revealHIV

rapid HIV antibody test

This package insert must be read carefully and completely prior to use of the Reveal® Rapid HIV Antibody Test. Instructions must be followed carefully. If directions are not followed exactly, inaccurate test results may occur.

NAME AND INTENDED USE

The Reveal® Rapid HIV Antibody Test (Reveal HIV) is a single use, qualitative immunoassay to detect antibodies to Human Immunodeficiency Virus (HIV) Type 1 and 2 in human serum or plasma. The Reveal HIV is intended for use as an aid in the diagnosis of infection with HIV-1 and/or HIV-2.

RESTRICTIONS

- **Sale of Reveal HIV is restricted to clinical laboratories that have an adequate quality assurance program, including planned systematic activities to provide adequate confidence that requirements for quality will be met and where there is assurance that operators will receive and use the instructional materials.**
- **Reveal HIV is approved for use only by an agent of a clinical laboratory.**
- **Reveal HIV is not approved to screen donors of blood, plasma, cells or tissues.**

SUMMARY AND EXPLANATION OF THE TEST

HIV causes Acquired Immune Deficiency Syndrome (AIDS). Of the two types of HIV, HIV-1 is far more prevalent within North America and in most regions worldwide. HIV is known to be transmitted through contact with the body fluids of an infected individual. Sexual contact, exposure to blood through contaminated syringes and needles or transfusion, or from an infected mother during the birthing process or through breastfeeding are the major modes of HIV transmission.

Infection with HIV-1 and/or HIV-2 elicits an immune response resulting in the production of corresponding HIV antibodies. Antibody detection tests for HIV-1/HIV-2 antibodies provide a means to aid in the diagnosis of HIV-infected individuals [1,2]. However, when utilizing HIV antibodies to diagnose HIV infection, corresponding clinical factors must also be considered. Following a recent exposure to HIV, it may take several months for the antibody response to reach detectable levels, during which time testing for antibodies to HIV will not be indicative of true infection status. On the other hand, newborns of HIV-infected mothers may carry maternal antibodies to HIV for up to eighteen months, which may not necessarily indicate the true infection status of the newborn.

Conventional laboratory testing for antibodies to HIV utilizes enzyme immunoassays (EIAs) followed by confirmation of repeatedly reactive EIAs using supplemental tests such as the Western blot test, both of which are complex, multi-step procedures. The EIA technology has proven to be extremely useful in the diagnosis of infection and is widely utilized as a screening tool. Although use of an EIA screening test is well suited for batch testing, the turnaround time could be several days to a few weeks. Additionally, the complexity and cost of EIA screen testing and the required equipment may prohibit its universal utilization in medical settings with limited resources and personnel.

Rapid, less complex HIV testing could improve the delivery of medical care and HIV prevention services with substantial time and cost savings [3,4]. Realizing the utility of rapid tests, the World Health Organization (WHO) recommends the use of alternative testing strategies using rapid and simpler HIV tests [5]. Similar recommendations were made by the United States Centers for Disease Control and Prevention (CDC) upon determining that large numbers of patients testing positive for HIV using conventional methods did not return to the medical facility to obtain test results. From a public health perspective, this high non-return rate has great implications for the health and welfare of an HIV-infected individual and his/her contacts [6]. Reveal HIV is a rapid, flow-through diagnostic immunoassay developed to utilize the performance characteristics of a conventional diagnostic immunoassay while simplifying the testing procedure to eliminate the requirement for expensive equipment and highly trained personnel, and decrease turnaround time.

BIOLOGICAL PRINCIPLES OF THE TEST

Reveal HIV is a manually performed, visually interpreted, rapid immunoassay. Reveal HIV is comprised of a single-use test cartridge containing an immunoreactive test membrane. The immunoreactive test membrane contains a combination of synthetic peptides corresponding to conserved regions of HIV-1 and HIV-2 structural proteins coated onto the membrane, which functions to capture HIV-1/2 antibodies present in human serum or plasma when a drop of the specimen is applied. The immunoreactive test membrane also contains a procedural and reagent control line. This is

comprised of protein A prepared in a proprietary buffered solution, which binds to all classes of IgG antibodies present in human serum and plasma regardless of the presence or absence of HIV antibodies. Following the application of the sample, the membrane is washed with Universal Buffer to remove any non-specifically bound antibodies. Captured HIV antibodies are visualized through a reaction with the Colorimetric Detection Agent (a proprietary protein A-colloidal gold conjugate) following a second washing step with Universal Buffer for clarification of the test result. A Reactive test result occurs only when the protein A portion of the conjugate binds to the captured HIV antibodies, producing a distinctive red dot in the test (T) zone. The test is validated by the presence of a red vertical procedural and reagent control line in the control (C) zone of the test membrane. In contrast, with the application of a specimen, which does not contain HIV antibodies, a red dot would not appear on the membrane. This represents a Non-Reactive result, and this is validated by the presence of only the red vertical procedural and reagent control line in the control zone (C) of the test membrane. If the vertical procedural and reagent control line is not present, the test result is considered Invalid, and testing must be repeated with a new test cartridge (refer to **Test Results and Interpretation of Results** section below).

