WHO Prequalification of Diagnostics Programme
PUBLIC REPORT

Product: Alere Determine HIV-1/2 Ag/Ab Combo
Number: PQDx 0034-013-00

Abstract

The Alere Determine HIV-1/2 Ag/Ab Combo with product codes[1] 7D2643 and 7D2243 manufactured by Alere Medical Co. Ltd., 357 Matsuhidai, Matsudo-shi, Chiba-ken 270-2214, Japan, "rest of the world" regulatory version (non CE-marked regulatory version), was accepted for the WHO list of prequalified diagnostics and was listed on 19 March 2012.

Alere Determine™ HIV-1/2 Ag/Ab Combo is an In Vitro, visually read, qualitative immunoassay for the simultaneous detection of free non-immunocomplexed HIV-1 p24 antigen (Ag) and antibodies (Ab) to HIV-1 and HIV-2 in human blood. The test specimen can be serum, plasma, fingerstick or venous whole blood. The test is intended as an aid to detect HIV-1 p24 antigen and antibodies to HIV-1/HIV-2 from infected individuals.

Specimen is added to the sample pad. The specimen mixes with a biotinylated anti-p24 antibody, selenium colloid-antigen conjugate and selenium colloid- anti p24 antibody. 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 free non immunocomplexed HIV-1 p24 antigen (Ag), 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.

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.

The test kit contains:

- Alere Determine® HIV-1/2 Ag/Ab Combo Test Cards[1]
- If whole blood test procedure, 1 bottle of Chase Buffer (2.5 ml) (List No 7D2243).

Storage:
The test kit should be stored at 2-30 °C.

Shelf-life upon manufacture:
10 months.

Summary of prequalification status for the Alere Determine HIV-1/2 Ag/Ab Combo

	Initial acceptance	
	Date	**Outcome**
Status on PQ list	16 March 2012	listed
Dossier assessment	12 January 2012	MR
Inspection status	24 October 2011	MR
Laboratory evaluation	8 March 2012	MR

MR: Meets Requirements
NA: Not Applicable

The Alere Determine HIV-1/2 Ag/Ab Combo was accepted for the WHO list of prequalified diagnostics on the basis of data submitted and publicly available information.

[1] 7D2643: 10 cards (10 tests per card) 100 tests
7D2243: Chase buffer, 1 Bottle (2.5 mL)

Background information

Alere Medical Co. Ltd. submitted an application for prequalification of the Alere Determine HIV-1/2 Ag/Ab Combo. Based on the established prioritization criteria, the Alere Determine HIV-1/2 Ag/Ab Combo was given priority for prequalification.

Product dossier assessment

Alere Medical Co. Ltd. submitted a product dossier for the Alere Determine HIV-1/2 Ag/Ab Combo as per the Instructions for compilation of a product dossier (PQDx_018 v1). The information submitted in the product dossier was reviewed by WHO staff and external experts (assessors) appointed by WHO in accordance with the internal report on the screening and assessment of a product dossier (PQDx_009 v2). Based on the product dossier screening and assessment findings, a recommendation was made to accept the product dossier for the Alere Determine HIV-1/2 Ag/Ab Combo for prequalification.

Commitments for prequalification:
The manufacturer committed to amend and submit additional documentation on the following issues:

1. analytical performance studies
2. clinical performance studies
3. stability studies
4. a new version of the instructions for use.

Manufacturing site inspection

An inspection was performed at the site of manufacture of the Alere Determine HIV-1/2 Ag/Ab Combo, with product codes 7D2643 and 7D2243 manufactured by Alere Medical Co. Ltd., at 357 Matsuhidai Matsudo-shi, Chiba-ken 270-2214, Japan, non CE-marked regulatory version, on 28 September to 1 October 2010. The inspection procedure is described in “Information for manufacturers on WHO prequalification inspection procedures for the sites of manufacture of diagnostics” (PQDx_014 v1).

