REVEAL® TP (Syphilis)

Antibody Test

REF **Cat. No. 815311005282**

For *in vitro* diagnostic use only
Not for donor screening

IVD ***In vitro* Medical Device**

Store at 2 - 30°C

Do not reuse

Reveal® TP (Syphilis) Antibody Test 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 in human whole blood specimens.

INTENDED USE

Reveal® TP (Syphilis) Antibody Test is a single-use, qualitative immunoassay for the detection of antibodies to *Treponema pallidum* bacteria (TP), the causative agent of syphilis in human whole blood (fingerstick) samples. Reveal® TP (Syphilis) Antibody Test is intended for use by healthcare professionals in Point of Care settings as an aid in the diagnosis of infection with TP.

TEST DESCRIPTION

Reveal® TP (Syphilis) Antibody Test is a manually performed, visually interpreted rapid vertical flow immunoassay. The test cartridge contains an immunoreactive test membrane comprised of TP recombinant antigens, coated onto a membrane matrix, which function to capture anti-TP antibodies present in human 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-TP antibodies are visualized through a reaction with the InstantGold™ cap, which contains a proprietary Protein A-colloidal gold conjugate. Specifically, for the detection of TP antibodies, the capture cocktail consists of 15 kDa, 17 kDa, and 47 kDa recombinant antigens.

PRODUCT FORMATS AND CONTENTS

Product Format	Contents
Reveal® TP (Syphilis) Antibody Test (POC) Cat. No. 815311005282 (Fingerstick Whole Blood)	20 Mylar bags each containing: 1 Auto-fill pipette 1 Universal Buffer Vial 1 1 Universal Buffer Vial 2 1 Lancet (sterile) 1 Alcohol swab 1 Package insert 1 Test Tray 1 Small mylar pouch containing: 1 Test Cartridge 1 InstantGold™ Cap 1 Silica gel packet

MATERIALS REQUIRED BUT NOT PROVIDED

1. Disposable gloves
2. Laboratory coat
3. Biohazard waste disposal bags suitable for autoclaving
4. Permanent marking pen
5. Disinfectant (household bleach)
6. Liquid waste discard container with a freshly prepared 1.0 % solution of sodium hypochlorite (20% solution of household bleach).

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 expired kits and 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.
7. Wipe spills promptly with a freshly prepared solution of 1% sodium hypochlorite (20% solution of household bleach) or other appropriate disinfectant. Contaminated materials should be disposed of as biohazardous waste.
8. Add an equal volume of freshly prepared 1% sodium hypochlorite solution (20% solution of household bleach) to liquid wastes and allow them to soak for at least 1 hour for disinfection.

HANDLING PRECAUTIONS

1. Use test components only once and dispose of them properly. Do not use expired kits.
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.

LIMITATIONS OF THE TEST

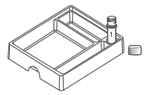
1. The test must be used in accordance with this package insert to ensure accurate results.
2. The test is for use only with fingerstick whole blood specimens. Use of other types of specimens may yield inaccurate results.
3. Test results are to be read and interpreted immediately upon completion of the test procedure. A delay in reading test results may yield inaccurate results.
4. A Reactive test result suggests the presence of anti-TP antibodies in the specimen.
5. The intensity of the red dot (Reactive test result) does not necessarily correlate with the antibody titre of the specimen.
6. A Non-Reactive test result indicates the absence of detectable antibodies to TP in the specimen but does not exclude the possibility of exposure to, or infection with TP.
7. All Reactive test results should be confirmed and evaluated with respect to an overall clinical evaluation before a diagnosis is made.
8. Reveal® TP is not approved for use to screen donors of blood, plasma, cells or tissues.
9. Some individuals are prone to thickened skin on their fingertips which may require a lancet with a deeper cut.
10. If an interruption occurs during sample collection and handling, blood clots in the pipette and sample coagulation on the membrane may occur.