The test results are to be read and interpreted **immediately** following the final washing step with Universal Buffer. Precision pipetting, sample manipulation or specialized equipment **is not required** to perform the Reveal HIV.

MATERIALS PROVIDED

Reveal HIV (Figure 1) is a unitized, ready-to-use test device that is packaged with all required test components. One box contains the following:

Component	Quantity for Catalogue # 815311000416
Test Cartridge Mylar pouch Each pouch contains: • 1 Test Cartridge • 1 Disposable pipette • 1 Desiccant packet	30
Colorimetric Detection Agent Package The poly zipper bag contains: **Colorimetric Detection Agent** Mylar pouch Each pouch contains: • 1 vial of lyophilized colorimetric detection agent comprised of protein A conjugated to colloidal gold in a buffered solution (Preservative: 0.1% sodium azide) • 1 Desiccant packet	1 2
HIV Test Control Mylar pouch The pouch contains: • 1 vial of Positive Test Control* (lyophilized, heat-inactivated human serum/plasma positive for HIV-1 antibodies and negative for Hepatitis B surface antigen and Hepatitis C antibodies, in a buffered solution). • 1 vial of Negative Test Control* (lyophilized human serum/plasma negative for HIV antibodies and antigen, Hepatitis B surface antigen, and Hepatitis C antibodies, in a buffered solution). • 1 Desiccant packet * Test Controls do not contain preservative	1
Poly zipper bag: The bag contains: • 1 Drop dispenser bottle containing 30 mL of **Universal Buffer** solution composed of Tris-buffered saline, synthetic polymers and an anti-microbial agent (Preservative: 0.1% sodium azide). • 1 Screw-cap bottle containing 30 mL of **Universal Buffer** solution composed of Tris-buffered saline, synthetic polymers and an anti-microbial agent (Preservative: 0.1% sodium azide).	1
Small Disposable pipettes (in a poly zipper bag)**.**	30
Large Graduated transfer pipettes (in a poly zipper bag)**.**	2
Package Insert	1

