

MULTISURE® HIV Rapid Test

Instructions For Use

CE 0123

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Note: Changes Highlighted.

REF 43030-020 (20 tests)

TRADE NAME AND INTENDED USE

The MP Diagnostics MULTISURE® HIV Rapid Test is a qualitative immunochromatographic assay for the rapid *in vitro* detection and differentiation of antibodies to HIV-1 and HIV-2 in human serum, plasma, finger pricked whole blood or whole blood with anti-coagulants. It is intended for professional use as a diagnostic test for HIV-1 and/or HIV-2 infection.

INTRODUCTION

Human Immunodeficiency Viruses (HIVs) are pathogenic retroviruses that cause HIV infection and the acquired immunodeficiency syndrome (AIDS)^[1], which remains one of the most important global public health threats. It was estimated that 35 million people worldwide are living with HIV, with 2.1 million newly infected; and 1.5 million of AIDS-related deaths (UNAIDS, 2013)^[2]. HIV infection causes gradual failure of the immune system in human, leading to an increased susceptibility of the body to life-threatening opportunistic infections and cancers.

HIV was first discovered in two separate research groups independently in 1983^[3-4]. Two types of HIV have been identified and characterized: HIV-1 and HIV-2. Both types are transmitted by sexual contact, through contaminated blood, body fluids and from mother to child during pregnancy or breastfeeding. HIV-1 is the major cause of HIV infection and AIDS in the world^[5]. HIV-2 is less common and less infective^[6]. Studies of the geographic distribution of HIV infections reveal that HIV-1 is the predominant type worldwide, HIV-2 is largely concentrated in West Africa^[6, 7].

Prevention and treatment of AIDS depends on the accurate laboratory diagnosis of HIV infections, which is essential to identify HIV infected persons who could benefit from treatment and to reduce HIV transmission^[8]. HIV infections elicit immune responses and induce HIV specific antibodies in human^[9]. The serological methods, such as Enzyme-linked Immunosorbent Assay (ELISA), Colloidal Gold Immunochromatographic Rapid Test, and Western Blot (WB) are widely used in the laboratory diagnosis of HIV-1 and HIV-2 infection^[10, 11].

The MP Diagnostics MULTISURE® HIV Rapid Test is intended as a rapid diagnostic test, developed to detect antibodies specific to HIV-1 gp120, HIV-1 gp41, HIV-1 p24 (also react with HIV-2) and HIV-2 gp36 antigens in human serum, plasma, finger pricked whole blood or whole blood with anti-coagulants.

CHEMICAL AND BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The MP Diagnostics MULTISURE® HIV Rapid Test kit is an indirect solid-phase immunochromatographic assay, based on MP Biomedicals' proprietary Reverse Flow technology (US Patent No.: 6,316,205) for simultaneous and differential detection of antibodies to HIV-1 and HIV-2 in human serum, plasma, finger pricked whole blood or whole blood with anti-coagulants.

Highly purified recombinant antigens gp120 and gp41 representing HIV-1, gp36 representing HIV-2 and p24 (reactive for both HIV-1 and HIV-2) are striped on the membrane as 4 separate test lines.

The antibodies in the test sample (serum, plasma, finger pricked whole blood or whole blood with anti-coagulants) form antibody antigen complexes with HIV specific recombinant antigens immobilized on nitrocellulose membrane in the test viewing window as the test sample migrates upward from the sample well.

The bound antibody-antigen complexes are subsequently detected by goat anti-human IgG gold conjugate carried by chase buffer that flows downward giving a pink-purple color. The control line containing protein A captures human IgG from patient's sample, subsequently binds with the anti-human IgG gold conjugate. The appearance of control line serves to validate the proper addition and migration of sample and chase buffer, as well as the resolubilised anti-human IgG gold conjugate.

DESCRIPTION OF SYMBOLS USED

The following are graphical symbols used in or found on MP Diagnostics' products and packaging. These symbols are the most common ones appearing on medical devices and their packaging.

