Infection

ichroma™ COVID-19/Flu Ag Combo

INTENDED USE

ichroma™ COVID-19/Flu Ag Combo is a fluorescence immunoassay (FIA) for the simultaneous qualitative detection of novel coronavirus (SARS-CoV-2), Influenza A virus and Influenza B virus in human nasopharyngeal swab. It is useful as an aid in the distinguish novel coronavirus and influenza infection in flu-like symptom.

For *in vitro* diagnostic use only.

INTRODUCTION

The third zoonotic human coronavirus (CoV) of the century emerged in December 2019. This virus, the newly identified coronavirus SARS-CoV-2, could cause risky pneumonia so that prevention and control of the infection has become highly required. The SARS-CoV-2 is a member of the Betacoronavirus Genus, that also includes Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV). Since it is identified that symptoms become rapidly severe without a proper treatment after onset of illness, early diagnosis of the virus infection is quite crucial. Currently, the spread of the viral transmission become fast so that the prevention of local transmission requires a point-of care test (POCT).

Influenza, or flu, known as 'febrile respiratory illness' can cause mild to severe symptoms, such as a high fever, chills, headache, muscle pains coughing and even death. These illness typically begins after exposure to the influenza virus in the respiratory epithelial cell from person-to- person through sneezing, coughing, or touching contaminated surfaces. Within 48 hours after the onset of symptoms, the patient is strongly recommended to visit the nearest medical facility for the diagnosis of Influenza A or B and to take the antiviral medication. The preventive measure is highly required for those at increased risk for severe illness, so that early and differential diagnosis between influenza types A or B is very essential.

PRINCIPLE

This test uses a sandwich immunodetection method.

The detector antibodies in buffer bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized antibodies on a test strip.

More antigens in the sample will form more antigen-antibody complexes, which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for ichroma™ tests to show the 'Positive'/ 'Negative' in the sample of SARS-CoV-2, influenza A and influenza B antigens in the sample respectively.

COMPONENTS

ichroma™ COVID-19/Flu Ag Combo consists of 'cartridges', 'detector tubes', 'extraction tube sets'.

- The cartridge contains the membrane called a test strip which has streptavidin, anti-influenza A antibodies, and anti-influenza B antibodies at the test line, and chicken IgY at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant, and they are further packaged in a box.
- The detector tube has a granule containing anti-SARS-CoV-2 NP-fluorescence conjugate, Anti-SARS-CoV-2 NP-Biotin conjugate, anti-influenza A-fluorescence conjugate, and anti-influenza B fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, BSA and sucrose as a stabilizer and sodium azide as a preservative in Tris-HCl buffer. All detector tubes are packed in a pouch.
- The extraction buffer tube contains sodium chloride, sodium azide as a preservative in Tris-HCl buffer, and it is pre-dispensed in extraction buffer tubes. The extraction buffer tubes are packed in a box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detector tube, extraction buffer tube and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges or detector tubes or extraction tube sets. A cartridge should be used for testing one sample only. A detector tube should be used for processing of one sample only. An extraction tube set should be used for processing of one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use cartridge, if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations.
- If test components and/or sample are stored in refrigerator, then allow cartridge, detector tube, extraction buffer tube and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, detectors, extraction buffer tubes, nozzles and swabs should be handled carefully and discarded by an appropriate method in accordance with the relevant local regulations.
- The detector tube and extraction buffer tube contain sodium azide (NaN_3), and it may cause certain health issues like convulsions, low blood pressure, low heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **ichroma™ COVID-**

19/Flu Ag Combo when biotin concentration in the sample was below 200 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.

- **ichroma™ COVID-19/Flu Ag Combo** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ COVID-19/Flu Ag Combo** should be used only in conjunction with the instrument for ichroma™ tests.

