multiplo
rapid TP/HIV test

Multiplo Rapid TP/HIV Test (Multiplo TP/HIV) is a qualitative rapid vertical flow test, developed and manufactured by MedMira Laboratories Inc., to detect the presence of antibodies to *Treponema pallidum* bacteria (TP), the causative agent of syphilis, and human immunodeficiency virus (HIV) type 1 and 2 in human serum, plasma or whole blood specimens.

INTENDED USE

Multiplo TP/HIV is a single-use, qualitative immunoassay for the detection of antibodies to *Treponema pallidum* bacteria (TP), the causative agent of syphilis and/or antibodies to human immunodeficiency virus Type 1 and Type 2 (anti-HIV-1/2) in human serum, plasma, and whole blood (fingerstick and venipuncture). Multiplo TP/HIV is intended for use by healthcare professionals as an aid in the diagnosis of infection with TP and/or HIV-1/2.

TEST DESCRIPTION

Multiplo TP/HIV is a manually performed, visually interpreted, rapid vertical flow immunoassay. The test cartridge contains an immunoreactive test membrane comprised of specially formulated synthetic peptides to gp36, gp41, gp120, HIV-1 group O, and TP recombinant antigens, coated onto a membrane matrix, which function to capture anti-TP and anti-HIV-1/2 antibodies present in human serum, plasma and whole blood when a drop of the specimen is applied. In addition, the test membrane has a procedural and reagent Control Line comprised of an optimized amount of protein A. Following the application of the sample, captured anti-HIV-1/2 antibodies and/or anti-TP antibodies are visualized through a reaction with the InstantGold™ cap, which contains a proprietary protein A-colloidal gold conjugate.

PRODUCT FORMATS AND CONTENTS

Product Format	Contents
Multiplo TP/HIV (POC) **Cat. No. 815311005015** *(Fingerstick Whole Blood)* Includes a test tray in each pouch	20 Mylar pouches each containing: 1 test cartridge 1 InstantGold cap 1 silica gel packet 1 auto-fill pipette 1 Universal Buffer vial 1 1 Universal Buffer vial 2 1 lancet (sterile) 1 alcohol swab 1 package insert 1 lancet use card
Multiplo TP/HIV (LAB+) **Cat. No. 815311004995** *(Venipuncture Whole Blood/Serum/Plasma)*	50 Mylar pouches each containing: 1 test cartridge 1 InstantGold cap 1 silica gel packet 2 bottles Universal Buffer 50 transfer pipettes 50 sample tubes 1 package insert
Multiplo TP/HIV (LAB S/P) **Cat. No. 815311005008** *(Serum/Plasma)*	50 Mylar pouches each containing: 1 test cartridge 1 InstantGold cap 1 silica gel packet 2 bottles Universal Buffer 50 transfer pipettes 1 package insert

WARNINGS AND SAFETY RECOMMENDATIONS

1. **The test is intended for in vitro diagnostic use by healthcare professionals. This product is not to be used for self-testing.**
2. **Read this package insert completely and carefully prior to use of this test. If the directions are not followed exactly, inaccurate test results may occur.**
3. Handle specimens, and all materials contacting specimens as if capable of transmitting infectious agents. It is recommended that all specimens and test reagents be handled according to Universal Precautions.
4. Do not smoke, eat, or drink in areas where specimens or test reagents are handled.
5. Wear disposable gloves, laboratory coat and eye protection throughout the test procedure.
6. Dispose of all test specimens and materials used in the test in a biohazard waste container. Follow local guidelines for the disposal of solid and liquid biohazardous waste.

HANDLING PRECAUTIONS

1. Use test components only once, excluding bottles of Universal Buffer in LAB+ and LAB S/P products, and dispose of properly. Once opened the bottles of Universal Buffer are stable throughout the expiration period of the product.
2. Do not touch the reaction membrane. Touching the membrane may compromise test results.
3. Store in a dry place at 2 - 30°C.
4. Exercise care in handling test components to prevent contamination.
5. Adequate lighting is required to read the test result.
6. Ensure that the Mylar pouch is intact and that the expiration date printed on the outside of the pouch is valid. If the pouch is not intact or is expired, discard and obtain a new pouch.
7. Allow the components to equilibrate to room temperature for 30-60 minutes before performing the test.
8. Keep the test cartridges and reagents sealed in packages until immediately prior to use. Using the notched corners, tear open the pouch and remove the components, placing them on a clean, flat surface.