IMPORTANT TEST PROCEDURE NOTES

- 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

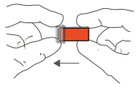
SPECIMEN COLLECTION & HANDLING

1. Uncap Universal Buffer vial 1 and place in the test tray.

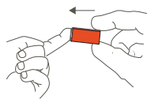


2. Using an alcohol swab, clean the index finger. Allow the finger to dry thoroughly.

3. Remove the protective cap from the sterile lancet provided with the test. Do not use lancet if damaged.

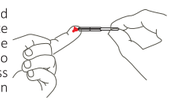


4. Firmly press the lancet against the puncture site to activate the device and puncture the skin.

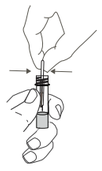


5. Point the lanced finger downward, apply gentle pressure beside the point of puncture to allow a drop of blood to form. Avoid squeezing the fingertip to make it bleed.

6. Use the auto-fill pipette provided to collect a drop of blood from the fingerstick site. To do this, touch the tip of the pipette to the blood sample in a horizontal position. The blood sample will be automatically drawn to the black fill line and stop. Do not squeeze the pipette bulb during filling. If there is excess blood around the pipette tip, please wipe it gently with a clean tissue.



7. Place the tip of the auto-fill pipette into the Universal Buffer in Universal Buffer vial 1. Squeeze the bulb to empty the blood sample into the vial. Discard the auto-fill pipette. Recap Universal Buffer vial 1.



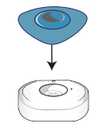
8. Hold Universal Buffer vial 1 and gently tap the side of the vial near the bottom until the mixture becomes a clear reddish color.

9. Proceed to TEST PROCEDURE

TEST PROCEDURE

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

2. Place the InstantGold™ cap on the test cartridge.

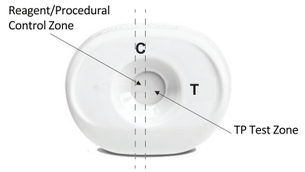


3. Pour the entire contents of Universal Buffer vial 2 onto the InstantGold™ cap and allow the solution to be absorbed completely.

   Remove the InstantGold™ cap and wait for the solution to absorb completely. Read test results immediately.

READING TEST RESULTS

The reaction membrane is made up of two zones: T test zone and reagent/procedural control 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 Reveal® TP (Syphilis) Antibody Test. If the control line is present, examine the T test zone for the presence of a dot of any intensity.



Non-Reactive Test Results

Probable Non-Exposure to TP

The presence of a vertical red line under the C and the absence of a red dot beside T on the test means that the individual has probably not been exposed to TP. Following an exposure to TP, 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 T on the test, regardless of intensity, indicates the individual might have been exposed to TP. Any visible dot in the T zone must be considered to be a Reactive result. It means that TP antibodies are probably present in the individual's blood and medical care should be sought 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, even if a dot appears beside T on the Test. The absence of the red 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 Reveal® TP (Syphilis) Antibody Test. If the problem persists, contact MedMira Customer Support.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity LoD Study

WHO International Standard for Syphilis (1st IS for human syphilitic plasma IgG, NIBSC code 05/122, 0.3 IU/mL) was diluted between 1/10 and 1/20 and tested at n=20 per dilution to determine the Limit of Detection. The lowest concentration detected ≥95% of the time during this study was the 1:15 dilution.

Analytical Specificity

Interference Studies

Interference studies were conducted to assess the impact of unrelated medical conditions or interfering substances on the sensitivity and specificity of the TP Test. 100% concordance was demonstrated with unrelated medical conditions as shown in Table 1.

Table 1: Table Values represent the number of results in agreement/total number of tests performed.

