ACCESS®
Immunoassay System
HIV combo

For the qualitative detection of HIV p24 antigen and antibodies to HIV-1/O/2 in human serum and plasma using the Access Immunoassay Systems.

ACCESS®
Immunoassay System
HIV combo Calibrators

The Access HIV combo Calibrators are intended to calibrate the Access HIV combo assay using the Access Immunoassay Systems.

ACCESS®
Immunoassay System
HIV combo QC

For monitoring the system performance of the Access HIV combo assay.

ACCESS®
Immunoassay System
HIV combo QC4 & QC5

For monitoring the system performance of the Access HIV combo assay.
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For the qualitative detection of HIV p24 antigen and antibodies to HIV-1/O/2 in human serum and plasma using the Access Immunoassay Systems.
1 Intended Use

The Access HIV combo assay is a paramagnetic-particle, chemiluminescent immunoassay for the qualitative detection of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum and plasma, using the Access Immunoassay Systems. The Access HIV combo assay is intended to be used as an aid in the diagnosis of HIV-1 or HIV-2 infection. This assay is not intended for testing or screening pooled specimens. An Access HIV combo assay result does not distinguish between the detection of HIV-1 p24 antigen, HIV-1 or HIV-1-O or HIV-2 antibodies.

2 Summary and Explanation of the Test

Acquired Immunodeficiency Syndrome (AIDS) is a virus-induced infectious disease expressed by a deep cellular immunity deficiency. Two types of viruses related to the lentivirus group were isolated from lymphocytes of patients with AIDS or its early syndromes.[1,2,3] The first virus called HIV-1 (Human Immunodeficiency Virus) was initially isolated in France and subsequently then in the USA. The second virus called HIV-2 was identified in two patients of African origin and found to be the origin of a new AIDS focus in West Africa.[4,5,6]

The knowledge of the genetic variability of HIV strains was gained from the sequencing of the GAG, POL and ENV genes of representative strains for each subtype.[7] A phylogenetic analysis enabled different groups of HIV-1 to be distinguished: group M (Major), group N (non-M, non-O), group O (Outlier) and group P.[8,9,10,11,12,13]

The group M of the HIV-1 includes 9 subtypes (A, B, C, D, F, G, H, J and K)[11] and circulating recombinant forms (CRFs).[11,14] The geographic distribution of the various subtypes is now fairly well defined.[15,16] Some HIV-1 variants have only 70% homology for GAG and POL genes with the main isolates, and only 50% for the ENV gene. These differences may account for the failure to diagnose the disease in some patients.[17] The various HIV-2 strains show common antigenic features with the simian immunodeficiency virus SIV, whichever viral protein is considered (envelope and core proteins; heterology: 30%). They show less than 40% homology with the envelope proteins of HIV-1.[8,18,19,20]

However, HIV-2 is less pathogenic than HIV-1, shows slower progression to disease, lower viral titers, and lower rates of vertical and horizontal transmission.[21,22,23,24]

HIV antigens and antibodies appear and are detectable at different stages of the infection.[25,26,27] Current diagnosis of HIV infection requires the detection of anti–HIV serum antibodies using an ELISA method.[28,29,30] However, there is a mean period of 3 weeks between exposure and the appearance of the first antibodies. During this period, p24 antigen may be detected in most people infected by HIV-1, whatever their geographical origin.[31,32] The Access HIV combo assay allows the simultaneous detection of both HIV-1 and HIV-2 antibodies. This assay also uses monoclonal antibodies in the reagents to detect HIV-1 p24 antigen prior to seroconversion, thereby decreasing the seroconversion window and improving early detection of HIV infection.[33,34,35,36]

3 Principles of The Procedure

The Access HIV combo assay is a sequential two-step immunoenzymatic (“sandwich”) assay. In the first test step, sample, coated paramagnetic particles, biotinylated monoclonal antibodies to p24 and particle additive are combined. The paramagnetic particles are coated with recombinant HIV-1 protein, HIV-1-O / HIV-2 polypeptides, and monoclonal antibodies against HIV-1 p24 antigen. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away.

In the second test step, 3 polypeptides and streptavidin labelled with alkaline phosphatase and also conjugate additive are then added. After incubation, the unbound reagents are removed by separation in a magnetic field and by washing. A chemiluminescent substrate Lumi-Phos 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is a function of the amount of enzyme conjugate present at the end of the reaction. The light quantity measured for a sample allows a determination of the presence of anti-HIV-1, or HIV-2 antibodies and/or antigen p24, by comparison to a cut-off value defined during the assay calibration on the instrument. If the light production is equal to or greater than the cut-off value, the sample is considered reactive in the Access HIV combo assay.
4 Product Information

4.1 Description

Access HIV combo Reagent Packs

<table>
<thead>
<tr>
<th>Identification on label</th>
<th>Description</th>
<th>Presentation/ preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1a</td>
<td>Paramagnetic particles: coated with recombinant HIV-1 protein (gp 160), HIV-1-O (gp 41) and HIV-2 (gp 36) polyptides and monoclonal antibodies to p24 HIV-1 antigen, suspended in TRIS buffered saline, with 0.1% sodium azide and ProClin 300 (0.25%).</td>
<td>2 x 50 tests Ready to use</td>
</tr>
<tr>
<td>R1b</td>
<td>Conjugate additive: TRIS buffered saline, with 0.1% sodium azide and ProClin 300 (0.25%).</td>
<td></td>
</tr>
<tr>
<td>R1c</td>
<td>Particle additive: TRIS buffer saline with biotinylated monoclonal antibodies to p24 HIV-1, with 0.1% sodium azide and ProClin 300 (0.25%).</td>
<td></td>
</tr>
<tr>
<td>R1d</td>
<td>Conjugates: HIV-1, HIV-1-O, HIV-2 polypeptides and streptavidin conjugated with alkaline phosphatase, with 0.1% sodium azide and ProClin 300 (0.25%).</td>
<td></td>
</tr>
</tbody>
</table>

4.2 Storage and Handling Conditions

- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C (reagent pack unopened).
- Mix the new, unpunctured packs by gently inverting them until the particles are in solution and no longer adhere to the seal or sides of the well. Do not invert packs that have been punctured.
- Stable at 2 to 10°C for 56 days on board after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e. broken elastomer), discard the pack.

5 Warnings and Precautions

- For in vitro diagnostic use. For healthcare professional use only.

5.1 Health and Safety Precautions

- This test kit should only be handled by qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately in accordance with Good Laboratory Practices.
- This test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Consequently, all human derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Universal Precautions for bloodborne pathogens as defined by OSHA, the guidelines from the current CDC/NHI Biosafety in Microbiological and Biomedical Laboratories and/or local, regional, national regulations.
- Biological spills: human source material spills should be treated as potentially infectious. Spills not containing acid should be immediately decontaminated, including the spill area, materials and any contaminated surfaces or equipment and with appropriate chemical disinfectant that is effective on the potential biohazards of the samples in question (commonly a 1:10 dilution of household bleach, 70-80% ethanol or isopropanol, an iodophor such as 0.5% Wescodyne™ Plus, etc.) and wiped dry. Spills containing acid should be appropriately absorbed (wiped up) or neutralized, the area flushed with water and wiped dry; materials used to absorb the spill may require hazardous waste disposal. The area should subsequently decontaminated with one of the chemical disinfectants.
• Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or bio-hazardous waste must be handled and discarded in accordance with all local, regional and national regulations.
• For hazard and precaution recommendations related to any chemical components in this test kit, please refer to the pictogram(s) featured on the labels and the information supplied in the section 5.2. The Safety Data Sheet (SDS) is available at www.bio-rad.com.