The inspection found that Alere Medical Co. Ltd. had an established quality management system and manufacturing practices in place that should ensure the manufacture of a product of consistent quality. The manufacturer's final responses to the major and minor nonconformities, and observations, noted at the time of the inspection, were accepted on 24 October 2011.

Commitments for prequalification:

1. Alere Medical Co. Ltd. will continue to review Risk Analysis and Risk Management for accuracy of assessment of risk, attributed to specific components of the product, and the mitigation of such risk, and to ensure ongoing due consideration of end

users in resource limited and environmentally challenging regions to which the product is distributed.

2. Alere Medical Co. Ltd. will inform the WHO Prequalification of Diagnostics Programme of changes made subsequent to the site inspection, such as change in location of site of manufacture of major components of the test, or other changes to the manufacturing process that may affect the quality of the product.

Laboratory evaluation

Alere Determine™ HIV-1/2 Ag/Ab Combo (Alere Medical Co. Ltd.) was evaluated by WHO in the fourth quarter of 2011 at the Institute of Tropical Medicine, Antwerp, Belgium – a WHO Collaborating Centre for HIV/AIDS Diagnostics and Laboratory Support. The laboratory evaluation was conducted according to the "WHO Protocol for the laboratory evaluation of HIV serology assays" (PQDx_030 V1.0), and drew the following conclusions:

Alere Determine™ HIV-1/2 Ag/Ab Combo (Alere Medical Co. Ltd.) is an immunochromatographic rapid diagnostic test for the detection of antibodies to HIV-1/2 and HIV-1 p24 antigen in human serum, plasma and, venous/capillary whole blood. A volume of 50 µL of specimen is required to perform the assay. This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory testing settings. Reading of the results can be done visually i.e. subjective reading.

In this limited evaluation on a panel of 1081 clinically-derived specimens, we found an initial sensitivity (95% CI) of 100% (99.1% - 100%) and an initial specificity (95% CI) of 98.78% (97.6% - 99.5%) compared to the reference assays. The final sensitivity (95% CI) was 100% (99.1% - 100%) and the final specificity (95% CI) was 98.78% (97.6% - 99.5%) compared to the reference assays. Lot to lot variation observed was within the acceptance range.

For eight seroconversion panels, Alere Determine™ HIV-1/2 Ag/Ab Combo detected on average 0.75 specimens earlier than the benchmark assay (Enzygnost Anti-HIV 1/2 Plus [Siemens Healthcare Diagnostics]) and on average 0.125 specimens earlier than Vironostika HIV Ag/Ab (bioMérieux).

For the mixed titer panel, Alere Determine™ HIV-1/2 Ag/Ab Combo correctly classified all but one specimen. For the HIV-1 p24 antigen panel, Alere Determine™ HIV-1/2 Ag/Ab Combo correctly classified all specimens. For the HIV culture supernatant panel, Alere Determine™ HIV-1/2 Ag/Ab Combo detected all HIV-1 subtypes, the HIV-2 culture isolate was not detected.

For the 1st International Reference Panel for anti-HIV [NIBSC code 02/210], Alere Determine™ HIV-1/2 Ag/Ab Combo detected all subtypes tested (HIV-1 A, HIV-1 B, HIV-C, HIV-1 CRF01_AE, HIV-1 O and HIV-2). For the HIV-1 p24 antigen standard [NIBSC code 90/636], Alere Determine™ HIV-1/2 Ag/Ab Combo detected to a dilution of 1:320