Specimen	Unaltered Negative	TP Spiked*
Cytomegalovirus (IgM)	15/15	15/15
Epstein-Barr Virus (IgM)	15/15	15/15
Multiple Blood Transfusion	15/15	15/15
Human Anti-Mouse Antibodies (HAMA)	15/15	15/15
Hashimoto's Thyroiditis	15/15	15/15
Graves disease	15/15	15/15
Anti-Lyme	15/15	15/15
Anti-E. coli	6/6	6/6
Pregnancy- First Trimester	60/60	69/69
Pregnancy- Second Trimester	60/60	71/71
Pregnancy- Third Trimester	60/60	66/66
Unknown Pregnant	8/8	17/17
Hepatitis B Vaccine	3/3	6/6
VZV IgG Positive	4/4	N/A
Multiparous female[1]	17/17	29/29
Self-reported drug user	2/2	N/A
HAV IgG Positive	3/3	4/4
Alkaline Phosphatase (ALP)	5/5	12/12
Cytomegalovirus (IgG)	19/19	30/30
Rubella IgG	12/12	25/25
Toxoplasmosis IgG	10/10	25/25
High Bilirubin	5/5	14/14
Alanine Aminotransferase (ALT)	4/4	9/9
Rheumatoid Factors (RF)	4/4	13/13
Epstein-Barr Virus (EBV) IgG	17/17	50/50
Parvovirus B-19 IgG	3/3	11/11
Herpes Simplex Virus (HSV) IgG	6/6	3/3
Anti-nuclear antibodies (ANA)	6/6	6/6
Influenza Vaccine Recipient	3/3	4/4
Non-Viral Liver disease	3/3	3/3
HBV	15/15	15/15
HCV	15/15	15/15
HIV-1/2	15/15	15/15

[1]11 multiparous specimens were received as TP Positive.
*The TP Test data collected was from the Multiplo® TP/HIV Study

Drug Interferences

A drug interference study was conducted with 19 common therapeutic drugs including common over-the-counter anti-inflammatory drugs, anti-bacterial, anti-parasitic, anti-tuberculosis, anti-malarial and anti-viral drugs used in Syphilis treatment. No interference was observed at the following tested concentrations as shown in the table below.

Table 2

Specimen Interferent	Concentration		
Atovaquone	600 µg/mL	3/3	3/3
Acetaminophen	180 µg/mL	3/3	3/3
Ampicillin	80 µg/mL	3/3	3/3
Artesunate	200 µg/mL	3/3	3/3
Acetylsalicylic Acid	1200 µg/mL	3/3	3/3
Chloroquine	600 µg/mL	3/3	3/3
Erythromycin	140 µg/mL	3/3	3/3
Ethambutol	750 µg/mL	3/3	3/3
Gentamycin Sulfate	20 µg/mL	3/3	3/3
Ibuprofen	220 µg/mL	3/3	3/3
Isoniazid	180 µg/mL	3/3	3/3
Primaquine	160 µg/mL	3/3	3/3
Pyrazinamide	1100 µg/mL	3/3	3/3
Rifampin	360 µg/mL	3/3	3/3
Suramin	120 µg/mL	3/3	3/3
Tetracycline Hydrochloride	200 µg/mL	3/3	3/3
Doxycycline	60 µg/mL	3/3	3/3
Diethylcarbamazine	120 µg/mL	3/3	3/3
Mefloquine	550 µg/mL	3/3	3/3
Total		**57/57**	**57/57**

*The TP Test data collected was from the Multiplo® TP/HIV Study.

Syphilis Performance with Pregnant Samples

A total of 98 samples from pregnant patients during different stages of pregnancy were tested to evaluate the performance of TP testing component. 38/38 of the syphilis positive pregnancy samples were reactive and 60/60 of the syphilis negative pregnancy samples were non-reactive as shown in the table below. These results were from patients in various stages of syphilis infection. 19 samples were from patients in the primary phase of infection, 7 samples were from patients in the secondary phase of infection and 6 samples were from patients in the latent stage of infection. Six samples were from patients with an unknown stage of infection.

Table 3 – Stratification of Pregnancy Samples

Pregnancy Sample Staging		TP Test* Result		Total
		Positive	Negative	
1st Trimester	Positive	9	0	9
	Negative	0	20	20
2nd Trimester	Positive	11	0	11
	Negative	0	20	20
3rd Trimester	Positive	6	0	6
	Negative	0	20	20
Unknown	Positive	12	0	12
	Negative	0	0	0
	Total	38	60	98

*The 98 pregnancy samples were tested on the Multiplo® Rapid TP/HIV Test which has the identical TP component as the Reveal® TP (Syphilis) Antibody Test.