5.2 Precautions Related to the Procedure

Warning:

H317: May cause an allergic skin reaction.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.
P302+P352: If on skin: Wash with plenty of soap and water.
P501: Dispose of contents/container in accordance with local/regional/national/international regulations.

• This product contains human or animal components. Handle with care.

6 Specimens

1. Serum (including serum separator tubes) and plasma (Li Heparin, including plasma separator tubes EDTA and CPDA-1) are the recommended samples.

2. Do not heat the samples.

3. Observe the following recommendations for handling, processing, and storing blood samples:\(^{37}\):
   • Collect all blood samples observing routine precautions for venipuncture.
   • Allow serum samples to clot completely before centrifugation.
   • Ensure that all residual fibrin and cellular matter has been removed prior to analysis.
   • Follow blood collection tube manufacturer’s recommendations for centrifugation.
   • Keep tubes tightly stoppered at all times.
   • Store samples at room temperature (15 to 23°C) for no longer than twenty-four hours.
   • If the assay is not completed within twenty-four hours, refrigerate the samples at 2 to 8°C.
   • If the assay is not completed within 8 days at 2 to 8°C, or for shipment of samples, freeze at -20°C or below.
   • Thaw samples no more than 3 times. A study of 25 fresh non-reactive sera and 25 fresh reactive sera exhibited no clinically significant dose changes after three freeze-thaw cycles.
   • After thawing, the sample must be thoroughly mixed, centrifuged again at 3,000 g for 10 minutes and transferred into a cup in order to remove any suspended fibrin particles or aggregates liable to yield false-positive results.

4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, occasionally, from lot to lot.
7 Procedure

7.1 Material Required

7.1.1 Materials Provided

R1 Access HIV combo Reagent Packs

7.1.2 Materials Required but Not Provided

1. Access HIV combo Calibrators
   Provided as one HIV-Ab negative serum and one anti-HIV-1 Ab positive serum
   Cat. No. A59429

2. Quality control materials:
   • Access HIV combo QC, provided as one HIV-Ab negative serum, one anti-HIV-1 positive serum
     and one HIV-1 antigen positive in Tris Buffer
     Cat. No. A59430
   • Access HIV combo QC4 & QC5, provided as one anti-HIV-2 antibodies positive serum and one
     anti-HIV-1-O antibodies positive serum in human negative serum.
     Cat. No. B22822
   • Other commercial control sera

3. Access Substrate
   Cat. No. 81906

4. Access 2:
   Wash buffer: Access Wash Buffer II, Cat. No. A16792

5. UniCel® DxI®:
   Wash buffer: UniCel DxI Wash Buffer II, Cat. No. 16793

6. Systems:
   Access 2, UniCel DxI (UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel
   DxC 680i, UniCel DxC 660i).

7.2 Assay Procedure

1. Refer to the appropriate system manuals and/or Help system for a detailed description of
   installation, start-up, principles of operation, system performance characteristics, operating
   instructions, calibration procedures, operational limitations and precautions, hazards, maintenance
   and troubleshooting.

2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before
   loading on the instrument. Do not invert open (punctured) packs.

3. One hundred ten (110) μL of sample is used for each determination (in addition to dead volume).

4. Time to first result is approximately 60 minutes.

5. The system default unit of measure for sample results is the Signal/Cut-off (S/CO) ratio.

7.3 Calibration

An active calibration point is required for all tests. For the Access HIV combo assay, calibration is
required every 56 days. Consequently, for the Access HIV combo assay, calibration is required every 56
days using C0 and C1 from the Access HIV combo Calibrators kit.

Refer to the appropriate system manuals and/or Help system for information on calibration theory,
configuring calibrators, entering calibrator test requests and reviewing calibration data.

7.4 Quality Control

Quality control materials simulate the characteristics of patient samples and are essential for monitoring
the system performance of immunochemical assays. Quality control is recommended at least, every 24
hours and on system start-up prior to running patient samples. Include Access HIV combo QC and
Access HIV combo QC4 & QC5 kits or other commercially available quality control materials that cover at
least two levels of analyte. More frequent use of these controls or the use of additional controls is left to
the discretion of the user based on good laboratory practices or laboratory accreditation requirements
and applicable laws. Follow the manufacturer’s instructions for reconstitution and storage. Each
laboratory should establish mean values and acceptable ranges to ensure proper performance. Quality
control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test
results generated since obtaining the last acceptable quality control test point for this analyte. The Access
HIV combo assay has been evaluated at a room temperature range of 18-32°C. For optimal results, assay calibration and patient sample testing should be conducted under similar temperature conditions. If ambient laboratory temperature varies by more than ± 5°C from the temperature of calibration, review quality control results and recalibrate as necessary. Refer to the appropriate system manuals and/or Help system for complete information about reviewing quality control results.

All manufactured and commercialized reagents are under subject to a comprehensive quality system starting from the reception of raw materials right up to the ultimate commercialization of the product.

Each lot is submitted to a quality control and is only released onto the market if it conforms to the acceptance criteria.

7.5 Calculation / Interpretation of the Results

Patient test results are calculated automatically by the system software using the cut-off value determined by active calibration. Results (Signal/Cut-Off = S/CO) are reported to be “reactive” or “non-reactive” as a function of their relationship with the “cut-off” (signal greater than or signal equal to or less than the cut-off value). However, results ~10% lower than the “cut-off value” should be cautiously interpreted and retested in duplicate. This recommended gray zone (from 0.9 to less than 1.0) should be stored by the user in the system software (refer to the appropriate system manuals and/or Help system for complete instructions on gray zone for a qualitative assay). In this way a distinctive mark will automatically be reported, enabling rapid identification of a result situated in the gray zone. Patient test results can be reviewed using the Sample Results screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing results.

First result analysis:
- Any sample with a ratio (S/CO) lower than 0.9 is considered to be non-reactive with the Access HIV combo assay.
- Samples with a ratio (S/CO) ≥ 0.9 and < 1 are in the gray zone and should be retested in duplicate before final interpretation.
- Samples with a ratio (S/CO) greater than or equal to 1, are initially considered to be reactive with the Access HIV combo and such samples should be retested in duplicate before final interpretation.

Second result analysis:
All samples that were initially reactive or in the gray zone should be retested in duplicate using the Access HIV combo assay:
- If the results of the duplicates are < 1.0 S/CO, the sample must be considered non-reactive (negative) for the Access HIV combo assay.
- If one of the 2 results is ≥ 1.0 S/CO, the initial result is repeatable and the sample is declared as “reactive” for the Access HIV combo assay.

However, in accordance with local regulations, it is necessary to analyze any “reactive” sample by supplementary tests, including at least a confirmatory method to clearly establish the positive result.

