IVD

Ver. 6.0 of September 2017

Please read this package insert carefully before use.

Capilia™ Flu Neo

INTENDED USE

To detect influenza A virus antigens and influenza B virus antigens in nasal aspirate, nasal swab, nasal discharge/nasal mucus or pharyngeal swab (to assist in the diagnosis of Influenza virus infectious disease).

SUMMARY AND EXPLANATION OF THE TEST

Influenza spreads around the world in seasonal epidemics, resulting in about 3 to 5 million annual cases of severe illness and about 250,000 to 500,000 annual deaths, rising to millions in some pandemic years.

Common symptoms are chills, fever, sore throat, muscle pains, headache, coughing, weakness/fatigue and general discomfort.

Diagnosis is difficult because the initial symptoms can be similar to those caused by other infectious agents.

The influenza A virus is usually more prevalent and is associated with the most serious influenza epidemics, while influenza B infections usually present more mild symptoms.

Because the influenza virus is highly contagious, rapid diagnosis and prompt treatment can have a positive effect on public health. And the ability to distinguish between A or B antigens can help the physician to prescribe an appropriate antiviral therapy.

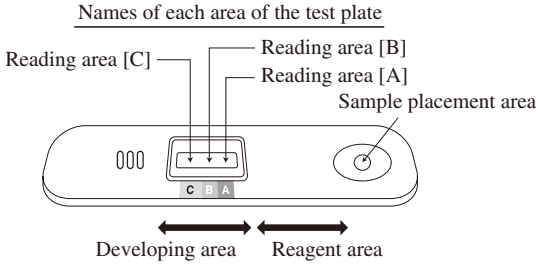
Administration of antiviral therapy within 48 hours of symptom onset is recommended for more rapid reduction of symptoms and to reduce viral shedding.

Capilia Flu Neo can provide rapid and accurate detection of influenza A and/or B viral antigens from symptomatic patients. No special instruments or equipment are required.

PRINCIPLE OF THE TEST

Measurement using this product is based on an immunochromatography assay using a monoclonal antibody that recognizes influenza virus 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-influenza A and B virus monoclonal antibody (mouse) (hereinafter referred to as “colloidal platinum-gold labeled antibody”), a reading area [A] that fixes the anti-influenza A virus monoclonal antibody (mouse) (hereinafter referred to as “anti-influenza A virus antibody”), a reading area [B] that fixes the anti-influenza B virus monoclonal antibody (mouse) (hereinafter referred to as “anti-influenza B virus antibody”), and a reading area [C] that fixes the anti-mouse immunoglobulin polyclonal antibody (rabbit) (hereinafter referred to as “anti-mouse immunoglobulin antibody”).



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

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

REAGENTS AND MATERIALS PROVIDED

REF CAFL0570 Capilia Flu Neo 20T/Box

Test plates

・Components

Colloidal platinum-gold labeled anti-influenza A, B virus monoclonal antibody (mouse)

Anti-influenza A virus monoclonal antibody (mouse)

Anti-influenza B virus 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

MATERIALS REQUIRED BUT NOT PROVIDED

Timer, micropipette, pipette tips, suction machine, suction trap, the specimen collecting sheet for nasal discharge, 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.

2. Precautions when using

1) This product reacts only with influenza A and B viruses and does not react with C virus.
2) This product is a rapid test for detecting influenza A and B virus antigen. **A definite diagnosis should be made by an attending physician, in combination with the clinical symptoms, the result of viral isolation culture test and other test results.**
3) This product should be used in accordance with the procedure stated in the package insert.
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 or stained.
10) 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.
11) 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.
12) When sampling a nasal discharge, be careful not to spill or scatter the samples, as it may cause a secondary infection.
13) Do not use any products beyond the expiration date.

3. Precautions for disposal

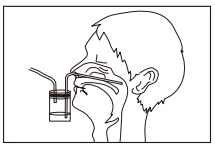
1) Because used test plates, swabs, tubes and nozzles after use, remaining samples, etc. may cause infections, they should be autoclaved (121°C, 20 min) or soaked in 0.1% sodium hypochlorite for more than one hour. When remaining reagents or their accessories are disposed of, they should be treated in 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

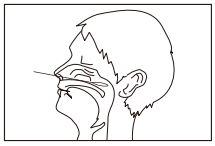
Storage : Store at 2°C to 30°C. **DO NOT FREEZE.**
Keep away from direct sunlight.
Do not use test plate or extraction buffer after expiration date.