For FINGERSTICK WHOLE BLOOD specimens go to A
For VENIPUNCTURE WHOLE BLOOD specimens go to B
For SERUM/PLASMA specimens go to C

IMPORTANT TEST PROCEDURE NOTES

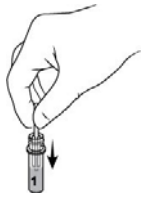
- Check the Cat. No. of the product you are using and select the corresponding procedure for your specimen type.
- All solutions must be completely absorbed into the test membrane before proceeding to the next step in the test procedure.
- Once the test has been started, all subsequent steps should be completed without interruption.
- Perform the test on a flat work surface to ensure that reagents and specimens uniformly flow through the test device.
- Read the test results immediately.

A. Fingerstick Whole Blood Specimens - Cat. No. 815311005015

SPECIMEN HANDLING & COLLECTION

1. Uncap and place Universal Buffer vial 1 into the hole of the test tray.
2. Using an alcohol swab, clean the finger. Allow the finger to dry thoroughly.
3. Using the lancet provided with the test, lance the fingertip in preparation for collection of the fingerstick whole blood specimen. Refer to Lancet Use Card included in the Mylar pouch for detailed instructions.

4. Use the auto-fill pipette provided to collect a drop of blood from the fingerstick site. To do this, hold the pipette horizontally and touch the drop of blood. The blood sample will be automatically drawn to the black fill line and stop. **Do not** squeeze the pipette bulb during filling.

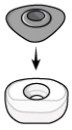


5. Place the tip of the pipette into the Universal Buffer in Universal Buffer vial 1. Squeeze the bulb to empty the blood sample into the vial. Recap Universal Buffer vial 1.

6. Hold Universal Buffer vial 1 and gently tap the side of the vial near the bottom until the mixture becomes a clear reddish colour. This can take 15-30 seconds of gentle tapping to mix properly.

TEST PROCEDURE

1. Pour the entire contents of Universal Buffer vial 1 into the center of the test cartridge. Allow the solution to absorb completely.



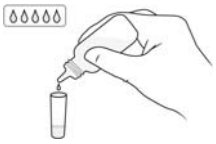
2. Place the InstantGold cap on the test cartridge.

3. Pour the entire contents of Universal Buffer vial 2 onto the InstantGold cap and allow the solution to absorb completely. Remove the InstantGold cap and wait for the solution to absorb completely. Read test results immediately.

B. Venipuncture Whole Blood Specimens - Cat. No. 815311004995

SPECIMEN HANDLING & COLLECTION

1. Use standard venous phlebotomy procedures to collect a whole blood sample. If specimens are not tested at the time of collection, they may be stored at 2 - 8°C for up to five (5) days prior to testing. If storage is necessary for over five (5) days, plasma should be separated from the whole blood specimen and stored at -20°C or below.



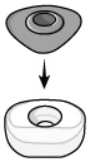
2. Place the sample tube in a secured rack on a flat surface and add five (5) drops from the bottle of Universal Buffer to the sample tube.

3. Using the transfer pipette provided, collect whole blood from the specimen collection tube. Add one (1) drop of whole blood to the sample tube prepared in Step 2.

4. Hold the sample tube and gently tap the side of the tube near the bottom until the mixture becomes a clear reddish colour. This can take 15-30 seconds of gentle tapping to mix properly.

TEST PROCEDURE

1. Pour the entire contents of the sample tube into the center of the test cartridge. Allow the solution to absorb completely.



2. Place the InstantGold cap on the test cartridge.

3. Dispense twelve (12) drops of Universal Buffer onto the InstantGold cap and allow the solution to absorb completely. Remove the InstantGold cap and wait for the solution to absorb completely. Add three (3) drops of Universal Buffer to clarify results. Allow the solution to absorb completely. Read test results immediately.