	Use by		In vitro diagnostic medical device
	Batch Code Synonyms for this are: Lot Number Batch Number		Catalogue Number Synonyms for this are: Reference Number Reorder Number
	Temperature Limitation		Caution
	Manufacturer		Consult Instructions for Use
	Contains sufficient for <n> tests		Do not reuse
	Authorized representative in the European Community		

KIT COMPONENTS		
DEVICE	MP Diagnostics MULTISURE® HIV Rapid Test Device Incorporated with recombinant HIV proteins. Packed in individually sealed pouch with a desiccant. Store at 2°C - 28°C	20 devices
APPLICATOR	SAMPLE APPLICATOR With marking of 20µl and 25µl.	20 pieces
BUFFER	CHASE BUFFER Contains sodium azide as preservative. Store at 2°C - 28°C	1 bottle (5 ml)
	INSTRUCTIONS FOR USE	1 copy

HEALTH AND SAFETY INFORMATION

- In case of an accident or contact with eyes, rinse immediately with plenty of water and seek medical advice.
- Consult a physician immediately in the event that contaminated materials are ingested or come in contact with open lacerations, or other breaks in the skin.
- Wipe any spills of sera, plasma or blood promptly with 0.5% sodium hypochlorite solution.
- Autoclave all used and contaminated materials at 121°C, 15 p.s.i. for 30 minutes before disposal. Alternatively, decontaminate materials in 0.5% sodium hypochlorite solution for 30-60 minutes before disposal in biohazard waste-bags.

Pursuant to EC regulation 1272/2008 (CLP), hazardous components are classified and labelled as follows:

Component:	Chase Buffer
Signal Word:	Warning
Pictogram:	
Hazard Statements:	H319 Causes serious eye irritation.
Precautionary Statements:	P264 Wash hands thoroughly after handling. P280 Wear protective gloves/protective clothing/eye protection/face protection.
Supplemental Statements:	EUH 210 Safety Data Sheet is available on request
Contains:	1% Triton X-100

ANALYTICAL PRECAUTIONS:

- The sample applicator is for single use only. DO NOT re-use the sample applicator.
- Each sealed test device is for single use only. DO NOT re-use the test device.
- For *in vitro* diagnostic use only.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when samples are assayed.

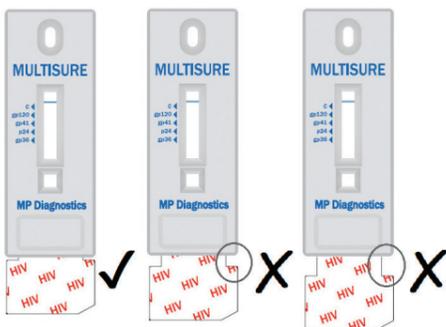
ASSAY PROCEDURE

IMPORTANT: Strict adherence to the assay procedure will ensure optimal performance. Deviations from the procedure may lead to aberrant results.

Note :

- Allow the kit to warm to room temperature (25°C ± 3°C) before running the assay.
- For best results, conduct the assay at room temperature (25°C ± 3°C).

- Open the pouch by tearing at the tear notch on the right side of the pouch to avoid accidental pulling of pull tab.
- Discard the device if the pull tab is not fully inserted into test device. Refer to diagrams below.



- Label the test device with the sample name.
- Proceed with the assay procedures as shown in the diagrams below.

