Medcaptain 麦科田

Instructions for Use

Insulin (CLIA)

[Product Name]

Insulin (CLIA)

[Packing Size]

24×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg

[Intended Use]

Insulin (CLIA) is a chemiluminescent immunoassay (CLIA) used for the quantitative determination of insulin in human serum, plasma, or whole blood, and it is mainly used for evaluation of the islet function.

Insulin is a peptide hormone with 51 amino acid residues and composed of two polypeptide chains, α and β, the molecular weight is 5808 Da. It is secreted by pancreatic islet β cells and enters into the blood circulation through the portal vein and liver [1, 2]. Insulin regulates the uptake and usage of glucose, and is also involved in the regulation of protein synthesis and triglyceride storage [3]. The most important clinical application of insulin is in the diagnosis and management of diabetes mellitus, which is caused by insufficient tissue uptake of glucose. Diabetes can be divided into two main types according to the secretion of insulin. The first category is insulin-dependent diabetes mellitus (IDDM) or type I diabetes. It is caused by autoimmunity destruction of pancreatic islet β cells [4]. When all pancreatic islet β cells are eventually destroyed, insulin secretion gradually decreases to negligible levels. In this case, only the injection of insulin can keep the patient alive. The second type is non-insulin-dependent diabetes mellitus (NIDDM) or type II diabetes. The pancreatic islet β cells of these diabetic patients can still secrete insulin, but the body is resistant to the hormone. When the glucose concentration in the circulation increases, the insulin response is slow and insufficient. More and more insulin are needed to keep glucose at the same level with the disease progression of type II diabetes. Depending on the patient's level of glucose control, patients may require medication to stimulate insulin secretion or insulin supplementation [5]. The measurement of insulin can be used for the auxiliary diagnosis of diabetes; the insulin level under basal conditions or after glucose processing can be used to evaluate the ability of the pancreas to secrete insulin. The insulin level of insulin-dependent diabetes (IDDM) patient is low, while patients with non-insulin-dependent diabetes (NIDDM) is normal or even elevated. The measurement of insulin can also be used to assess the duration of the body's response to various insulin at the beginning of therapy for diabetes treatment [6-8].

[Principle of the Assay]

This assay takes the double-antibody sandwich format. The detection principle is described below:

(1) Mix the sample with magnetic microparticle coated with an anti-Insulin antibody, add another acridinium labeled anti-Insulin antibody. After mixing and incubation, Insulin in the sample will react with anti- Insulin antibody coated on the microparticle, acridinium labeled anti-Insulin antibody will react with another site on Insulin, forming antigen-antibody complex;

(2) A magnet captures the microparticle, and then unbound substance is washed off. Add pre-trigger and trigger solution to the reaction mixture sequentially to initiate chemiluminescence reaction;

(3) A photomultiplier tube is used to measure photons generated from the reaction. Signal is amplified exponentially. The count is proportional to Insulin concentration in the sample. Insulin concentration is determined by an internal calibration curve.

[Main Components]

Packing Size

Component \ Packing Size		Fill Volume		
		24×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg
Insulin Reagent Cartridge	Microparticle (R1)	24×50 μL	60×50 μL	60×50 μL
	Conjugate (R2)	24×100 μL	60×100 μL	60×100 μL
	Reaction diluent (R3)	24×100 μL	60×100 μL	60×100 μL
Insulin Calibrator C1		1×1.0 mL	1×1.0 mL	/
Insulin Calibrator C2		1×1.0 mL	1×1.0 mL	/
Calibration Card		1 pcs	1 pcs	/

Main Composition

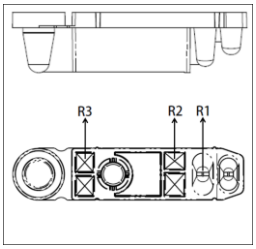
Component	Main Composition	
Insulin Reagent Cartridge	Microparticle (R1)	Anti-Insulin antibody coated microparticle, ~0.3 g/L; Tris buffer, 50 mmol/L; ProClin 300, 0.5 g/L
	Conjugate (R2)	Acridinium labeled anti-Insulin antibody, ~200 μg/L; MES buffer, 50 mmol/L; ProClin 300, 0.5 g/L
	Reaction diluent (R3)	Tris buffer, 50 mmol/L; ProClin 300, 0.5 g/L
Insulin Calibrator C1	Insulin; Tris buffer, 25 mmol/L; ProClin 300, 0.5 g/L	
Insulin Calibrator C2	Insulin; Tris buffer, 25 mmol/L; ProClin 300, 0.5 g/L	
Calibration Card	Calibration curve and calibrator information	

Note: (1) Components in different lots of reagent cannot be mixed or exchanged for use.

