Infection

ichroma™ Strep A

INTENDED USE

ichroma™ Strep A is a fluorescence immunoassay (FIA) for the qualitative **determination of Streptococcus** A in human throat specimen. It is useful as an aid in management and monitoring of Group A Streptococcal infection.

For *in vitro* diagnostic use only.

INTRODUCTION

Group A Streptococcus is one of the most common causes of acute upper respiratory tract infection. Early diagnosis and treatment of Group A Streptococcal pharyngitis has been shown to reduce the severity of symptoms and serious complications such as rheumatic fever and glomerulonephritis.

Conventional procedures for identification of Group A Streptococcus from throat swabs involve the culture, isolation, and subsequent identification of viable pathogen at 24 to 48 hours or longer for results.

PRINCIPLE

The test uses a sandwich immunodetection method. The detector antibodies in the conjugate pad bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto the 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 concentration of Group A Streptococcus. This signal then is interpreted by the reader to display 'Positive'/ 'Negative' on the screen.

COMPONENTS

- **ichroma™ Strep A** consists of 'cartridges', 'extraction tubes', 'controls' (Strep A Positive Control Swab, Strep A Negative Control Swab).
- The cartridge contains the membrane called a test strip which has anti Strep A at the test line, with streptavidin at the control line.
- The test strip contains anti strep A-fluorescence conjugate, biotin-BSA-fluorescence conjugate and Biotin-BSA-fluorescence conjugate and sucrose as a stabilizer in drying condition. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant, and they are further packaged in a box.
- The extraction buffer contains sodium nitrite and citric acid, and it is pre-dispensed in tube. The extraction buffers is packed in a box.
- Strep A positive control swab: 1/10 diluted heat inactivated GABHS(Group A beta-hemolytic Streptococcus pyogenes) (ATCC 19615) solution with PBS/1% BSA, 1% sucrose
- Strep A negative control swab: non-treated.
- All sealed cartridges and extraction tubes are packed in a box which also contains extraction buffer packs, swabs, controls and an ID chip.

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.
- Lot numbers of all the test components (cartridge, extraction tube, control 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, extraction tubes extraction buffer packs and control swaps. A cartridge should be used for testing one sample only. An extraction buffer tube and extraction buffer pack 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 the 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 instrument for ichroma™ tests may generate slight vibration during use.
- 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.
- Used cartridges, extraction buffers and swaps should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The extraction buffer contains sodium azide (NaN_3), and they may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **ichroma™ Strep A** 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 throat. 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 applicable local requirement.

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.

STORAGE AND STABILITY

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

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

MATERIALS SUPPLIED

REF CFPC-74

Components of **ichroma™ Strep A**

- Cartridge box:
  - Cartridge 25
  - Extraction tube 25
  - Extraction buffer pack 25
  - Swab 25
  - Control
    - Strep A Positive Control Swab 1
    - Strep A Negative Control Swab 1
  - Tube holder 3
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ Strep A.**

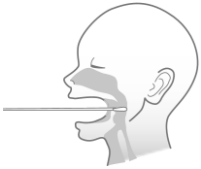
Please contact our sales division for more information.

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

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ Strep A** is human throat specimen.

- Sample Collection
  To collect samples, insert a sterile swab into the throat trying not to touch tongue, oral cavity and teeth. Let the swab touch the faucal or tonsil with inflammation and gently rotate it to collect sufficient amount of sample.



- It is recommended to test the sample immediately after collection. Unless the sample is tested immediately, it should be stored at 2-8 °C or -20 °C.
- Samples stored at 2-8 °C for 2 days showed no performance difference.
- Samples stored frozen at -20 °C for a week showed no performance difference.
- Once the sample was frozen, it should be thawed only once because repeated freezing-and-thawing can cause erroneous results.

TEST SETUP

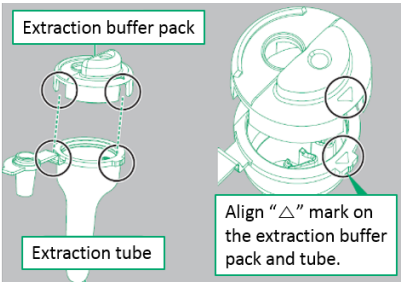
- Check the contents of **ichroma™ Strep A**.
- Sealed test cartridges, extraction tubes, extraction buffer packs, swabs, controls, ID chip and instructions for use.
- Ensure that the lot number of the cartridge matches that of the ID Chip.
- If the sealed cartridge, extraction tube and extraction buffer pack 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'.