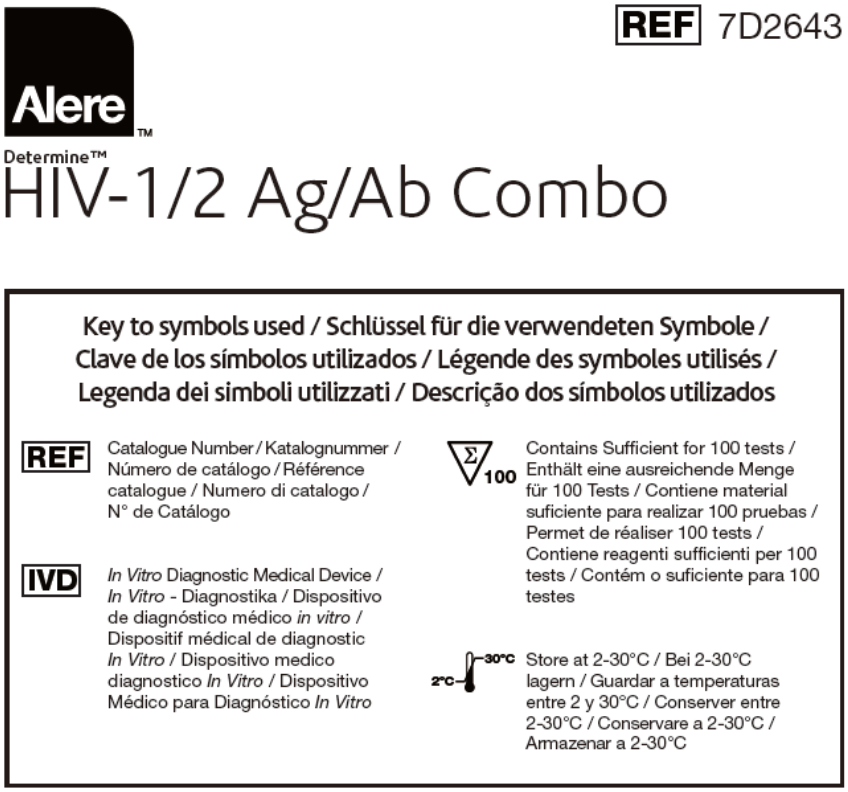
(corresponding to 3.125 international units). In contrast, Vironostika HIV Ag/Ab (bioMérieux) detected to 12.5 international units.

In this study, 0% of the results were recorded as indeterminate. Results were interpreted independently by three technicians; the overall inter-reader variability was 0.7%. The invalid rate was 0%.

Labelling

1. **Labels**
2. **Instructions for use**

1. Labels



2. Instructions for use

June 2011
240726/R5

Determine™ HIV-1/2 Ag/Ab Combo

EN

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

Alere Determine™ HIV-1/2 Ag/Ab Combo is an *in Vitro*, visually read, qualitative immunoassay for the simultaneous detection of free non immunocomplexed HIV-1 p24 antigen (Ag) and antibodies (Ab) to HIV-1 and HIV-2 in human blood. The test specimen can be serum, plasma, fingerstick or venous whole blood. The test is intended as an aid to detect HIV-1 p24 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[1,2] followed by the production of specific antibodies to either HIV-1 or HIV-2.[3,4,5]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

Alere Determine™ 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, selenium colloid-antigen conjugate and selenium colloid- anti p24 antibody. 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 free non immunocomplexed HIV-1 p24 antigen (Ag), 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

Alere Determine™ HIV-1/2 Ag/Ab Combo 100 Test (7D2643)

- **Alere** Determine™ HIV-1/2 Ag/Ab Combo Test Card, 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

1 Bottle (2.5 mL) Chase Buffer (7D2243) prepared in phosphate buffer.
Preservatives: Antimicrobial Agents.
Whole Blood (fingerstick assay)
EDTA Capillary Tubes (7D2222)
Microsafe Capillary Tube (7D2223)
Lancet

WARNINGS AND PRECAUTIONS

For *in Vitro* Diagnostic Use.
For Professional use only.
Safety data sheet available for professional user on request.
Patients with elevated triglycerides levels may test false reactive with the Alere Determine™ HIV-1/2 Ag/Ab Combo.

CAUTION:

Appropriate biosafety practices[7,8] 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.[7]
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local regulations.[7,8]

STORAGE

Alere Determine™ 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:[6]

EDTA Capillary Tubes or Microsafe Capillary Tube can be used.
Before collecting a fingerstick specimen, place an EDTA capillary tube on a clean dry surface. (Refer to the Microsafe Capillary Tube package insert for additional information.)

