directive 98/79/EC on *in vitro* diagnostic medical devices)	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device		Do not reuse
2℃ 30℃	Temperature limitation		Manufacturer/Manufactured by
	Use by YYYY-MM		Consult instructions for use
LOT	Batch code		Caution, consult accompanying documents
REF	Catalog number		Keep away from sunlight
Σ n	Contents sufficient for <n> tests		Fragile, handle with care
	Open here		