C. Serum/Plasma Specimens - Cat. No. 815311004995 OR Cat. No. 815311005008

SPECIMEN HANDLING & COLLECTION

1. Plasma obtained used EDTA, heparin, or sodium citrate as anticoagulants is suitable for testing.
2. Fresh serum or plasma specimens may be tested immediately upon receipt or stored at 2 - 8°C for up to five (5) days prior to testing. If storage is necessary for over five (5) days, serum or plasma specimens should be stored at -20°C or below.
3. Particulate matter can block the reaction test membrane or cause high background making the results difficult to interpret. Cloudy, viscous, or highly hemolyzed specimens should not be used for testing.
4. For serum or plasma that has been previously frozen:
   a. Thaw completely at room temperature (15 - 27°C) and mix thoroughly by inverting the tube several times.
   b. Centrifuge an aliquot of the specimen in a small, capped tube at room temperature (15 - 27°C) at 3361 g (radius of rotor 8.35 cm = 6000 rpm) for at least five (5) minutes and use only the clear supernatant for testing.
5. Avoid multiple freeze-thaw cycles. A specimen should not be frozen and thawed for more than twice prior to use with this test.

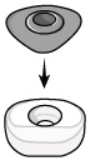
TEST PROCEDURE

1. Add three (3) drops of Universal Buffer to the center of the test cartridge. Allow the solution to absorb completely.

2. Apply one (1) drop of serum or plasma to the center of the test cartridge. Allow the specimen to absorb completely.

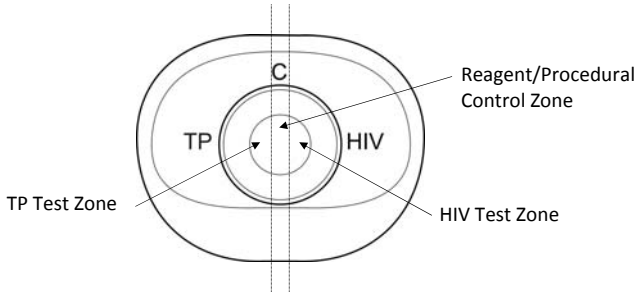
   If the serum or plasma specimen is not absorbed within 30 seconds, centrifuge an aliquot of the specimen in a small, capped tube at room temperature (15 - 27°C) at 3361 g (radius of rotor 8.35 cm = 6000 rpm) for at least five (5) minutes. Test the clear supernatant using a new test cartridge. If slow absorption persists after centrifugation, the specimen may not be suitable for use.

3. Place the InstantGold cap on the test cartridge. Dispense twelve (12) drops of Universal Buffer onto the InstantGold cap and allow the solution to absorb completely. Remove the InstantGold cap and wait for the solution to absorb completely. Add three (3) drops of Universal Buffer to clarify results. Allow the solution to absorb completely. Read test results immediately.



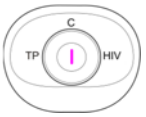
READING TEST RESULTS

The reaction membrane is made up of THREE zones: TP test zone, reagent/procedural control zone, and HIV test zone. The first step in reading test results is to look for a vertical line in the control zone. A solid line in the control zone validates the test. If no solid line is present repeat the test with a new Multiplo TP/HIV test. If the control line is present, examine the TP and HIV test zones for the presence of a dot of any intensity.



Non-Reactive Test Result

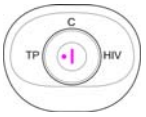
Probable Non-Exposure to TP and HIV-1/2



The presence of a vertical red line under the **C** and the absence of a red dot beside **TP** and absence of a red dot beside **HIV** on the test means that the individual has probably not been exposed to TP or HIV-1/2. Following an exposure to TP or HIV, it may take several months for the antibody response to reach detectable levels. If there is reason for concern, the individual should repeat the test within three to six months or consult a healthcare provider.

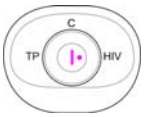
Reactive Test Results

Probable Exposure to TP



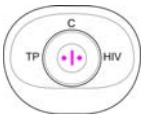
The presence of a vertical red line under the **C** and a red dot beside **TP** on the test, regardless of intensity, indicates the individual might have been exposed to TP. Any visible dot in the TP zone must be considered to be a Reactive result. It means that TP antibodies are probably present in the individual's blood and he/she should seek medical care as soon as possible. All reactive test results should be confirmed and evaluated with respect to clinical evaluation before a diagnosis is made.

