


# Determine<sup>®</sup>

## HIV-1/2 Ag/Ab Combo

### Key to symbols used


**REF** Catalogue Number

**IVD** *In Vitro* Diagnostic Medical Device

 Consult instructions for use

 Manufacturer

 Store at 2-30°C

 Contains Sufficient for 20 or 100 tests

 Expiration Date

**LOT** Lot Number

**EDTA CAPILLARY TUBES** EDTA Capillary Tubes

**CHASE BUFFER** Chase Buffer

 CE Mark

# Determine<sup>®</sup>

## HIV-1/2 Ag/Ab Combo

This package insert must be read carefully prior to use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are deviations from the instructions in this package insert.

### NAME AND INTENDED USE

Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo is an *In Vitro*, visually read, qualitative immunoassay for the simultaneous detection of HIV p24 antigen (Ag) and antibodies (Ab) to HIV-1 and HIV-2 in human serum, plasma or whole blood. The test is intended as an aid to detect HIV antigen and antibodies to HIV-1/HIV-2 from infected individuals.

### SUMMARY AND EXPLANATION OF THE TEST

AIDS (Acquired Immunodeficiency Syndrome) is characterized by changes in the population of T-cell lymphocytes. In an infected individual, the virus causes depletion of helper T-cells, which leaves the person susceptible to opportunistic infections and some malignancies. The virus that causes AIDS exists as two related types known as HIV-1 and HIV-2. The presence of HIV first elicits the secretion of p24 antigen<sup>1,2</sup> followed by the production of specific antibodies to either HIV-1 or HIV-2.<sup>3,4,5</sup>

### BIOLOGICAL PRINCIPLES OF THE PROCEDURE

Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo is an immunochromatographic test for the qualitative detection of p24 antigen and antibodies to HIV-1 and HIV-2.

Specimen is added to the sample pad. The specimen mixes with a biotinylated anti-p24 antibody and selenium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized avidin, recombinant antigens and synthetic peptides at the patient window sites.

If antibodies to HIV-1 and/or HIV-2 are present in the specimen, the antibodies bind to the antigen-selenium colloid and to the immobilized recombinant antigens and synthetic peptides, forming one red bar at the patient HIV Antibody window site. If antibodies to HIV-1 and/or HIV-2 are absent the antigen-selenium colloid flows past the patient window, and no red bar is formed at the patient HIV Antibody window site.

If p24 antigen is present in the specimen, the antigen binds to the biotinylated anti-p24 from the sample pad and the selenium colloid anti-p24 antibody and it binds to an immobilized avidin forming a red bar at the patient HIV Antigen window site. If p24 antigen is not present both the biotinylated anti-p24 and selenium colloid anti-p24 antibody flow past the patient window, and no red bar is formed at the patient HIV Antigen window site.

To ensure assay validity, a procedural control bar is incorporated in the assay device.

### CONTENTS

Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo 20 Test (7D2646) or 100 Test (7D2647)

- Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo Test Card, 2 or 10 cards (10 tests/card) coated with HIV-1/2 recombinant antigen and synthetic peptides, anti-p24 antibodies and avidin.

### ACCESSORIES (required but not provided)

For testing Whole Blood samples.

**CHASE BUFFER** (2.5 mL) Chase Buffer (7D2247) prepared in phosphate buffer. Preservatives: Antimicrobial Agents.

Whole Blood (fingerstick assay)

**EDTA CAPILLARY TUBES** (7D2227)

### WARNINGS AND PRECAUTIONS

For *In Vitro* Diagnostic Use.

For Professional use only.

Safety data sheet available for professional user on request.

### CAUTION:

Appropriate biosafety practices<sup>7,8</sup> should be used when handling specimens and reagents. These precautions include, but are not limited to the following:

- Wear gloves.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in areas where these materials are handled.
- Clean and disinfect all spills of specimens or reagents using suitable disinfectant, such as 0.5% sodium hypochlorite, or other suitable disinfectant.<sup>6</sup>
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local regulations.<sup>7,8</sup>

### STORAGE

Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo Test Cards and Chase Buffer must be stored at 2-30°C until expiration date.

- Kit components are stable until expiration date when handled and stored as directed. Do not use kit components beyond expiration date.
- Immediately reseal all unused tests in the foil pouch containing the desiccant by pressing seal from end to end to close.
- Do not use devices that have become wet or if the packaging has become damaged.