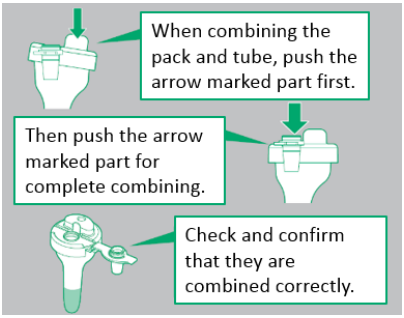
※ Please refer to the instrument for ichroma™ tests operation manual for complete information and operating instructions.

TEST PROCEDURE

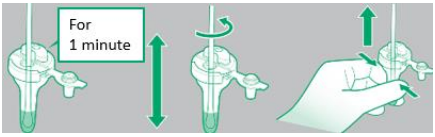
▶ **Sample preparation**

1) Assemble an extraction tube and extraction buffer pack into one. (A structure in the extraction tube will puncture sealing of extraction buffer pack. Then solution A and solution B will flow to the bottom of the extraction tube and be mixed.)





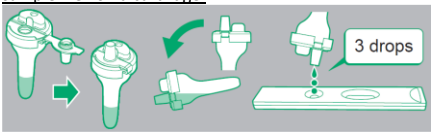
2) Collect of sample with a swab and then put it into the extraction tube.
(Spin and squeeze the swab to extract the sample into the buffer.)
3) Leave the sample-mixed extraction buffer tube at room temperature for 1 minute.
4) Assemble a nozzle with the extraction tube.



▶ **ichroma™ II, ichroma™ M2**

Multi test mode

1) Load only three drops of sample mixture onto the sample well on a cartridge.



2) Leave the cartridge at room temperature for 5 minutes.

⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*

3) 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.
4) Tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M2 is tested automatically after inserting.)
5) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
6) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

1) Load only three drops of sample mixture onto the sample well on a cartridge.
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 is tested automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 5 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**

1) Insert the tip array in the tip station.
2) Insert the cartridges in the cartridge magazine individually.
3) After transferring the prepared extraction buffer-sample mixture to the sample tube, insert the sample tube into the tube rack.
4) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
5) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
6) 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.
7) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
8) Set the number of pipette tips by tapping.
9) 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
Strep A: Positive	Strep A positive (Contain strep A antigen)
Strep A: Negative	Strep A negative (Not contain strep A antigen)
Invalid	Result invalid. Need to retest.

QUALITY CONTROLS

- The **Strep A Positive Control Swab** and **Strep A Negative Control Swab** are intended for *in vitro* diagnostic use in the quality control of **ichroma™ Strep A** assay Kit.
- Each cartridge box of **ichroma™ Strep A** contains following two dry swab controls:
  - Strep A Positive Control Swab 1
  - Strep A Negative Control Swab 1
- Do not use **Strep A Positive Control Swab** and **Strep A Negative Control Swab** to collect human throat specimen.
- Exercise proper precautions that would be normally required for handling laboratory reagents.
- The control tests should be performed after opening a new cartridge box or receiving a new lot to ensure the test performance.
- Strep A Positive and Negative controls material are not derived from human-derived substances. However, since no method can offer complete assurance as to the absence of infectious agents, Strep A Positive and Negative controls should be handled as though capable of transmitting infectious diseases and should be disposed of as hazardous wastes.
- 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™ Strep A**. 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) 0.079

  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)	Result
< 0.68 RFU	"Negative, -"
≥ 0.68 RFU	"Positive, +"

- **Analytical Specificity**
  - **Cross reactivity**

    ichroma™ Strep A test results did not show any significant cross-reactivity with 34 various other viruses and 40 various bacteria.