Probable Exposure to HIV-1 and/or HIV-2



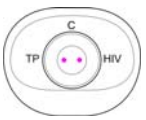
The presence of a vertical red line under the **C** and a red dot beside **HIV** on the test, regardless of intensity, indicates the individual may have been exposed to HIV-1 and/or HIV-2. Any visible dot in the HIV zone must be considered to be a Reactive result. It means that HIV-1 and/or HIV-2 antibodies are probably present in the individual's blood and he/she should seek medical care as soon as possible. All reactive test results should be confirmed and evaluated with respect to clinical evaluation before a diagnosis is made.

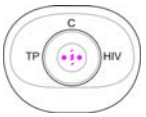
Probable Exposure to TP and HIV-1/2

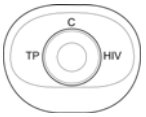


The presence of a vertical red line under the **C** with a red dot beside **TP** and a red dot beside **HIV** on the test, regardless of the intensity of each dot, means the individual might have been exposed to both TP and HIV -1/2. Any visible dot in the TP zone or any visible dot in the HIV zone must be considered to be a Reactive result. It means that TP and HIV-1/2 antibodies are probably present in the individuals blood and he/she should seek medical care as soon as possible. All reactive test results should be confirmed and evaluated with respect to clinical evaluation before a diagnosis is made.

Invalid Test Results







The result is Invalid if no red line appears under the **C** or if the red line under the **C** appears broken, even if a dot appears beside **TP** or a dot appears beside **HIV** on the test. The absence of the red line under the **C** or the presence of a broken line under the **C** indicates that there has been a problem, with either the test or the specimen, during the Test Procedure.

If an invalid test result occurs, the test procedure should be repeated with a new Multiplo TP/HIV test. If the problem persists, contact MedMira Customer Support.

QUALITY CONTROL

It is the responsibility of the user to establish an adequate quality assurance program to ensure the proper performance of this rapid test under its conditions of use.

Built-in Control Features

This rapid test includes a built-in procedural and reagent Control Line that demonstrates the validity of the testing procedure and reagent function. A vertical red line under the "**C**" (Control Zone) on the test cartridge indicates that specimen has been added to the test cartridge, and that the test reagents are functioning properly. The Control Line will appear on all valid tests, regardless of whether the test result is Reactive or Non-Reactive (see **Test Results** section).

LIMITATIONS OF THE TEST

1. The test must be used in accordance with this package insert to ensure accurate results.
2. The test is for use only with serum, plasma, or whole blood specimens. Use of other types of specimens may yield inaccurate results.
3. Test results are to be read and interpreted immediately upon completion of the test procedure. A delay in reading test results may yield inaccurate results.
4. Serum or plasma specimens that do not pass through the membrane in 30 seconds may be unsuitable for testing.
5. A Reactive test result suggests the presence of anti-HIV antibodies and/or anti-TP antibodies in the specimen.
6. The intensity of the red dot(s) (Reactive test results) does not necessarily correlate with the antibody titre of the specimen.
7. A Non-Reactive test result indicates the absence of detectable antibodies to HIV and TP in the specimen but does not exclude the possibility of exposure to, or infection with HIV and/or TP.
8. All Reactive test results should be confirmed and evaluated with respect to an overall clinical evaluation before a diagnosis is made.

PERFORMANCE CHARACTERISTICS

HIV Sensitivity

Sensitivity studies were performed using HIV-1 antibody positive specimens. The sensitivity of the rapid HIV test was 99.8% when 1967 Western blot confirmed positive specimens (different clades) were tested (Table 1). The rapid HIV test was found to be 100% sensitive when 44 specimens of various clades of HIV-1 group M, 10 HIV-1 group O specimens, and 299 HIV-2 specimens were tested (Table 2).

Table 1—Sensitivity with HIV –1 Clades by Region

Country	Prevalence	Number of Specimens	Sensitivity
Canada	B	836	99.8%
India	C,A,B	20	100%
Kenya	C,A	205	100%
Peru	B,F	20	100%
South Africa	C	250	100%
Tanzania	C,A,D	14	100%
Thailand	E,B	20	100%
Trinidad	B	20	100%
United States	B	582	99.7%
TOTAL		**1967**	**99.8%**

Table 2—Sensitivity with HIV-1 group M, group O, and HIV-2

Specimen (group, Clade)	Number of Specimens	Sensitivity
HIV-1 (M,A)	10	100%
HIV-1 (M,B)	10	100%
HIV-1 (M,C)	11	100%
HIV-1 (M,D)	5	100%
HIV-1 (M,E)	3	100%
HIV-1 (M,F)	3	100%
HIV-1 (M,G)	2	100%
HIV-1 (O)	10	100%
HIV-2	299	100%

TP Sensitivity

Sensitivity was evaluated through in-house testing. Results indicated 100.0 % sensitivity when 50 *Treponema pallidum* positive specimens were tested. Included in the evaluation of sensitivity was 50 dually infected (for TP and HIV antibodies) specimens. Multiplo TP/HIV device sensitivity to these specimens was 100.0%.

