TiSENC Cardiac Troponin I (CLIA) PACKAGE INSERT

IVD

INTENDED USE

Cardiac Troponin I (CLIA) is a Chemiluminescence Immunoassay (CLIA) test for the quantitative measurement of circulating cardiac troponin I (cTnI) in human serum, plasma and whole blood, which is intended as an aid to diagnosis of myocardial infarction.
The assay can be used for samples over the range of 0.05 ng/mL~50 ng/mL.
The test must be performed on the ACCRE series analyzers (including ACCRE 6, ACCRE 8, ACCRE 90, ACCRE 100, ACCRE 120 and other ACCRE series analyzers).

For *in vitro* diagnostic use only. For professional use only.

SUMMARY

Troponin I together with troponin T (cTnT) and troponin C (cTnC) forms a complex that plays a fundamental role in transmission of intracellular calcium signal of actin-myosin interaction. The physiological effect of troponin I is to inhibit the activity of ATP enzyme in actin-myosin complex in the absence of calcium ion to prevent muscle contraction. The integrity of myocardial cell membrane is destroyed during myocardial necrosis, which is often accompanied by the release of structural proteins and other intracellular macromolecules into myocardial stroma. These biomarkers of myocardial necrosis include cardiac troponin I and T (cTnI and cTnT), creatine kinase isoenzyme MB (CM-MB), myoglobin (MYO) and so on. Compared with other available myocardial markers, cardiac troponin has good sensitivity and tissue specificity for myocardial injury, and is the first choice for the detection of myocardial injury. It can assist in the diagnosis of myocardial infarction (MI) and risk stratification of acute coronary syndrome (ACS) in acute coronary syndrome. According to the new definition of myocardial infarction by the European College of Cardiology (ESC) and the American Society of Cardiology (ACC), MI can be diagnosed when the concentration of cardiac troponin I in blood is higher than the 99th percentile of the normal control group (the precision of cTnI test at 99th percentile is less than or equal to 10%). In patients with acute myocardial infarction (AMI), the concentration of serum cTnI increased at 3-6 hours after chest pain, reached the highest level at 12-16 hours, and lasted for 4 to 9 days. It has been reported that the concentration of cTnI is also increased in unstable angina pectoris (UAP) and congestive heart failure (CHF). The concentration of cardiac troponin I can be detected in patients with UAP and patients without ST segment elevation, which is related to the incidence of death. Therefore, the determination of cardiac troponin I can also be used to grade patients for risk level.

ASSAY PRINCIPLES

The principle of Cardiac Troponin I (CLIA) hereinafter also referred to as the "cTnI" combines a two-site sandwich immunoassay method with enzyme catalytic chemiluminescence detection (CLIA). The principle is described as following:
Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent cartridges. All the assay steps are performed automatically by the ACCRE analyzer.
The sample is manually pipetted into the sample well of reagent cartridge, then sample, cTnI antibody labeled with alkaline phosphatase and cTnI antibody coated magnetic particles are mixed thoroughly together, incubating at 37 °C. The antigen in the sample, labelled antibody and antibody coated with magnetic particles are bonded together as an antibody-antigen sandwich immunocomplex. The immunocomplex is then washed in the magnetic field to eliminate the unbound components in the sample. The substrate is added to trigger the chemiluminescent reaction, the result of chemiluminescent reaction is measured by photomultiplier tube (PMT) as relative light units (RLUs). The concentration of the substance to be detected in the sample is proportional to the luminescence intensity. At the end, the results are automatically calculated by the ACCRE analyzer in relation to the calibration curve stored.

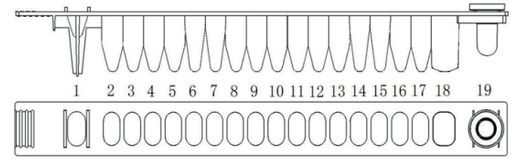
CONTENT OF THE KIT

Package: 60 tests/kit with quality controls, 36 tests/kit with quality controls, 60 tests/kit without quality controls, 36 tests/kit without quality controls.
The calibrator in the kit has been traced to Abbott fully automated chemiluminescence immunoassay analyzer and ARCHITECT STAT Troponin-I assay. For specific calibrator concentration values, see the Calibrator Barcode Sheet for each lot.