SPECIMEN COLLECTION AND PREPARATION

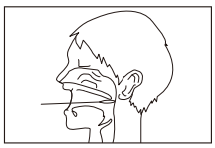
1. Methods of specimen collection



1) Sampling of nasal aspirate
Firmly insert one tube of the 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 a 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.



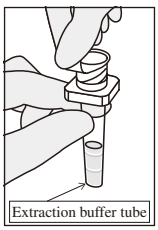
2) Sampling of nasal swab
Firmly insert a nasal swab into the nasal cavity and collect mucosal epithelium by swabbing the nasal turbinate several times.



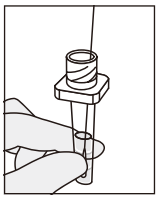
3) Sampling of pharyngeal swab
Firmly insert a pharyngeal swab into the pharynx through the oral cavity, and collect the mucosal epithelium by swabbing the posterior wall of the pharynx and the palatine tonsil several times, centering around the rubefacient portion. Avoid touching saliva.
If the specimen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

4) Sampling of nasal discharge/nasal mucus
When the patient's condition is judged to be suitable for collecting nasal discharge, the patient should blow his/her nose using the specimen collecting sheet. Swab the collected nasal discharge with a nasal swab. Or directly swab the nostril to obtain the specimen.
If either sampling method collects insufficient samples, try other methods.

2. Sample preparation

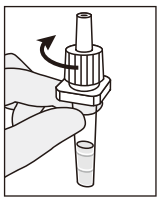


Remove the aluminum sealing cap from the extraction buffer tube, while taking care not to spill the liquid.



Soak the swab that collected the specimen in the extraction buffer, and stir well.
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.

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 8 minutes** and interpret the result according to the "READING TEST RESULTS."

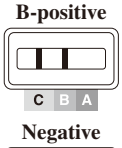
READING TEST RESULTS

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

A-positive

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

B-positive

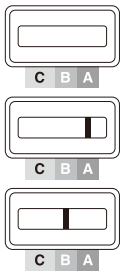


When black lines are seen at both [B] and [C] in the reading area (two lines), the result is read as positive for influenza B virus antigen. When a very faint black line is seen in the reading area [B], the result is interpreted as positive.

Negative

When no black line is seen at [A] and [B] 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 the 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. If the amount of antigens is very high, a very thick line may be seen at [A] or [B] in the reading area and no line may be seen at [C] in the reading area. In that case, dilute the sample with the extraction buffer and perform the test again.

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

(Note)

1. Black lines seen both at [A] or [B] and [C] in the reading area 3 to 8 minutes after sample dripping are read as A-positive or B-positive. No black line at [A] and [B] in the reading area even 8 minutes after sample dripping indicates a negative result.
2. An A-positive result does not rule out the presence of B-infection. Contrarily, a B-positive result does not rule out the presence of A-infection. On rare occasions, the result shows positivity for both A and B.
3. Do not use the test plate for a reading result beyond the judgment time (8 minutes) as the result may change due to drying, etc.
4. 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.
5. If the amount of antigen is very high, a very thick line may be seen at [A] or [B] in the reading 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.
6. The line is valid even if there is unevenness in depth and there are breaks in the line.
7. When decoloration of the test plate is delayed due to some factor in the specimen, or white coloration is observed on the line at [A] or [B] in the reading area, the visibility may be improved by extending the judgment time for a further 5 minutes after 8 minutes have elapsed showing sample dripping.

LIMITATIONS

1. This product is a rapid test for detecting influenza A and B virus antigen.
   A definite diagnosis should be made by an attending physician, in combination with the clinical symptoms, the result of viral isolation culture test and other test results.
2. If a pharyngeal swab, nasal discharge or nasal mucus is used as a specimen, pay special attention to the method of collection, as the test tends to be less sensitive than those of nasal swabs and aspirates.
3. 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.
4. This product should be used for *in vitro* diagnosis only and should not be used for any other purposes.
5. 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.
6. The extraction buffer contains sodium azide. If the solution comes into contact with the 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

The result of the clinical performance evaluation in Japan (Comparison with isolation culture method).

Nasal swab, nasal aspirate, pharyngeal swab : Exams carried out in the flu season in 2006 to 2007.

Nasal discharge/nasal mucus : Exams carried out in 2008.

