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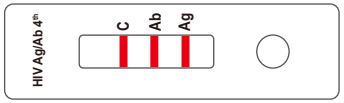
HIV Ag/Ab 4th Gen. Rapid Test Instructions for Use

PRODUCT NAME
HIV Ag/Ab 4th Gen. Rapid Test

INTENDED USE
HIV Ag/Ab 4th Gen. Rapid Test is a lateral flow immunoassay for the qualitative detection of anti-HIV-1 (including O) and anti-HIV-2 virus antibodies (IgG, IgM, IgA), and HIV-1 p24 antigen in human serum, plasma or whole blood. It is intended to be used by healthcare professionals to aid in the diagnosis of infection with HIV.
Any use or interpretation of this preliminary test result must also rely on other clinical findings and the professional judgment of health care providers. Alternative test method(s) should be considered to confirm the test result obtained by this device.

SUMMARY
Human immunodeficiency virus type I and type II (HIV-1 and HIV-2) are enveloped, single- stranded, positive-sense RNA viruses. The causative relationship between HIV-1 and HIV-2 viruses and acquired immunodeficiency syndrome (AIDS) has been established over decades. HIV-1 has been isolated from patients with AIDS and AIDS-related complex and from healthy individuals with a high risk for developing AIDS1. HIV-2 has been isolated from West African AIDS patients and from sero-positive asymptomatic individuals. HIV-1 is much more prevalent than HIV-2 worldwide. Recent studies have shown that over 30 million people have been infected with HIV-1.
Both HIV-1 and HIV-2 viruses can elicit strong immune responses including the production of antiviral antibodies. Presence of specific anti-HIV-1 or HIV-2 virus antibodies in whole blood, serum or plasma indicates the exposure of an individual to HIV-1 or HIV-2 which is of great value for clinical diagnosis. Tests that detect HIV p24 antigen may be useful for the early diagnosis of HIV as p24 antigen is one of the earliest markers of HIV infection. It has been suggested that HIV infection is detectable with an HIV p24 antigen test 6 days earlier than an antibody test.
The HIV Ag/Ab 4th Gen. Rapid Test utilizes recombinant gp-120-4th, gp36 and anti-p24 antibodies to qualitatively detect antibodies (IgG, IgM, IgA) to anti-HIV-1 (including O) or HIV-2 viruses and HIV-1 p24 antigen in patient serum, plasma or whole blood. The test can be performed within 15 minutes by minimally skilled personnel without cumbersome laboratory equipment.

PRINCIPLE
The HIV Ag/Ab 4th Gen. Rapid Test is a lateral flow immunochromatographic assay. The test strip in the cassette consists of: 1) a colored conjugate pad containing recombinant HIV- gp120-41 and gp-36 antigens conjugated with colloidal gold (HIV conjugates), monoclonal anti-HIV-p24 antibody conjugated with colloidal gold (p24 conjugates) and a control antibody conjugated with colloidal gold, 2) a nitrocellulose membrane strip containing two test lines (Ag line and Ab line) and a control line (C line). The Ab line is pre-coated with HIV-gp120-41 and HIV-2 gp-36 antigens for the detection of antibodies to HIV-1 including O or HIV-2, the Ag line is pre-coated with another monoclonal anti-HIV-p24 antibody for the detection of p24 antigen, and theCline is pre-coated with a control line antibody.
When an adequate volume of test specimen is dispensed into the sample well of the test cassette, the specimen migrates by capillary action across the cassette. IgG, IgM or IgA antibodies to HIV- 1 or HIV-2, if present in the specimen, migrate through the conjugate pad where they bind to the HIV conjugates. The immunocomplex is then captured on the membrane by the pre-coated HIV- 1+2 antigens forming a colored Ab line, indicating a positive test result. Absence of the Ab line suggests an HIV-1 and HIV-2 antibody negative result.
HIV-1 p24 antigen, if present in the specimen, migrates through the conjugate pad where it binds to the p24 conjugates. The immunocomplex is then captured on the membrane by the pre-coated HIV-p24 antibody, forming a colored Ag line, indicating a positive test result. Absence of the Ag line suggests a HIV-p24 antigen negative result.
The test contains an internal control (C line) which should exhibit a colored line of the immunocomplex of control antibodies regardless of the presence of any colored test lines. If the C line does not develop, the test result is invalid and the specimen must be retested with another device.