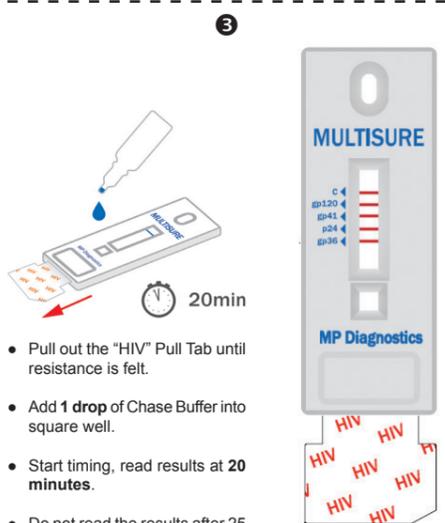
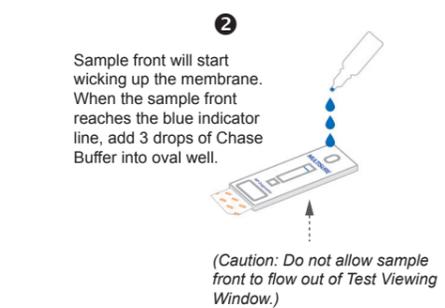
Assay Procedures for MULTISURE® HIV Rapid Test

1

For Serum/Plasma Samples For Whole Blood Samples

Add 25µl serum/plasma sample into square well.

Add 20µl whole blood sample into square well, followed by 1 drop of chase buffer into the same well.



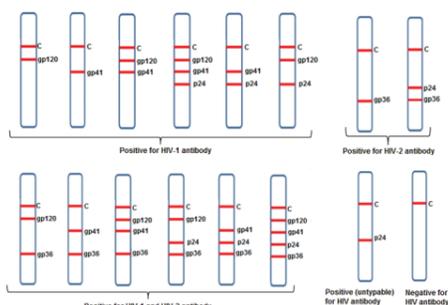
- Pull out the "HIV" Pull Tab until resistance is felt.
- Add 1 drop of Chase Buffer into square well.
- Start timing, read results at 20 minutes.
- Do not read the results after 25 minutes.

Example of test device with all visible test lines

QUALITY CONTROL

The control line is an internal procedure control. Absence of control line indicates insufficient/improper sample volume, incorrect assay technique used or faulty device. The assay procedure should be reviewed before repeating with a new device.

INTERPRETATION OF RESULTS



1. Positive for HIV-1 antibody

A test is HIV-1 positive if it meets any of the following criteria:

- Control Line (C) appears with visible gp120 test line (with or without visible gp41 and/or p24 test lines)
- Control Line (C) appears with visible gp41 test line (with or without visible gp120 and/or p24 test lines)
- Control Line (C) appears with visible gp120 & gp41 test lines (with or without visible p24 test line)

2. Positive for HIV-2 antibody

A test is HIV-2 positive if Control Line (C) appears with visible gp36 test line (with or without visible p24 test line)

3. Positive for HIV-1 and HIV-2 antibody

A test is HIV-1 and HIV-2 positive if it meets any of the following criteria:

- Control Line (C) appears with visible gp120 & gp36 test lines (with or without visible gp41 and/or p24 test lines)
- Control Line (C) appears with visible gp41 & gp36 test lines (with or without visible gp120 and/or p24 test lines)
- Control Line (C) appears with visible gp120 & gp41 & gp36 test lines (with or without visible p24 test line)

4. Positive (untypable) for HIV antibody

A test is HIV positive (untypable) if Control Line (C) appears with visible p24 test line only.

5. Negative for HIV antibody

A test is negative if Control line (C) appears and Test line(s) are not visible.

6. Invalid

A test is invalid if Control line (C) is absent. The assay should be repeated using a new device.

Note: Any test line (with any shade of intensity) that appears at 20-25 minutes indicates HIV positive result and should be interpreted based on the criteria above.

LIMITATIONS OF THE PROCEDURE

The MP Diagnostics MULTISURE® HIV Rapid Test is for *in vitro* diagnostic use and for the detection and differentiation of HIV antibodies in serum, plasma, finger pricked whole blood or whole blood with anti-coagulants. This test is not for determining the quantitative value or the rate of increase in HIV antibodies.

Optimal assay performance requires the strict adherence to the assay procedure described. Deviation from the procedure may lead to aberrant results.