Table 1: Access HIV combo result interpretation

<table>
<thead>
<tr>
<th>Result Ratio: Signal/Cut-Off</th>
<th>Interpretation</th>
<th>Supplementary tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Result Analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S/CO &lt; 0.9</td>
<td>Non-reactive</td>
<td>HIV-1 p24 and/or HIV-1/HIV-1-0/HIV-2 Ab not detected</td>
</tr>
<tr>
<td>S/CO ≥ 1.0</td>
<td>Reactive</td>
<td>“Initial Reactive”</td>
</tr>
<tr>
<td>0.9 ≤ S/CO &lt; 1.0</td>
<td>Gray zone</td>
<td>“Initial Reactive”</td>
</tr>
<tr>
<td><strong>Second Result Analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retest in duplicate: if the 2 results are &lt; 1.0</td>
<td>Non-reactive</td>
<td>HIV-1 p24 and/or HIV-1/HIV-1-0/HIV-2 Ab not detected</td>
</tr>
<tr>
<td>Retest in duplicate: if one of the 2 results is ≥ 1.0</td>
<td>Reactive</td>
<td>HIV-1 p24 and/or HIV-1/HIV-1-0/HIV-2 Ab detected “Repeat Reactive”</td>
</tr>
</tbody>
</table>
8 Test Limitations

1. The Access HIV combo assay is strictly limited to the detection of HIV-1 antigen and HIV-1/HIV-1-O/HIV-2 antibodies in human serum or plasma (Li heparin, EDTA and CPDA-1). The performance characteristics using other sample types have not been established or are limited.

2. The Access HIV combo results should be interpreted in light of the total clinical presentation of the patient, including: clinical history, data from additional tests and other appropriate information.

3. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.

4. Transplant patient samples have to be tested before freezing.

5. Performance has not been established using cadaver samples or body fluids other than human serum and plasma.

6. The magnitude of the measured result, above the cut-off, is not indicative of the total amount of antibody and/or antigen present.

7. A non-reactive result indicates that the tested sample contains no antigen and no antibodies detectable with Access HIV combo assay. This does not preclude the possibility of infection by HIV-1 and/or HIV-2.

8. For an infection to be declared, a reactive result obtained with the Access HIV combo assay should be confirmed by an appropriate method.

9. Immunocompromised individuals and conditions such as severe infection and immunosuppressive drug therapy can result in the suppression of antibody levels below the detection threshold of the assay. Results obtained with such samples should be interpreted with caution.

9 Performance Characteristics

9.1 Precision Measurement

A repeatability and intermediate precision study were realized on a panel constituted of 13 samples: 1 negative sample, 3 HIV-1 antibody positive samples, 3 HIV-1/O antibody positive samples, 3 HIV-2 antibody positive samples and 3 HIV-1 antigen positive samples at different amounts. A reproducibility study was then realized on three different sites (1 lot per site) on a sample panel constituted of 13 samples during 20 days, in triplicate, one run per day. Additionally one of the site tested the same panel on the three different lots during 5 days, in triplicate, 1 run per day.

All the studies were realized on the UniCel DxI 800 systems.

9.1.1 Repeatability

The 13 samples were tested in 30 replicates during the same run on one system. Mean, Standard Deviation (SD) and Coefficient of Variation (CV) were determined on ratio values (S/CO) for each sample.

Table 2: Repeatability results expressed in ratio S/CO

<table>
<thead>
<tr>
<th>ID</th>
<th>Sample Panel</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Negative</td>
<td>30</td>
<td>0.28</td>
<td>0.03</td>
<td>10.6</td>
</tr>
<tr>
<td>2</td>
<td>HIV-1 low</td>
<td>30</td>
<td>0.96</td>
<td>0.06</td>
<td>5.9</td>
</tr>
<tr>
<td>3</td>
<td>HIV-1 medium</td>
<td>30</td>
<td>2.19</td>
<td>0.09</td>
<td>4.1</td>
</tr>
<tr>
<td>4</td>
<td>HIV-1 high</td>
<td>30</td>
<td>2.86</td>
<td>0.16</td>
<td>5.8</td>
</tr>
<tr>
<td>5</td>
<td>HIV-1-O low</td>
<td>30</td>
<td>1.16</td>
<td>0.05</td>
<td>4.6</td>
</tr>
<tr>
<td>6</td>
<td>HIV-1-O medium</td>
<td>30</td>
<td>1.91</td>
<td>0.05</td>
<td>2.6</td>
</tr>
<tr>
<td>7</td>
<td>HIV-1-O high</td>
<td>30</td>
<td>3.34</td>
<td>0.14</td>
<td>4.2</td>
</tr>
<tr>
<td>8</td>
<td>HIV-2 low</td>
<td>30</td>
<td>0.95</td>
<td>0.04</td>
<td>4.4</td>
</tr>
<tr>
<td>9</td>
<td>HIV-2 medium</td>
<td>30</td>
<td>2.20</td>
<td>0.10</td>
<td>4.7</td>
</tr>
<tr>
<td>10</td>
<td>HIV-2 high</td>
<td>30</td>
<td>3.81</td>
<td>0.13</td>
<td>3.4</td>
</tr>
<tr>
<td>11</td>
<td>HIV-1 Ag low</td>
<td>30</td>
<td>1.20</td>
<td>0.05</td>
<td>4.6</td>
</tr>
<tr>
<td>12</td>
<td>HIV-1 Ag medium</td>
<td>30</td>
<td>2.41</td>
<td>0.12</td>
<td>5.0</td>
</tr>
<tr>
<td>13</td>
<td>HIV-1 Ag high</td>
<td>30</td>
<td>3.27</td>
<td>0.12</td>
<td>3.7</td>
</tr>
</tbody>
</table>
9.1.2 Intermediate Precision

The sample panel (N= 13) was tested on 1 lot, in duplicate, in 2 different runs per day for a period of 20 days on one system.

For each sample, descriptive statistics will be realized, with calculations of the mean, the standard deviation and the percent coefficient of variation (CV) on Ratio (S/CO) values. Within-run, between-run, between-day and total precision were expressed in % CV. Nested ANOVA method was used to determine within-run, between-run, between-day, between lot and total precision.

