BIO TECHNOLOGY boditech

Infection

ichroma™ RSV

INTENDED USE

ichroma™ RSV the *in vitro* diagnostic device for the qualitative determination of RSV infection to detect RSV (Respiratory syncytial virus) viral antigen in nasopharyngeal swab and nasal aspirate specimens taken from symptomatic patients.

For *in vitro* diagnostic use only.

INTRODUCTION

RSV is a causative agent of highly contagious, acute, viral infection of the respiratory tract in pediatric and elderly populations. Respiratory syncytial virus is a single-stranded RNA virus. Nearly half of all children become infected by RSV in their first year of life. It is also the major viral cause of nosocomial illness in children already hospitalized for other reasons.

Respiratory syncytial virus (RSV) infection is a common viral infection of the respiratory tract in young children, occurring as a winter epidemic in temperate climates. A rapid and reliable diagnosis of in children is very important for clinical management. Prompt institution of infection control measures is necessary to limit the spread of infection.

This product is for in vitro diagnostic medical devices with which the infection of RSV viruses can be determined within 10 minutes, much quicker and easier than the conventional diagnostic methods like PCR or viral culture which takes more than 24 to 48 hours for diagnosis.

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antibodies in conjugate pad 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 result as ‘ Positive/Negative’.

COMPONENTS

ichroma™ RSV consists of ‘cartridges’, ‘extraction tubes’, ‘swabs’, ‘controls (RSV Positive control swab, Negative control swab).

- The cartridge contains the membrane called a test strip which has mouse monoclonal anti-human RSV 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 cartridge box.
- The test strip contains mouse monoclonal anti-RSV antibody-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, BSA and sucrose as a stabilizer in drying condition.
- The extraction buffer contains Tween20 and BSA, in Tris-HCl buffer as surfactant and stabilizer respectively.
- The extraction buffer is pre-dispensed in a tube.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this ‘Instructions for use’.
- Use only fresh samples and avoid direct sunlight.
- 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 extract buffers or control swaps. A cartridge should be used for testing one sample only. A extract buffer should be used for processing of one sample only.
- Lot numbers of all the test components (cartridge, extract buffer, control and ID chip) must match each other.
- 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.
- If test components and/or sample are stored in refrigerator, then allow cartridge, extraction buffer and sample to be at room temperature for approximately 30 minutes before use.
- The extraction buffer contains NaN3 as preservatives, of which the contact to eyes, skin or clothing should be avoided. If it happens, please wash with running water immediately.
- Please apply the exact drops for accurate test result. Or it may cause erroneous 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.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, extraction buffer tubes, nozzles, and swabs should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- **ichroma™ RSV** will provide accurate and reliable results, when it is used only in conjunction with the instrument for ichroma™ tests.

WARNINGS AND PRECAUTIONS FOR SAMPLE

- It is recommended to test the sample immediately after sample collection.
- Refrain from smoking or eating, while sample is collected.

- Do not collect samples outside of the nasopharynx. In any cases, pre-education for user is required for the proper sample collection.
- Please use fresh swab to avoid the cross-reactivity between samples. Never reuse the sterile swab.
- The improper samples such as those from an individual who has recently taken any interfering medicine or samples mistakenly mixed up with different patients shall cause inaccurate test results.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with the relevant local regulations.

STORAGE AND STABILITY

Storage condition		
Component	Storage Temperature	Shelf life
Cartridge	1 - 30 °C	18 months
Extraction buffer tube	1 - 30 °C	18 months
Control swab	1 - 30 °C	18 months

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

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 antigen 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 antigen with time and/or temperature may also cause false negative result as it makes the antigen 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.

MATERIALS SUPPLIED

REF CFPC-88

Components of **ichroma™ RSV**

- Cartridge box:
  - Cartridge 25
  - Extraction buffer tube set
    - Extraction buffer tube 25
    - Nozzle 25
  - Swab 25
  - Control
    - RSV Positive control Swab 1
    - RSV Negative control Swab 1
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ RSV.**

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™-50** REF FPRR022
  - **ichroma™ M2** REF FPRR031

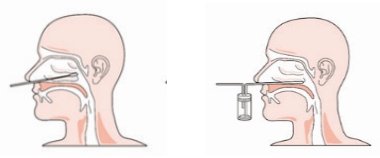
SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ RSV** is human nasopharyngeal swab and nasal aspirate specimens.