HIV Specificity

The overall specificity of the rapid HIV test was 99.7% when 11,669 negative specimens were tested.

TP Specificity

Specificity was evaluated through in-house testing. Results indicated 100% specificity when 100 *Treponema pallidum* negative specimens were tested.

Reactivity with Seroconversion Panels

Thirty seroconversion panels were tested in comparison to licensed anti-HIV-1,2 EIA. Each panel consisted of a series of sequential specimens obtained from a single individual undergoing seroconversion. The 30 seroconversion panels consisted of 219 specimens. In this study, the rapid HIV test detected seroconversion similarly to the licensed HIV-1,2 EIA.

Reactivity with Low Titre HIV-1 Antibody Performance Panels

A low titre HIV-1 antibody panel consisting of 15 specimens, obtained from a commercial source, was tested in comparison with licensed anti-HIV EIA tests. The rapid HIV test was capable of detecting antibodies to HIV-1 similarly to the licensed anti-HIV EIA tests.

Interference Studies

Interference studies were carried out on 1220 specimens, the results indicate that EDTA, heparin, sodium citrate, abnormal levels of chemistry markers (i.e. alkaline phosphatase, alanine aminotransferase, lactate dehydrogenase, thyroid stimulating hormone, glucose, cholesterol, amylase, and various ions), seromarkers associated with unrelated medical condition (i.e. rheumatoid factor, infectious mononucleosis, Helicobacter pylori, hepatitis A, B, or C, herpes simplex virus, mycoplasma, mumps, measles, rubella, and syphilis), and specimens obtained from pregnant women did not interfere with the test.

Repeatability and Reproducibility

Three blind coded panels were tested with three lots of the test, on three testing days at three sites. Results of these studies indicated 100% repeatability and reproducibility.

Equivalence of Analytes

When serum, plasma, and whole blood was collected from the same individual and tested with the rapid HIV test 100% correlation was observed between the three analytes and a reference test (EIA).

PRODUCT WARRANTY

MedMira Laboratories Inc. guarantees the quality of this product if stored and used as instructed. Any component of the test found to be defective shall be replaced free of charge upon return of the defective product. MedMira Laboratories Inc. disclaims any implied warranty of merchantability or fitness for a particular purpose, and in no event shall MedMira Laboratories Inc. be liable for consequent damage.

REFERENCE DOCUMENTS

1. Operational characteristics of commercially available assays to detect antibodies to HIV-1 and/or HIV-2 in human sera. Report 9/10. World Health Organization, Geneva. January 1998.
2. Canadian Biosafety Standard: 2nd Edition, Public Health Agency of Canada, 2015.
3. Canadian Biosafety Handbook: 2nd Edition, Public Health Agency of Canada, 2016.
4. World Health Organization. 2004. Laboratory biosafety manual. Third edition. Geneva.
5. CDC. Recommendations for Preventing Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Patients During Exposure-Prone Invasive procedures. MMWR Recommendations and Reports. 1991, 40 (RR-08) 1-9
6. Whidmer, A.F. & R. Frei. 2003. "Decontamination, Disinfection and Sterilization. In: Murray PR, ed. Manual of Clinical Microbiology. 9th edition. ASM Press. 2007. pp 65-96.
7. CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. MMWR Recommendations and Reports. 2006, 55 (RR-14).

Explanation of Symbols

	Temperature Limit		Use by
	Manufacturer		Do not reuse
REF	Catalogue number	IVD	*in vitro* diagnostic medical device
LOT	Lot number		Consult instructions before use
EC REP	Authorized Representative in the European Community	CE	CE Marking of Conformity

EC REP

EU Auth. Rep.
Advena Ltd.
Pure Offices, Plato Close
Warwick, CV34 6WE, UK

CE 0318 (HIV detection only)

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