Table 3: Intermediate precision results expressed in ratio S/CO

<table>
<thead>
<tr>
<th>ID</th>
<th>Sample Panel</th>
<th>N</th>
<th>Mean</th>
<th>Within-run SD</th>
<th>CV%</th>
<th>Between-run SD</th>
<th>CV%</th>
<th>Between-day SD</th>
<th>CV%</th>
<th>Total precision SD</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Negative</td>
<td>80</td>
<td>0.30</td>
<td>0.03</td>
<td>8.9</td>
<td>0.00</td>
<td>NA</td>
<td>0.01</td>
<td>4.7</td>
<td>0.03</td>
<td>10.1</td>
</tr>
<tr>
<td>2</td>
<td>HIV-1 low</td>
<td>80</td>
<td>1.02</td>
<td>0.04</td>
<td>4.1</td>
<td>0.02</td>
<td>2.1</td>
<td>0.03</td>
<td>3.2</td>
<td>0.06</td>
<td>5.6</td>
</tr>
<tr>
<td>3</td>
<td>HIV-1 medium</td>
<td>80</td>
<td>2.35</td>
<td>0.08</td>
<td>3.5</td>
<td>0.07</td>
<td>2.9</td>
<td>0.08</td>
<td>3.3</td>
<td>0.13</td>
<td>5.6</td>
</tr>
<tr>
<td>4</td>
<td>HIV-1 high</td>
<td>80</td>
<td>3.04</td>
<td>0.10</td>
<td>3.3</td>
<td>0.10</td>
<td>3.5</td>
<td>0.05</td>
<td>1.7</td>
<td>0.16</td>
<td>5.1</td>
</tr>
<tr>
<td>5</td>
<td>HIV-1-O low</td>
<td>80</td>
<td>1.15</td>
<td>0.04</td>
<td>3.8</td>
<td>0.04</td>
<td>3.1</td>
<td>0.00</td>
<td>NA</td>
<td>0.66</td>
<td>4.9</td>
</tr>
<tr>
<td>6</td>
<td>HIV-1-O medium</td>
<td>80</td>
<td>1.88</td>
<td>0.07</td>
<td>3.8</td>
<td>0.04</td>
<td>2.3</td>
<td>0.03</td>
<td>1.4</td>
<td>0.09</td>
<td>4.6</td>
</tr>
<tr>
<td>7</td>
<td>HIV-1-O high</td>
<td>80</td>
<td>3.23</td>
<td>0.14</td>
<td>4.5</td>
<td>0.02</td>
<td>0.5</td>
<td>0.03</td>
<td>1.0</td>
<td>0.15</td>
<td>4.6</td>
</tr>
<tr>
<td>8</td>
<td>HIV-2 low</td>
<td>80</td>
<td>1.03</td>
<td>0.04</td>
<td>4.1</td>
<td>0.04</td>
<td>3.9</td>
<td>0.00</td>
<td>NA</td>
<td>0.66</td>
<td>5.6</td>
</tr>
<tr>
<td>9</td>
<td>HIV-2 medium</td>
<td>80</td>
<td>2.37</td>
<td>0.10</td>
<td>4.0</td>
<td>0.07</td>
<td>2.8</td>
<td>0.03</td>
<td>1.3</td>
<td>0.12</td>
<td>5.1</td>
</tr>
<tr>
<td>10</td>
<td>HIV-2 high</td>
<td>80</td>
<td>3.99</td>
<td>0.17</td>
<td>4.1</td>
<td>0.08</td>
<td>1.9</td>
<td>0.07</td>
<td>1.8</td>
<td>0.20</td>
<td>4.9</td>
</tr>
<tr>
<td>11</td>
<td>HIV-1 Ag low</td>
<td>80</td>
<td>1.17</td>
<td>0.04</td>
<td>3.3</td>
<td>0.04</td>
<td>3.6</td>
<td>0.00</td>
<td>NA</td>
<td>0.66</td>
<td>4.9</td>
</tr>
<tr>
<td>12</td>
<td>HIV-1 Ag medium</td>
<td>80</td>
<td>2.35</td>
<td>0.13</td>
<td>5.6</td>
<td>0.12</td>
<td>4.9</td>
<td>0.03</td>
<td>1.4</td>
<td>0.18</td>
<td>7.6</td>
</tr>
<tr>
<td>13</td>
<td>HIV-1 Ag high</td>
<td>80</td>
<td>3.12</td>
<td>0.12</td>
<td>4.7</td>
<td>0.07</td>
<td>4.0</td>
<td>0.02</td>
<td>2.4</td>
<td>0.15</td>
<td>4.7</td>
</tr>
</tbody>
</table>

9.1.3 Reproducibility study

The sample panel was tested in triplicate on each on 3 sites (1 lot and 1 system per site during 20 days). Each QC (1-5) was run in triplicate at the same time as the sample panel.

Table 4: Inter site study: results expressed in ratio S/CO

<table>
<thead>
<tr>
<th>ID</th>
<th>Sample Panel</th>
<th>N</th>
<th>Mean ratio</th>
<th>Within assay SD</th>
<th>CV%</th>
<th>Between assay SD</th>
<th>CV%</th>
<th>Between site SD</th>
<th>CV%</th>
<th>Total precision SD</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>QC1</td>
<td>Negative</td>
<td>180</td>
<td>0.36</td>
<td>0.05</td>
<td>14.6</td>
<td>0.04</td>
<td>10.2</td>
<td>0.05</td>
<td>14.3</td>
<td>0.08</td>
<td>22.8</td>
</tr>
<tr>
<td>QC2</td>
<td>HIV-1 Ab</td>
<td>180</td>
<td>2.78</td>
<td>0.15</td>
<td>5.4</td>
<td>0.16</td>
<td>5.8</td>
<td>0.23</td>
<td>8.5</td>
<td>0.32</td>
<td>11.6</td>
</tr>
<tr>
<td>QC3</td>
<td>HIV-1 Ag</td>
<td>180</td>
<td>5.51</td>
<td>0.33</td>
<td>6.1</td>
<td>0.18</td>
<td>3.3</td>
<td>0.20</td>
<td>3.7</td>
<td>0.43</td>
<td>7.8</td>
</tr>
<tr>
<td>QC4</td>
<td>HIV-2 Ab</td>
<td>179</td>
<td>3.40</td>
<td>0.18</td>
<td>5.3</td>
<td>0.11</td>
<td>3.3</td>
<td>0.00</td>
<td>N/A*</td>
<td>0.21</td>
<td>6.2</td>
</tr>
<tr>
<td>QC5</td>
<td>HIV-1-O Ab</td>
<td>180</td>
<td>3.33</td>
<td>0.15</td>
<td>4.5</td>
<td>0.17</td>
<td>5.0</td>
<td>0.23</td>
<td>7.0</td>
<td>0.32</td>
<td>9.7</td>
</tr>
<tr>
<td>P1</td>
<td>Negative</td>
<td>180</td>
<td>0.34</td>
<td>0.05</td>
<td>14.6</td>
<td>0.02</td>
<td>5.3</td>
<td>0.05</td>
<td>13.4</td>
<td>0.07</td>
<td>20.5</td>
</tr>
<tr>
<td>P2</td>
<td>HIV-1 non B Ab</td>
<td>180</td>
<td>0.82</td>
<td>0.06</td>
<td>7.1</td>
<td>0.04</td>
<td>4.8</td>
<td>0.09</td>
<td>10.5</td>
<td>0.11</td>
<td>13.5</td>
</tr>
<tr>
<td>P3</td>
<td>HIV-1 non B Ab</td>
<td>180</td>
<td>1.53</td>
<td>0.09</td>
<td>5.8</td>
<td>0.07</td>
<td>4.6</td>
<td>0.17</td>
<td>11.3</td>
<td>0.21</td>
<td>13.5</td>
</tr>
<tr>
<td>P4</td>
<td>HIV-1 non B Ab</td>
<td>180</td>
<td>2.88</td>
<td>0.18</td>
<td>6.4</td>
<td>0.13</td>
<td>4.5</td>
<td>0.31</td>
<td>10.6</td>
<td>0.38</td>
<td>13.2</td>
</tr>
<tr>
<td>P5</td>
<td>HIV-1-O Ab</td>
<td>180</td>
<td>0.88</td>
<td>0.05</td>
<td>6.0</td>
<td>0.04</td>
<td>4.9</td>
<td>0.03</td>
<td>3.6</td>
<td>0.08</td>
<td>8.6</td>
</tr>
<tr>
<td>P6</td>
<td>HIV-1-O Ab</td>
<td>180</td>
<td>1.73</td>
<td>0.09</td>
<td>5.4</td>
<td>0.08</td>
<td>4.7</td>
<td>0.02</td>
<td>1.3</td>
<td>0.13</td>
<td>7.3</td>
</tr>
<tr>
<td>P7</td>
<td>HIV-1-O Ab</td>
<td>180</td>
<td>3.22</td>
<td>0.15</td>
<td>4.8</td>
<td>0.14</td>
<td>4.4</td>
<td>0.00</td>
<td>N/A*</td>
<td>0.21</td>
<td>6.5</td>
</tr>
<tr>
<td>P8</td>
<td>HIV-2 Ab</td>
<td>180</td>
<td>0.86</td>
<td>0.06</td>
<td>7.0</td>
<td>0.06</td>
<td>6.7</td>
<td>0.07</td>
<td>8.7</td>
<td>0.11</td>
<td>13.0</td>
</tr>
<tr>
<td>P9</td>
<td>HIV-2 Ab</td>
<td>180</td>
<td>1.50</td>
<td>0.07</td>
<td>4.8</td>
<td>0.07</td>
<td>4.5</td>
<td>0.15</td>
<td>9.8</td>
<td>0.18</td>
<td>11.8</td>
</tr>
<tr>
<td>P10</td>
<td>HIV-2 Ab</td>
<td>180</td>
<td>3.05</td>
<td>0.14</td>
<td>4.7</td>
<td>0.15</td>
<td>5.0</td>
<td>0.27</td>
<td>8.8</td>
<td>0.34</td>
<td>11.1</td>
</tr>
<tr>
<td>P11</td>
<td>HIV-1 Ag</td>
<td>180</td>
<td>1.00</td>
<td>0.06</td>
<td>6.2</td>
<td>0.05</td>
<td>4.8</td>
<td>0.03</td>
<td>2.8</td>
<td>0.08</td>
<td>8.4</td>
</tr>
<tr>
<td>P12</td>
<td>HIV-1 Ag</td>
<td>180</td>
<td>1.78</td>
<td>0.09</td>
<td>5.0</td>
<td>0.10</td>
<td>5.6</td>
<td>0.06</td>
<td>3.6</td>
<td>0.15</td>
<td>8.3</td>
</tr>
<tr>
<td>P13</td>
<td>HIV-1 Ag</td>
<td>180</td>
<td>3.46</td>
<td>0.18</td>
<td>5.1</td>
<td>0.14</td>
<td>3.9</td>
<td>0.16</td>
<td>4.5</td>
<td>0.27</td>
<td>7.8</td>
</tr>
</tbody>
</table>