Contents	Quantities				Notice
	REF W121A	REF W121C	REF W12A	REF W12C	
cTnI Reagents Cartridges	60 strips	36 strips	60 strips	36 strips	Ready to Use
cTnI Calibrator 1 (CAL1)	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Lyophilized powder; Tris Buffer, 50mM; Proclin300, 0.48g/L; BND, 0.2g/L
cTnI Calibrator 2 (CAL2)	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Lyophilized powder; Recombinant cardiac troponin I protein, 0.3 ng/mL
cTnI Calibrator3 (CAL3)	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	Lyophilized powder; Recombinant cardiac troponin I protein, 10 ng/mL
cTnI Quality Control Level 1 (QC1)	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	/	/	Lyophilized powder; Recombinant cardiac troponin I protein, 0.5 ng/mL Only for the configuration with Quality Controls
cTnI Quality Control Level 2(QC2)	Dissolved to 1.0 mL x 1 vial	Dissolved to 1.0 mL x 1 vial	/	/	Lyophilized powder; Recombinant cardiac troponin I protein, 5 ng/mL Only for the configuration with Quality Controls
Instruction for Use	1	1	1	1	N/A
Reagent Registration Card	1	1	1	1	N/A
Calibrator Barcode Sheet	1	1	1	1	N/A
Quality Control Sheet	1	1	/	/	Only for the configurations with Quality Controls

Note: Refer to the target value list of the controls from Quality Control Sheet within the kit.

The Reagents Cartridge
The strip consists of 19 wells. The 1st well is the sample well and the last 19th is the reading well for chemiluminescent signal. From the 2nd to the 18th well are all covered with a label, aluminum foil seal. The label comprises a barcode which mainly indicates the reagent assay information, reagent lot number and expiration date. All reagents components needed for the assay are ready-to-use and pre-dispensed in the cartridge. And please do not interchange integral component from different reagents or lots.



Description of the reagent cartridge

Well	Component	Content	Volume
3	Sample treatment solution (R3)	Tris buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	50μL
5	Enzyme Label (R2)	ALP (alkaline phosphatase) labeled anti-cTnI antibody (mouse), 3.0mg/L; MES Buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	50μL
7	Magnetic Particles (R1)	Anti-cTnI antibody (mouse) coated magnetic particles, 0.2g/L; Tris buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	50μL
10, 11, 12, 14	Wash Solutions	Tris buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	350μL
16	Substrate Solution	Disodium [(4-chlorophenyl)sulfanyl] (10-methyl-9(10H)-acridinylidene) methyl phosphate	200μL

Note: Well 1, 2, 4, 6, 8, 9, 13, 15, 17, 18 are empty.

MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED

- Sample diluent (manufactured by Tisenc)
- Pipette with disposable tip to dispense 200 μL.
- Powerless, disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User Manual.
- Instruments of the ACCRE series analyzers.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- For professional use only by qualified laboratory personnel.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest; do not inhale).
- Do not use reagents after the expiration date indicated on the box label.
- Do not use if the packaging of reagent cartridge is damaged or leaked.
- Do not use the reagents if the quantity is obviously insufficient.
- If any component adheres to inside wall of wells or aluminum film of the reagent cartridge, please gently switch the reagent cartridge to let the component back the wells.
- Do not reverse the reagent cartridge. Otherwise, the result will be unreliable.
- Do not mix reagents (or disposables) from different lots.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.
- Use powderless gloves, as powder has been reported to cause false results for certain enzyme immunoassay tests.

STORAGE

- Store the Cardiac Troponin I (CLIA) kits including reagent cartridges, calibrators and quality controls **upright** at 2-8 °C, kit can be in dark place and the kit can be valid for 18 months from manufactured date.
- After the reagent cartridge is on-board in the ACCRE analyzer，the testing should be finished within 2 hours.
- When opened and re-dissolved, the calibrators and quality controls will be stable for 45 days at -20°C and below -20°C. Calibrators and quality controls can be frozen and thawed 3 times.
- Keep away from sunlight.
- Do not freeze reagent cartridges.

SAMPLES

The sample volume for Cardiac Troponin I (CLIA) assay is 50μL, please note that at least 75μL of sample should be pipetted into the reagent cartridge.