A **POSITIVE** result may indicate infection with HIV-1 or HIV-2 virus, a diagnosis of AIDS can only be made clinically if a person meets the case definition of AIDS established by the Centre for Disease Control (USA), the World Health Organization or other relevant authorities. Specimens obtained from HIV patients who are undergoing HIV treatment may result in weak test line(s) or negative results on MP Diagnostics MULTISURE® HIV Rapid Test. A **NEGATIVE** result does not exclude the possibility of exposure to or infection with HIV.

- Handle all samples as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of samples.
- Optimal assay performance requires **STRICT ADHERENCE** to the assay procedure described in this Instruction For Use. Deviations from the procedure may lead to aberrant results.
- Do not interchange reagents between kit lots.
- Do not use kit components beyond the expiry date printed on the kit box.
- The chase buffer reagent contains sodium azide as a preservative. Handle reagent carefully to avoid spills on work surface. Clean up spills with absorbent paper and water.
- Reagents supplied should not present a hazard to health if used in accordance to the instructions stated.
- For best results, allow all reagents and samples to reach room temperature (25°C ± 3°C) before use.
- Humidity and temperature can adversely affect results.
- DO NOT use the test device if the seal of the pouch is broken.
- Conduct the test as soon as possible within 1 hour after removing the test device from the pouch.
- DO NOT use the test device if the pull tab is not fully inserted, i.e. pre-pulled.
- Ensure lighting is adequate for the interpretation of results. The test should be read from a comfortable distance without manipulating the test device. As a rule of thumb, lighting is sufficient if text printed on the test device can be read without difficulty.

STORAGE

- Store the kit and its components at 2°C - 28°C.
- Do not freeze the kit and its components.
- The test device must remain in the sealed pouch until use.
- Do not use after the expiry date printed on the pouch.

MATERIAL REQUIRED BUT NOT PROVIDED

- Timer
- Lancet
- Alcohol swabs

SPECIMEN COLLECTION

Whole blood can be collected in anti-coagulant containing tubes and used as outlined in the assay procedure immediately or stored at 2°C to 8°C for not more than 72 hours before use.

The presence of 6 anti-coagulants, Acid Citrate Dextrose (ACD), Citrate-phosphate-dextrose (CPD), Ethylenediaminetetraacetic acid (EDTA), Potassium Oxalate (K-Oxalate), Lithium Heparin (Li Hep) and Sodium Citrate (Na Citrate) were found to have no effects on the performance of MP Diagnostics MULTISURE® HIV Rapid Test.

Serum / plasma samples should be stored at 2°C to 8°C if the test is to be run within 7 days of collection or frozen at -20°C or colder if the test is to be delayed for more than 7 days. Clear, nonhemolyzed samples are preferred. Lipemic, icteric or contaminated (particulate or bacterial) samples should be filtered (0.45µm) or centrifuged before testing.

Repeated freeze-thawing of the sample is not recommended. Do not use specimens (serum & plasma) with more than five (5) freeze-thaw cycles.

PERFORMANCE CHARACTERISTICS

Total Diagnostic Performance

Diagnostic Parameter	Performance of MP Diagnostics MULTISURE® HIV Rapid Test	95% Confidence Interval
Sensitivity (n=801)	100.00%	99.54% to 100.00%
Specificity (n=2057)	99.12%	98.62% to 99.48%
Positive Predictive Value	97.80%	96.55% to 98.69%
Negative Predictive Value	100.00%	99.82% to 100.00%

Sensitivity

Study	Category	Total Sample Size	Diagnostic Sensitivity of MP Diagnostics MULTISURE® HIV Rapid Test
In-house Study	HIV-1 positive	516	100.00% (516/516)
	HIV-2 positive	122	100.00% (122/122)
	HIV positive (untypable)	3	100.00% (3/3)
Clinical Evaluation	HIV positive	160	100.00% (160/160)
Total		801	100.00% (801/801)