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigens to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigens with time and/or temperature may also cause false negative result as it makes the antigens unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.
- If the test result is “Negative” even though the patient has significant infectious symptoms, it should be recommended to conduct additional test including PCR or culture test.
- The accurate determination of test result as “Positive” should be confirmed by additional clinical evaluation.
- “Negative” result should be considered with possibilities of other infections. Positive result should be considered with additional infections by another pathogenic bacterium.
- If the product has positive results, any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.
- In case of antigen concentration is low, the test may yield false negative results. Therefore, the negative results cannot exclude the possibility of infection completely.

STORAGE AND STABILITY

Storage condition			
Component	Storage temperature	Shelf life	Note
Cartridge	2 - 30 °C	20 months	Disposable
Detector tube	2 - 30 °C	20 months	Disposable
Extraction buffer tube	2 - 30 °C	20 months	Disposable

- After the cartridge pouch is opened, the test should be performed immediately.

MATERIALS SUPPLIED

REF CFPC-117

Components of **ichroma™ COVID-19/Flu Ag Combo**

- Cartridge box:
  - Cartridge 25
  - Detector tube 25
  - Extraction tube set
    - Extraction buffer tube 25
    - Nozzle 25
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **ichroma™ COVID-19/Flu Ag Combo.**

Please contact our sales division for more information.

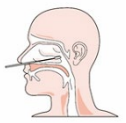
- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M2** REF FPRR031
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 PLUS** REF FPRR036
- **Boditech COVID-19/Flu Ag Control** REF CFPO-298

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ COVID-19/Flu Ag Combo** is human nasopharyngeal swab.

- It is highly recommended that **ichroma™ COVID-19/Flu Ag combo** test would be performed on the nasopharyngeal swab specimens directly collected from patients with provided extraction buffer.

Nasopharyngeal swab sample collection method



Nasopharyngeal swab

- To collect samples, insert a sterile swab in the nasal cavity and spin it smoothly in the nasopharynx.
- It is recommended to test the sample immediately after collection.
- The samples may be stored for 3 days at 2-8 °C prior to being tested.
- Do not collect samples outside of the nasopharynx. In any cases, pre-education for user is required for the proper sample collection.

TEST SETUP

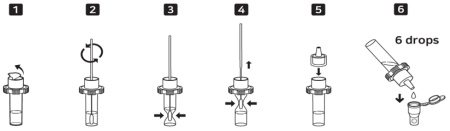
- Check the contents of **ichroma™ COVID-19/Flu Ag Combo**: Sealed cartridges, detector tubes, extraction tube sets, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the detector tube, the extraction buffer tube as well as an ID chip.
- If the sealed cartridge, the detector tube and the extraction buffer tube have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.

- Turn on the instrument for ichroma™ tests.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for ichroma™ tests operation manual for the complete information and operating instructions.**

TEST PROCEDURE

▶ **ichroma™ II, ichroma™ M2**



Multi test mode / Read now mode

1) Open the extraction buffer tube by removing its aluminum foil seal.
2) Collect samples with a sterile swab and then put it into the extraction buffer tube. Spin the sterile swab 5 times.
3) Squeeze the sterile swab to extract the sample into the extraction buffer.
4) Squeeze the bottom to extract the sample into the buffer and start pushing the swab to the top and pushing the swab to the top of the extraction buffer tube to pull it out of the tube.
5) Assemble a nozzle to the top of the extraction buffer tube.
6) Apply 6 drops of sample mixture onto the detector tube.
7) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 20 times.
   (The sample mixture must be used immediately. Do not exceed 30 seconds.)
8) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
9) Leave the cartridge at room temperature for 20 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*
10) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose,
11) Tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
    (ichroma™ M2 will start the test automatically after inserting.)
12) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
13) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode/ Walk away mode

1) The test procedure is same with the 'Multi test mode 1) – 8)'.
2) Insert the sample-loaded cartridge into the holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
3) Tap the 'Start' button on the instrument for ichroma™ tests.
   (ichroma™ M2 will start the test automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 20 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ **ichroma™ III**

1) The test procedure is same with the 'Single test mode'.