1. Choose the fingertip of the middle, ring, or index finger (whichever is the least calloused). 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*. Avoid air bubbles.

*If EDTA Capillary Tubes (No. 7D2222) 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 10,000*g* for 5 min at room temperature. Carefully remove the 50 µL 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.

  If stored at 2-8°C, bring specimen to room temperature before testing. Mix specimen well by gentle inversion of the tube immediately before testing.
- 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 50 µL of sample (precision pipette) to the sample pad (marked by the arrow symbol).
   b. Wait a minimum of 20 minutes from addition of the sample (up to 30 minutes maximum) and read result.
3. For whole blood (venipuncture) samples:
   a. Apply 50 µL 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 from addition of the chase buffer (up to 30 minutes maximum) and read result.
4. For whole blood (fingerstick) samples using an EDTA capillary tube:
   a. Place the capillary tube containing the blood sample onto the sample pad (marked by the arrow symbol).
   b. Wait until all the blood is transferred from the capillary tube to the sample pad and then immediately apply one drop of Chase Buffer to the sample pad. *Caution: do not lift the capillary from the sample pad before all the blood has been transferred – a bubble may form which will prevent the complete transfer of sample and invalidate the test.*
   c. Wait a minimum of 20 minutes from addition of the chase buffer (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". Any visible line (even very faint) in the control window should be interpreted as a valid result. 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 interpreted as positive.

Antibody Positive

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.

Antigen Positive

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.

Antigen and Antibody Positive

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").

Negative

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.

Invalid Invalid

NOTES:

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

LIMITATIONS OF THE PROCEDURE

- **Alere** Determine™ HIV-1/2 Ag/Ab Combo is designed to simultaneously detect antibodies to HIV-1 and/or HIV-2 and free non immunocomplexed HIV-1 p24 antigen (Ag), 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-1 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 **Alere** Determine™ 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. In addition, 90 fresh matched samples confirmed positive for HIV-1 were tested. The performance evaluations were conducted in nine clinical studies in Europe, Africa, Asia and South America.

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 Alere Determine™ HIV-1/2 Ag/Ab Combo

Types	Number of Specimens Tested	Positive by Alere Determine™ HIV 1/2 Ag/Ab Combo	Sensitivity
HIV-1	885	885	100.00 %
HIV-1 group O	7	7	100.00 %
HIV-1 non B subtypes*	154	154	100.00 %
HIV-2	133	133	100.00 %
Total	1179	1179	100.00 %

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

A total of 1179 confirmed HIV Ab positive specimens were tested (Table I). The diagnostic sensitivity of **Alere** Determine™ HIV-1/2 Ag/Ab Combo on this population of specimens is calculated to be 100%.

Table II
Comparison of results obtained with Alere 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)	
91	91	91	91	-	100 %
20	-	-	20	20	100 %
9	-	9	9	-	100 %
22	22	22	-	22	100 %
Total Number of specimens tested					
142	113	122	120	42	100 %

Multiple (matched) specimens:
Seropositive specimens from a total of 142 individuals from Africa, Europe and South America were tested. Multiple (matched) specimens were obtained from several of these donors. From these 142 individuals, 113 serum specimens, 122 plasma specimens, 120 whole blood (venipuncture) specimens and 42 whole blood (fingerstick) specimens were obtained in various combinations.
Whole Blood (venipuncture) specimens:
120 whole blood (venipuncture) specimens were tested. Of these, 91 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 **Alere** Determine™ HIV-1/2 Ag/Ab Combo gives identical results for these types of specimen matrices.

