Access®
Immunoassay Systems

BIO-RAD

HIV combo
REF A59428

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 (Li heparin), 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 and as screening test for blood and plasma donors. 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.

IVD For *In Vitro* Diagnostic Use

All manufactured and commercialized reagents are under complete quality system starting from reception of raw material to the final commercialization of the product.
Each lot is submitted to a quality control and is only released on the market when conforming to the acceptance criteria.
The records relating to production and control of each single lot are kept within our company.

Summary and Explanations

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 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[3,4,5,6].

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 allowed to distinguish different groups of HIV-1: 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, whatever viral protein is considered (envelope and core proteins; heterology: 30%).They show less than 40% homology with the envelope proteins of HIV-1[3,18,19,20]. However, HIV-2 is less pathogenic than HIV-1, and 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].

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 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.

Product Information

Access HIV combo Reagent Packs

Cat. No. A59428: 100 determinations, 2 packs, 50 tests/pack

- Provided ready to use.
- 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 not opened)
- 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.

R1a:	Paramagnetic particles coated with recombinant HIV-1 protein (gp 160), HIV-1-O (gp 41) and HIV-2 (gp 36) polypeptides and monoclonal antibodies to p24 HIV-1 antigen, suspended in TRIS buffered saline, with 0.1% sodium azide and ProClin**300 (0.25%).
R1b:	Conjugate additive: TRIS buffered saline, with 0.1% sodium azide and ProClin**300 (0.25%).
R1c:	Particle additive: TRIS buffer saline with biotinylated monoclonal antibodies to p24 HIV-1, with 0.1% sodium azide and ProClin**300 (0.25%).
R1d:	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%).

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines[37].
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal flush with a large volume of water to prevent azide build-up[38].
  ProClin**300 is a potential skin sensitizer. Avoid spilling or splashing this reagent on skin or clothing. In case of contact with the reagent, flush thoroughly with soap and water.
  Xn. Harmful: 0.1% Sodium Azide and 0.25% ProClin**300.

  R 22: Harmful if swallowed.

  R 43: May cause sensitization by skin contact.

  S 23: Do not breathe gas/fumes/vapour/spray

  S 24: Avoid contact with skin.

  S 37: Wear suitable gloves.

  S 60: This material and its container must be disposed of as hazardous waste.
- The Material Safety Data Sheet (MSDS) is available upon request.

Specimen Collection and Preparation

1. Serum (including serum separator tubes) and plasma (Li Heparin, including plasma separator tubes) are the recommended samples.
2. **Do not heat the samples.**
3. Observe the following recommendations for handling, processing, and storing blood samples[39]:
   - Collect all blood samples observing routine precautions for venipuncture.
   - Allow serum samples to clot completely before centrifugation.
   - Keep tubes stoppered at all times.
   - Store samples tightly stoppered at room temperature (15 to 23°C) for no longer than twenty-four hours.
   - If the assay will not be completed within twenty-four hours, refrigerate the samples at 2 to 8°C.
   - If the assay will not be completed within 8 days at 2 to 8°C, or for shipment of samples, freeze at -20°C or colder.
4. Use the following guidelines when preparing specimens:
   - Ensure residual fibrin and cellular matters have been removed prior to analysis.
   - Follow blood collection tube manufacturer's recommendations for centrifugation.
5. 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, at times, from lot to lot.
6. 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.
7. After thawing, the sample must be thoroughly mixed, centrifuged again at 3,000 g for 15 minutes and transferred into a cup in order to remove any suspended fibrin particles or aggregates liable to yield false positive results.
8. 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.

Materials Provided

R1 Access HIV combo Reagent Packs

Materials Required But Not Provided

1. Access HIV combo Calibrators
   Provided as one HIV-Ab negative serum and one 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
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 800 and 600 Immunoassay Systems, UniCel DxC 880i, 860i, 680i and 660i Synchron® Access Clinical Systems.

Procedural Comments

1. Refer to the appropriate system manuals and/or Help system for a specific 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. Use one hundred ten (110) µL of sample for each determination in addition to the sample container and system dead volumes. Refer to the appropriate system manuals and/orand/or Help system for the minimum sample volume required.
4. Time to first result is approximately 60 minutes.
5. The system default unit of measure for sample results is Signal/Cut-off (S/CO) ratio.