▶ **ichroma™-50, ichroma™-50 PLUS**

1) The test procedure is same with the 'Multi test mode 1) – 5)'.
2) Squeeze the extraction buffer tube gently to completely fill a sample tube.
3) Insert the tip array in the tip station.
4) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
5) Insert the cartridge magazine with the cartridges into the magazine station.
6) Insert the sample tube including extraction buffer into the tube rack and load the tube rack into the sampling station (loading part).
7) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip that you want to use.
8) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
9) Set the number of pipette tips by tapping.
10) Tap the 'Start' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays as below.

Display		Interpretation
COVID-19	Positive	SARS-CoV-2 antigen present
	Negative	No SARS-CoV-2 antigen detected
Influenza A	Positive	Influenza A virus antigen present
	Negative	No Influenza A virus antigen detected
Influenza B	Positive	Influenza B virus antigen present
	Negative	No Influenza B virus antigen detected
Invalid		Result invalid. Need to retest.

- This product cannot be used as a tool for confirmation. The false positive and false negative results can be caused by various causes.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ichroma™ COVID-19/Flu Ag Combo**. For more information regarding the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**

- **LOD**

Virus type		Conc.
SARS-CoV-2	SARS-CoV-2 (USA/WA1/2020)	35.15 TCID50/mL
Influenza A	A/Brisbane/02/2018 (H1N1)pdm09-like virus	4.4 x 10^2 pfu/mL
	A/Kansas/14/2017 (H3N2)-like virus	1.5 x 10^3 pfu/mL
Influenza B	B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)	2.0 x 10^4 pfu/m
	B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)	2.9 x 10^3 pfu/mL

- **Analytical specificity**

- **Cross-reactivity**
  There was no significant cross-reactivity on 30 various other viruses and 36 various bacteria with the **ichroma™ COVID-19/Flu Ag Combo** test.

Virus			
1	Adenovirus type1	16	Echovirus 6
2	Adenovirus type2	17	Echovirus 9
3	Adenovirus type3	18	Enterovirus 71
4	Adenovirus type4	19	HCMV-AD-169
5	Adenovirus type6	20	HSV-1 - F(3A20)
6	Adenovirus type7	21	HSV-2 - MS(4A6)
7	Coronavirus - FCV(3A2)	22	Measles virus
8	Coronavirus - FIP(2A4)	23	Mumps virus
9	Coxsackievirus A2	24	Polio virus - sin(3A4)
10	Coxsackievirus A4	25	Respiratory Syncytial virus A
11	Coxsackievirus B1 - conn5	26	Rhinovirus - RV21
12	Coxsackievirus B3–nancy (5A1)	27	Rhinovirus -RV14
13	Dengue virus	28	Rhinovirus -RV71
14	Echovirus 25	29	Rubella virus
15	Echovirus 3	30	Zika virus

Bacteria			
1	*Candida albicans*	19	*Neisseria gonorrhoeae*
2	*Candida glabrata*	20	*Neisseria meningitidis*
3	*Candida tropicalis*	21	*Neisseria sicca*
4	*Citrobacter freundii*	22	*Proteus mirabilis*
5	*Corynebacterium sp.*	23	*Proteus vulgaris*
6	*Corynebacterium diphtheriae*	24	*Pseudomonas aeruginosa*
7	*Enterococcus faecalis*	25	*Serratia marcescens*
8	*Enterococcus gallinarum*	26	*Staphylococcus aureus*
9	*Escherichia coli*	27	*Staphylococcus epidermidis*
10	*Hemophilus influenzae*	28	*Stenotrophomonas maltophilia*
11	*Hemophilus parainfluenzae*	29	*Streptococcus sp. (Group D)*
12	*Klebsiella oxytoca*	30	*Streptococcus agalactiae (Group B)*
13	*Klebsiella pneumoniae*	31	*Streptococcus anginosus (Group F)*
14	*Lactobacillus sp.*	32	*Streptococcus dysgalactiae (Group C)*
15	*Legionella spp*	33	*Streptococcus dysgalactiae (Group G)*
16	*Listeria monocytogenes*	34	*Streptococcus mutans*
17	*Moraxella catarrhalis*	35	*Streptococcus pneumoniae*
18	*Mycobacterium tuberculosis*	36	*Streptococcus pyogenes*

- **Interference**
  Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ichroma™ COVID-19/Flu Ag Combo** test results did not show any significant interference with these materials.