Kind of samples	Type	Sensitivity (%)	Specificity (%)	Accuracy (%)	Total number
Nasal swab	Type A	94.3 (100/106)	95.4 (187/196)	95 (287/302)	302
	Type B	100 (69/69)	98.7 (230/233)	99 (299/302)	302
Nasal aspirate	Type A	95.1 (58/61)	98.4 (188/191)	97.6 (246/252)	252
	Type B	100 (61/61)	100 (191/191)	100 (252/252)	252
Pharyngeal swab	Type A	87.3 (55/63)	94.8 (128/135)	92.4 (183/198)	198
	Type B	91.5 (75/82)	99.1 (115/116)	96 (190/198)	198
Nasal discharge/ nasal mucus	Type A	84.1 (53/63)	96.9 (94/97)	91.9 (147/160)	160
	Type B	96.2 (50/52)	98.1 (106/108)	97.5 (156/160)	160

2. Sensitivity (Detection limit)

The minimum detection limit is 7.5×10^3 $TCID_{50}$/test for the influenza A virus antigen and is 7.5×10^4 $TCID_{50}$/test for the influenza B virus antigen.

3. Reactivity

Reactivity was found in the following strains :

1) Human origin type A virus

A/New Jersey/8/76 (H1N1)
A/Sendai/782/06 (H1N1) A/Sendai/197/07 (H1N1) A/Adachi/1/57 (H2N2)
A/Sendai/F492/06 (H3N2) A/Sendai/958/07 (H3N2) A/Aichi/2/68 (H3N2)
A/Anhui/1/2013 (H7N9)

2) Human origin A(H1N1)pdm09

A/Osaka/50/09	A/Osaka/51/09	A/Osaka/52/09	A/Osaka/55/09
A/Osaka/56/09	A/Osaka/57/09	A/Osaka/58/09	A/Osaka/59/09
A/Osaka/60/09	A/Osaka/61/09	A/Osaka/63/09	A/Osaka/64/09
A/Osaka/65/09	A/Osaka/66/09	A/Osaka/69/09	A/Osaka/70/09
A/Osaka/71/09	A/Osaka/72/09	A/Osaka/78/09	A/Osaka/83/09
A/Osaka/84/09	A/Osaka/85/09	A/Osaka/90/09	A/Osaka/91/09
A/Osaka/100/09	A/Osaka/101/09	A/Osaka/102/09	A/Osaka/103/09
A/Osaka/104/09	A/Osaka/105/09	A/Osaka/106/09	A/Osaka/107/09
A/Osaka/108/09	A/Osaka/109/09	A/Osaka/110/09	A/Osaka/112/09
A/Osaka/114/09	A/Osaka/115/09	A/Osaka/116/09	A/Osaka/118/09
A/Osaka/119/09	A/Osaka/126/09	A/Osaka/130/09	A/Osaka/139/09
A/Osaka/143/09	A/Osaka/144/09	A/Osaka/146/09	A/Osaka/148/09
A/Osaka/157/09	A/Osaka/164/09	A/Osaka/165/09	A/Osaka/167/09
A/Osaka/168/09	A/Osaka/169/09	A/Osaka/171/09	A/Osaka/172/09
A/Osaka/174/09	A/Osaka/176/09	A/Osaka/193/09	

3) Type A virus of other than human origin

A/duck/Tottori/723/80 (H1N1)	A/duck/Hokkaido/17/01 (H2N3)
A/duck/Mongolia/4/03 (H3N8)	A/duck/Czechoslovakia/1/56 (H4N6)
A/chicken/Yamaguchi/7/04 (H5N1)	A/whooper swan/Hokkaido/1/08 (H5N1)
A/whooper swan/Mongolia/3/05 (H5N1)	A/duck/Pennsylvania/10218/84 (H5N2)
A/duck/HongKong/820/80 (H5N3)	A/turkey/Massachusetts/3740/65 (H6N2)
A/shearwater/Austlalia/1/72 (H6N5)	A/chicken/Italy/99 (H7N1)
A/chicken/Pakistan/447/95 (H7N3)	A/seal/Massachusetts/1/80 (H7N7)
A/chicken/Netherlands/2586/03 (H7N7)	A/tufted duck/Shimane/124R/80 (H7N7)
A/duck/Mongolia/119/2008 (H7N9)	A/duck/Mongolia/129/2010 (H7N9)
A/turkey/Ontario/67 (H8N4)	A/turkey/Ontario/6118/68 (H8N4)
A/turkey/Wisconsin/66 (H9N2)	A/chicken/Germany/N/49 (H10N7)
A/duck/England/1/56 (H11N6)	A/duck/Alberta/60/76 (H12N5)
A/gull/Maryland/704/77 (H13N6)	A/mallard/Astrakhan/263/82 (H14N5)
A/duck/Australia/341/83 (H15N8)	A/black-headed gull/Sweden/5/99 (H16N3)
A/swine/Iowa/15/30 (H1N1)	A/swine/Niigata/1/77 (H1N1)
A/swine/Niigata/1/78 (H1N1)	A/swine/Toyama/1/78 (H1N1)
A/swine/Kanagawa/1/78 (H1N1)	A/swine/Shizuoka/1/78 (H1N1)
A/swine/Shimane/1/78 (H1N1)	A/swine/Hokkaido/80 (H1N1)
A/swine/Hokkaido/2/81 (H1N1)	A/swine/Saitama/96 (H1N2)
A/swine/Miyagi/5/03 (H1N2)	A/swine/Hong Kong/126/82 (H3N2)
A/swine/Obihiro/10/85 (H3N2)	A/swine/Chonburi/02 (H3N2)