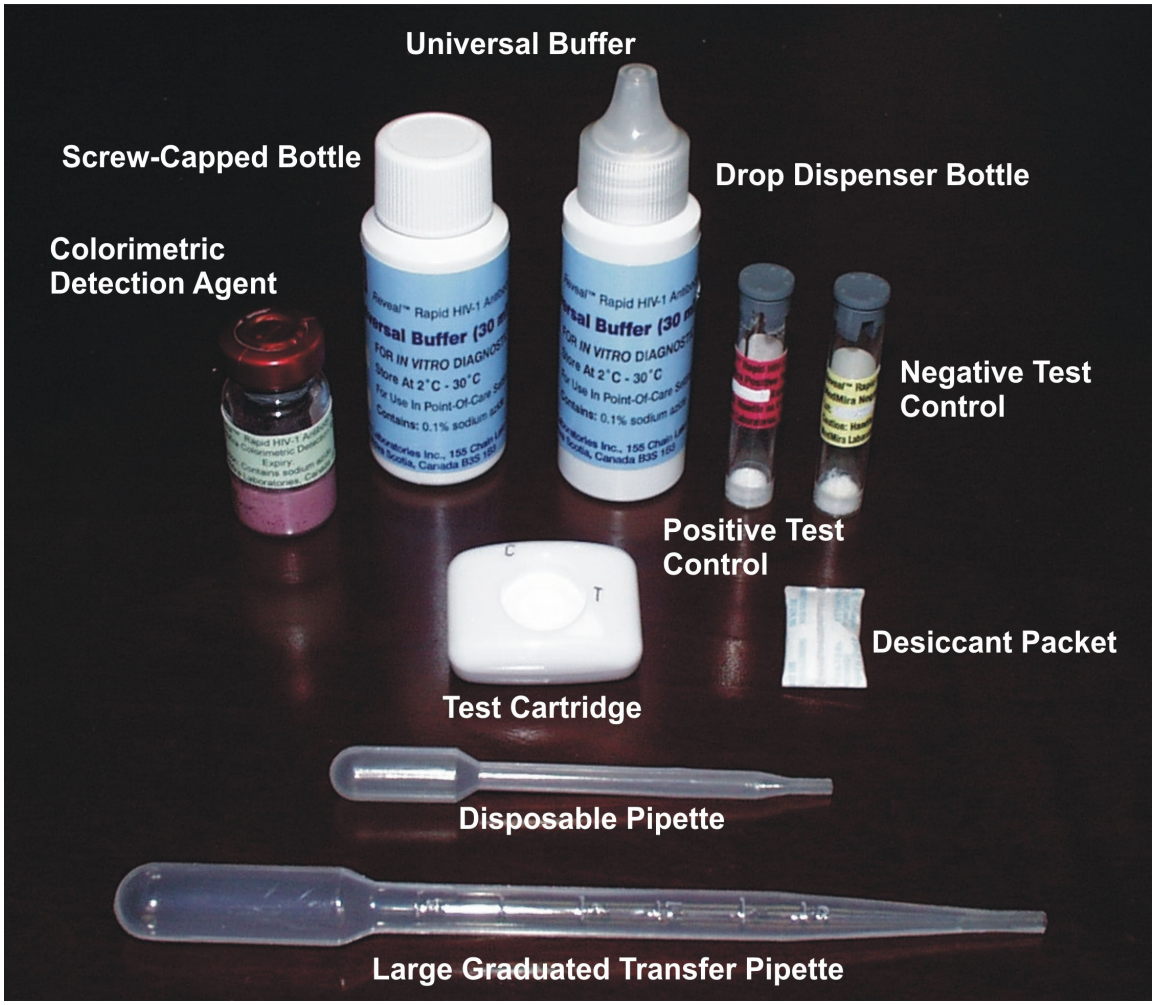


Figure 1. Components of Reveal HIV

MATERIALS PROVIDED AS AN ACCESSORY TO THE TEST
Additional components may be purchased from MedMira's Sales and Marketing Department, subject to availability.

Component	Description	Catalogue Number
Universal Buffer	One 30 mL Drop Dispenser bottle One 30 mL Screw-Capped bottle	1009785RDB 1009785RSB
Colorimetric Detection Agent	1 Mylar pouch containing 1 vial of Colorimetric Detection Agent	1009785RCG
HIV Test Controls	1 Mylar pouch containing 1 Positive and 1 Negative Test Control	1009785RCP
Small Disposable pipettes	1 poly zipper bag containing 20 pipettes	1009785RPI
Large Graduated transfer pipettes	1 poly zipper bag containing 2 graduated pipettes	1009785RRP

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

For *In Vitro* Diagnostic Use

1. **Read the Package Insert completely and carefully prior to use of Reveal HIV. If the directions are not followed exactly, inaccurate test results may occur.**
2. **Health Canada has approved this test for use with serum or plasma specimens only. Use of this test with specimens other than those specifically approved may result in inaccurate test results.**
3. **Perform Reveal HIV at room temperature (15-27°C).**
4. **Perform Reveal HIV on a flat work surface to ensure that reagents and specimens uniformly flow through the test device.**

PRECAUTIONS

Safety Precautions

1. Handle specimens, HIV Test Controls, and all materials contacting specimens as if capable of transmitting infectious agents. It is recommended that all specimens and test reagents be handled in accordance with biosafety level 2 practices as described in Laboratory Biosafety Guidelines, Health Canada[7], the CDC/NIH publication on Biosafety in Microbiological and Biomedical Laboratories [8], WHO biosafety manual [9] or CDC Universal Precautions[10].
2. Do not smoke, eat, or drink in areas where specimens or test reagents are handled. Do not pipette by mouth.
3. Wear disposable gloves, laboratory coat and eye protection throughout the test procedure. Upon completion of the test, gloves must be treated as biohazardous waste and disposed of accordingly. Wash hands thoroughly after disposing of gloves.
4. Wipe spills promptly with a freshly prepared solution of 1% sodium hypochlorite (20% solution of household bleach) or other appropriate disinfectant [11]. Contaminated materials should be disposed of as biohazardous waste.
5. 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.
6. Dispose of all test specimens and materials used in the Reveal HIV in a biohazardous waste container. The recommended method of disposal is autoclaving for a minimum of 1 hour at 121^0 C or by incineration. **Note: Do not autoclave solutions that contain bleach.**
7. Sodium azide is used as a preservative in the Universal Buffer. Sodium azide forms lead or copper azide in laboratory plumbing and may explode on percussion, such as hammering. To prevent formation of lead or copper azide, flush drains thoroughly with water after disposing of solutions containing sodium azide.

Handling Precautions

1. Use each test cartridge and specimen pipette only once and dispose of properly (see *Safety Precautions*). **Do not reuse these components.**
2. **Do not touch the immunoreactive test membrane.**
3. Do not use Reveal HIV or any of its components beyond the expiration date. The expiration date is printed on all labels. Always check the expiration date prior to testing. Reconstituted Test Controls are stable for up to 7 days, and reconstituted Colorimetric Detection Agent is stable for up to 30 days when stored at 2 - 8°C.
4. Do not interchange reagents or devices from different lots.
5. To prevent contamination, do not interchange stoppers on Test Control vials.
6. Exercise care in handling test components to prevent contamination.
7. Adequate lighting is required to read the test result.

