BIO TECHNOLOGY boditech

ichroma™ Total IgE

INTENDED USE

ichroma™ Total IgE is a fluorescence immunoassay (FIA) for the quantitative determination of total IgE in human whole blood/serum/plasma. It is useful as an aid in diagnosis and management of allergic disease.

For *in vitro* diagnostic use only.

INTRODUCTION

Immunoglobulin E (IgE) was discovered for its involvement in allergic reactions (Type I hypersensitivity)[1]. Type I hypersensitivity is an allergic reaction provoked by re-exposure to a specific type of antigen referred to as an allergen.

The sequence of events in the allergic reaction consists of the production of IgE antibodies in response to an allergen, binding of IgE to of mast cells, cross-linking of the bound IgE by the allergen upon re-exposure, and release of mast cell mediators such as histamine, lipid mediators and cytokines. Some mast cell mediators cause rapid increase in vascular permeability and smooth muscle contraction, resulting in many of the symptoms.

The IgE concentration in serum is normally very low (<0.001% of the total serum immunoglobulin). The serum concentration of IgE is age-related, increasing during childhood until about 10 years of age, after which it reaches values that are maintained during adult life [2), 3)].

Measurement of total IgE is often used as a tool in the diagnosis and management of atopic diseases, and elevated level of IgE can be found in patients with allergic disease such as asthma, hay fever, atopic dermatitis and urticarial [4), 5), 6)].

It has been used to distinguish atopic from non-atopic individuals presenting allergy-like symptoms. In addition, studies have also shown that increased levels of IgE in cord blood and infants may be predictive of future atopic tendencies [7)].

Serum IgE levels may vary as a result of diet, genetic background, geographical location and other factors. It is therefore recommended that total IgE measurements be used in conjunction with other clinical tests when establishing diagnoses [8)].

PRINCIPLE

The test uses a sandwich immunodetection method; the detector antibody in buffer binds to total IgE in sample, forming IgE-anti IgE complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-anti IgE on test strip.

The more IgE in sample forms the more IgE-anti IgE complex and leads to stronger intensity of fluorescence signal. This signal then is interpreted by the reader to display the total IgE concentration in the sample.

COMPONENTS

ichroma™ Total IgE consists of 'Cartridges', 'Detection Buffer Tubes', and an 'ID Chip'.

- The cartridge contains a test strip, the membrane which has anti IgE at the test line, with streptavidin at the control line.
- Each cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed cartridges are packed in cartridge box which also contains an ID Chip.
- The detection buffer contains anti-IgE fluorescence conjugate, BSA-Biotin fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.
- The detection buffer is dispensed in a tube. 25 detection buffer tubes are packaged in detection buffer box.

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow instructions and procedures described in this 'Instruction for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, ID Chip and detection buffer) 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 detection buffer tubes. A detection buffer tube should be used for processing of one sample only. A cartridge should be for testing 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. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- Allow cartridge, detection 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.
- Used detection buffer tubes, pipette tips and cartridges should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **ichroma™ Total IgE** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ Total IgE** should be used only in conjunction with instrument for ichroma™ tests.
  - Have to use recommended anticoagulant sample.

Sample type	Recommended anticoagulant
Whole blood	EDTA, heparin, Sodium citrate
Plasma	
Serum	Not applicable.

STORAGE AND STABILITY

- The cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4-30 °C.
- The detection buffer dispensed in a tube is stable for 20 months if stored at 2-8 °C.
- Once 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 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 antigen unrecognizable by the antibodies.
- An interference can be found for samples from patients treated with Xolair (omalizumab) or similar drugs containing anti IgE

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 including clinical symptoms and other relevant test results.

MATERIALS SUPPLIED

REF CFPC-91

Components of **ichroma™ Total IgE**

- Cartridge Box:
  - Cartridge 25
  - ID Chip 1
  - Instruction For Use 1
- Detection Buffer Box
  - Detection Buffer Tube 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ Total IgE**. Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
- **Boditech Total IgE Control** REF CFPO-219

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ Total IgE** is human whole blood/ serum /plasma.

- It is recommended to test the sample within 24 hours after collection.
- The serum should be collected using standard sampling tubes or tubes containing separating gel.
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood. If longer storage is required, e.g. if the test could not be performed within 24 hours, serum or plasma should be keep at 2- 8 °C or below -20 °C.
- The sample is stable for 1 month at 2- 8 °C, 3 month at -20 °C. Once the sample was frozen, it should be used one time only for test, because repeated freezing and thawing can result in the change of test values.
- However, the whole blood sample should not be kept in a freezer in any cases.
- The listed sample types were tested with a selection of sample collection tubes, not all available tubes of all manufacturers. Sample collection system from various manufacturers may contain differing materials which could affect the test results in some cases.

TEST SETUP

- Check the contents of **ichroma™ Total IgE**: Sealed Cartridges, Detection Buffer Tubes and ID Chip.
- Ensure that the lot number of the cartridge matches that of the ID Chip as well as the detection buffer.
- Keep the sealed cartridge (if stored in refrigerator) and the detection buffer tube at room temperature for at least 30 minutes just prior to the test. Place the cartridge on a clean, dust-free and flat surface.
- Turn on the instrument for ichroma™ tests.
- Insert the ID Chip into the ID Chip port of the instrument for ichroma™ tests**.**
- Press the 'Start' button on the instrument for ichroma™ tests.