Procedure

Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

Calibration Details

An active calibration point is required for all tests. For the Access HIV combo assay, calibration is required every 56 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Quality Control

Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. 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[40]. Include Access HIV combo QC 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 manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure 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. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

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 control sera results.

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, respectively). However, results ~10% lower than the "cut-off value" should be prudently 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 automatically will be reported, permitting 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 ratio (S/CO) lower than 0.9 is considered to be non-reactive with the Access HIV combo test.
- Samples with ratio (S/CO) $\geq$ 0.9 and < 1 are in the gray zone and should be retested in duplicate before final interpretation.
- Samples with 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 HIV combo assay.
- If one of the 2 results is $\geq$ 1.0 S/CO, the initial result is repeatable and the sample is declared as "reactive" for the Access HIV combo test.

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

Result Ratio : Signal/Cut-Off			Interpretation	Supplementary tests
First Result Analysis	S/CO < 0.9	Non reactive	HIV-1 p24 and/or HIV-1/HIV-1-O/HIV-2 Ab not detected	NA
	S/CO ≥ 1	Reactive	"Initial Reactive"	To retest in duplicate
	0.9 ≤ S/CO < 1.0	Gray zone	"Initial Reactive"	To retest in duplicate
Second Result Analysis	Retest in duplicate: If the 2 results are < 1	Non reactive	HIV-1 p24 and/or HIV-1/HIV-1-O/HIV-2 Ab not detected	NA
	Retest in duplicate: if one of the 2 results is ≥ 1	Reactive	HIV-1 p24 and/or HIV-1/HIV-1-O/HIV-2 Ab detected "Repeat Reactive"	Confirmatory test

Limitations of the Procedure

1. The Access HIV combo assay is intended for use with human serum or plasma (Li heparin) sample only. The performance characteristics using other sample types have not been established or are limited.
2. 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).
3. The results obtained with Access HIV combo assay must correlate with the symptoms if any and with the clinical report history.
4. 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 interferes with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples[41,42].
   Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.
5. Transplant patient samples have to be tested before freezing.
6. Performance has not been established using cadaver samples or body fluids other than human serum and plasma.
7. The magnitude of the measured result, above the cut-off, is not indicative of the total amount of antibody and/or antigen present.
8. 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.
9. 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.
10. For an infection to be declared, a reactive result obtained with the Access HIV combo assay should be confirmed with an appropriate method.
11. 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 on such samples should be interpreted with caution.

Specific Performance Characteristics

Sensitivity

Sensitivity studies with Access HIV combo were performed by testing confirmed HIV Ab samples, specimens from acute infected patients, commercial seroconversion panels, and HIV Ag samples (neat or diluted).

1. Analytical sensitivity

The Access HIV combo assay shows an analytical sensitivity < 2 IU/mL to HIV-1 p24 Antigen. The regression analysis of NIBSC 90/636 Panel WHO and Bio-Rad Internal HIV Ag Standard allowed determining the assay sensitivity limit.

2. Clinical sensitivity

- **Confirmed HIV Ab positive samples**
  - The HIV-1 sensitivity was investigated on 674 confirmed positive samples and found equal to **100%** (95% CI: 99.45 – 100%).

  The samples include genotyped subtypes and variants samples:

  - Group M : A, B, C, D, F, G, H, J, K, CRF 01-02-05-06-08-09-10-11-12-13-14-15-19-27
  - Group O
  - Group N

  As requested, a minimum of 3 samples per subtype have been tested.

  - The HIV-2 sensitivity was evaluated by testing 126 well-documented samples and declared equal to **100%** (95% CI: 97.11 – 100%).

- **Specimens from acute infected patients and from commercial seroconversion panels**
  - The HIV-1 sensitivity on preseroconversion and perseroconversion was investigated on 86 specimens.
  - Seroconversion sensitivity of the Access HIV combo assay was evaluated by testing sequential specimens from 61 well–documented commercial HIV seroconversion panels (with 131 early seroconversion samples).

Table 2 shows results from 6 seroconversion panels.