(2) Traceability: This quantification method can be traced back to Insulin National Reference Materials code 150519, which can be traced back to the 1st IRP WHO Reference Standard 66/304 (NIBSC).

(3) Information about the calibrators (such as lot number and concentration etc.) can be found on the instrument interface after scanning the Calibrator Card.

The position of each component in the reagent pack is shown in the front view (Upper) and vertical view (Down) of the reagent cartridge.



Instruments and accessories needed but not included (Medcaptain has the supplies)

(1) Medcaptain Immu F6/F6S Automatic Chemiluminescent Immunoassay Analyzers;

(2) Pre-trigger solution;

(3) Trigger solution;

(4) Washing solution;

(5) 500 μL pipette tips;

(6) Diabetes Controls.

[Storage and Shelf-life]

Storage: Store sealed reagent cartridges and calibrators at 2~8℃ in upright position, and avoid freezing.

Shelf life: 14 months.

Stability of Calibrators: Sealed vial of calibrators can be kept at 2~8℃ in dark for 14 months. After calibrator C1 or C2 is uncapped and sealed again, it can be stored at 10~30 ℃ for 5 days, and at 2~8 ℃ for 60 days.

The dates of manufacturing and expiration can be found on the labels.

[Matched Instruments]

Medcaptain Immu F6/F6S Automatic Chemiluminescent Immunoassay Analyzers

[Specimen Types]

Serum, plasma, and whole blood (collected with EDTA-K_2, EDTA-K_3, lithium heparin, and sodium heparin as the anti-coagulants) can be used in the testing.

Sample volume for each test: 20 μL.

The collected sample should be tested as soon as possible. Whole blood must be tested within 4 hours after sample collection. Serum and plasma can be kept at 10~30℃ for 8 hours, at 2~8℃ for 2 days, and at -20℃ or below for 60 days. Frequent freeze-thaw cycles should be avoided, and only one freeze-thaw cycle is allowed. If the sample contains precipitate or frozen floccule, centrifugation is needed to clear the sample before testing.

Sample collection tubes from different manufacturers may lead to variation in testing results, due to the difference in tube material and additives in the tubes. Medcaptain has not evaluated all types of sample collection tubes from different manufacturers. Each laboratory should make its own judgment about the usability of sample collection tubes.

[Test Procedure]

Reagent Preparation

Reagent: Insulin reagent cartridge (containing magnetic microparticle R1, acridinium labeled conjugate R2，and reaction diluent R3) is ready for use. It can be loaded directly into the instrument after opening the package.

Calibrators: Calibrator C1 and C2 are ready for use. Each calibrator can be added to a sample cup, and the cups are loaded to a sample rack. The sample rack can be pushed directly into the instrument for calibrator testing.

Calibration

Refer to the relevant chapters in the operation manual of each chemiluminescent immunoassay analyzer. Calibration tests should be ordered before the first time use of Insulin assay. Medcaptain provides Insulin reagent pack and matched calibrators to calibrate the instrument.

Before calibration, scan the calibration card provided in the kit, and the calibration curve and calibrator information will be scanned into the system. Take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.); Put calibrators on a sample rack, load the sample rack into the instrument. On the screen interface of “Reagent > Request Calibration”, select test name and lot number to request a calibration. Select the position of each calibrator on the sample rack, set the number of repeat tests, start calibration. Automatic immunoassay analyzer makes use of calibration data to validate the calibration, and adjust the calibration curve automatically. Instrument calibration is effective for 60 days. A new calibration is needed in the following situation:

(1) Change into a new lot of reagent;

(2) Control test results are out of the target range;

(3) The lot of reagent has been used on the same instrument for more than 60 days.

Refer to the Chapter of “Calibration” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about calibration.

Control Testing

Diabetes Controls are matched with Insulin reagent pack. There are two levels of controls: Low Control (L) and High Control (H).

Test two levels of controls with Insulin reagent on the instrument within 24 hours before testing real samples. Control testing is highly recommended every time the lot of reagent has been changed, the instrument has been re-calibrated, or after trouble shooting/maintenance service.