4) Human origin type B virus

B/Sendai/1708/05 B/Sendai/942/07 B/Lee/40

4. Cross reactivity

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

1) Viruses

Adenovirus Type 1-6, 11	Influenza virus C
Parainfluenza virus Type 1-4	Respiratory syncytial virus (A) (B)
Rhinovirus Type 2	Coxsackie virus Type A9, A16, B1-6
Echovirus Type 4, 6, 9, 11, 14, 16	Cytomegalovirus
Human Metapneumovirus	

2) Bacteria

Acinetobacter baumannii	*Bacillius cereus*
Bacteroides fragilis	*Bordetella pertussis*
Branhamella catarrhalis	*Capnocytophaga ochracea*
Citrobacter freundii	*Eikenella corrodens*
Enterococcus faecalis	*Enterobacter cloacae*
Fusobacterium nucleatum	*Gardnerella vaginalis*
Haemophilus influenzae	*Haemophilus parainfluenzae*
Kingella kingae	*Klebsiella oxytoca*
Lactobacills casei	*Mycobacterium abscesus*
Mycobacterium avium	*Mycobacterium intracellulare*
Mycobacterium tuberculosis	*Neisseria meningitidis*
Nocardia asteroides	*Pasteurella multocida*
Peptostreptococcus anaerobius	*Porphyromonas asaccharolyticus*
Prevotella intermedia	*Prevotella melaninogenica*
Salmonella choleraesuis (sub, minnesota)	*Serratia marcescens*
Staphylococcus aureus	*Staphylococcus epidermidis*
Streptococcus bovis (Ⅱ Group D)	*Streptococcus* sp. group A, B, C, F, G
Streptococcus milleri	*Streptococcus mutans*
Streptococcus oralis	*Streptococcus pneumoniae*
Streptococcus sanguis	*Chlamydophila pneumoniae*
Chlamydophila psittaci	

INTERFERING SUBSTANCES

The following substances were found to have no effect on the results at the concentrations indicated.

Whole blood (0.25%), acetylsalicylic acid (20 mg/mL), ambroxol hydrochloride (375 ng/mL), dequalinium hydrochloride (6.25 ng/mL), oxymetazoline hydrochloride (100 ng/mL), dried Platycodon extract (555 ng/mL), disodium cromoglycate (5 mg/mL), zanamivir (500 ng/mL), diphenhydramine hydrochloride (10 mg/mL), cyproheptadine hydrochloride hydrate (200 ng/mL), cefixime (2.5 mg/mL), dextromethorphan hydrobromide monohydrate (10 mg/mL), Naphazoline nitrate (125 ng/mL), (R) - (-) -phenylephrine hydrochloride (1 mg/mL), fluticasone propionate (127.5 ng/mL), chlorpheniramine maleate (5 mg/mL)

REFERENCES

1) Kudo K, Takasaki J, Manabe T, Uryu H, Yamada R, et al. Systemic Corticosteriods and Early Administation of Antiviral Agents for Pneumonia with Acute Wheezing due to Influenza A (H1N1) pdm09 in Japan. *PLoS ONE.* 2012;7(2):e32280.
2) Iwaki N, et al. Review on the Epidemic of Influenza from 2009 to 2010 in Japan. *Jpn J Clin Exp Med.* 2010;87:1489-1499.
3) Kurita I, Kamiya C, Kouga K, Amano T. Evaluation of rapid influenza test kit and detection of influenza A (H1N1) pdm09 using RT-PCR. *J Clin Lab Inst Reag.* 2010;33(5):645-648.
4) Takasaki Y, et al. Evaluation of Rapid Influenza Test Kit “ImunoAce Flu” Using Pt-Au Colloid. *Jpn J Clin Exp Med.* 2008;85:1804-1807.

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		