REAGENTS AND MATERIALS PROVIDED
1. Individually sealed foil pouches containing:
   a. One cassette device
   b. One desiccant
2. Capillary tubes (20 μL)
3. Sample diluent (5 mL/bottle)
4. Instructions for Use

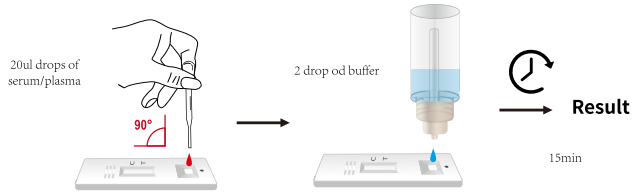
MATERIALS REQUIRED BUT NOT PROVIDED
1. Clock or timer
2. Lancing device for whole blood test

WARNINGS AND PRECAUTIONS
For In Vitro Diagnostic Use
1. Read these Instructions for Use completely before performing the test. Failure to follow the instructions could lead to inaccurate test results.
2. Do not open the sealed pouch until ready to conduct the assay.
3. Do not use expired devices or components.
4. Bring all reagents to room temperature (15-30°C) before use.
5. Do not use components from any other type of test kit as a substitute for the components in this kit.
6. Do not use hemolyzed blood for testing.
7. Wear protective clothing and disposable gloves while handling the kit reagents and clinical specimens. Wash hands thoroughly after performing the test.
8. Users of this test should follow the US CDC Universal Precautions for prevention of transmission of HIV, HBV and other blood-borne pathogens.
9. Do not smoke, drink or eat in areas where specimens or kit reagents are being handled.
10. Dispose of all specimens and materials used to perform the test as bio-hazardous waste.
11. Handle the negative and positive controls in the same manner as patientspecimens.
12. The test result should be read 15-20 minutes after a specimen is applied to the sample well of the device. Any results interpreted outside 15-20 minutes should be considered invalid and must be repeated.
13. Do not perform the test in a room with strong air flow, i.e. an electric fan or strong air conditioning.

REAGENT PREPARATION AND STORAGEINSTRUCTIONS
All reagents are ready to use as supplied. Store unused test devices unopened at 2-30°C. If stored at 2-8°C, ensure that the test device is brought to room temperature before opening. The test device is stable through the expiration date printed on the sealed pouch. Do not freeze or expose the kit to temperatures above 30°C.

SPECIMEN COLLECTION AND STORAGE
Consider any materials of human origin as infectious and handle them using standard bio-safety procedures.
Plasma/Serum
Step 1: Collect blood specimen into collection tube containing EDTA, citrate or heparin for plasma or collection tube containing no anticoagulants for serum by venipuncture.
Step 2: To make plasma specimen, centrifuge collected specimens and carefully withdraw the plasma into a new pre-labeled tube.
Step 3: To make serum specimen, allow blood to clot, then centrifuge collected specimens and carefully withdraw the serum into a new pre-labeled tube.
Test specimens as soon as possible after collecting. Store specimens at 2-8°C, if not tested immediately. The specimens can be stored at 2-8°C for up to 5 days. The specimens should be frozen at -20°C for longer storage.
Avoid multiple freeze-thaw cycles. Prior to testing, bring frozen specimens to room temperature slowly and mix gently. Specimens containing visible particulate matter should be clarified by centrifugation before testing.
Do not use samples demonstrating gross lipemia, gross hemolysis or turbidity in order to avoid interference with result interpretation.
Whole Blood
Step 1: Drops of whole blood can be obtained by either fingertip puncture or venipuncture. Collect blood specimen into a collection tube containing EDTA, citrate or heparin. Do not use hemolyzed blood for testing.
Whole blood specimens should be stored in refrigeration (2-8°C), if not tested immediately. The specimens must be tested within 24 hours of collection.