In addition, 12 pregnant samples were identified in the clinical studies conducted in Alberta with the Multiplo® Rapid TP/HIV Test, which contains the same TP component as the Reveal® TP (Syphilis) Antibody Test. Eight of these samples were EIA reactive and three were EIA non-reactive. One patient sample was removed from the analysis as the test was invalid. The TP component of the test was able to produce negative results, when the EIA was reactive, for the 2 biologically false positive cases found during clinical testing. The table below shows the serology results, the syphilis status/stage of infection, stage of pregnancy and the TP Test result. Additionally, during clinical trials conducted in Saskatchewan, 23 pregnant samples were tested using the Reveal® TP (Syphilis) Antibody Test. Among these, two cases were both Reveal® TP and EIA reactive, with RPR titers ≥1:8, while one case was Reveal® TP non-reactive but EIA reactive, with an RPR titer ≥1:4. Another case involved a previously treated syphilis infection. The remaining 19 cases were non-reactive on both the Reveal® TP and EIA tests. Stratification data for these samples is not available.

Table 4 – Stratification of Pregnant Subjects

Pregnant Sample ID	Serology Result	Syphilis Status / Stage of Infection	Stage of Pregnancy (Trimester)	TP Test Result
1	EIA R, RPR R, 128 dils, TPPA PP	Infectious/Primary	Second	Positive
2	EIA R, RPR R, 2 dils, TPPA PP	Previously Positive	Second	Positive
3	EIA R, RPR R, 1 dil, TPPA PP	Previously Positive	Second	Positive
4	EIA R, RPR R, 8 dils, TPPA PP	Infectious/Early Latent	Second	Positive
5	EIA R, RPR R, 2 dils, TPPA PP	Previously Positive	First	Positive
6	EIA NR	Non Case	Second	Negative
7*	EIA R, RPR NR, TPPA NR	Biological False Positive	First	Negative
8*	EIA R, RPR NR, TPPA indeterminate	Biological False Positive	First	Negative
9	EIA NR	Non Case	Second	Negative
10	EIA R, RPR R, 8 dils, TPPA PP	Previously Positive	First	Positive
11	EIA NR	Non Case	Not Available	Negative

NR = Non-reactive, PP = Previously Positive, R = Reactive
*Pregnant Samples 7 & 8 are from the same patient on separate visits.

Clinical Evaluation

Alberta Clinical Trial

The diagnostic performance of the TP testing was evaluated in clinical trials carried out in five (5) different study sites across Alberta. Results obtained with fingerstick whole blood specimens were compared to standard testing for syphilis from serum-based specimens. Performance characteristics were evaluated by means of agreement analysis, and Positive Percent Agreement (PPA), Negative Percent Agreement (NPA), Positive Predictive Value (PPV), and Negative Predictive Value (NPV) with 95% binomial confidence intervals were calculated separately for the TP component of Multiplo® TP/HIV. In addition, diagnostic performance for TP antibody detection was stratified by RPR titre (Non-Reactive, 1:8 dilutions).