### SPECIMEN COLLECTION

Serum, Plasma, and Whole Blood Collection by Venipuncture.

Human serum, plasma, and whole blood collected by venipuncture should be collected aseptically in such a way as to avoid hemolysis.

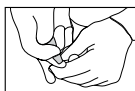
Separate the serum from the clot or plasma from the packed cells as soon as possible to avoid any hemolysis.

**NOTE: For whole blood and plasma specimens, EDTA collection tubes must be used.**

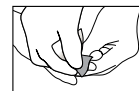
### Whole Blood Collection by Fingerstick<sup>9</sup>

Before collecting a fingerstick specimen, place an EDTA capillary tube on a clean dry surface.

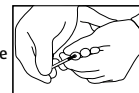
1. Choose the fingertip of the middle, ring, or index finger (whichever is the least callused). Warm the hand as needed with a warm, moist towel or warm water to increase blood flow.



2. Clean fingertip with alcohol; allow to air dry.



3. Position the hand palm-side up. Place the lancet off-center on the fingertip. Firmly press the lancet against the finger and puncture the skin. Dispose of the lancet in an appropriate biohazard sharps container.



4. Wipe away the first drop of blood with a sterile gauze pad.

5. Hold the finger lower than the elbow and apply gentle, intermittent pressure to the base of the punctured finger several times. Touch the tip of the EDTA Capillary Tube to the drop of blood<sup>9</sup>. Avoid air bubbles.

<sup>9</sup>If EDTA Capillary Tubes (No. 7D2227) will be used, fill the tube with blood between the 2 marked lines.

### SPECIMEN STORAGE

- Serum and plasma specimens should be stored at 2-8°C if the test is to be run within 7 days of collection. If testing is delayed more than 7 days, the specimen should be frozen (-20°C or colder).
- Avoid repeated freeze/thaw cycles. Specimens that have been frozen and thawed more than 3 times cannot be used.
- All frozen specimens must be centrifuged at 10,000g for 5min at room temperature. Carefully remove the 50µL test sample from the supernatant. If a lipid layer is formed on the surface of the liquid, ensure that the sample is taken from the clear liquid below that layer.
- Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 7 days of collection. Do not freeze whole blood specimens.
- Whole blood collected by fingerstick should be tested immediately.

### TEST PROCEDURE

The desired number of test units from the 10-test card can be removed by bending and tearing at the perforation.

#### NOTE:

- Removal of the test units should start from the right side of the test card to preserve the lot number which appears on the left side of the test card.
- Assay should be initiated within 2 hours after removing the protective foil cover from each test.

1. Remove the protective foil cover from each test.

2. For serum or plasma samples:

- a. Apply 50µL of sample (precision pipette) to the sample pad (marked by the arrow symbol).
- b. Wait a minimum of 20 minutes (up to 30 minutes maximum) and read result.

3. For whole blood (venipuncture) samples:

- a. Apply 50µL of sample (precision pipette) to the sample pad (marked by the arrow symbol).
- b. Wait one minute, then apply one drop of Chase Buffer to the sample pad.
- c. Wait a minimum of 20 minutes (up to 30 minutes maximum) and read result.

4. For whole blood (fingerstick) samples:

- a. Apply 50µL of sample (by EDTA capillary tube) to the sample pad (marked by the arrow symbol).
- b. Wait until blood is absorbed into the sample pad, then apply one drop of Chase Buffer to the sample pad.
- c. Wait a minimum of 20 minutes (up to 30 minutes maximum) and read result.

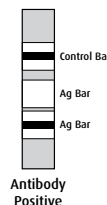
### QUALITY CONTROL

To ensure assay validity, a procedural control is incorporated in the device and is labeled "Control". If the control bar does not turn red by assay completion, the test result is invalid and the sample should be retested.

### INTERPRETATION OF RESULTS

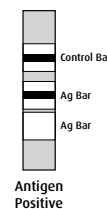
#### ANTIBODY POSITIVE (Two Bars - Control and Ab Bars)

Red bars appear in both the control window (labeled "Control") and in the Ab bar window (labeled "Ab") of the strip. Any visible red (or grey-red) color in the patient window should be



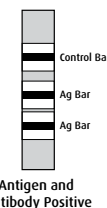
#### ANTIGEN (p24) POSITIVE (Two Bars - Control and Ag Bars)

Red bars appear in both the control window (labeled "Control") and in the Ag bar window (labeled "Ag") of the strip. Any visible red (or grey-red) color in the patient window should be interpreted as positive. The presence of only an antigen response suggests that the infection is at an early stage. Follow up testing may be suggested in order to track the expected future detection of antibodies.