STORAGE INSTRUCTIONS

Unopened Reveal HIV tests should be stored in a dry area at 2 - 30^0 C.

Keep the test cartridges and reagents in sealed packages until use.

Following reconstitution, the HIV Test Controls may be stored at 2 - 8°C for up to 7 days. Vials of Colorimetric Detection Agent should be reconstituted one at a time as required. Reconstituted Colorimetric Detection Agent may be stored at 2 - 8°C for up to 30 days. Ensure that stoppers are secure during storage.

DIRECTIONS FOR USE

A. Specimen Collection

1. Reveal HIV can be used to test either serum or plasma specimens. Plasma obtained using EDTA, heparin, or sodium citrate, as an anticoagulant is suitable for testing.
2. Specimens may be tested immediately upon receipt or stored at 2 - 8 ^{0} C for up to 5 days prior to testing. Specimens should be stored at -20 ^{0} C or below if storage is necessary for more than 5 days.
3. Particulate matter can block the test membrane or cause high background colour making interpretation of results difficult. **Cloudy or viscous specimens should not be used for testing.**

B. Specimen Shipping

1. If specimens are to be shipped, dispatch by the fastest means available. Package the specimens in compliance with IATA Packing Instructions 650 and transport as diagnostic specimens.
2. Serum or plasma specimens may be shipped overnight at ambient temperature. However, if the transit time is expected to exceed 24 hours and/or the ambient temperature is >35^{0}C, specimens should be shipped under refrigeration.

C. Specimen Handling

1. For serum or plasma that has been previously frozen:
    a) Thaw completely at room temperature (15-27°C) and mix thoroughly by gently tapping the bottom of the capped tube.
    b) Centrifuge an aliquot of the specimen at room temperature (15-27°C) at 6000 rpm for at least 5 minutes and use only the clear supernatant for testing.
2. Avoid multiple freeze-thaw cycles. A specimen should not be frozen and thawed more than twice prior to use with Reveal HIV.

D. General Test Preparation

1. Allow all test components and specimens to equilibrate to room temperature (15-27°C) for 30-60 minutes prior to opening the specimen container or Mylar pouch.
2. Using the notched corners, tear open the required number of Test Cartridge Mylar pouches. Ensure that a desiccant packet is present in each pouch. If the desiccant packet is not present, discard the test cartridge and open a new pouch.
3. Inspect each test cartridge to ensure that a faint blue line is visible in the control zone under the letter **C** on the test cartridge. If this blue line is not visible, discard the test cartridge and open a new pouch.
4. Align the test cartridges in front of the specimens to be tested. Label test cartridges on the white plastic casing with a permanent marking pen. **Do not label or make any marks on the immunoreactive test membrane.**

E. Reconstitution of Reagents

I. Colorimetric Detection Agent

Reconstitute the Colorimetric Detection Agent as required. When reconstituted, one vial of the Colorimetric Detection Agent contains sufficient quantity to perform 15 tests. Reconstituted Colorimetric Detection Agent is stable for up to 30 days at 2-8ºC.

1. Using the notched corners, tear open the required number of Colorimetric Detection Agent Mylar pouches. One vial of Colorimetric Detection Agent is packaged in each Mylar pouch, and is sufficient to perform 15 tests.
2. Carefully tear off the metal closure and remove the stopper from the vial of the Colorimetric Detection Agent.
3. Remove the cap from the screw-capped bottle of Universal Buffer. Using the large transfer pipette provided, draw the Universal Buffer into the channel of the pipette to the 2 ml mark and deliver all of it into one vial of Colorimetric Detection Agent. Replace the stopper of the vial tightly. Gently mix the Colorimetric Detection Agent by tapping the bottom of the vial until all material has dissolved. **Do not mix by inverting the vial,** as this will cause excess foaming.
4. After mixing, ensure that the solution is a rose pink colour and free of precipitate by visual inspection. If the solution is blue or if precipitate is present, discard the solution and reconstitute another vial following steps 2-4. If the problem recurs, contact the MedMira Sales and Marketing Department for replacement.
5. Note the date of reconstitution, and expiration with a 30-day post dating on the vial with a permanent marking pen. Store the unused reconstituted Colorimetric Detection Agent upright in the stoppered vial at 2 - 8°C.
6. Discard reconstituted Colorimetric Detection Agent not used within the 30-day expiry dating. The Colorimetric Detection Agent can be disposed of in the sink and flushed with water.