A total of 1371 participants had complete syphilis serology and point of care testing during a clinical trial in Alberta using the Multiplo® Rapid TP/HIV Test, which has the identical TP component to the Reveal® TP (Syphilis) Antibody Test with results shown in Table 5. When compared to serology, the overall PPA was 86.0% (95% CI:82.7-89.0), NPA was 99.5% (95% CI:98.8-99.9%), PPV was 99.1% (97.6-99.7%), NPV was 92.7% (91.0-94.0%). The test performance revealed a PPA of 98.3% (95% CI: 95.7-99.5%), NPA of 99.5% (95% CI: 98.8-99.9%), PPV of 98.3% (95% CI: 95.6-99.4%) and NPV of 99.5% (95% CI: 98.8-99.9%) for syphilis with a RPR titre of ≥ 1:8 dilutions. A PPA of 89.8% (95% CI: 83.7-94.1%), NPA of 99.5% (95% CI: 98.8-99.9%), PPV of 97.1% (95% CI: 92.5-98.9%) and NPV of 98.3% (95% CI: 97.3-99.0%) for syphilis with a RPR titre of <1:8 dilutions and a PPA of 54.6% (95% CI: 44.8-64.1%), NPA of 99.5% (95% CI: 98.8-99.9%), PPV of 93.8% (95% CI: 84.8-97.6%), NPV of 94.6% (95% CI: 93.4-95.6%) for syphilis with a non-reactive RPR was also revealed in this study. The TP component is most sensitive to those who have RPR dilutions greater than or equal to 1:8 dilutions; this titre is generally considered to be the marker for an infectious case. This titre made up for an estimated 80% of newly diagnosed infectious syphilis cases in Alberta during the study.

Table 5

TP Test*	PPA (%) (95% CI)	NPA (%) (95% CI)	PPV (%) (95% CI)	NPV(%) (95% CI)
Syphilis (any RPR titre)	86.0% (82.7-89.0%) N=494 425/(425+69)	99.5% (98.8-99.9%) N=877 873/(873+4)	99.1% (97.6-99.7%) N=429 425/(425+4)	92.7% (91.0-94.0%) N=942 873/(873+69)
Syphilis sub-analysis for different RPR dilutions				
Syphilis (RPR non-reactive)	54.6% (44.8-64.1%) N=110 60/(60+50)	99.5% (98.8-99.9%) N=877 873/(873+4)	93.8% (84.8-97.6%) N=64 60/(60+4)	94.6% (93.4-95.6%) N=923 873/(873+50)
Syphilis (RPR <1:8 dilutions)	89.8% (83.7-94.1%) N=147 132/(132+15)	99.5% (98.8-99.9%) N=877 873/(873+4)	97.1% (92.5-98.9%) N=136 132/(132+4)	98.3% (97.3-99.0%) N=888 873/(873+15)
Syphilis (RPR ≥1:8 dilutions)	98.3% (95.7-99.5%) N=237 233/(233+4)	99.5% (98.8-99.9%) N=877 873/(873+4)	98.3% (95.6-99.4%) N=237 233/(233+4)	99.5% (98.8-99.9%) N=877 873/(873+4)

*The TP Test data collected was from the Multiplo® TP/HIV Study.

Saskatchewan Clinical Trials

A total of 389 participants with complete syphilis serology and point-of-care testing data from a clinical trial conducted in Saskatchewan using the Reveal® TP (Syphilis) Antibody Test are included in Table 6. When compared to standard serology, the overall positive percent agreement (PPA) was 70.9% (95% CI: 61.0–79.3%), negative percent agreement (NPA) was 98.3% (95% CI: 96.2–99.3%), positive predictive value (PPV) was 92.4% (95% CI: 83.5–96.9%), and negative predictive value (NPV) was 92.3% (95% CI: 88.9–94.8%).

Test performance among syphilis cases with an RPR titer of ≥1:8 showed a PPA of 87.5% (95% CI: 69.0–95.7%), NPA of 98.3% (95% CI: 96.2–99.3%), PPV of 80.8% (95% CI: 63.5–91.0%), and NPV of 99.0% (95% CI: 97.2–99.7%). For cases with RPR titers <1:8, the PPA was 80.0% (95% CI: 62.7–90.5%), NPA 98.3% (95% CI: 96.2–99.3%), PPV 82.8% (95% CI: 66.4–92.1%), and NPV 98.0% (95% CI: 96.0–99.0%). For cases with non-reactive RPR, the PPA was 50.0% (95% CI: 33.6–66.4%), NPA 100% (95% CI: 80.6-100%), PPV 76.2% (95% CI: 55.7–89.1%), and NPV 94.9% (95% CI: 92.9–96.3%).

These results demonstrate that the Reveal® TP test is most sensitive in individuals with RPR titers ≥ 1:8, which is generally considered indicative of an infectious syphilis case.