- **Collection method for sample**

- Nasopharyngeal swab specimens
  To collect samples, insert a sterile rayon swab in the nasal cavity and spin it smoothly in the nasopharynx.

- Nasal aspirate specimens
  To use suction catheter, insert pipe in the nasopharynx. Operate suction machine and collect sample. Collected samples should be used with a sterile rayon swab for this test.



< Nasopharyngeal swab> <Nasal aspirate>

- It is recommended to test the sample immediately after collection. If do not use the sample immediately, it should be stored at 2-8 °C or -70 °C.
- Samples stored at 2-8 °C for 3 days showed no performance difference.
- Samples stored frozen at -70 °C for a year showed no performance difference.
- Once the sample was frozen, it should be thawed only one time and only for test, because repeated freezing and thawing can cause erroneous results.

TEST SETUP

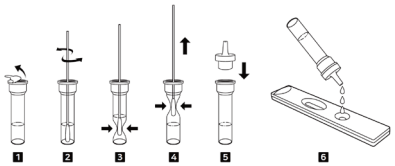
- Check the contents of **ichroma™ RSV**:
  Sealed test cartridges, swabs, extraction tube sets, controls, an ID Chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the extraction buffer as well as an ID chip.
- If the sealed cartridge, and the extraction buffer 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 complete information and operating instructions.**

TEST PROCEDURE

▶ ichroma™ II, ichroma™ M2

1) Open the extraction buffer tube.
2) Sample Collection
   - With a sterile swab
     Collect samples with a sterile swab and then put it into the extraction tube (Spin 5 times). Then go to the step 3).
   - Sample in VTM or UTM
     Collect 700 µL of samples with a pipette and put the collected samples into the extraction tube. Close the extraction buffer tube and gently invert it 10 times. Open the extraction buffer tube. Then go to the step 5).
3) Squeeze the bottom to extract the sample into the buffer and start pushing the swab to the top.
4) Continue squeezing and pushing the swab to the top of extraction tube to pull it out of tube.
5) Assemble a nozzle with the extraction tube.
6) Load only three drops of sample mixture onto the sample well on a cartridge.
   (When using swab sample by transport media, mix extracted samples in transport media with extraction buffer in the same volume. Then load only three drops onto the sample well on a cartridge.)



7) For scanning, refer to the following steps.

Single test mode/ Walk away mode

8) 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.
9) Tap the 'Start' button on the instrument for ichroma™ tests.
   (ichroma™ M2 is tested automatically after inserting.)
10) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 10 minutes.

Read the test result on the display screen of the instrument for ichroma™ tests.

Multi test mode / Read now mode

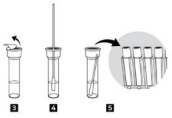
1) Leave the cartridge at room temperature for 10 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*
2) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. 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.
3) Tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
   (ichroma™ M2 is tested automatically after inserting.)
4) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
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

1) Insert the tip array in the tip station.
2) Insert the cartridges in the cartridge magazine individually.
3) Open the extraction buffer tube.
4) Put the sample collected swab into the extraction buffer tube and cut the swab (Please refer to the below instruction). The swab length should be shorter than tube height.
5) Insert the extraction buffer tube into the tube rack.



6) Tap the button located in the upper side of the No. of test cartridge region to select ID chip what you want to use.
7) When the selected cartridge slot is activated, set the number of test cartridge by tapping.
8) Tap the button located in the upper side of the No. of reagent region to select ID chip what you want to use.
9) When the selected slot is activated, set the number of Detector by tapping.
10) Set the number of pipette tips by tapping.
11) 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 Positive/Negative.
- If test result is Invalid, you need to perform a new test with a new test cartridge and a new test sample.

Display	Judgment
RSV: Positive	RSV positive (Contain RSV antigen)
RSV: Negative	RSV negative
Invalid	Result invalid. Need to retest.

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 with **ichroma™ RSV**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.