II. Positive and Negative Test Controls

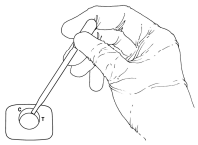
Reconstitute the Test Controls as required. When reconstituted, each vial of the Test Controls contains sufficient quantity to perform 5 tests. Reconstituted Test Controls are stable for up to 7 days at 2-8ºC.

1. Using the notched corners, tear open a *HIV Test Control* Mylar pouch.
2. Take the Negative Test Control vial and carefully remove the stopper.
3. Hold the Universal Buffer bottle with the drop dispenser on a slight angle from vertical (See **Testing Procedure** section) directly above the vial to avoid air bubbles. Add 6 drops of the Universal Buffer by gently squeezing the bottle.
4. Replace the stopper tightly, and gently mix by tapping the bottom of the vial until all material has dissolved. **Do not mix by inverting the vial,** as this will cause excess foaming.
5. After mixing, the solution should be clear with a slight yellow tint. If this is not the case, contact the MedMira Sales and Marketing Department for replacement.
6. Repeat steps 2-5 above with the Positive Test Control.
7. Note the date of reconstitution, and expiration with a 7-day post dating on the vials with a permanent marking pen. Store the unused reconstituted Test Controls upright in the stoppered vials at 2 - 8°C.
8. Discard reconstituted Test Controls not used within the 7 day expiry dating. The Test Controls should be treated as infectious liquid waste and disposed of according to local guidelines. The recommended method of disposal is autoclaving for a minimum of 1 hour at 121^0 C or by incineration.

F. Testing Procedure

- ***Perform the test on a flat work surface to ensure that reagents and specimens uniformly flow through the test device.***
- ***Once the assay has been started, all subsequent steps should be completed without interruption.***
- ***All solutions must be completely absorbed into the test membrane before proceeding to the next step in the testing procedure.***
- ***Read the test results immediately. Failure to do so may result in inaccurate test results.***

1. Holding the Universal Buffer bottle with the drop dispenser on a slight angle from vertical, apply **3** drops of the buffer to the centre of the test membrane. Allow the buffer to absorb completely.



2. Uncap the specimen tube(s). With the disposable pipette provided in the Test Cartridge Mylar pouch, draw the specimen into the channel of the pipette. Apply 1 drop of specimen to the centre of the test membrane. If the specimen does not completely absorb into the test membrane within 30 seconds, centrifuge an aliquot of the specimen at room temperature (15 - 27°C) at 6000 rpm for at least 5 minutes. Retest the clear supernatant using a new test before proceeding to the next step.

3. Holding the Universal Buffer bottle with the drop dispenser on a slight angle from vertical apply 3 drops of the buffer to the centre of the test membrane. Allow the buffer to absorb completely. **Do not touch the membrane with the drop dispenser tip.**

4. Apply **4** drops of the reconstituted Colorimetric Detection Agent (see above **Section E. Reconstitution of Reagents; part I, Colorimetric Detection Agent**) to the centre of the test membrane using a small disposable pipette provided in the poly zipper bag. Allow the solution to absorb completely. **Do not touch the test membrane with the pipette tip.**

5. Holding the Universal Buffer bottle with the drop dispenser on a slight angle from vertical apply **3** drops of the buffer to the centre of the test membrane. Allow the buffer to absorb completely. **Do not touch the test membrane with the drop dispenser tip.**

Read results immediately as indicated in the Test Results and Interpretation of Results section below.

After recording the test results, dispose of the test cartridges, empty Colorimetric Detection Agent and Test Control vials, disposable pipettes and other testing materials in a biohazard waste container.

QUALITY CONTROL

Built-in Control Feature

Reveal HIV includes a built-in procedural and reagent control that demonstrates the validity of the testing procedure and reagent function. A red vertical line under the letter 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 procedural and reagent control line will appear on all valid tests, regardless of whether the test result is Reactive or Non-Reactive (see **Test Results and Interpretation of Results** section below).

External Quality Control

One HIV Test Control Package is provided with the test kit, and is only for use with Reveal HIV. Additional packages are available as an accessory to the test. The Test Control Package includes a Positive and a Negative Test Control. Each test control is reconstituted as described above (**Section E. Reconstitution of Reagents; part II, Positive and Negative Test Controls**).