Virus				
	Strain	Conc.	Unit
1	Adenovirus type1	6.31×10^5	$TCID_{50}$/ml
2	Adenovirus type2	6.31×10^6	$TCID_{50}$/ml
3	Adenovirus type3	2×10^4	$TCID_{50}$/ml
4	Adenovirus type4	6.31×10^3	$TCID_{50}$/ml
5	Adenovirus type6	6.31×10^6	$TCID_{50}$/ml
6	Adenovirus type7	3.89×10^4	$TCID_{50}$/ml
7	Coxaievirus A2	1×10^8	$TCID_{50}$/ml
8	Coxaievirus A4	5.01×10^5	$TCID_{50}$/ml
9	Coxaievirus B2	5.01×10^6	$TCID_{50}$/ml
10	Echovirus 3	3.16×10^7	$TCID_{50}$/ml
11	Echovirus 6	1×10^8	$TCID_{50}$/ml
12	Echovirus 9	1×10^6	$TCID_{50}$/ml
13	Echovirus 25	3.16×10^7	$TCID_{50}$/ml
14	Enterovirus 71	2×10^6	$TCID_{50}$/ml
15	Rubella virus	3.16×10^4	$TCID_{50}$/ml
16	Mumps virus	1.26×10^6	$TCID_{50}$/ml
17	Meales virus	2×10^4	$TCID_{50}$/ml
18	Respiratory Syncytial virus A	8.5×10^5	pfu/mL
19	Coxakie virus B1 - conn5	8.7×10^{-7}	$CCID_{50}$/ml
20	Coxakie virus B3 - nancy(5A1)	2.3×10^{-8}	$CCID_{50}$/ml
21	Polio virus - sabin(3A4)	4×10^{-7}	$CCID_{50}$/ml
22	Corona virus - FCV(3A2)	1.5×10^{-5}	$CCID_{50}$/ml
23	Corona virus - FIP(2A4)	3.0×10^{-6}	$CCID_{50}$/ml
24	HSV-1 F(3A20)	2.4×10^{-6}	$CCID_{50}$/ml
25	HSV-2 MS(4A6)	2.6×10^{-5}	$CCID_{50}$/ml
26	RSV - Strain B WV/14617/82(VR-1400)	2.4×10^{-6}	$CCID_{50}$/ml
27	Adenovirus(type 5)	2.4×10^{-6}	$CCID_{50}$/ml
28	Rhinovirus-RV71	5.6×10^{-4}	$CCID_{50}$/ml
29	Rhinovirus-RV14	3.7×10^{-6}	$CCID_{50}$/ml
30	Influenza A - H3N2(HK)	3.5×10^6	PFU/ml
31	Influenza B-Lee	8.6×10^5	PFU/ml
32	Influenza A - H1N1(PR8)	5.1×10^6	PFU/ml
33	Rhinovirus - RV21	1.1×10^{-4}	$CCID_{50}$/ml
34	HCMV(AD-169)	1×10^{-6}	$CCID_{50}$/ml

Bacteria			
	Strain	Conc.	Unit
1	*S. Dysgalactiae subsp. dysgalactiae*	3.2×10^9	CFU/ml
2	*S. mitis*	2.8×10^9	CFU/ml
3	*S. Mutans*	3.7×10^9	CFU/ml
4	*S. Canis*	5×10^9	CFU/ml
5	*S. Aglactiae*	2.7×10^9	CFU/ml
6	*S. Aglactiae*	1.9×10^9	CFU/ml
7	*S. Paraganguis*	1.5×10^9	CFU/ml
8	*S. Equisimilis subsp. equisimilis*	2.8×10^9	CFU/ml
9	*S. thermophilus*	1.9×10^9	CFU/ml
10	*S. Anginosis*	3.8×10^9	CFU/ml
11	*S. Pneumoniae*	1.5×10^9	CFU/ml
12	*S. Porcinus*	1.2×10^9	CFU/ml
13	*Candida albicans*	6×10^8	CFU/ml
14	*Candida glabrata*	6×10^8	CFU/ml
15	*Candida tropicalis*	6×10^8	CFU/ml
16	*Citrobacter freundii*	6×10^8	CFU/ml
17	*Corynebacterium sp.*	6×10^8	CFU/ml
18	*Corynebacterium diphtheriae*	6×10^8	CFU/ml
19	*Enterococcus faecalis*	6×10^8	CFU/ml