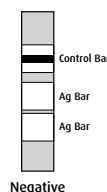
#### ANTIBODY POSITIVE AND ANTIGEN (p24) POSITIVE (Three Bars - Control, Ab and Ag Bars)

Red bars appear in the Control window (labeled "Control"), the Ab bar window (labeled "Ab") and Ag bar window (labeled "Ag") of the strip. Any visible red (or grey-red) color in the Ab bar and Ag bar windows should be interpreted as positive. The presence of an antigen response suggests that the infection is at an early stage.



#### NEGATIVE (One Bar)

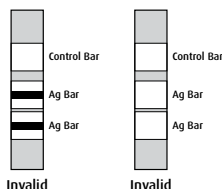
One red bar appears in the control window of the strip (labeled "Control"), and no red bar appears in the patient windows of the strip (labeled "Ag" and "Ab").



# Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo

## INVALID (No Bar)

If there is no red bar in the control window of the strip, and even if a red bar appears in one of the patient windows of the strip, the result is invalid and should be repeated. If the problem persists, contact your local distributor or call Inverness Medical Technical Support on: +44 (0) 1234 835959 or email: product.support@invmed.com.



## NOTES:

- The test result is positive even if the patient bars appear lighter or darker than the control bar.
- If an invalid test result occurs repeatedly, or for technical assistance, contact your local distributor or call Technical Support, as detailed above.

## LIMITATIONS OF THE PROCEDURE

- Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo is designed to simultaneously detect antibodies to HIV-1 and/or HIV-2 and HIV p24 antigen in human serum, plasma and whole blood. Other body fluids or pooled specimens may not give accurate results and should not be used.
- The intensity of the Ab and Ag bars does not correlate to the titer of antibody and antigen in the specimen.
- No test provides absolute assurance that a specimen does not contain low levels of HIV p24 antigen and/or antibodies to HIV-1 and HIV-2 such as those present at a very early stage of infection. A negative result for both antibodies to HIV and p24 antigen does not preclude the possibility of exposure to or infection with HIV-1 or HIV-2 viruses. A positive result for antibodies to HIV with a negative result for p24 antigen does not preclude the possibility of acute infection.
- Positive results should be confirmed using another method and the results should be evaluated in light of the overall clinical evaluation before a diagnosis is made.

## PERFORMANCE CHARACTERISTICS

The performance of Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo has been determined by testing specimens from random blood donors, from patients with HIV infection, patients at risk of HIV infection or in other clinical categories and commercial seroconversion panels. The performance evaluations were conducted in seven clinical studies in Europe, Africa and Asia

## SENSITIVITY

Sensitivity has been evaluated by testing confirmed HIV Ab positive samples, commercial seroconversion panels and specimens from primary (acute) HIV infected patients.

### 1. HIV Antibody positive specimens:

Table I  
Sensitivity of Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo

Types	Number of Specimens Tested	Positive by Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo	Sensitivity
HIV-1	870	870	100.00%
HIV-1 group O	7	7	100.00%
HIV-1 non B subtypes*	118	118	100.00%
HIV-2	133	133	100.00%
<b>Total</b>	<b>1128</b>	<b>1128</b>	<b>100.00%</b>

\*Subtypes: A, C, D, F, G, H, J, K, and CRF AE, AG, AD, BD, 06, 09 and 011.

A total of 1128 confirmed HIV Ab positive specimens were tested (Table I). The diagnostic sensitivity of Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo on this population of specimens is calculated to be 100%.

Table II  
Comparison of results obtained with Determine HIV 1/2 Ag/Ab Combo using matched specimens of whole blood (venipuncture and fingerstick), serum and plasma.

Specimens					Correlation between matrices
Type of Specimen					
No. of matched specimens tested	Serum	Plasma	Whole Blood (venipuncture)	Whole Blood (fingerstick)	
70	70	70	70	-	100%
20	-	-	20	20	100%
9	-	9	9	-	100%
22	22	22	-	22	100%

### Multiple (matched) specimens:

Seropositive specimens from a total of 121 individuals from Africa and Europe were tested. Multiple (matched) specimens were obtained from several of these donors. From these 121 individuals, 92 serum specimens, 101 plasma specimens, 99 whole blood (venipuncture) specimens and 42 whole blood (fingerstick) specimens were obtained in various combinations.