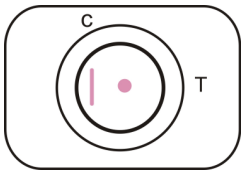
Using individual test cartridges run one Positive and one Negative Control to monitor proper test performance under the following circumstances:

- **With each new operator prior to performing testing on patient specimens.**
- **When beginning testing with a new lot of test devices.**
- **On each new shipment of tests received.**
- **At periodic intervals as required.**

Positive and Negative Test Controls are tested as per the **Testing Procedure** described above, replacing the specimen in step 2 of the **Testing Procedure**. The Positive Control will produce a Reactive test result indicated by both the red dot in the test (T) zone and a red vertical procedural and reagent control line in the control (C) zone upon completion of the test procedure. In contrast, the Negative Control will produce a Non-Reactive test result indicated by the absence of the red dot in the test zone and the presence of only the red vertical procedural and reagent control line in the control zone.

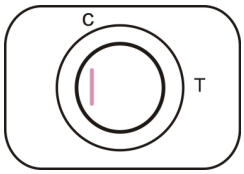
It is the responsibility of each laboratory using Reveal HIV to establish an adequate quality assurance program to ensure the proper performance of the device under its conditions of use. Contact MedMira's Sales and Marketing Department if the Positive and/or Negative Test Controls do not produce the expected results.

TEST RESULTS AND INTERPRETATION OF RESULTS



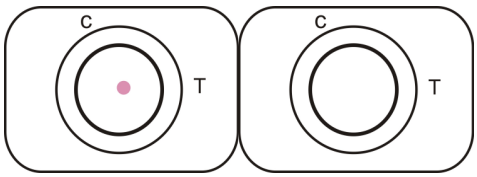
Reactive Result

This diagram is an example of a *Reactive Result*. The presence of a red dot, regardless of intensity, on the test membrane across from the letter **T** indicates that HIV-1 and/or HIV-2 antibodies have been detected. The presence of the red vertical control line under the letter **C** validates the test. Accordingly, the test result is interpreted as *Preliminary Positive* for HIV-1/HIV-2 antibodies.



Non-Reactive Result

The diagram is an example of a *Non-Reactive* result. The absence of a red dot on the test membrane across from the letter **T** indicates that HIV-1 and HIV-2 antibodies were not detected. The presence of the red vertical control line under the letter **C** validates the test. Accordingly, the test result is interpreted as *Negative* for HIV-1/HIV-2 antibodies. (A uniform, faint pinkish background may be visible on the test membrane).



Invalid Result

The diagrams are examples on an *Invalid* result. The absence of the red vertical control line under the letter **C** or the presence of a broken control line indicates that there has been a problem with the test reagents or the testing procedure. Also, a problem with the test specimen will occasionally result in a high background colour on the test membrane, which will not permit reading of the test result. Accordingly, in all of these instances (as shown in the diagrams to the left), the test result is deemed *Invalid* regardless of the specimen test result.

- Any specimen with a Reactive result should be retested in duplicate to confirm the initial result, and all repeatedly Reactive results confirmed by appropriate supplemental tests such as the Western blot test, or by suitable tests of multi-test algorithms.
- If an Invalid test result is obtained, testing should be repeated using a new test cartridge.
- Specimens yielding a high background colour should be tested using an alternate method.

PERFORMANCE CHARACTERISTICS

Reveal HIV was evaluated in independent pre-clinical and clinical trials conducted in Canada, United States, Bahamas, Uganda, Sierra Leone, and India both in low and high HIV prevalence populations. These studies were done using characterized repository specimens as well as fresh serum/plasma specimens in real-time in routine clinical settings. These studies have determined the safety and effectiveness of the Reveal HIV. The performance data of Reveal HIV are summarized below.

Sensitivity

The sensitivity of Reveal HIV was determined based on confirmed HIV-1 and HIV-2 positive serum or plasma specimens from persons with AIDS, HIV high risk groups such as gay men, intravenous drug users and sex traders etc, and from low risk general population infected with HIV. The overall sensitivity of Reveal HIV was 99.4% (95% C.I: 99.2, 99.6) when 2,958 HIV-1 positive specimens were tested. This included 1026 confirmed HIV-1 antibody positive serum and plasma specimens obtained from various parts of the world to determine the sensitivity of the Reveal HIV for the detection of antibodies to HIV-1 group M subtypes A, B, C, D, E, F, G; with this subset, the sensitivity was 99.8%. (95%C.I: 99.0, 100). Reveal HIV showed a sensitivity of 100% when 9 HIV-1 group O positive specimens were tested, and 99.6% (95% C.I: 98.9, 100) when 273 HIV-2 positive specimens tested.

Specificity

The specificity of Reveal HIV was determined based on reference screen HIV negative serum or plasma specimens presumed to be negative for HIV antibodies. The overall specificity of the test was 99.3% (95% C.I: 99.2, 99.4) when 16,968 HIV-1/HIV-2 negative specimens were tested.

Predictive Values and Agreement

In the above field trials, the mean positive predictive value of Reveal HIV was found to be 96.0% (range: 50.9% to 100%), the mean negative predictive value 99.1% (range: 98.0% to 100%), and the mean agreement with the reference methods 99.3% (range: 98.2% to 100%).

