HIV Ag/Ab Combo (CLIA) PACKAGE INSERT

IVD

[INTENDED USE]

HIV Ag/Ab Combo (CLIA) is a Chemiluminescence Immunoassay test for the qualitative detection of HIV Ag/Ab Combo (HIV Ag/Ab) , clinically mainly used as an auxiliary diagnosis for human immunodeficiency virus infection.
The test must be performed on the ACCRE series analyzers (including ACCRE 6, ACC RE 8, ACCRE 90, ACCRE 100, ACCRE 120, and all other ACCRE series analyzers).

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

[SUMMARY]

AIDS, or Acquired immunodeficiency syndrome, is a seriously contagious immunodeficiency disease caused by the Human immunodeficiency virus (HIV) infection. The global epidemic of HIV can be divided into two types: HIV-1 and HIV-2. When HIV invades the human body, the main target of its attack is a basic component of the immune system cells (T4 lymphocytes: containing CD4 surface antigen), and it will lead to a large number of T4 lymphocytes death, resulting in a sharp reduction of the cells in the human body, and then destroy the immune function of the infected person, causing immune deficiency and reduce or lose resistance to some diseases. After HIV infection, viral RNA is detected first, then p24 antigens, and finally antibodies. Within 10 to 14 days after infection, the level of viral RNA increases exponentially, and then decreases and remains at a stable level, entering the asymptomatic phase of HIV. The level of p24 antigen develops with the increase of viral RNA level. After HIV-1 invasion, p24 antigen appears in the acute infection phase and is considered as an indirect marker of viral replication. Therefore, detection of p24 antigen can shorten the window period of seroconversion.

[ASSAY PRINCIPLES]

The HIV Ag/Ab Combo (CLIA) hereinafter also referred to as the "HIV Ag/Ab" is a sandwich immunoassay. The principle is described as following:
Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent cartridge. All the assay steps are performed automatically by the ACCRE analyzer.
The first step is to add the sample and sample treatment solution to the magnetic beads coated with HIV-1 antigen, HIV-2 antigen and HIV-1 p24 antibody, and then mix, incubate and wash. The second step is to react with the HIV-1 antigen, HIV-2 antigen and HIV-1 P24 antibody labeled with alkaline phosphatase, and then mix and incubate to form a double antigen sandwich immune complex. After the reaction is completed, the magnetic beads are adsorbed by the magnetic field, and unbound substances are removed by washing. After the substrate solution is added, the luminescence intensity is detected by a photomultiplier tube (PMT). After calculating the luminescence signal value of the sample, the S/CO value of Human immunodeficiency virus antigen and antibody in the sample is obtained.

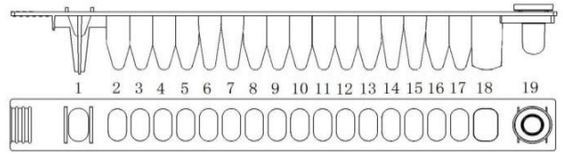
[CONTENT OF THE KIT]

Package: 60 tests/kit with quality controls, 36 tests/kit with quality controls.
Traceability: The calibrators of this kit can be traced to the internal reference substance. For specific calibrator concentration values, see the Calibrator Barcode Sheet for each lot.

Contents	Quantities		Notice
	REF W80A	REF W80C	
HIV Ag/Ab reagent cartridge	60 strips	36 strips	Ready to use
HIV Ag/Ab Calibrator 1 (CAL 1)	1.0mL×1 vial	1.0mL×1 vial	Tris buffer, ProClin300,Tween20 BND, BSA .
HIV Ag/Ab Calibrator 2 (CAL 2)	1.0mL×1 vial	1.0mL×1 vial	Tris buffer, ProClin300, Tween20 BND, BSA, HIV-1 positive sample.
HIV Ag/Ab Quality Control level 1 (QC 1)	1.0mL×1 vial	1.0mL×1 vial	Tris buffer, ProClin300, Tween20 BND, BSA.
HIV Ag/Ab Quality Control level 2 (QC 2)	1.0mL×1 vial	1.0mL×1 vial	Tris buffer, ProClin300, Tween20 BND, BSA, HIV-1 positive sample.
HIV Ag/Ab Quality Control level 3 (QC 3)	1.0mL×1 vial	1.0mL×1 vial	Tris buffer, ProClin300, Tween20 BND, BSA, HIV-1 p24 Antigen.
Instruction for Use	1	1	N/A
Reagent Registration Card	1	1	N/A
Calibrator Barcode Sheet	1	1	N/A
Quality Control Sheet	1	1	N/A

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

The Reagent Cartridge
The strip consists of 19 wells. The 1st well is the sample well and the last 19th well is the reading well for chemiluminescent signal. From the 2nd to the 18th well are all covered with a labeled, 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 cartridges. And please do not interchange integral component from different reagents or lots.