2. HIV seroconversion specimens:

Table III
Seroconversion panels

	Alere Determine™ HIV 1/2 Ag/Ab Combo results compared to Alere Determine™ 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 **Alere** Determine™ HIV-1/2 Ag/Ab Combo results were compared to the results of the CE marked **Alere** Determine™ 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). **Alere** Determine™ HIV-1/2 Ag/Ab Combo detected HIV infection 2-20 days earlier than the **Alere** Determine™ HIV-1/2 (3rd generation) antibody test, depending on the panel tested.

3. **Early seroconversion:**
   40 early sero-conversion HIV samples were tested. The results conform to the state of art.
4. **Primary HIV infection specimens:**
   A total of 117 specimens from primary HIV infected patients (pre- or per-seroconversion) were tested. **Alere** Determine™ HIV-1/2 Ag/Ab Combo detected 108 (92.31%) of the samples when compared to commercial CE marked 4th generation EIA.
5. The analytical sensitivity of the **Alere** Determine™ HIV-1/2 Ag/Ab Combo was evaluated by testing Whole blood, Serum and EDTA Plasma for WHO international standard 1963 HN-1 p24 Ag (NIBSC code 90/636). A detection limit of 2 IU/ml was reached.

SPECIFICITY

A total of 2343 confirmed negative serum, plasma or whole blood specimens were tested by **Alere** Determine™ HIV-1/2 Ag/Ab Combo and specificity was determined for the Antibody Test line and for the Antigen Test line (Table IV). In both tests the specificity is more than 99 %.

Table IV
Specificity of Alere Determine™ HIV-1/2 Ag/Ab Combo

Population	Number of Specimens Tested	Negative by Alere Determine™ HIV 1/2 Ag/Ab Combo Ab Test line	Specificity (%) of the Antibody Test line	Negative by Alere Determine™ HIV 1/2 Ag/Ab Combo Ag Test line	Specificity (%) of the Antigen Test line
Seronegative specimens	1783	1769	99.21 %	1776	99.61 %
Pregnant women	200	200	100.00 %	199	99.50 %
Disease States Other than HIV and Potentially Interfering Substances*	360	356	98.89 %	360	100.00 %
Total	2343	2325	99.23 %	2335	99.66 %

*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, multiparous, (HBV, HCV, HTLV, CMV, Toxo IgG, Syphilis, HSV 1/2, EBV, Flu vaccinated patients and Chlamydia IgG/IgM).
A total of 1783 negative specimens (included in table IV) were tested in nine different clinical sites from four major geographic areas and specificity was determined for the Antibody Test line and for the Antigen Test line (Table V).

Table V
A comparison of Alere Determine™ HIV-1/2 Ag/Ab Combo Specificity by geographic area

Area	Number of Specimens Tested	Negative by Alere Determine™ HIV 1/2 Ag/Ab Combo Ab Test line	Specificity (%) of the Antibody Test line	Negative by Alere Determine™ HIV 1/2 Ag/Ab Combo Ag Test line	Specificity (%) of the Antigen Test line
Europe	237	236	99.58 %	237	100.00 %
Africa	1383	1370	99.06 %	1376	99.49 %
Asia	82	82	100.00 %	82	100.00 %
South America	81	81	100.00 %	81	100.00 %
Total	1783	1769	99.21 %	1776	99.61 %

Table VI
A comparison of Alere Determine™ HIV-1/2 Ag/Ab Combo Specificity in whole blood and paired serum and plasma specimens

No. of Individuals	Serum	Plasma	WB venipuncture
64	64	64	64
20	-	20	20
Total			
84	64	84	84

Multiple (matched) specimens:
Seronegative specimens from a total of 84 individuals from Africa and South America were tested. Multiple (matched) specimens were obtained from several of these donors. A total of 84 whole blood (venipuncture) specimens were tested. Of these, 64 were matched pairs with serum and plasma, and 20 were matched pairs with plasma specimens.
The results obtained from all specimen matrices showed 100% correlation, demonstrating that **Alere** Determine™ HIV-1/2 Ag/Ab Combo gives identical results for these types of specimen matrices.

Advice Line (See Back Page)

BIBLIOGRAPHY (See Back Page)