*Negative value for variance component was estimated at 0
9.1.4 Inter-lot Precision

In one site, (Bio-Rad, Steenvoorde), the sample panel was run in triplicate on the 3 lots in parallel during 5 days on the same system.

Table 5: Between-Lot precision study

| ID   | Sample Panel       | N  | Mean | Within run SD | Between run CV | Between day SD | Between day CV | Between lot SD | Between lot CV | Total precision SD | Total precision CV |
|------|--------------------|----|------|---------------|----------------|----------------|----------------|---------------|----------------|-----------------|-------------------|-------------------|
| QC1  | Negative           | 45 | 0.34 | 0.024         | 6.9            | 0.015          | 4.4            | 0.024         | 7.1            | 0.037            | 10.9              |
| QC2  | HIV-1 Ab           | 45 | 2.85 | 0.091         | 3.2            | 0.084          | 2.9            | 0.121         | 4.3            | 0.173            | 6.1               |
| QC3  | HIV-1 Ag           | 45 | 5.51 | 0.168         | 3.0            | 0.205          | 3.7            | 0.549         | 10.0           | 0.610            | 11.1              |
| QC4  | HIV-2 Ab           | 45 | 3.50 | 0.102         | 2.9            | 0.115          | 3.3            | 0.188         | 3.3            | 0.243            | 7.0               |
| QC5  | HIV-1-O Ab         | 45 | 3.43 | 0.119         | 3.5            | 0.121          | 3.5            | 0.434         | 12.7           | 0.466            | 13.6              |
| P1   | Negative           | 45 | 0.34 | 0.029         | 8.6            | 0.010          | 2.9            | 0.021         | 6.2            | 0.000            | 11.0              |
| P2   | HIV-1 non B Ab     | 45 | 0.86 | 0.044         | 5.1            | 0.025          | 2.9            | 0.040         | 4.7            | 0.064            | 7.5               |
| P3   | HIV-1 non B Ab     | 45 | 1.57 | 0.046         | 2.9            | 0.072          | 4.6            | 0.066         | 4.2            | 0.108            | 6.9               |
| P4   | HIV-1 non B Ab     | 45 | 3.01 | 0.227         | 7.6            | 0.000          | 0.0            | 0.096         | 3.2            | 0.247            | 8.2               |
| P5   | HIV-1-O Ab         | 45 | 0.90 | 0.031         | 3.5            | 0.028          | 3.2            | 0.000         | 0.0            | 0.042            | 4.7               |
| P6   | HIV-1-O Ab         | 45 | 1.76 | 0.055         | 3.1            | 0.029          | 1.7            | 0.069         | 3.9            | 0.093            | 5.3               |
| P7   | HIV-1-O Ab         | 45 | 3.28 | 0.136         | 4.2            | 0.170          | 5.2            | 0.097         | 3.0            | 0.238            | 7.3               |
| P8   | HIV-2 Ab           | 45 | 0.87 | 0.050         | 5.8            | 0.029          | 3.3            | 0.013         | 1.5            | 0.059            | 6.8               |
| P9   | HIV-2 Ab           | 45 | 1.54 | 0.057         | 3.7            | 0.073          | 4.7            | 0.012         | 0.8            | 0.093            | 6.1               |
| P10  | HIV-2 Ab           | 45 | 3.15 | 0.100         | 3.2            | 0.092          | 2.9            | 0.030         | 1.0            | 0.139            | 4.4               |
| P11  | HIV-1 Ag           | 45 | 0.99 | 0.042         | 4.3            | 0.015          | 1.5            | 0.030         | 3.1            | 0.054            | 5.5               |
| P12  | HIV-1 Ag           | 45 | 1.74 | 0.051         | 2.9            | 0.063          | 3.6            | 0.135         | 7.7            | 0.157            | 9.0               |
| P13  | HIV-1 Ag           | 45 | 3.50 | 0.109         | 3.1            | 0.153          | 4.4            | 0.304         | 8.7            | 0.358            | 10.2              |

9.2 Diagnostic Performance

A multicenter study was conducted to establish the performance of the Access HIV combo assay in the following populations: pregnant women, individuals of unknown HIV status who asked for an HIV screening, patients infected or not, individuals of unknown HIV status belonging to groups recognized to be at risk for HIV infection. Specimens that were repeatedly reactive with Access HIV combo assay and/or a Canadian licensed HIV Ab /Ag assay, supplemental testing was performed using HIV Western blot, and HIV-1 p24 Antigen assays.