20	*Enterococcus gallinarum*	6 x 10^8	CFU/ml
21	*Escherichia coli*	6 x 10^8	CFU/ml
22	*Hemophilus influenzae*	6 x 10^8	CFU/ml
23	*Hemophilus parainfluenzae*	6 x 10^8	CFU/ml
24	*Klebsiella oxytoca*	6 x 10^8	CFU/ml
25	*Klebsiella pneumoniae*	6 x 10^8	CFU/ml
26	*Lactobacillus sp.*	6 x 10^8	CFU/ml
27	*Legionella spp*	6 x 10^8	CFU/ml
28	*Listeria monocytogenes*	6 x 10^8	CFU/ml
29	*Moraxella catarrhalis*	6 x 10^8	CFU/ml
30	*Mycobacterium tuberculosis*	6 x 10^8	CFU/ml
31	*Neisseria gonorrhoeae*	6 x 10^8	CFU/ml
32	*Neisseria meningitidis*	6 x 10^8	CFU/ml
33	*Neisseiria sicca*	6 x 10^8	CFU/ml
34	*Proteus mirabilis*	6 x 10^8	CFU/ml
35	*Proteus vulgaris*	6 x 10^8	CFU/ml
36	*Pseudomonas aeruginosa*	6 x 10^8	CFU/ml
37	*Serratia marcescens*	6 x 10^8	CFU/ml
38	*Staphylococcus aureus*	6 x 10^8	CFU/ml
39	*Staphylococcus epidermidis*	6 x 10^8	CFU/ml
40	*Stenotrophomonas maltophilia*	6 x 10^8	CFU/ml

- **Interference**

Interference materials such as below the ones in the table were added to the test sample(s) the same as the below concentrations. **ichroma™ Strep A** test results did not show any significant interference with these materials.

	Interference material	Conc.
1	Nasal sprays drops	20 %
2	Nasal corticosteroids	20 %
3	Homeopathic allergy relief medicine	5 mg/ml
4	Throat lozenges, oral anesthetic & analgesic	5 mg/ml
5	Anti-viral drugs (TAMIFLU)	5 mg/ml
6	Antibiotic (Bactroban, cream)	10 mg/ml
7	Antibacterial, systemic (cefadroxil)	5 mg/ml
8	Whole blood	10 %
9	Acetaminophen	10 mg/ml
10	Ibuprofen	10 mg/ml
11	Povidone-iodine	3.50 %
12	Acetylsalicylic acid (Aspirin)	30 mg/ml
13	Mouth wash (LISTERIN)	20.00 %
14	Throat candy (Cetylpyridinium chloride – candy, VICKS)	20 mg/ml
15	Throat candy (Lysozyme chloride)	20 mg/ml

■ **Precision**

- Single-site study

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision

3 Lots of **ichroma™ Strep A** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

- Multi-site study

Reproducibility

1 Lot of **ichroma™ Strep A** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

		Single-site study	
		Repeatability	Within-laboratory precision
std. 1	Judgment/Nr.	40/40	80/80
	Detection ratio(%)	100	100
std. 2	Judgment/Nr.	40/40	80/80
	Detection ratio(%)	100	100
std. 3	Judgment/Nr.	40/40	80/80
	Detection ratio(%)	100	100
std. 4	Judgment/Nr.	40/40	80/80
	Detection ratio(%)	100	100
		Single-site study	Multi-site study
		Lot to lot precision	Reproducibility
std. 1	Judgment/Nr.	120/120	75/75
	Detection ratio(%)	100	100
std. 2	Judgment/Nr.	120/120	75/75
	Detection ratio(%)	100	100
std. 3	Judgment/Nr.	120/120	75/75
	Detection ratio(%)	100	100
std. 4	Judgment/Nr.	120/120	75/75
	Detection ratio(%)	100	100

■ **Clinical performance evaluation**

ichroma™ Strep A have demonstrated the following clinical performance results.

		ichroma™ Strep A		Total
		Positive	Negative	
Culture method	Positive	99	7	106
	Negative	1	47	48
Total		100	54	154

- Clinical sensitivity: 93.39 % (95% CI: 86.39% ~ 97.07%)
- Clinical specificity: 97.91 % (95% CI: 87.52% ~ 99.89%)

■ **Comparability**

		ichroma™ Strep A		Total
		Positive	Negative	
Reference reagent	Positive	95	0	95
	Negative	5	54	59
Total		100	54	154

- Overall percent agreement (%): 96.75 %

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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

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