Before the control testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

Put controls on a sample rack, and load the sample rack into the instrument; Select “Control” on the interface of test menu, select test name and control lot; Click on “Start” and begin the testing. Check the results after control test is finished.

Control test results should fall into a specific range. If it is out of the target range, the user should check the system, such as expiration date of the controls, storage condition, instrument performance and status. After root cause analysis and corrective action, the user should test controls again. If the same problem exists, please contact customer service of Medcaptain.

Each laboratory should set up its own control range and frequency of control testing, based on its own practice. Refer to the Chapter of “Control Testing” in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about control testing.

Sample Testing

Before sample testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

If a sample collection tube is directly loaded to the instrument for testing, the sample volume should be at least 1.0 mL; Un-cap sample collection tubes, put samples on a sample rack, and push the sample rack into the instrument; Select “Sample” on the interface of test menu, enter information of samples, select test name; Click on “Start” and begin the testing. Check the results after sample test is finished.

The reagent usage for each test is: R1 50 μL, R2 100 μL, and R3 100 μL. The instrument aspirates and mixes each component in the reagent cartridge and incubates at 37℃. Time duration from sampling to result is about 15 min.

Refer to the Chapter of "Sample Testing" in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about sample testing.

Result Calculation

Based on the built-in calibration curve, the instrument automatically calculate Insulin concentration of each sample, in a unit of μIU/mL or pmol/L, 1.0 pmol/L = 6.945μIU/mL

[Reference Intervals]

Samples for the study of reference intervals come from local area in Guangdong Province. A total of 210 healthy and normal people has been recruited (Male: 108; Female: 102), age ranges from 13 to 80 years old. Serum obtained from fasting individuals give a reference interval of 2.5th percentile to 97.5th percentile as: 2.63~25.12 μIU/mL (18.27~174.46 pmol/L).

Due to the differences in geography, race, sex, and age of tested population, the reference interval may vary in different laboratories. It is highly recommended for each clinical lab to establish its own reference intervals.

[Interpretation of Test Results]

The test data is for clinical reference only. It cannot be used as the only confirmatory evidence nor to eliminate the possibility of diseases. Clinical diagnosis of patients should take clinical symptoms, body sign, disease history, other lab test results, and treatment response into comprehensive consideration.

The measurement range of this assay is: 0.4~1000 μIU/mL (2.78~6945 pmol/L). If Insulin concentration is lower than LoD, it will be reported as <0.4 μIU/mL (<2.78 pmol/L); If Insulin concentration is over the upper limit, it will be reported as >1000 μIU/mL (>6945 pmol/L). For a sample with Insulin concentration of >1000 μIU/mL (>6945 pmol/L), sample diluent can be used to dilute the sample manually (a dilution factor of 1:2 is recommended). Test the diluted sample in duplicate to obtain more accurate results.

When the instrument shows a warning sign of "SMPL", it means there is insufficient sample volume. Make sure enough sample is added for repeating the test. When the instrument shows a warning sign of "SMPJ", it means the sample probe has been blocked. Clean sample clot in the probe before repeating the test. Some results are tagged with other signs. Refer to the Chapter of "Result Signs" in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about results tagged with signs.

[Limitation of the Test Method]

The test data is for clinical reference only. It cannot be used individually as the evidence to confirm or eliminate the possibility of diseases.

There is no Hook effect for a sample with Insulin concentration of ≤20000 μIU/mL. For each endogenous interference substance with concentration less than the value shown in the table below, measurement error caused by the interference is within ±10%.

Endogenous interference substance	Concentration of interference substance
Total Protein	≤12 g/dL
Bilirubin	≤90 mg/dL
Hemoglobin	≤1000 mg/dL
Triglyceride	≤1800 mg/dL

For therapeutic drug with concentration less than the value shown in the table below, measurement error caused by the interference is within ±10%.