Specificity

Study	Category	Total Sample Size (n)	Diagnostic Specificity of MP Diagnostics MULTISURE® HIV Rapid Test
In-house Study	Blood Donors /Healthy Donors	1184	99.32% (1176/1184)
In-house Study	Hospitalized/ Clinical	193	100.00% (193/193)
Clinical evaluation	Clinical	222	98.20% (218/222)
In-house Study	Cross-reactive	100	99.00% (99/100)
In-house Study	Interference	103	100.00% (103/103)
In-house study /Clinical evaluation	Pregnancy	235	97.87% (230/235)
Clinical evaluation	Anti <i>E-coli</i> Positive	20	100.00% (20/20)
Total		2057	99.12% (2039/2057)

Potential cross-reacting

Sample Profile	Total Sample Size	Performance of MP Diagnostics MULTISURE® HIV Rapid Test
Rheumatoid Factor (RF)	10	90.00% (09/10)
Syphilis	11	100.00% (11/11)
Hepatitis A	10	100.00% (10/10)
HBsAg	10	100.00% (10/10)
Hepatitis C	10	100.00% (10/10)
Epstein-Barr virus (EBV)	10	100.00% (10/10)
Human T-lymphotropic Virus Type I (HTLV-I)	11	100.00% (11/11)
Human T-lymphotropic Virus Type II (HTLV-II)	8	100.00% (08/08)
Cytomegalovirus (CMV)	10	100.00% (10/10)
Hepatitis E	10	100.00% (10/10)
Total	100	99.00% (99/100)

Potential Interferences

Sample Profile	Total Sample Size	Performance of MP Diagnostics MULTISURE® HIV Rapid Test
Icteric (= 1-10mg/DL)	10	100.00% (10/10)
Hemolyzed (= 25-100mg/DL)	10	100.00% (10/10)
Triglyceride (1100 – 2593mg/dL)	12	100.00% (12/12)
Lipemic (= 60-150mg/DL)	10	100.00% (10/10)
Total Protein (9.1-9.6 g/dL)	8	100.00% (08/08)
Total bilirubin (5.5 – 42.9 g/dL)	10	100.00% (10/10)
Anti-streptolysin O (ASO) (200-400IU/ml)	10	100.00% (10/10)
Antinuclear Antibody (ANA)	10	100.00% (10/10)
Autoimmune Disease	11	100.00% (11/11)
Diabetes	4	100.00% (04/04)
Intravenous Drug User	8	100.00% (08/08)
Total	103	100.00% (103/103)

Differentiation of HIV-1 and HIV-2

Serotype	Total Sample Size	Accuracy of differentiation by MP Diagnostics MULTISURE® HIV Rapid Test
HIV-1	530	97.55% (517/530)
HIV-2	132	93.94% (124/132)

Detection of HIV-1 and HIV-2 subtypes

Serotype^	Total Sample Size	Performance of MP Diagnostics MULTISURE® HIV Rapid Test
HIV-1	89*	100% (89/89)
HIV-2	4	100% (4/4)

* Including Group M (Subtype A, B, C, D, E, F, G, H, J, K, BC, C/E, CRF01_AE, CRF02_AG, CRF02_AB, E/F, G/CRF02, H/A1, K/CRF09, CRF01/CRF15) & Group O

^ Source of panels:

- HIV worldwide Performance Panel WWRB301, Sera Care Life Sciences
- HIV worldwide Performance Panel WWRB304, Sera Care Life Sciences
- HIV worldwide Performance Panel WWRB305, Sera Care Life Sciences
- WHO International Standard-NIBSC Code 02/210, NIBSC
- National Reference for Confirmation Reagent of HIV Antibody, China

Sero-conversion panels

A total of 30 sero-conversion panels purchased from SeraCare Life science, Boston Biomedica, Inc and Zeptomatrix Corporation were tested on MP Diagnostics MULTISURE® HIV Rapid Test. The reactivity and average days of detection from 1st bleed of MP Diagnostics MULTISURE® HIV Rapid Test was found to be better or comparable with the commercially available Rapid Test kits and Western Blot kits.