Additionally, 16 out of 32 subjects previously positive for syphilis (EIA reactive, RPR non-reactive, and TPPA reactive) showed a reactive result with the Reveal® TP test. One case was identified as an EIA false positive.

Table 6

Reveal® TP (Syphilis) Antibody Test	PPA (%) (95% CI)	NPA (%) (95% CI)	PPV (%) (95% CI)	NPV(%) (95% CI)
Syphilis (any RPR titre)	70.9% (61.0-79.3%) N=86 61/(61+25)	98.3% (96.2-99.3%) N=303 298/(298+5)	92.4% (83.5-96.9%) N=66 61/(61+5)	92.3% (88.9-94.8%) N=323 298/(298+25)
Syphilis sub-analysis for different RPR dilutions				
Syphilis (RPR non-reactive)	50.0% (33.6-66.4%) N=32 16/(16+16)	100% (80.6-100.0%) N=16 16/(16+0)	76.2% (55.7-89.1%) N=21 16/(16+5)	94.9% (92.9-96.3%) N=314 298/(298+16)
Syphilis (RPR <1:8 dilutions)	80.0% (62.7-90.5%) N=30 24/(24+6)	98.3% (96.2-99.3%) N=303 298/(298+5)	82.8% (66.4-92.1%) N=29 24/(24+5)	98.0% (96.0-99.0%) N=304 298/(298+6)
Syphilis (RPR ≥1:8 dilutions)	87.5% (69.0-95.7%) N=24 21/(21+3)	98.3% (96.2-99.3%) N=303 298/(298+5)	80.8% (63.5-91.0%) N=26 21/(21+5)	99.0% (97.2-99.7%) N=301 298/(298+3)

A total of 1760 participants had complete syphilis serology and point of care testing during the clinical trials in Alberta, using the Multiplo® Rapid TP/HIV Test (which has the identical TP component to Reveal® TP (Syphilis) Antibody Test) and Saskatchewan using the Reveal® TP (Syphilis) Antibody Test and are included in Table 7. When compared to serology, the overall PPA was 83.8% (95% CI: 80.5-86.7%), NPA was 99.2% (95% CI: 98.6-99.7%), PPV was 98.2% (95% CI: 96.6-99.0%) and the NPV was 92.6% (95% CI: 91.2-93.8%). The test performance revealed a PPA of 97.3% (95% CI: 94.6-98.9%), NPA of 99.2% (95% CI: 98.6-99.7%), PPV of 96.6% (95% CI: 93.6-98.2%) and NPV of 99.4% (95% CI: 98.8-99.7%) for syphilis with a RPR titre of ≥ 1:8 dilutions. A PPA of 88.1% (95% CI: 82.4-92.5%), NPA of 99.2% (95% CI: 98.6-99.7%), PPV of 94.5% (95% CI: 90.0-97.1%) and NPV of 98.2% (95% CI: 97.4-98.8%) for syphilis with a RPR titre of <1:8 dilutions and a PPA of 53.5% (95% CI: 45.0-61.9%), NPA of 99.6% (95% CI: 98.9-99.9%), PPV of 89.4% (95% CI: 81.2-94.3%), NPV of 94.7% (95% CI: 93.7-95.5%) for syphilis with a non-reactive RPR was also revealed in this study. The TP component is most sensitive to those who have RPR dilutions greater than or equal to 1:8 dilutions.

Table 7- Reveal® TP (Syphilis) Test – TP Component Results from Saskatchewan and Alberta Trials

	Sample Size (n)	PPA (95% CI)	NPA (95% CI)	PPV (95% CI)	NPV (95% CI)
Syphilis (any RPR titre)	1760	83.8% (80.5-86.7%)	99.2% (98.6-99.7%)	98.2% (96.6-99.0%)	92.6% (91.2-93.8%)
Syphilis (RPR Non-Reactive)	1322	53.5% (45.0-61.9%)	99.6% (98.9-99.9%)	89.4% (81.2-94.3%)	94.7% (93.7-95.5%)
Syphilis (RPR titre <1:8)	1357	88.1% (82.4-92.5%)	99.2% (98.6-99.7%)	94.5% (90.0-97.1%)	98.2% (97.4-98.8%)
Syphilis (RPR titre ≥1:8)	1141	97.3% (94.6-98.9%)	99.2% (98.6-99.7%)	96.6% (93.6-98.2%)	99.4% (98.8-99.7%)