Drugs	Concentration (mg/L)
Euglucon	10
Tolbutamide	3

For potential cross-reactant with concentration less than the value shown in the table below, the following negligible cross-reactivity is reported:

Cross-reactant	Concentration	Cross-reactivity (%)
Bovine insulin	20000 pmol/L	10
Porcine insulin	10000 pmol/L	20
Human proinsulin	111000 pmol/L	0.3
C-peptide	33000 pmol/L	0
Glucagon	280 pmol/L	0
Somatostatin	60 pmol/L	0
Insulin-like growth factor I	10000 pmol/L	0

Heterophilic antibodies in human serum may react with immunoglobulin in the reagent, and interfere with immunoassay *in vitro*. More clinical or diagnostic information is needed to confirm disease diagnosis of patients. Some patients have frequent contact with animals, or have been treated or diagnosed with mouse monoclonal antibodies. They may have generated heterophilic antibodies. For example, some patients under monoclonal antibody treatment may have human anti-mouse antibodies (HAMA) in blood circulation, leading to false positive or false negative results. Anti-interference components are added to this reagent formulation to minimize the impact of HAMA and ANA, but the problem may not be totally eliminated, and some sample testing may still be impacted. More clinical and diagnostic information is needed to make a solid conclusion.

Samples with the titer of no less than 1:1000 by anti-nuclear IgG test kit (indirect immune-fluorescence method) were studied in interference tests. It has shown less than ±10% error in the test results. For RF at a concentration of less than 1500 IU/mL, and for multiple representative human HAMA samples, the measurement error caused by the interference is within ±10%.

[Property and Performance]

1 Limit of Blank

LoB ≤ 0.2 μIU/mL (1.39 pmol/L).

2 Limit of Detection

LoD ≤0.4 μIU/mL (2.78 pmol/L).

3 Accuracy

a) Test the National Standard for Insulin within the linear range specified by the kit. The relative deviation between the measurement result and the theoretical concentration traced to the National Standard must not exceed 10.0 %;

b) Test the accuracy reference samples at two concentration levels multiple times respectively. The relative deviation between measurement result and the target value must not exceed 10.0 %.

4 Linearity

Test Insulin samples with concentration in the range of 1~1000 μIU/mL (6.95 ~6945 pmol/L), the linearity correlation coefficient r≥0.9900.

5 Repeatability

Coefficient of variation (CV) for the test results of low (2.5±0.5 μIU/mL) and high (25±5 μIU/mL) corporate reference sample is less than 8.0%.

6 Lot-to-lot Variation

Coefficient of variation (CV) for the test results of low (2.5±0.5 μIU/mL) and high (25±5 μIU/mL) corporate reference sample with three batches of reagents is less than 10.0%.

7 Accuracy of Calibrator Value Assignment

Use primary calibrators with values assigned from higher level measurement procedure, calibrate the immunoassay analyzer, and use the same lot of reagent to measure the value of each product calibrator. The measured value of Calibrator C1 or C2 has a relative deviation within ±10.0% from its assigned value.

8 Homogeneity of Calibrators

8.1 Within-vial Homogeneity

Within-vial homogeneity of Calibrator C1 or C2 is represented with coefficient of variation, and CV≤8.0 %.

8.2 Between-vial Homogeneity

Between-vial homogeneity of calibrator C1 or C2 is represented with coefficient of variation, and CV≤5.0%.

[Attention Notes]

1 It is for in-vitro diagnosis only.
2 It can only be used by professionals.
3 Never use expired reagent kit.
4 Never mix components from different kits, or from different reagent lots.
5 Do not put the reagent cartridges upside down.
6 Measurement of Insulin in a sample using different detection systems may yield different results, due to difference in test methods, assay specificity, and factors of interference. The measured values from different systems should not be directly compared to avoid inappropriate clinical interpretation.
7 Strictly follow the protocol in the package insert, and operate according to the lab guidelines.
8 The test results can only be used for clinical reference. Clinical diagnosis of patients should take symptoms, body sign, disease history, other laboratory test results, and response to treatment for comprehensive assessment.
9 User should wear gloves, safety goggles, and lab coat. Rinse with water if skin is in contact with the reagent. Flush eyes with copious of water if eyes are in touch with the reagent, and see a doctor immediately.
10 Take all samples and reaction waste as potential biohazard. All waste must be handled following the local government regulation.
11 This product is a single-use cartridge. Reagent cartridges should be put back into refrigerator and stored at 2~8℃ if they have been placed at room temperature but not opened yet.

[Interpretation of Signs]

	Temperature limit.		Date of manufacturing
	*In-vitro* diagnostic medical device		Catalogue number
	Batch Code		Consult instructions for use or consult electronic instructions for use
	Use-by Date		Authorized representative in the European Community/ European Union

	This way up		CE marking
	Manufacturer		Unique device identifier

[References]

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[Basic Information]

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