Stability

A panel of 19 specimens comprising 11 HIV-1 strongly reactive specimens, 6 HIV-1 weakly reactive specimens and 2 HIV-1/2 negative specimens was tested in triplicate using 3 master lots of Reveal HIV which had been stored at, 2 to 8°C, 20 to 25°C, 27 to 30°C, or 37°C for 12 to 18 months. All tests consistently yielded the expected results validating the stability of Reveal HIV under the conditions of storage.

Reproducibility

A panel of 19 specimens comprising 11 HIV-1 strongly reactive specimens, 6 HIV-1 weakly reactive specimens and 2 HIV-1/2 negative specimens was tested ten times each in a single assay. The intra-assay reproducibility of Reveal HIV was found to be 100%. The above panel of 19 specimens was also tested in triplicate using 3 master lots of Reveal HIV in 3 centres on 3 occasions to determine the intra- and inter-lot and intra- and inter-assay reproducibility of the test. The reproducibility of Reveal HIV was found to be 100% in these studies.

Reactivity with Seroconversion Panels

Five characterized commercial seroconversion panels (Boston Biomedica Inc. MA) and 15 clinical seroconversion panels were tested by Reveal HIV in comparison with Abbott HIVAB HIV-1/HIV-2 (rDNA) EIA or Biochem Pharma EIA and Western blot. Each panel consisted of a series of sequential specimens obtained from individual HIV infected cases during seroconversion. In five cases, Reveal HIV detected HIV antibody earlier than the reference EIA assays. In one instance, a sample obtained during seroconversion, which tested positive by EIA was negative by Reveal HIV; this sample yielded an indeterminate result by Western blot. In the rest, Reveal HIV was positive as early as the reference EIA assays. In six cases, Reveal HIV was positive earlier than Western blot in that the latter only showed "indeterminate" result with subsequent specimens yielding positive Western blot results thus confirming the initial Reveal HIV result. In the remaining cases, there was a 100% correlation with the Western blot results. Reveal HIV results on three representative seroconversion panels are summarized in Tables 1.1., 1.2., 1.3.

Table 1.1. Seroconversion Panel A

Bleed dates	Days since 1st bleed	Reveal HIV result	Abbott HIV 1/2 result	Western blot	Western blot band pattern						
					p24	p31	gp41	p51	p55	p65	Gp 120/160
08/14/95	0	Neg	Neg	-	-	-	-	-	-	-	-
08/16/95	2	Neg	Neg	-	-	-	-	-	-	-	-
08/21/95	7	Neg	Neg	-	-	-	-	-	-	-	-
08/23/95	9	Neg	Neg	-	-	-	-	-	-	-	-
08/29/95	15	Pos	Neg	-	-	-	-	-	-	-	-
09/11/95	28	Pos	Pos	-	-	-	-	-	-	-	-
09/16/95	33	Pos	Pos	+	+	-	-	-	-	-	+
09/18/95	35	Pos	Pos	+	+	-	+	+	-	+	+
09/25/95	42	Pos	Pos	+	+	-	+	+	-	+	+

Table 1.2. Seroconversion Panel B

Date of bleed	Days since 1st bleed	Reveal HIV result	Abbott HIV 1/2 result	Western blot	Western blot band pattern						
					p24	p31	gp41	p51	p55	p65	Gp 120/160
04/29/81	0	Neg	Neg	-	-	-	-	-	-	-	-
05/20/81	21	Neg	Neg	-	-	-	-	-	-	-	-
06/17/81	49	Pos	Neg	-	-	-	-	-	-	-	-
07/30/81	92	Pos	Pos	+	+	-	+	-	+	+	+
08/06/81	99	Pos	Pos	+	+	-	+	+	+	+	+

Table 1.3. Seroconversion Panel C

Date of bleed	Days since 1st bleed	Reveal HIV result	Abbott HIV 1/2 result	Western blot	Western blot band pattern						
					p24	p31	gp41	p51	p55	p65	Gp 120/160
01/13/89	0	Neg	Neg	-	-	-	-	-	-	-	-
01/20/89	7	Neg	Neg	-	-	-	-	-	-	-	-
01/25/89	12	Neg	Neg	-	-	-	-	-	-	-	-
02/01/89	19	Neg	Neg	-	-	-	-	-	-	-	-
02/08/89	26	Neg	Neg	-	-	-	-	-	-	-	-
02/10/89	28	Pos	Pos	+	+	-	+	+	-	+	+

Comparability with Approved Rapid HIV Tests

Reveal HIV was evaluated in comparison with the Red Dot HIV test, a WHO approved rapid HIV screen test similar to that of Reveal HIV. In parallel testing of 885 serologically defined specimens, the overall agreement of Reveal HIV was found to be 99.7% (Table 2).

