Diabetes ichroma™ HbA1c Neo

INTENDED USE

ichroma™ HbA1c Neo is a fluorescence immunoassay (FIA) for the quantitative determination of HbA1c (Hemoglobin A1c) in human whole blood. It is useful as an aid in management and monitoring of the long-term glycemic status in patients with diabetes mellitus.

For *in vitro* diagnostic use only.

INTRODUCTION

Glycated protein is formed post-translationally through the slow, nonenzymatic reaction between glucose and amino groups on proteins. HbA1c is a clinically useful index of mean glycemia during the preceding 120 days, the average life span of erythrocytes. Carefully controlled studies have documented a close relationship between the concentrations of HbA1c and mean glycemia. HbA1c is considered as a more reliable parameter in monitoring glycemia over the glycemic reading with the conventional glucometer.

PRINCIPLE

The 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 content of glycated hemoglobin in terms of percent of the total hemoglobin in the blood.

COMPONENTS

ichroma™ HbA1c Neo consists of 'cartridges', 'detector tubes', 'detector diluents'.

- The cartridge contains the membrane called a test strip which has streptavidin 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-Hemoglobin A0-fluorescence conjugate, biotin-anti-HbA1c antibody conjugate, anti-chicken IgY-fluorescence conjugate and sodium azide as a preservative in phosphate buffered saline (PBS). All detector tubes are packed in a pouch.
- The detector diluent contains tween 20 and antifoam B emulsion (Polydi methylsiloxane) as a detergent, n-Teradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, Potassium hexacyanoferrate (Ⅲ) as a hemoclastic and sodium azide as a preservative in phosphate buffered saline (PBS), and it is pre-dispensed in 2 vials. The detector diluents 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, detector diluent and ID chip) must match each other.
- After using the detector diluent, keep it closed.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect of test result(s).
- Do not reuse cartridges or detector tubes. A cartridge should be used for testing one sample only. A detector tube 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, detector tube, detector diluent 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, detector tubes, detector diluents, capillary tube and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detector tube and the detector diluent contain sodium azide (NaN_3), and they 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™ HbA1c Neo** when biotin concentration in the sample was up to 3,500 ng/mL. If a patient has been taking biotin at dosage of more than 300 mg a day, it is recommended to collect blood 24 hours after discontinuation of biotin intake.
- **ichroma™ HbA1c Neo** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ HbA1c Neo** should be used only in conjunction with the instrument for ichroma™ tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2EDTA, K_3EDTA, Na_2EDTA, Lithium heparin, Sodium citrate

- **The capillary tube should be used when the following conditions are met.**
  - The capillary tube provided with the kit is recommended to obtain correct test result.
  - Whole blood should be immediately tested after collection.
  - Excess whole blood around the capillary tube should be wiped off.
  - In order to avoid cross-contamination, please do not re-use capillary tube for multiple samples.

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
Detector diluent	2-30°C	20 months	Unopened
	2-30°C	12 months	Opened

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

LIMITATIONS 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 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.
- The test environment conditions for **ichroma™ HbA1c Neo** are below.
  - Temperature: 20-30 °C
  - Humidity: 10-70 %
  - i-chamber target temperature: 30 °C

MATERIALS SUPPLIED

REF **CFPC-137**

Components of **ichroma™ HbA1c Neo**

- Cartridge Box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 2
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ HbA1c Neo**. Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF **FR203**
  - **ichroma™ II** REF **FPRR021**
  - **ichroma™ III** REF **FPRR037**
  - **ichroma™ M3** REF **FPRR035**
  - **ichroma™-50 PLUS** REF **FPRR036**
- **Printer** REF **FPRR007**
- **i-Chamber** REF **FPRR009**
- **Boditech HbA1c Control** REF **CFPO-96**
- **5 µL Capillary tube** REF **CFPO-32**

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ HbA1c Neo** is human whole blood.

- It is recommended to test the sample within 24 hours after collection when collected sample is stored at room temperature.
- The samples (whole blood) may be stored for a week at 2-8°C prior to being tested.
- However, the whole blood sample should not be kept in a freezer in any case.
- Whole blood sample may be used to collect according to below.

① Wear disposable gloves and protective equipment for safety.
② Open the bottle which has capillary tubes.
③ Take out the capillary tube and check for damage or contamination.
④ Hold the handle of the capillary tube and touch the surface of blood with the capillary tube.
⑤ Fill it with blood completely.
(Make sure that no air bubbles are present in the capillary tube. Do not get blood on the surface of the capillary tube. If the blood gets on the surface of the capillary tube, remove it gently with gauze.)

TEST SETUP

- Check the components of the **ichroma™ HbA1c Neo**: Sealed cartridges, detection tubes, detector diluents, ID chip and instructions for use.
- Ensure that the lot number of the test cartridges matches that of detector tube, detector diluent as well as an ID chip.
- If the sealed cartridge, the detector tube, and the detector diluent have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Temperature of i-chamber should be 30 °C.
- Turn on the instrument for ichroma™ tests.

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

CAUTION

- To minimize erroneous test results, we suggest that the ambient temperature of the cartridge should be 30°C during the reaction time after loading sample mixture to the cartridge.
- To maintain the ambient temperature to 30°C, you can use various devices such as an i-Chamber or an incubator and so on.