9.2.1 Diagnostic Specificity

The specificity of the Access HIV combo assay demonstrated a specificity \( \geq 99.5\% \). This specificity was investigated by testing the following samples:

A prospective study was conducted on 3 sites in France: A total of 3,073 fresh collected samples from low and high risk populations were tested with the Access HIV combo Assay and Canadian licensed 4th generation HIV Ag/Ab assay. The population included samples from pregnant women, samples from individuals of unknown HIV status who asked for an HIV screening, samples from patients infected or not, samples from individuals of unknown HIV status belonging to groups recognized to be at risk for HIV infection due to lifestyle, behavior, occupation, prisoners or known exposure subjects who asked for an HIV screening and who lived in a high prevalence area.
The results are presented in the following table:

### Table 6: Specificity study

<table>
<thead>
<tr>
<th>Population</th>
<th>Total</th>
<th>Canadian licensed HIV Ag Ab assay</th>
<th>Canadian licensed HIV Ag Ab assay</th>
<th>Repeat reactive</th>
<th>WB</th>
<th>HIV-1 Ag</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Non reactive Access HIV combo</td>
<td>Reactive Access HIV combo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number of initial reactive</td>
<td>Repeat reactive (false positive)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant women</td>
<td>492</td>
<td>487</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Population with anonymous screening</td>
<td>498</td>
<td>482</td>
<td>2</td>
<td>2</td>
<td>14</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Hospitalised patients</td>
<td>1,526</td>
<td>1,516</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>HIV-1</td>
</tr>
<tr>
<td>At risk population</td>
<td>507</td>
<td>281</td>
<td>3</td>
<td>1</td>
<td>224</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Prisoner population</td>
<td>50</td>
<td>50</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Total</td>
<td>3,073</td>
<td>2,816</td>
<td>13</td>
<td>5</td>
<td>252</td>
<td></td>
</tr>
</tbody>
</table>

Specificity on this population is 2,811/2,816 = 99.82% with a 95% confidence interval of [99.59 – 99.94%]. Additionally, 200 frozen serum samples from pregnant women were tested with Access HIV Combo; all were found negative (100%).

### 9.2.2 Diagnostic Sensitivity

- **Detection of HIV-1 antibodies**

Cumulating the data from all the sites (retrospective and prospective samples), a total of 1,355 serum and plasma samples collected from HIV infected individuals, confirmed positive for HIV-1 antibodies by western blot were tested with Access HIV Combo Assay. All were found positive 1,355/1,355= 100%.

Among these samples, 338 subtypes HIV-1 samples including B subtypes, and non-B subtypes (i.e. A, C, D, F, G, H, J, CRF recombinant subtypes (CRF 02_AG, CRF 01_AE, CRF 08_BC, CRF 06-cpx, CRF01/CRF15, CRF03_AB, G/ CRF02, H/A1, H/A1, CRF05, CRF06, CRF09, CRF10, CRF11, CRF12, CRF13, CRF14, CRF15, CRF19, CRF27)) as well as group O and N were analyzed. All were found positive.

- **HIV-1 Seroconversion Panels**

55 commercial seroconversion panels were tested with Access HIV combo and compared to two Canadian licenced 4th generation HIV combo screening assays.

From the 55 panels, 53 were compared with one predicate; 29 with the other predicate.

**Comparison to the first predicate assay:**

53 seroconversion panels were compared; 40 have the same level of detection; for 3 of them Access HIV combo detected in advance; for 10 of them, Access HIV combo has a delay of detection of 1 sample. All these 10 panels were early seroconversions; the samples not seen with Access were negative for HIV Ab, and positive for HIV antigen when HIV antibody assay and HIV–1 Ag p24 assays were analysed.

**Comparison to the second predicate assay:**

Among the 29 seroconversion panels tested with Access HIV combo assay, 25 panels were detected at the same time for both Access HIV combo and the predicate; for 2 of them Access was in advance and for 2 of them the predicate was in advance.
• **Detection of HIV-2 antibodies**

241 HIV-2 well characterized positive samples collected on the different sites were tested with Access HIV combo assay. All were found positive: 100% (241/241).

• **Detection of HIV-1 antigen**

362 positive for HIV-1 Ag coming from commercial panels, patients samples and early seroconversion samples were tested with Access HIV combo assay. Additionally, 44 samples from cell culture supernatant of different subtypes (A, B, C, D, E, F, G, H, J) were tested. 14 samples were not detected with Access HIV combo assay: 2 samples negative for HIV-Ab from commercial panels and 12 samples negative for HIV-Ab came from early seroconversion panels.

9.3 **Analytical Sensitivity**

**HIV-1 p24 Analytical sensitivity**

The Access HIV combo assay was designed to have an analytical sensitivity <2 IU/mL on the WHO HIV-1 p24 Ag international standard NIBSC 90/636. In an internal study, the results demonstrated an antigen sensitivity of 1.1 IU/mL with a 95% confidence interval (range of 0.55 – 1.72 IU/mL) on the WHO standard.

9.4 **Analytical Specificity**

9.4.1 Cross-reactivity Study

478 samples from individuals with medical conditions unrelated to HIV infection were tested on the Access HIV combo assay on two sites. Pregnancy (5); Multiparous women (10); Cirrhotos (5); renal and hepatitis transplanted (51); transplanted patient under lenograstim (9); Multi-transfusion (10); renal failure (5); cancer (breast, lung, stomach, colon) (5); samples with anti-mouse human immunoglobulin (5); Anti-Nuclear Antibodies (ANA) (5); Autoimmune as Systemic Lupus erythematous (5 SLE), Rheumatoid factor (36); Myeloma IgG (5) and IgM (10); Dialysis patients (5).

And viral, bacterial or parasitic infections:
HTLV I/ II (44); Hepatitis C (30 HCV); Hepatitis B (5 anti-HBs, 5 HBs Ag) and Hepatitis A (10 HAV); HAMA (5); Cytomegalovirus (10 CMV); Epstein-Barr (15 EBV); Varicelle-Zona (24 VZV); Herpes Simplex (20 HSV); Dialysis (5); Syphilis (88); Rubella (10); Measles (5); Mumps (5); Mycoplasma pneumoniae (5); Influenzae vaccines (5), parvovirus (6) Malaria (5); Toxoplasma (15).

Over the total 478 difficult samples, 5 samples were found repeat reactive with Access HIV combo (1 HTLVl, 1 HTLVII, 3 syphilis samples) leading to a specificity of 473/478= 98.95% with a 95% confidence interval of [97.58 – 99.66%].

9.4.2 Interference Study

Samples containing up to 200 mg/L and 300 mg/L for unconjugated and conjugated bilirubins respectively, up to 90 g/L albumin, lipemic samples containing the equivalent of 30 g/L triolein (triglyceride) and hemolyzed samples containing up to 2 g/L hemoglobin, do not affect the results.

9.4.3 Hook effect

The hook effect was studied by testing 5 high-titer specimens. Two HIV-1 Ag p24 samples (at 2 μg/mL and 10μg/mL), 2 HIV-1 Ab positive samples and 1 HIV-2 Ab positive sample were tested neat and diluted (from dilution 10-1 to 10-8). All results demonstrated a downward trend of ratio values with increased dilution and that high dose hook effect was not present in the Access HIV combo assay.
The Access HIV combo Calibrators are intended to calibrate the Access HIV combo assay using the Access Immunoassay Systems.
1 Intended Use

The Access HIV combo Calibrators are intended to calibrate the Access HIV combo assay for the qualitative detection of HIV-1 antigen and HIV-1/HIV-1-O/HIV-2 antibodies in human serum and plasma (Li heparin, EDTA and CPDA-1) using the Access Immunoassay Systems.