	Interference materials	Conc.
1	Nasal sprays drops	20%
2	Nasal corticosteroids	20%
3	Homeopathic allergy relief medicine	20%
4	Mouth wash (Listerine)	5 mg/mL
5	Throat lozenges, oral anesthetic & analgesic	5 mg/mL
6	Antiviral drugs (Tamiflu; Oseltamivir)	5 mg/mL
7	Antibiotic nasal ointment (Bactroban; mupirocin)	5 mg/mL
8	Whole blood	1%
9	Analgesic (Acetaminophen)	10 mg/mL
10	Analgesic (Ibuprofen)	10 mg/mL
11	Povidone-iodine	1%
12	Acetylsalicylic acid (Aspirin)	20 mg/mL
13	Antibacterial (cefadroxil)	5 mg/mL
14	Mucin (Porcine stomach)	0.5%
15	Throat lozenge (VICKS; cetylpyridinium chloride)	20 mg/mL
16	Throat lozenge (dipotassium glycyrrhizinate)	20 mg/mL
17	Throat lozenge (Nandina extraction)	20 mg/mL
18	Biotin	200 ng/mL

- **Precision**

- Between lots
  One person tested three different lots of **ichroma™ COVID-19/Flu Ag Combo**, ten times at each concentration of the control standard.
- Between persons
  Three different persons tested one lot of **ichroma™ COVID-19/Flu Ag Combo**, ten times at each concentration of the control standard.
- Between days
  One person tested one lot of **ichroma™ COVID-19/Flu Ag Combo** for three days, ten times at each concentration of the control standard.
- Between sites
  One person tested **ichroma™ COVID-19/Flu Ag Combo** at three different site, ten times at each concentration of the control standard.

	Cal No.	Between lot		Between person	
		Positive / No.	Positive rate	Positive / No.	Positive rate
COVID-19	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%
Flu A	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%

Flu B	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%
	Cal No.	Between day		Between site	
		Positive / No.	Positive rate	Positive / No.	Positive rate
COVID-19	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%
Flu A	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%
Flu B	1	0/30	0%	0/30	0%
	2	30/30	100%	30/30	100%
	3	30/30	100%	30/30	100%

- **Clinical performance evaluation**

ichroma™ COVID-19/Flu Ag Combo has demonstrated the following clinical performance results. (predicate: RT-PCR)

	COVID-19	Influenza A	Influenza B
Clinical Sensitivity	100 % (31/31)	93.8 % (30/32)	93.8 % (30/32)
Clinical Specificity	98.3 % (115/117)	100 % (74/74)	100 % (74/74)

* **COVID-19 Ag**
- Clinical Sensitivity (%)=100% (95%CI: 86.3% ~ 100%)
- Clinical Specificity (%)=98.3% (95%CI: 93.3% ~ 99.7%)

* **Influenza A**
- Clinical Sensitivity (%)=93.8% (95%CI: 77.8% ~ 98.9%)
- Clinical Specificity (%)=100% (95%CI: 93.9% ~ 100%

* **Influenza B**
- Clinical Sensitivity (%)=93.8% (95%CI: 77.8% - 98.9%)
- Clinical Specificity (%)=100% (95%CI: 93.9% - 100%)

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Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
LOT	Batch code
REF	Catalog number
	Caution
	Manufacturer
EC REP	Authorized representative of the European Community
IVD	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
CE	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

For technical assistance, please contact:
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