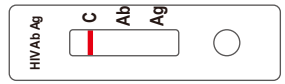
ASSAYPROCEDURE
Step 1: Bring the specimen and test components to room temperature if refrigerated or frozen.
Once the specimen is thawed, mix well prior to performing the assay.
Step 2: When ready to test, open the pouch at the notch and remove the device. Place the test device on a clean, flat surface.
Step 3: Be sure to label the device with the specimen's ID number.
Step 4: Fill the capillary tube with specimen not exceeding the specimen line as shown in the images below. The volume of specimen is approximately 20 μL. For better precision, transfer specimen using a pipette capable of delivering a 20 μL volume.
Holding the capillary tube vertically, dispense the entire specimen into the center of the sample well making sure that there are no air bubbles.
Immediately add 2 drops (about 60-80 μL) of sample diluent to the sample well with bottle positioned vertically.



Step 5: Set up the timer.
Step 6: Read results at 15-20 minutes. Positive results may be visible as soon as 1 minute. Negative results must be confirmed at the end of the 20 minutes only. However, any results interpreted outside 15-20 minutes should be considered invalid and must be repeated. Discard used device after interpreting the results following local laws governing the disposal of device.

QUALITY CONTROL
1. Internal Control: This test contains a built-in control feature, the C line. The Cline Copyright 2020 by CTK Biotech, Inc.
develops after adding the specimen and the sample diluent. If the Cline does not develop, review the entire procedure and repeat the test with a new device.
2. External Control: Good Laboratory Practice recommends using external controls, positive and negative, to assure the proper performance of the assay, particularly under the following circumstances:
a. A new operator uses the kit, prior to performing the testing of the specimens.
b. A new lot of test kits is used.
c. A new shipment of kits is used.
d. The temperature during storage of the kits falls outside of 2-30°C.
e. The temperature of the test area falls outside of 15-30°C.
f. To verify a higher than expected frequency of positive or negative results.
g. To investigate the cause of repeated invalid results.

INTERPRETATION OF ASSAYRESULT
1. NEGATIVE RESULT: If only the C line develops, the absence of any color in both test lines (Ab and Ag) indicates that neither HIV antibodies nor HIV p24 antigen is detected in the specimen. The result is negative or non-reactive.



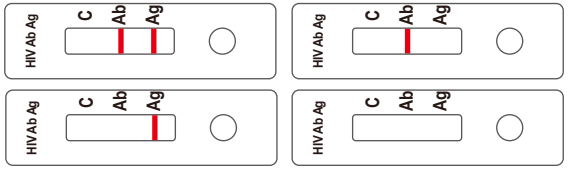
2. POSITIVE OR REACTIVE RESULT:
2.1 In addition to the presence of the C line, if the Ab line develops, the test indicates the presence of antibodies to HIV-1 and/or HIV-2 in the specimen. The result is HIV 1+2 Ab positive or reactive.

2.2 In addition to the presence of the C line, if the Ag line develops (including faint line), the test indicates the presence of HIV p24 antigen in the specimen. The result is HIV p24 antigen positive or reactive.

2.3 In addition to the presence of the C line, if both the Ab line and the Ag line develop, the result is both HIV 1+2 Ab and p24 antigen positive or reactive.

Samples with reactive results should be confirmed with alternative testing method(s) and clinical findings before a diagnosis is made.

3 INVALID: If no C line develops, the assay is invalid regardless of any color in the test line as indicated below. Repeat the assay with a new device.



PERFORMANCE CHARACTERISTICS

1. Clinical Performance

A total of 350 clinical samples were collected and tested by the OnSite HIV Ag/Ab 4th Gen. Rapid Test and by an SFDA licensed HIV 1+2 Ab reference kit. Comparisons for all subjects are shown in the following table:

Reference		EIA		Total Results
HIV Ag/Ab 4th Gen. Rapid Test	Results	Positive	Negative	
	Positive	105	0	105
	Negative	0	245	245
Total Results		105	245	350

Relative Sensitivity: 100% (95% CI:97.5-100%)
Relative Specificity: 100% (95% CI:98.9-100%)
Overall Agreement: 100% (95% CI:99.2-100%)

2. Specificity

The specificity of the OnSite HIV Ag/Ab 4th Gen. Rapid Test was evaluated with 1,000 specimens from a normal population and 200 specimens from pregnant women. No false positive results were detected.