### Whole Blood (venipuncture) specimens:

99 whole blood (venipuncture) specimens were tested. Of these, 70 were matched with serum and plasma, 9 were matched pairs with plasma and 20 were matched pairs with whole blood (fingerstick) specimens.

### Whole Blood (fingerstick) specimens:

42 whole blood (fingerstick) specimens were tested. Of these, 22 were matched with serum and plasma and 20 were matched pairs with whole blood (venipuncture) specimens.

The results obtained from all specimen matrices showed 100% correlation, demonstrating that Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo gives identical results for these types of specimen matrices.

### 2. HIV seroconversion specimens:

Table III  
Seroconversion panels

Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo results compared to Determine <sup>®</sup> HIV 1/2			
33 seroconversion panels	Earlier detection (at least one bleed)	Equivalent detection (Same sample recognized as positive)	Later detection
Number of seroconversion panels	23	10	0

A total of 33 seroconversion panels were studied and the Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo results were compared to the results of the CE marked Determine<sup>®</sup> HIV-1/2 (Table III).

With the exception of one panel, there was at least one specimen and up to 5 specimens reactive for the Ag bar, and recognized as acute infection (verified as positive for Ag according to the panel data sheet). Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo detected HIV infection 2-20 days earlier than the Determine<sup>®</sup> HIV-1/2 (3rd generation) antibody test, depending on the panel tested.

### 3. Primary HIV infection specimens:

A total of 116 specimens from primary HIV infected patients (pre- or per-seroconversion) were tested. Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo detected 107 (92.24%) of the samples when compared to commercial CE marked 4th generation EIA.

4. The analytical sensitivity of the Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo was evaluated by testing the EFS Ag HIV panel (HIV Ag panel from the French Blood Establishment). A detection limit of 25 pg/mL was reached.

The analytical sensitivity was also tested with purified HIV-1 p24 native protein (ABI, Maryland USA) showing limit of detection of 12.5 pg/mL.

## SPECIFICITY

A total of 2232 confirmed negative serum, plasma or whole blood specimens were tested by Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo (Table IV).

Table IV  
Specificity of Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo

Population	Number of Specimens Tested	Negative by Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo Ab line	Specificity (%) of the Ab line	Negative by Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo Ag line	Specificity (%) of the Ag line
Seronegative specimens	1722	1708	99.19%	1715	99.59%
Pregnant women	200	200	100.00%	199	99.50%
Disease States Other than HIV and Potentially Interfering Substances*	310	306	98.71%	310	100.00%
<b>Total</b>	<b>2232</b>	<b>2214</b>	<b>99.19%</b>	<b>2224</b>	<b>99.64%</b>

\*IV drug users, rheumatoid factor, cancer, alcoholic cirrhosis, autoimmune (ANA), high cholesterol, lipemic, high bilirubin, hemolyzed, anti mouse IgG and other viral or bacterial infections (HBV, HCV, HAV, HTLV, CMV, Toxo IgG, Syphilis, HSV 1/2, EBV, Flu vaccinated patients and Chlamydia IgG/IgM).

A total of 1722 negative specimens (included in table IV) were tested in 8 different clinical sites from three major geographic areas (Table V).

Table V  
A comparison of Determine<sup>®</sup> HIV-1/2 Ag/Ab Combo Specificity by geographic area

Area	Number of Specimens Tested	Negative by Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo Ab line	Specificity (%) of the Ab line	Negative by Determine <sup>®</sup> HIV 1/2 Ag/Ab Combo Ag line	Specificity (%) of the Ag line
Europe	237	236	99.58%	237	100.00%
Africa	1403	1390	99.07%	1396	99.50%
Asia	83	82	100.00%	82	100.00%
<b>Total</b>	<b>1722</b>	<b>1708</b>	<b>99.19%</b>	<b>1715</b>	<b>99.59%</b>

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## Advice Line

For further information, please contact your distributor, or call Inverness Medical Technical Support on: +44 (0) 1234 835959 or email: product.support@invmed.com

www.determinetest.com



Unipath Ltd, Bedford MK44 3UP, UK  
Tel: +44 (0) 1234 835000  
Fax: +44 (0) 1234 835009