2 Summary and Explanation of the Test

The Access HIV combo Calibrators are used to establish calibration (determine the cut-off value) for the Access HIV combo assay. By comparing the light intensity generated by a sample to the cut-off value, the presence or absence of HIV-1 antigen and/or HIV-1/HIV-1-O/HIV-2 antibodies in the sample is determined.

3 Product Information

3.1 Description

Access HIV combo Calibrators

<table>
<thead>
<tr>
<th>Identification on label</th>
<th>Description</th>
<th>Presentation/preparation A59429</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0 Negative Calibrator</td>
<td>Negative Calibrator: (non-reactive) human serum for HIV-1 antigen and HIV-1/HIV-1-O/HIV-2 antibodies with 0.1% sodium azide and 0.25% ProClin 300.</td>
<td>1 x 1.7 mL Ready to use</td>
</tr>
<tr>
<td>C1 Positive Calibrator</td>
<td>Positive Calibrator: (reactive) human serum for anti-HIV-1 antibodies with 0.1% sodium azide and 0.25% ProClin 300.</td>
<td>1 x 1.7 mL Ready to use</td>
</tr>
<tr>
<td>Calibration card</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

3.2 Storage and Handling Conditions

- Store upright and refrigerate at 2 to 10°C.
- Mix contents by gently inverting before use. Avoid bubble formation.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Vial is stable at 2 to 10°C for 120 days after initial use.
- Out-of-range control values are a possible sign of deterioration.

4 Warnings and Precautions

- For in vitro diagnostic use. For healthcare professional use only.

4.1 Health and Safety Precautions

- This test kit should only be handled by qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately in accordance with Good Laboratory Practices.
- This test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Consequently, all human derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Universal Precautions for bloodborne pathogens as defined by OSHA, the guidelines from the current CDC/NHI Biosafety in Microbiological and Blended Laboratories and/or local, regional, national regulations.
- Biological spills: human source material spills should be treated as potentially infectious. Spills not containing acid should be immediately decontaminated, including the spill area, materials and any contaminated surfaces or equipment and with appropriate chemical disinfectant that is effective on the potential biohazards of the samples in question (commonly a 1:10 dilution of household bleach, 70-80% ethanol or isopropanol, an iodophor such as 0.5% Wescodyne™ Plus, etc.) and wiped dry. Spills containing acid should be appropriately absorbed (wiped up) or neutralized, the area flushed with water and wiped dry; materials used to absorb the spill may require hazardous waste disposal. The area should subsequently be decontaminated with one of the chemical disinfectants.
- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or bio-hazardous waste must be handled and discarded in accordance with all local, regional and national regulations.
- For hazard and precaution recommendations related to any chemical components in this test kit, please refer to the pictogram(s) featured on the labels and the information supplied in the section 4.2. The Safety Data Sheet (SDS) is available at www.bio-rad.com.

4.2 Precautions Related to the Procedure

Warning:

![Exclamation Mark]

H317: May cause an allergic skin reaction.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.
P302+P352: If on skin: Wash with plenty of soap and water.
P501: Dispose of contents/container in accordance with local/regional/national/international regulations.

- This product contains human or animal components. Handle with care.

5 Procedure

Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, entering calibrator test requests and reviewing calibration data.

Calibration

The Access HIV combo Calibrators are provided as negative (C0) and positive (C1). The Access HIV combo assay requires a calibration curve (determination of the cut-off value) every 56 days in order to have an active “calibration” for only one lot of reagents well identified by its bar code. At the end of the 56 days or if another lot of reagents is loaded on the system, the curve is automatically invalidated. Each calibration requires 220 µL of the C0 calibrator (determination in duplicate) and 330 µL of the C1 calibrator (determination in triplicate) in addition to the sample container and system dead volume. One drop is equal to approximately 40 µL.

6 Test Limitation

If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.
ACCESS® Immunoassay System

HIV combo QC

For monitoring the system performance of the Access HIV combo assay.

B42396D - [CA] - 2015/06
1 Intended Use
The Access HIV combo QC is intended for monitoring the system performance of the Access HIV combo assay.

2 Summary and Explanation of the Test
Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of the Access HIV combo assay. In addition, they are an integral part of good laboratory practices [36-47]. When performing assays with Access reagents for HIV-1 antigen and anti HIV-1/HIV-1-O/HIV-2 antibodies, include quality control materials to validate the integrity of the assays. The assayed values should fall within the acceptable range if the test system is working properly.

3 Product Information

3.1 Description
Access HIV combo QC

<table>
<thead>
<tr>
<th>Identification on label</th>
<th>Description</th>
<th>Presentation/ preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>QC1 Negative QC</td>
<td>Negative QC: Human serum negative (non-reactive) for HIV-1 antigen and anti HIV-1/HIV-1-O/HIV-2 antibodies, with 0.1% sodium azide and 0.25% ProClin 300.</td>
<td>A59430 2 x 4.4 mL Ready to use</td>
</tr>
<tr>
<td>QC2 Anti-HIV-1</td>
<td>Anti-HIV-1, positive QC: Human serum positive (reactive) for anti-HIV-1 antibodies with 0.1% sodium azide and 0.25% ProClin 300.</td>
<td>2 x 4.4 mL Ready to use</td>
</tr>
<tr>
<td>QC3 HIV-1 Ag</td>
<td>HIV-1 Ag, positive QC: Purified HIV-1 antigen heat inactivated with a chaotropic agent in Tris Buffer with 0.1% ProClin 300</td>
<td>2 x 4.4 mL Ready to use</td>
</tr>
<tr>
<td>QC card</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

3.2 Storage and Handling Conditions
- Store upright and refrigerate at 2 to 10°C.
- Mix contents by gently inverting before use. Avoid bubble formation.
- QC are stable until the expiration date stated on the label when stored at 2 to 10°C.
- Vial is stable at 2 to 10°C for 120 days after initial use.
- Out-of-range quality control values are a possible sign of deterioration.
- Refer to the QC value card for mean values and standard deviations (SDs).

4 Warnings and Precautions
- For in vitro diagnostic use. Healthcare professional use only.

4.1 Health and Safety Precautions
- This test kit should only be handled by qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately in accordance with Good Laboratory Practices.
- This test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Consequently, all human derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Universal Precautions for bloodborne pathogens as defined by OSHA, the guidelines from the current CDC/NHI Biosafety in Microbiological and Biomedical Laboratories and/or local, regional, national regulations.
- Biological spills: human source material spills should be treated as potentially infectious. Spills not containing acid should be immediately decontaminated, including the spill area, materials and any contaminated surfaces or equipment and with appropriate chemical disinfectant that is effective on the potential biohazards of the samples in question (commonly a 1:10 dilution of...
household bleach, 70-80% ethanol or isopropanol, an iodophor such as 0.5% Wescodyne™ Plus, etc.) and wiped dry. Spills containing acid should be appropriately absorbed (wiped up) or neutralized, the area flushed with water and wiped dry; materials used to absorb the spill may require hazardous waste disposal. The area should subsequently be decontaminated with one of the chemical disinfectants.