Analytical Sensitivity

With the titration of one anti HIV-1 positive and one anti HIV-2 positive specimens, the reactivity end point for MP Diagnostics MULTISURE® HIV Rapid Test were found to be at 1:2560 dilution (HIV-1) and 1:10240 dilution (HIV-2) respectively. The results are comparable with commercially available Rapid Test kit.

Precision

The inter-assay (between-run) and intra-assay (within-run, within-day and day-to-day) reproducibility of MP Diagnostics MULTISURE® HIV Rapid Test have been evaluated using a set of control panel members. All results obtained consistently fall within the acceptance criteria, indicating the MP Diagnostics MULTISURE® HIV Rapid Test is robust, reproducible and consistent in three lots studied.

REFERENCES

- Weiss RA. "How does HIV cause AIDS?". Science 1993; 260:1273-1279.
- http://www.unaids.org/en/media/unaids/contentassets/documents/document/2014/2014gapreports/slides/HIV2013Estimates_1990-2013_22July2014.xlsx
- Gallo RC, Sarin PS, Gelmann EP, Robert-Guroff M, Richardson E, Kalyanaraman VS, Mann D, Sidhu GD, Stahl RE, Zolla-Pazner S, Leibowitch J, Popovic M. Isolation of human T-cell leukemia virus in acquired immune deficiency syndrome (AIDS). Science 1983; 220:865-867.
- Barré-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruest J, Dauguet C, Axler-Blin C, Vézinet-Brun F, Rouzioux C, Rozenbaum W, Montagnier L. Isolation of a Tlymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 1983; 220:868-871.
- McCutchan FE. Global epidemiology of HIV. J Med Virol 2006; 78:S7-S12.
- De Cock KM, Adjorlolo G, Ekpini E, Sibailly T, Kouadio J, Maran M, Brattegaard K, Vetter KM, Doorly R, Gayle HD. Epidemiology and transmission of HIV-2: why there is no HIV-2 pandemic. JAMA 1993; 270:2083-2086.
- Reeves JD, Doms RW. "Human Immunodeficiency Virus Type 2". Journal of General Virology 2002; 83:1253-1265.
- CDC. Vital signs: HIV prevention through care and treatment—United States. MMWR Morb Mortal Wkly Rep. 2011;60(47):1618-1623. Available at: <http://www.cdc.gov/mmwr/PDF/wk/mm6047.pdf>.
- Sarngadharan MG, Popovic M, Bruch L, Schüpbach J, Gallo RC. Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS. Science 1984; 224:506-508.
- CLSI. Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection; Approved Guideline. CLSI document M53-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.
- US Centers for Disease Control and Prevention (CDC). Laboratory Testing for the Diagnosis of HIV Infection Updated Recommendations. 27 June 2014.

LIMITED EXPRESSED WARRANTY DISCLAIMER

The manufacturer makes no express warranty other than that the test kit will function as an *in vitro* diagnostic assay within the specifications and limitations described in the product Instruction Manual when used in accordance with the instructions contained therein. The manufacturer disclaims any warranty expressed or implied, including such expressed or implied warranty with respect to merchantability, fitness for use or implied utility for any other purposes. The manufacturer is limited to either replacement of the product or refund of the purchase price of the product. The manufacturer shall not be liable to the purchaser or third parties for any damage, injury or economic loss howsoever caused by the product in the use or in the application thereof.

TECHNICAL PROBLEMS / COMPLAINTS

Should there be a technical problem / complaint, please do the following:

- Note the kit lot number and the expiry date.
- Retain the kits and the results that were obtained.
- Contact the nearest MP Biomedicals office or your local distributor.



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