3. Boston Biomedica Inc (BBI) Seroconversion Panel

The performance of the HIV Ag/Ab 4th Gen. Rapid Test was evaluated using BBI seroconversion panel PRB967. The results are shown in the following table:

PRB-967 panel		BioMerieux HIV Ag pg/mL	Abbott HIV1/2 Ab s/co	HIV Ag/Ab 4th Gen. Rapid Test	
Members ID	Days bleed			Ag reactivity	Ab reactivity
PRB967-04	17	>400.0	2.5	Positive	Positive
PRB967-05	19	>400.0	8.3	Negative	Positive
PRB967-06	24	10.5	8.4	Negative	Positive

Note: s/co < 1: Negative, s/co >=1: Positive

4. Cross-Reactivity

No false positive antibodies to HIV-1 and/or HIV-2 or HIV p24 antigen test results were observed on 4-20 specimens from the following disease states or special conditions, respectively:

HAV	HBV	HCV	HEV	H. pylori
TB	Syphilis	ANA	HAMA	RF (up to 2,500 IU/mL)

5. Interference

Common substances (such as pain and fever medication and blood components) may affect the performance of the HIV Ag/Ab 4th Gen. Rapid Test. This was studied by spiking these substances into three levels of HIV Ag and HIV Ab standard controls (negative, weak positive, strong positive). The results demonstrate, at the concentrations tested, the substances studied do not affect the performance of the HIV Ag/Ab 4th Gen. Rapid Test.

List of potentially interfering substances and concentrations tested:

1. Bilirubin	20 mg/dL	5. Human IgG	150 mg/dL
2. EDTA	3.4 μmol/L	6. Heparin	3,000 U/L
3. Glucose	55 mmol/L	7. Salicylic acid	4.34 mmol/L
4. Hemoglobin	2 g/L	8. Sodium citrate	3.8%

LIMITATIONS OF TEST

1. The Assay Procedure and the Interpretation of Assay Result sections must be followed closely when testing for the presence of antibodies to HIV and/or p24 antigen in serum, plasma or whole blood from individual subjects. Failure to follow the procedure may give inaccurate results.
2. The HIV Ag/Ab 4th Gen. Rapid Test is limited to the qualitative detection of antibodies to HIV-1 and/or HIV-2 and HIV p24 in human serum, plasma or whole blood. The intensity of the test line does not correlate with the antibody titer or antigen level of the specimen.
3. A negative or non-reactive result for an individual subject indicates absence of detectable anti-HIV-1, anti-HIV-2 and/or HIV p24 antigen. However, a negative or non-reactive test result does not preclude the possibility of exposure to or infection with HIV-1 and/or HIV- 2.
4. A negative or non-reactive result can occur if the quantity of the anti-HIV-1/anti-HIV-2 antibodies and/or HIV p24 antigen present in the specimen is below the detection limits of the assay or the antibodies/antigen that are detected are not present during the stage of disease in which a sample is collected.
5. Infection may progress rapidly. If the symptoms persist while the result from HIV Ag/Ab 4th Gen. Rapid Test is negative or non-reactive, it is recommended to test with alternative test methods.
6. Some specimens containing unusually high titers of heterophile antibodies or rheumatoid factor may affect expected results.
7. The results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

INDEX OF SYMBOLS

Symbol	Used For	Symbol	Used For
	Use-by date		Consult instructions for use
LOT	Batch code	IVD	In vitro diagnostic medical device
	Temperature limit		Manufacturer
	Please don't reuse it		Keep away from sunlight
	Don't use the product when the package is damaged		Keep dry
	Date of manufacture	Σ	Tests per kit
CE	CE Mark		Biological Risks
EC REP	Authorized representative in the European Community		