Table 2. Comparability with the Red Dot Rapid HIV Test

		Red Dot test		Reveal HIV test		% Agreement
		+	-	+	-	
Abbott EIA screen/ Western blot Confirmatory test	+	192	0	191	1	99.5
	-	0	693	2	691	99.7
Total		192	693	193	692	99.7

Reveal HIV was also evaluated in comparison with the SUDS rapid HIV-1 test, a FDA approved rapid test. In parallel testing of 200 serologically defined specimens, both tests showed identical results with 100% accuracy (Table 3).

Table 3. Comparability with the SUDS Rapid HIV-1 Test

		SUDS test		Reveal HIV test		% Agreement
		+	-	+	-	
Abbott EIA screen/ Western blot Confirmatory test	+	50	0	50	0	100
	-	0	150	0	150	100
Total		50	150	50	150	100

Interference study

The possible effects of anticoagulants, medical conditions other than HIV infection, and non-specific interfering substances on the outcome of Reveal HIV were assessed. The results indicated that EDTA, heparin and sodium citrate did not interfere with the test. It also indicated Reveal HIV to have a significantly better specificity than the Abbott HIV EIA screen, and showed no false positive results with other types of specimens tested with the exception of 6 specimens, which also tested falsely positive by the reference EIA (Table 4).

Table 4. Interference Study Data

Nature of specimen	Number of specimens tested	Reveal HIV test	
		-	+
Abbott HIV-1/2 EIA positive/Western blot negative[1]	49	43	6
Viral infections other than HIV[2]	91	91	0
Bacterial infections[3]	35	35	0
Other [4]	20	20	0
Total	195	189	6

[1] Falsely positive by Abbott EIA screen
[2] Includes HTLV-1, hepatitis B, hepatitis C, CMV, HSV, measles, rubella, and varicella positive specimens
[3] Includes ASO, mycoplasma and syphilis positive specimens
[4] Includes rheumatoid factor and CRP positive specimens

HIV Antibody Detection Limits

For this purpose, 10 well-characterized HIV positive plasma specimens were utilized. These were obtained from 10 individual cases that were in different stages of HIV/AIDS disease. These specimens were serially diluted 2-fold using HIV negative plasma yielding 6 dilutions from 1:2 to 1:64. Each of these 6 dilutions along with the undiluted specimen were simultaneously tested using Reveal HIV in comparison with the Abbott HIVAB HIV-1/ HIV-2 (rDNA) EIA as the reference method. This study indicated that the Reveal HIV could reliably detect HIV antibodies in specimens diluted up to 1:4. This level of performance for a rapid test of this nature is considered to be satisfactory.

LIMITATIONS OF THE TEST

1. Reveal HIV must be used in accordance with this Package Insert to ensure accurate results. Health Canada has approved this test for serum or plasma specimens only. Testing of other types of specimens may not yield accurate results.
2. Test results are to be read and interpreted immediately following the final washing step with Universal Buffer. A delay in reading test results may yield inaccurate results.
3. Specimens that do not pass through the membrane within 30 seconds after centrifugation (see **Testing Procedure, step 2**) are unsuitable for testing with this test.
4. Lipemic samples or specimens contaminated with bacteria may not pass through the membrane within 30 seconds, and therefore may be unsuitable for testing with this test.
5. Limited studies were conducted to determine the performance of the test on fresh serum and plasma specimens.
6. Limited studies were conducted to determine the potential effect of interfering substances and unrelated medical conditions on the performance of the test.
7. A Reactive test result using Reveal HIV suggests the presence of HIV-1 and or HIV-2 antibodies in the specimen. This test is intended to be used as an aid in the diagnosis of infection with HIV-1/HIV-2. AIDS and AIDS-related conditions are clinical syndromes and their diagnosis can only be established clinically. Therefore, results of this test should not be used in isolation, but in conjunction with the clinical status, history, and risk factors of the individual being tested.
8. The intensity of the red dot (Reactive test result) does not necessarily correlate with the antibody titre of the specimen.
9. A Non-Reactive test result with Reveal HIV indicates the absence of detectable antibodies to HIV in the specimen. However, a Non-Reactive test result does not exclude the possibility of exposure to, or infection with HIV. Following a recent exposure to HIV, it may take several months for the antibody response to reach detectable levels, during which time testing for antibodies to HIV will not be indicative of true infection status. A comprehensive risk history and clinical judgement should be considered before concluding that an individual is not infected with HIV.

PRODUCT WARRANTY

The MedMira Laboratories Inc. guarantees the quality of this product if stored and used as stipulated. 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 the MedMira Laboratories Inc. be liable for consequent damage.

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