Description of the reagent cartridge

Well	Component	Content	Volume
5	Enzyme Label (R2)	ALP (alkaline phosphatase) labeled HIV-1 antigen, HIV-2 antigen and HIV-1 p24 antibody, MES Buffer, ProClin300	100µL
7	Magnetic Particles (R1)	HIV-1 antigen, HIV-2 antigen and HIV-1 p24 antibody coated magnetic particles ,Tris buffer, ProClin300	50µL
9	Sample Treatment Solution (R3)	BSA, Tris buffer, ProClin300	50uL
2, 3, 10, 11, 12	Wash Solutions	Tris buffer, ProClin300, BND	350µL
16	Substrate Solution	Disodium [(4-chlorophenyl)sulfanyl] (10-methyl-9(10H)-acridinylidene) methyl phosphate	200µL

Note: Well 1,4,6,8,13,14,15,17,18 are empty.

[MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED]

- Sample diluent (manufactured by Tisenc), if needed.
- Pipette with disposable tip to dispense 200 µL.
- Powderless and disposable gloves.
- Disposable tips for ACCRE analyzer
- 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.
- 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 HIV Ag/Ab Combo (CLIA) upright at 2-8 °C, and kit can be stored for 18 months from manufactured date. After the reagent cartridge is taken out from the refrigerator to equilibrate, the testing should be completed within 2 hours.
- Store the calibrators and quality controls at 2-8 °C till expiry date. When opened, the calibrators and/or controls will be stable for 30 days at 2-8 °C.
- Keep away from sunlight.
- Do not freeze reagents cartridge.

[SAMPLES]

The sample volume for HIV Ag/Ab Combo (CLIA) assay is 100µL, please note that at least 125µL of sample has to be pipetted manually into the reagent cartridge.

Sample type and collection
Human serum or plasma (Heparin lithium/Heparin sodium/Sodium citrate/EDTA-K_2/EDTA-Na_2)
Types of tubes:
- Plastic tube with clot activator,
- Plastic tube with clot activator and separation gel,
- Plastic tube with heparin lithium,
- Plastic tube with heparin sodium,
- Plastic tube with sodium citrate,
- Plastic tube with EDTA-K_2,
- Plastic tube with EDTA-Na_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 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 a vortex-type mixer. If necessary, clarify samples by centrifuging before testing.

Sample stability
Samples (serum and plasma) can be stored at room temperature (15-30 ℃) for up to 8 hours or at 2-8 ℃ for up to 14 days; if longer storage is required, freeze the serum or plasma at -20 °C or below -20 °C, without exceeding 3 freeze/thaw cycle.

[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.
Calibration is necessary under the following conditions:
(1) New reagent lot number applied;
(2) Same lot of reagents used more than 4 weeks;
(3) QC out of control;
(4) When necessary, for example: system maintenance or repair that may affect the analytic performance.

Test Procedure
1. Remove the kit from storage at 2-8 °C and take out the required number of reagent cartridges. Allow the reagent cartridges, specimens, calibrators, and/or controls to equilibrate to room temperature (15-30°C) prior to testing.
2. Use each assay strips for each sample, calibrator or control, respectively.
3. Place the reagent cartridges into the reagent rack.
4. Manually pipette the Sample, Calibrator, or Control into the sample well of each reagent cartridge .
Please note that at least 125μL sample has to be pipetted manually into the reagent cartridge and 100μL sample 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 USER MANUAL.
8. HIV Ag/Ab Combo (CLIA) assay 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.

Quality control
Quality control should 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
After completing the calibration test, use the RLU values of two calibration samples to calculate and set a correct and effective critical value for the system, which is Cut off.
Calculate the sample results based on the critical values, using the following formula:
S/CO=Sample RLU/CUT OFF.

Interpretation of Results
By detecting samples of 248 HIV infected individuals and 450 normal individuals, the positive judgment value is determined using the receiver operating characteristic curve (ROC) method as follows:
S/CO < 1.0, indicates negative result.
S/CO ≥ 1.0, indicates positive result.
In interpreting the results, patient's clinical condition including symptoms, diseases history, and other relevant data and information should be considered.

[LIMITATIONS]

1. The test results of this reagent kit are for clinical reference only and should not be used as the sole basis for clinical diagnosis and treatment. They should be used in conjunction with other clinical tests, medical history, and laboratory test results.
2. This reagent kit has not yet established performance indicators for body fluid samples other than serum and plasma.
3. If the test results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
4. Unreasonable sample collection, transportation, processing, and improper experimental operations and environments may lead to false negative or false positive results.

[PERFORMANCE CHARACTERISTICS]

Detection Limit
Limit of Detection (LoD): 1.05 S/CO
The Limit of Detection was determined in accordance with the CLSI® EP17-A2 recommendations.

Precision
The precision study was performed according to CLSI® EP05-A3 recommendations.
The within-lot precision CV% is less than 10%.

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

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin	≤ 20 mg/dL
Triglyceride	≤ 3000 mg/dL
Rheumatoid factor	≤ 200 IU/mL

Cross-reactivity
No cross-reactivity with positive samples for Treponema Pallidum (TP), hepatitis C virus (HCV), macrophage virus (CMV), herpes simplex virus (HSV), hepatitis A virus (HAV), hepatitis B virus antigen, etc.

[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
	*In vitro* diagnostic medical device		Use-by date		Do not re-use
	Temperature limit		Batch code		Catalogue number
	Keep away from sunlight		Keep dry		Manufacturer
	Do not roll		Do not use if package is damaged		Contains biological material of animal origin
	Biological risks		Caution		Control
	Upright		Fragile, handle with care		

[REFERENCES]

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