TEST PROCEDURE

▶ **ichroma™ Reader, ichroma™ II, ichroma™ M3**

1) Take out a cartridge from the pouch and insert the half it into the i-Chamber slot (30 °C).
2) Take 400 µL of detector diluent using a pipette and dispense it to the detector tube containing a granule. When the granule form is completely dissolved in the tube, it becomes detection buffer.
(The detection buffer must be used immediately. Do not exceed 30 seconds.)
3) Take 5 µL of sample (Whole blood/control) using a pipette or capillary tube and put it to the detector tube.
(Do not make air bubbles in the capillary tube and careful not to get blood on the surface of the capillary tube. If blood gets on the surface of the capillary tube, remove it gently with gauze.)
4) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 15 times.
(The sample mixture must be used immediately. Do not exceed 30 seconds.)
5) Take out the half of the cartridge from i-Chamber slot.
6) Take 75 µL of the sample mixture and dispense it into a sample well of the cartridge.
7) Wait till the sample mixture flow appears in the windows. (about 10 seconds)
8) Insert the sample-loaded cartridge into the slot of the i-Chamber or an incubator (30 °C).
9) Leave the sample-loaded cartridge in the i-Chamber of an incubator for 12 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) Press 'Select' or tap 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M3 is tested automatically after inserting.)
12) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ **ichroma™ III**

1) The test procedure is same with the 'ichroma™ Reader, ichroma™ II, ichroma™ M3 test procedure 2) ~ 6)'.
2) 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 'Start' button on ichroma™ III to start the scanning process.
4) The cartridge goes inside and ichroma™ III will automatically start scanning the sample-loaded cartridge after 12 minutes.
5) Read the test result on the display screen of the ichroma™ III.

▶ **ichroma™-50 PLUS**

1) Insert the tip array in the tip station.
2) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
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 HbA1c concentration of the test sample in terms of % (NGSP), mmol/mol (IFCC), mg/dL (eAG).
- Reference value
  - NGSP (%): 4.5-6.5 %
  - IFCC (mmol/mol): 26-48 mmol/mol
- Working range
  - NGSP (%): 4-15 %
  - IFCC (mmol/mol): 20.2-140.4 mmol/mol
  - eAG (mg/dL): 68.1-383.8 mg/dL

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™ HbA1c Neo**. For more information regarding obtaining 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**
  - Limit of Blank (LoB) 2.00 %
  - Limit of Detection (LoD) 2.50 %
  - Limit of Quantitation (LoQ) 4.00%

- **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™ HbA1c Neo** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactants	Concentration
HbA0	20 mg/mL
HbA1a, A1b	20 mg/mL
Acetylated hemoglobin	100 mg/mL
Carbamylated hemoglobin	100 mg/mL
Glycated h-Albumin	100 mg/mL
HbA1d	100 mg/mL
Acetylaldehyde hemoglobin	100 mg/mL

  - Interference
  Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ichroma™ HbA1c Neo** test results did not show any significant interference with these materials.

Interferents	Concentration
Acetaminophen	20 mg/dL
L-ascorbic acid	500 mg/dL
Bilirubin [conjugated]	2 g/dL
D-glucose	1,000 mg/dL
Intralipid	8,000 U/L
Triglyceride	327 M
Urea	10 g/dL
Biotin	3,500 ng/mL

- **Precision**

- **Single-site study**

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision
3 Lots of **ichroma™ HbA1c Neo** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

Single-site study						
HbA1c [%]	Repeatability		within-laboratory precision		Lot to lot precision	
	AVG [%]	CV (%)	AVG [%]	CV (%)	AVG [%]	CV (%)
4.8	4.94	4.19	4.93	4.24	4.92	4.21
7.4	7.61	4.19	7.59	4.58	7.60	4.35
13.0	13.32	4.69	13.2	4.72	13.29	4.31

- **Multi-site study**

Reproducibility
1 Lot of **ichroma™ HbA1c Neo** 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.

Multi-site study		
HbA1c [%]	Reproducibility	
	AVG [%]	CV (%)
4.8	4.68	1.53
7.4	7.22	1.43
13.0	12.67	1.51

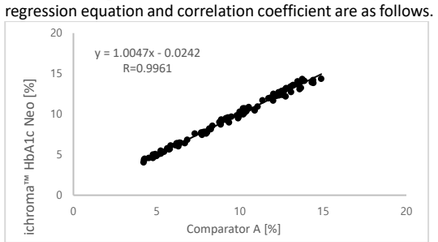
- **Accuracy**

The accuracy was confirmed by testing with 3 different lots of **ichroma™ HbA1c Neo**. The tests were repeated 10 times in each different concentration of the control standard.

HbA1c [%]	Lot 1	Lot 2	Lot 3	AVG [%]	Recovery (%)
4.8	4.76	4.72	4.80	4.76	99
7.4	7.39	7.32	7.36	7.36	99
10.1	10.11	10.07	9.98	10.06	100
13.0	12.90	12.94	12.98	12.94	100

- **Comparability**

HbA1c concentrations of 100 clinical samples were quantified independently with **ichroma™ HbA1c Neo (ichroma™ II)** and Comparator A as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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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:
Boditech Med Inc.'s Technical Services
Tel: +(82) -33-243-1400
E-mail: TS@boditech.co.kr

Boditech Med Inc.
43, Geodudanji 1-gil, Dongnae-myeon, Chuncheon-si,
Gang-won-do, 24398, Republic of Korea
Tel: +(82) -33-243-1400
Fax: +(82) -33-243-9373
www.boditech.co.kr

EC REP **Obelis s.a**
Bd. Général Wahis 53, 1030 Brussels, Belgium
Tel: +(32) -2-732-59-54
Fax: +(32) -2-732-60-03
E-Mail: mail@obelis.net

CE IVD