Sample type and collection
Human serum or plasma/whole blood (Heparin lithium/EDTA-K_2) are recommended.
Types of tubes:
- Plastic tube with clot activator,
- Plastic tube with clot activator and separation gel,
- Plastic tube with Heparin lithium,
- Plastic tube with EDTA-K_2.

It is recommended to validate collection tubes before using them as some may contain substances which interfere with test results.
Note: Blood sampling tube results may vary from one manufacturer to another depending on the materials and additives used.
It is the responsibility of each laboratory to validate the type of sample tube used and to follow the manufacturer's recommendations for use.

Sample preparation
The current revision of the WHO/DIL/LAB/99.1 document provides recommendations for the preparation of samples.
For use of the sample tubes, follow the tube manufacturer's instructions for use.
The pre-analytical step, including the preparation of blood samples, is an essential part of medical analyses. In accordance with Good Laboratory Practice, this step is performed under the responsibility of the laboratory manager.
Insufficient clot time can result in the formation of fibrin with micro-clots that are invisible to the naked eye. The presence of fibrin, red blood cells, or suspended particles can lead to erroneous results.
Samples containing suspended fibrin particles or erythrocyte stroma should be centrifuged before testing.
If there is a lipid layer over the sample after centrifuging, please transfer the clear sample into a new sample tube without transferring the lipid layer.
Severe hemolysis samples (hemoglobin >500mg/dL) or heat-inactivated samples are not recommended for applying on the reagents.
Preparation of frozen-stored samples: after thawing, these samples must be thoroughly mixed before testing.
Mix using with a vortex-type mixer. If necessary, clarify samples by centrifuging before testing.

Sample stability
Serum and plasma samples can be stored at 15~30°C for up to 2 hours or at 2-8°C for up to 24 hours; if longer storage is required, freeze the serum or plasma at -20°C or below -20 °C for up to 30 days, without exceeding 1 freeze/thaw cycle.

Whole blood samples can be stored at 15~30°C for up to 2 hours or at 2-8°C for up to 24 hours and not undergo freeze/thaw cycles.

INSTRUCTIONS FOR USE

For complete instructions, see the Instrument User Manual.

When using the assay for the first time. Register the assay using the registration code in the reagent kit before any assay is used in the ACCRE analyzer for the first time. Calibration, QC and sample test are only available after assay was registered successfully.

When opening a new lot of reagents. Each new lot of reagent must be registered by using the registration code in Reagent Registration Card within the reagent kit.

Calibration

Calibration must be performed with the reagents and calibrators from Manufacturer. Each bottle of lyophilized calibrator should be re-dissolved by purified water to 1.0mL before use.

Calibration is necessary under the following conditions:

(1) New reagent lot number applied;

(2) Same lot of reagents used more than 4 weeks;

(3) Quality control out of control;

(4) When necessary, for example: system maintenance or repairment that may affect the analytical performance.

Test Procedure

1. Remove the kit from storage at 2-8 °C and take out the required number of reagent cartridge. Allow the reagent cartridges. specimens, calibrators, and/or controls to equilibrate to room temperature (15-30°C) prior to testing.
2. Use each assay cTnI strips for each sample, calibrator or control respectively.
3. Place the reagent cartridge into the reagent rack.
4. Manually pipette the Sample, Calibrator, or Controls into the sample well of each reagent cartridge.

Please note that at least 75μL of sample must be pipetted manually into the reagent cartridge and 50μL is needed for each test.

** Before pipetting: Mix the samples using a vortex-type mixer if necessary, and ensure that the samples and sample diluent (if applicable) DO NOT have any bubbles, the same for calibrators and controls.*

5. Put the sample rack into the reagent chamber of ACCRE analyzer.
6. Place the assay tips into the reagent chamber of ACCRE analyzer.
7. Input Sample ID, sample type, dilution etc. into the software as directed by the USER MANUAL.
8. Cardiac Troponin I (CLIA) assay completed within approximately 15 minutes. Assays will be performed automatically by the ACCRE analyzer.
9. After assay is completed, remove the reagent rack from the ACCRE analyzer. Dispose the used reagent cartridge into an appropriate recipient.

Dilution

Samples with concentrations above 50 ng/mL can be diluted with negative serum or plasma manually. The recommended dilution is 1:10. And the concentration after dilution should be more than 5ng/mL. After manual dilution, multiply the result by the dilution factor. ACCRE analyzer cannot perform automatic dilution for samples.