Syphilis staging for the EIA positive results when compared to TP Test results performed during the Clinical Trial in Alberta can be shown in Table 8 below. Concordance for TP Test ranged from 82.6% for Late Latent to 100% for Secondary, Early and Late Neurosyphilis staging.

Table 8 - Syphilis Staging for EIA Positive Results by TP Test Results (N=505)

		TP Test Result		Total
		Positive (N)	Negative (N)	
Newly Diagnosed	Primary	57 (91.9%)	5 (8.1%)	62
	Secondary	18 (100%)	0	18
	Early Latent	118 (95.2%)	6 (4.8%)	124
	Early Neurosyphilis	2 (100%)	0	2
	Late Latent	19 (82.6%)	4 (17.4%)	23
	Late Neurosyphilis	1 (100%)	0	1
	Subtotal	**215 (93.5%)**	**15 (6.5%)**	**230**
Other	Previously Positive	210 (78.9%)	56 (21.1%)	266
	Biological False Positive	1 (14.3%)	6 (85.7%)	7
	Other	0	2 (100%)	2
	Subtotal	**211 (76.7%)**	**64 (23.3%)**	**275**
Grand Total		**426 (84.4%)**	**79 (15.6%)**	**505**

Clinical Trials performed in Saskatchewan identified 20 newly diagnosed cases. Of these cases, 2 primary, 1 secondary, 1 early latent and 15 late latent/unknown cases were identified. One case was unable to be staged.

Matrix Equivalency Study

The Matrix equivalency study was conducted using 42 matched fingerstick whole blood, venous whole blood, plasma (anticoagulant: sodium citrate) and serum specimens. All 42 matching sets of fingerstick whole blood, plasma with sodium citrate, venous whole blood with sodium citrate and serum specimen met the acceptance criteria and were concordant with the expected results. It can be concluded from these results that the *Treponema pallidum* (TP) antibody detection are not adversely affected in different matrices.

Prozone Effect

A prozone effect study was performed using the TP Test which aimed to assess the potential prozone effect using highly reactive plasma specimens at four different dilution levels (neat, 1:10, 1:100 and 1:1000). The prozone effect study was completed with one operator and three different lots. All results were as expected with no observation of an increase in signal upon dilution of or highly reactive TP specimens.

Precision Study

The Precision study of the TP component was conducted across three sites with three operators testing three different lots of Multiplo® Rapid TP/HIV Test over a period of 5 days. A panel of 7 blinded panel members, which included weakly reactive HIV-1, weakly reactive HIV-2 and weakly reactive TP panel members were tested per panel with each member tested 5 times. All the results were as expected for all 1575 tests performed with no discordant results occurring giving an overall reproducibility result of 100% for TP and HIV.

Usability study with Intended Operators

The usability study was conducted using nine (9) untrained Health Care Professionals at 3 different sites with one lot of the Reveal® TP (Syphilis) Antibody Test and a panel consisting of 10 panel members. Two (2) discordant results were observed when completing the reproducibility portion of the study, which were both weak reactive results which were observed as negative by the same untrained operator.

Each operator reviewed a total of 25 contrived test results. During the result interpretation portion of the study zero (0) discordant results were observed.

The reproducibility of the Reveal® TP (Syphilis) Antibody Test when performed by untrained users was calculated to be 97.8% (95% CI: 96.401 –99.115) and the accuracy of result interpretation was calculated to be 100%.

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 Reading Test Results section).

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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.

Explanation of Symbols

	Temperature Limit		Use by date
	Manufacturer		Do not reuse
REF	Catalogue number	IVD	*In Vitro* diagnostic medical device
LOT	Lot number		Consult instructions before use

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