PERFORMANCE CHARACTERISTICS

- **Analytical Sensitivity**
  - **Limit of detection (LoD)**

List	Conc.
RSV A long	2.23 X 10^2 pfu/mL
RSV A2	3.86 X 10^2 pfu/mL
RSV B	6.60 X 10^2 pfu/mL

  - **Cut-off**
    The cut-off value is 0.68 RFU (Relative Fluorescence Unit) as COI (Cut off index) that is obtained from algorithm of the instrument.

COI (Cut off index)	Judgment
< 0.68 RFU	Negative (-)
≥ 0.68 RFU	Positive (+)

- **Analytical Specificity**
  - **Cross reactivity**
    Biomolecules listed in the following table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **ichroma™ RSV** test results did not show any significant cross-reactivity with these 16 various other viruses and 16 various bacteria.

	Virus
1	HSV-1 F(3A20)strain
2	HSV-2 MS(4A6)strain
3	Corona FCV(4A1)strain
4	Corona FIP(2A4)strain
5	Coxakie B1 conn5 strain
6	Coxakie B3 nancy (5A1) strain
7	Polie virus sabin (3A4) strain
8	Rhino virus RV14 strain
9	Rhino virus RV21strain
10	Rhino virus RV71strain
11	Adeno virus type 5 4A1 strain
12	HCMV AD-169
13	Influenza A virus H1N1 PR8
14	Influenza A virus H3N2 Hongkong
15	Influenza B virus B/Lee/40
16	Entero virus 71 strain H(5A2)
	Bacteria
1	S. Canis
2	S. Dysgalactiae subsp Dysgalactiae
3	S. Pneumoniae
4	S. Anginosis
5	S. Mutans
6	S. Equisimilis subsp equisimilis
7	S. mitis
8	S. Aglactiae
9	S. Aglactiae
10	S. Dysgalacteae subsp. Equisimilis
11	S. Paraganguis
12	S. Porcinus
13	S. thermophilus
14	S. pyogenes
15	Escherichia coli
16	Mycoplasma pneumonia

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

	Materials	Conc.
1	Nasal spray drops	30%
2	Nasal corticosteroids	30%
3	Antihistamine drug	7.5 mg/ml
4	Antiviral drugs (Oseltamivir)	7.5 mg/ml
5	Nasal ointment	7.5 mg/ml
6	Antibiotic (Cefadroxin Cap.)	7.5 mg/ml
7	Whole blood	10%
8	Acetaminophen	20 mg/ml
9	Ibuprofen	20 mg/ml
10	Povidone-iodine	3.5%
11	Acetylsalicylic acid (Aspirin)	30 mg/ml
12	Mucin	1.0%
13	Throat candy (Cetylpyridinium chloride –candy, VICKS)	30 mg/ml
14	Throat candy (South Tomorrow Extract)	30 mg/ml
15	Throat candy (Dipotassium glycyrrhizinat)	30 mg/ml

- **Precision**
  - Between Lot
    One person tested three different lots of **ichroma™ RSV**, ten times at each concentration of the control standard.
  - Between Person
    Six different persons tested **ichroma™ RSV**, three times at each concentration of the control standard.
  - Between Day
    One person tested **ichroma™ RSV** during five days, three times at each concentration of the control standard.
  - Between Site
    One person tested **ichroma™ RSV** at three different sites, three times at each concentration of the control standard.

Cal.	Between lot		Between person	
	# pos./ # runs.	Detection rate	# pos./ # runs.	Detection rate
Negative	0/30	0%	0/18	0%
Positive (low, mid, high)	88/90	97.8%	53/54	98.1%
Cal.	Between day		Between site	
	# pos./ # runs.	Detection rate	# pos./ # runs.	Detection rate
Negative	0/15	0%	0/9	0%
Positive (low, mid, high)	45/45	100%	27/27	100%

Comparative analysis on commercial products

		Commercial product		
		Positive	Negative	Total
ichroma™ RSV	Positive	126	18	144
	Negative	1	130	131
	Total	127	148	275
Positive percent agreement (%)		99.2		
Negative percent agreement (%)		87.8		
Total percent agreement (%)		93.0		

■ **Clinical performance evaluation**

ichroma™ RSV have demonstrated the following clinical performance results.

	Result
Clinical Sensitivity	91.3% (137/150) (95%CI: 85.5% - 95.3%)
Clinical Specificity	100% (125/125) (95%CI: 97.1% - 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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