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or bio-hazardous waste must be handled and discarded in accordance with all local, regional and national regulations.
- For hazard and precaution recommendations related to any chemical components in this test kit please refer to the pictogram(s) featured on the labels and the information supplied in the section 4.2 The Safety Data Sheet (SDS) is available at www.bio-rad.com.

4.2 Precautions Related to the Procedure

Warning:

H317: May cause an allergic skin reaction.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.
P302+P352: If on skin: Wash with plenty of soap and water.
P501: Dispose of contents/container in accordance with local/regional/national/international regulations.

- This product contains human or animal components. Handle with care.

5 Procedure

The Access HIV combo QC should be treated in the same way as patient specimens and run in accordance with the instructions accompanying the instrument and/or method being used. To process the Access HIV combo QC, 110 μL of sample is required for each of the 3 levels in addition to the sample container and system dead volume (single determination). One drop is equal to approximately 40 μL.

Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Refer to the appropriate system manuals and/or Help system for information on quality control theory, configuring controls, entering quality control sample test requests and reviewing quality control data.

6 Test Limitations

1. The use of the Access HIV combo QC has not been established with assays other than the Access HIV combo assay.
2. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte.
3. If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

7 Expected Values

The expected means (x) and SDs (σ) for the Access HIV combo QC1, QC2 and QC3 are provided on the QC value card contained in the kit. Each laboratory should establish its own acceptability criteria by selecting the QC rules to be applied to the control results. Individual control results should fall within the initial acceptance range. However, each laboratory should update the mean and SD once sufficient data has been collected.

Given that specific levels of reactivity may vary by assay manufacturer, by procedure, by lot number and by laboratory, each laboratory should determine the specific level of reactivity and establish its own range of acceptable values. The acceptable range might include all values within ± 2 SD of the mean of 20 data points out of 20 determinations over a period of 30 days.
ACCESS® Immunoassay System

HIV combo QC4 & QC5

For monitoring the system performance of the Access HIV combo assay.

[IVD] CE 0459

B42396D - [CA] - 2015/06
1 Intended Use
The Access HIV combo QC4 & QC5 is intended for monitoring the system performance of the Access HIV combo assay.
Access HIV combo QC4 is an anti-HIV-2 quality control and Access HIV combo QC5 is an anti-HIV-1-O quality control.

2 Summary and Explanation of the Test
Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of the Access HIV combo assay. In addition, they are an integral part of good laboratory practices (36,41-47). When performing assays with Access reagents for HIV-1 antigen and anti-HIV-1/HIV-1-O/HIV-2 antibodies, include quality control materials to validate the integrity of the assays. The assayed values should fall within the acceptable range if the test system is working properly.

3 Product Information
3.1 Description
Access HIV combo QC4 & QC5

<table>
<thead>
<tr>
<th>Identification on label</th>
<th>Description</th>
<th>Presentation/preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>QC4 Anti-HIV-2</td>
<td>Anti-HIV-2, positive QC: Anti-HIV-2 rabbit serum in human negative serum with 0.1% sodium azide and 0.25% ProClin 300</td>
<td>2 x 4.4 mL Ready to use</td>
</tr>
<tr>
<td>QC5 Anti-HIV-1-O</td>
<td>Anti-HIV-1-O, positive QC: Anti-HIV-1-O rabbit serum in human negative serum with 0.1% sodium azide and 0.25% ProClin 300</td>
<td>2 x 4.4 mL Ready to use</td>
</tr>
<tr>
<td>QC card</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

3.2 Storage and Handling Conditions
- Store upright and refrigerate at 2 to 10°C.
- Mix contents by gently inverting before use. Avoid bubble formation.
- QC are stable until the expiry date stated on the label when stored at 2 to 10°C.
- Vial is stable at 2 to 10°C for 120 days after initial use.
- Out-of-range quality control values are a possible sign of deterioration.
- Refer to the QC value card for mean values and standard deviations (SDs).

4 Warnings and Precautions
- For in vitro diagnostic use. Healthcare professional use only.

4.1 Health and Safety Precautions
- This test kit should only be handled by qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately in accordance with Good Laboratory Practices.
- This test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Consequently, all human derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Universal Precautions for bloodborne pathogens as defined by OSHA, the guidelines from the current CDC/NHI Biosafety in Microbiological and Biomedical Laboratories and/or local, regional, national regulations.
- Biological spills: human source material spills should be treated as potentially infectious. Spills not containing acid should be immediately decontaminated, including the spill area, materials and any contaminated surfaces or equipment and using the appropriate chemical disinfectant that is effective on the potential biohazards of the samples concerned (commonly a 1:10 dilution of household bleach, 70-80% ethanol or isopropanol, an iodophor such as 0.5% Wescodyne™ Plus, etc.), and wiped dry. Spills containing acid should be appropriately absorbed (wiped up) or neutralized, the area flushed with water and wiped dry; materials used to absorb the spill may require hazardous waste disposal.
The area should subsequently be decontaminated using one of the chemical disinfectants.

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or bio-hazardous waste must be handled and discarded in accordance with all local, regional and national regulations.
- For hazard and precaution recommendations related to any chemical components in this test kit, please refer to the pictogram(s) featured on the labels and the information supplied in the section 4.2. The Safety Data Sheet (SDS) is available at www.bio-rad.com.

4.2 Precautions Related to the Procedure

Warning:

H317: May cause an allergic skin reaction.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.
P302+P352: If on skin: Wash with plenty of soap and water.
P501: Dispose of contents/container in accordance with local/regional/national/international regulations.
- This product contains human or animal components. Handle with care.

5 Procedure

The Access HIV combo QC4 & QC5 should be treated in the same way as patient specimens and run in accordance with the instructions accompanying the instrument and/or method being used.

To process the Access HIV combo QC4 & QC5, 110 μL of sample is required for each of the 2 levels in addition to the sample container and system dead volume (single determination). One drop is equal to approximately 40 μL.

Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

Refer to the appropriate system manuals and/or Help system for information on quality control theory, configuring controls, entering quality control sample test requests and reviewing quality control data.

6 Test Limitations

4. The use of the Access HIV combo QC4 & QC5 has not been established with assays other than the Access HIV combo assay.

5. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte.

6. If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

7 Expected Values

The expected means (x) and SDs (σ) for the Access HIV combo QC4 and QC5 are provided on the QC value card contained in the kit. Each laboratory should establish its own acceptability criteria by selecting the QC rules to be applied to the control results. Individual control results should fall within the initial acceptance range. However, each laboratory should update the mean and SD once sufficient data has been collected.

Given that specific levels of reactivity may vary by assay manufacturer, by procedure, by lot number and by laboratory, each laboratory should determine the specific level of reactivity and establish its own range of acceptable values. The acceptable range might include all values within ± 2 SD of the mean of 20 data points out of 20 determinations over a period of 30 days.
Bibliography References


2. Popovic M., Sarngadhar M.G., Read E., Gallo R.C.: Detection, isolation and continuous production of cytopathic retroviruses (HTLV III) from patients with AIDS AND pre-AIDS. Science, 1984, 224, 497-500


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