(Please refer to the 'Instrument for **ichroma™ II** Tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

1) Transfer of 50 uL (human serum/ plasma/ control) or 100 uL (human whole blood) of sample with a pipette dispense it into the detection buffer tube.
2) Shake 5 times or more the closed tube until the mixture mix well. The mixture has to be used within 30 seconds.
3) Load only 75 uL of the mixture onto the sample well of the cartridge.
4) Leave the cartridge at room temperature for 12 min before inserting the device into the holder.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inexact test result.*
5) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the test cartridge before pushing it all the way inside the test cartridge holder. An arrow has been marked on the test cartridge especially for this purpose.
6) Press 'Start' button on the instrument ichroma™ for tests to start the scanning process.
7) Instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
8) Read the test result on the display screen of the instrument for ichroma™ tests.
   (Please refer to the ichroma™ II operation manual for complete information and operation instructions.)

INTERPRETATION OF TEST RESULT

- Instrument for ichroma™ tests calculates the test result automatically and displays total IgE concentration of the test sample in terms of IU/mL.
- To convert the IU/mL of the result to mass unit per volume, the conversion factor can be used as follow:
  1 IU/mL = 2.44 ng/mL
- The concentration of IgE in the serum is highly age dependent.
- Total IgE concentrations were measured in human serum samples from non-atopic healthy adult and child subjects using the **ichroma™ Total IgE**. The observed ranges of total IgE concentrations are shown below for each age group represented:

Age group	Geometric mean *	ichroma™ Total IgE
		Mean + 1SD
< 1 year	3.2 IU/mL	13.6 IU/mL
1 – 5 year	12.1 IU/mL	43.3 IU/mL
6 – 9 year	20.6 IU/mL	80.1 IU/mL
10 – 15 year	51.1 IU/mL	209.2 IU/mL
≥16 year	13.2 IU/mL	88.4 IU/mL

*Reference values for serum IgE in healthy non-atopic children and adults. *Clin Chem.* 1982;**28**(7):1556.

- Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.
- Working range : 1.00 IU/mL – 1,000 IU/mL

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.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are not provided with **ichroma™ Total IgE**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instruction for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 0.50 IU/mL
  - Limit of Detection (LoD) 0.75 IU/mL
  - Limit of Quantification (LoQ) 1.75 IU/mL
  - Reportable range
    Reportable range of the undiluted sample is 1.00 IU/mL – 1,000 IU/mL. Samples with total IgE concentrations above 1,000 IU /mL can be diluted with saline (0.9% NaCl in distilled water, not provided). The recommended dilution is 1:10 or 1:100.
    After dilution, multiply the result by the dilution factor. Please follow the below equation to obtain final sample concentration.
    [Final sample conc. = Reported conc. x Dilution factor (10 or 100)]

- **High-dose Hook Effect**
  There is no high-dose hook effect at IgE concentration up to 15,000 IU/mL.

- **Analytical specificity**
  - Cross-reactivity
    No cross-reactivities with the immunoglobulin G, A and M were detectable in following conditions:

Immunoglobulin	Concentration
Immunoglobulin G	20 mg/mL
Immunoglobulin A	20 mg/mL
Immunoglobulin M	20 mg/mL

  - Interference
    No interference was observed from hemoglobin, bilirubin, triglyceride, rheumatoid factor and human serum albumin, biotin in following conditions. But If interference materials are higher concentration than this table, **ichroma™ Total IgE** may be shown interference.

Interference Materials	Concentration
Hemoglobin	200 mg/dL
Bilirubin	0.4 mg/mL
Triglyceride	2,000 mg/dL
Rheumatoid factor	78 IU/mL
Human serum albumin	12 g/dL
Biotin	10 ng/mL

- **Precision**
  - Between-lot
    One person tested three different lots of **ichroma™ Total IgE**, ten times at each sample.
  - Between person
    Three different persons tested **ichroma™ Total IgE**, ten times at each sample.
  - Between day
    One person tested **ichroma™ Total IgE** during five days, ten times at each sample.
  - Between site
    One person tested **ichroma™ Total IgE** at three different sites, ten times at each sample.
    The following results were obtained:

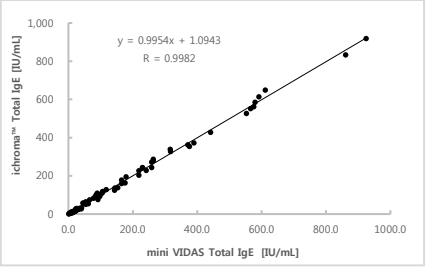
Expected value [IU/mL]	Between-lot		Between-person		Between-day		Between-site	
	Mean [IU/mL]	CV (%)	Mean [IU/mL]	CV (%)	Mean [IU/mL]	CV (%)	Mean [IU/mL]	CV (%)
5.0	4.98	8.6	5.05	8.0	4.90	8.1	5.07	9.5
100.0	100.73	3.7	101.49	4.3	101.18	3.6	104.76	7.2
500.0	520.05	2.8	527.25	5.7	514.54	2.6	534.28	5.6

- **Accuracy**
  The accuracy was determined by 3 different lots testing six times each human serum.

Expected value [IU/mL]	Value [IU/mL]			Mean [IU/mL]	Bias (%)
	Lot 1	Lot 2	Lot 3		
15.00	14.97	15.15	15.29	15.14	1%
52.50	50.48	49.93	49.88	50.10	-5%
252.50	259.80	263.27	261.65	261.57	4%
400.00	420.10	423.13	420.40	421.21	5%

- **Comparability**
  Diluted standard materials test results from the **ichroma™ Total IgE** assay (y) were compared with that of the mini VIDAS (x): The method comparison shows a good correlation between both methods with the following results:

  Linear regression: y =0.9954x + 1.0943; R=0.9982



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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
	Batch code
	Catalog number
	Caution
	Manufacturer
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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