Quality control

Each bottle of lyophilized quality control should be re-dissolved by purified water to 1.0mL before use.

Quality control can be performed in accordance with local regulations or requirements related to accreditation, as well as requirements defined in the laboratory's quality control procedure.

RESULTS AND INTERPRETATION

Calculation of Results

The results are automatically calculated by the ACCRE analyzer using stored calibration curve which generate by 3-point calibration, and calculated according to a predefined mathematical model, the results expressed in ng/mL.

Interpretation of Results

The detection range is from 0.05ng/mL to 50ng/mL. For samples with cTnI below the upper limit of detection, quantitative determination can be performed; if the sample is lower than the lower limit of detection, the reported result is <0.05ng/mL; if the sample is higher than the upper limit of detection, the reported result is >50ng/mL.

Results of Cardiac Troponin I (CLIA) assays were determined by testing serum specimens from a study in clinical centers with group of totally 328 healthy adult individuals in China. The 99th percentile value is 0.10 ng/mL.

** Please note that results may differ between laboratories due to variations in population and test method. If necessary, each laboratory should establish its own reference range.*

In interpreting the results, patient's clinical condition including symptoms, diseases history, and other relevant data and information should be considered.

LIMITATIONS

1. If the test results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
2. For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
3. Please note that heterophile antibody in human serum, plasma or whole blood can interfere the test result.
4. High concentration of HAMA can also cause a false positive or false negative result.

PERFORMANCE CHARACTERISTICS

Detection limit

LOB (Limit of Blank) = 0.045ng/mL

LOB was determined according to CLSI® EP17-A2 recommendations.

Measurement range

The measurement range is the range of values corresponding to the acceptable performance limits (precision and linearity).

The measurement range of the Cardiac Troponin I (CLIA) assay is: 0.05ng/mL~50 ng/mL.

Linearity

Linearity was evaluated according to CLSI® EP06-A recommendations. The Cardiac Troponin I (CLIA) assay is linear between 0.05ng/mL to 50ng/mL. The absolute linear correlation coefficient (r) is greater than 0.9900.

Precision

A precision study was performed according to CLSI® EP05-A3 recommendations.

The within-lot precision CV% is less than 8%.

The between-lot precision CV% is less than 10%.

Accuracy

The sample which is a control with trueness traceability is used for the detection, and the relative deviation between the detection result and the calibration concentration is within ±10%.

Interference

Potential interference substances were studied according to CLSI® EP07-A3 recommendations. No significant interference was detected up to the maximum.

Substance	Concentration
Hemoglobin	≤500mg/dL
Bilirubin	≤20mg/dL
Triglyceride	≤3000mg/dL
Total Protein	≤10g/dL
Rheumatoid factor	≤1500IU/mL

Cross-reactivity

The Cardiac Troponin I (CLIA) assay is specific for cardiac troponin I. The following muscle proteins were tested and found to have an insignificant effect on the measured cTnI.

Substance	Concentration	Percent Cross-reactivity
Troponin C (cardiac)	1000ng/mL	≤0.1%
Troponin T (cardiac)	1000ng/mL	≤0.1%
Troponin I (skeletal)	1000ng/mL	≤0.1%

HAMA

Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

Hook effect

No hook effect was found up to cardiac troponin I concentrations of 1000ng/mL.

WASTE DISPOSAL

Dispose used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.

It is the responsibility of each laboratory to handle waste and effluents produced according to their nature and degree of hazardousness and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

INDEX OF SYMBOLS

Symbol	Meaning	Symbol	Meaning	Symbol	Meaning
	Consult instructions for use		Contains sufficient for <n> tests		Date of manufacture
IVD	*In vitro* diagnostic medical device		Use-by date		Do not re-use
	Temperature limit	LOT	Batch code	REF	Catalogue number
	Keep away from sunlight		Keep dry		Manufacturer
EC REP	Authorized representative in the European Community/ European Union		Do not use if package is damaged and consult instructions for use	BIO	Contains biological material of animal origin
	Biological risks		Caution	CE	CE marking
	Upright		Fragile, handle with care		Do not roll
CONTROL	Control				

REFERENCES

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4. Kricka L. Interferences in immunoassays - still a threat. Clin Chem 2000; 46: 1037-1038.
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