Table 2: Seroconversion panels

Panel	Sample ID	Days after 1st bleed	Access® HIV combo (S/CO)	PCR*	Western Blot*
BBI 9012	9012-05	14	0.53	Positive	Negative
	9012-06	16	1.21	Positive	Negative
	9012-07	21	25.36	Positive	Negative
BBI 9017	9017-04	10	0.32	Positive	Positive
	9017-06	13	1.19	Positive	Positive
	9017-07	17	3.48	Positive	Positive
	9017-08	20	4.15	Positive	Positive
	9017-09	24	2.44	Positive	Positive
	9017-10	28	5.67	Positive	Positive
	9017-11	31	42.27	Positive	Positive
BBI 9022	9022-07	23	0.77	Positive	Negative
	9022-08	25	5.81	Positive	Negative
	9022-09	32	161.31	Positive	Negative
PRB 950	PRB950-01	0	0.29	Negative	Negative
	PRB950-02	18	1.12	Positive	Negative
	PRB950-03	21	8.03	Positive	Negative
	PRB950-04	28	21.15	Positive	Positive
BBI 9034	9034-10	42	0.28	Negative	Negative
	9034-11	47	1.75	Positive	Negative
	9034-12	51	20.47	Positive	Negative
Zeptometrix 6243	6243-06	20	0.37	Positive	Indeterminate
	6243-07	25	1.37	Positive	Indeterminate
	6243-08	27	1.89	Positive	Indeterminate
	6243-09	30	6.68	Positive	Indeterminate
	6243-10	32	18.06	Positive	Indeterminate

* Data from the vendors

- **HIV-1 Antigen samples**

  Sensitivity = **100%** (104/104) (95% CI: 96.52 – 100%)

Sensitivity of the assay was evaluated by testing 104 well documented samples including:

- 44 HIV Ag culture cells supernatants of HIV-1 group M from the following genotypes: 10A, 5B, 8C, 5D, 10E, 1F, 2G, 1H, 2J
- 21 HIV-Ag commercial positive samples
- 39 HIV-Ag positive samples from the 86 serum samples at different stage of seroconversion

- **Fresh samples**

  103 HIV positive samples were tested within 1 day after blood collection.

Specificity

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

Sample type	IR specificity			RR specificity		
	n	%	95% Confidence Interval	n	%	95% Confidence Interval
Blood donors	7656 / 7664	99.90	[99.79-99.95%]	7664 / 7664	100.00	[94.95 - 100%]
Selected Hospitalized patients	1961 / 1969	99.59	[99.20-99.82%]	1966 / 1969	99.85	[99.56 - 99.97%]
Not selected Hospitalized patients	1121 / 1122	99.91	[99.50-100%]	1121 / 1122	99.91	[99.50 - 100%]
Pregnant women	200 / 200	100.00	[98.17-100%]	200 /200	100.00	[98.17 - 100%]
Overall mean	10938 / 10955	**99.84**	[99.75-99.91%]	10951 / 10955	**99.96**	[99.91 - 99.99%]

477 Samples have been tested from patients showing different pathologies or status not linked to the HIV: pregnant women, rheumatoid factor, cirrhotic, chronic renal failure, dialysis, transplants, patients under lenograstim, human anti-mouse Ig, antinuclear antibodies, *mycoplasma pneumoniae*, erythrovirus B19, myeloma, other viral or bacterial infections (HAV, HBV, HCV, Rubella, Toxoplasmosis, Syphilis, Mumps, Measles, CMV, HSV, EBV, VZV, HTLVI, Malaria, Flu vaccinated patients).

Specificity was equal to 98.10% (414/422) (95% CI: 96.30 – 99.18%) without the frozen transplant population (see limitation of the procedure, point n°5).

Five non-specific reactions were found with:

- VZV positive samples (7.7%)
- EBV positive samples (6.7%)
- HCV positive samples (2.9%)
- Rheumatoid factor (7.1%)
- Syphilis positive samples (2.3%)

Precision

The precision of the Access HIV combo assay was determined by the analysis of 13 samples: 1 negative sample, 1 low positive sample (Low1), 1 sample close to cut off (low 2), 1 medium positive sample for HIV1, HIV2, HIV-1-O and HIV Ag.

The intra assay precision was assessed by testing these 13 samples in one run with 30 replicates on 1 system. The CVs were determined.

The inter assay precision was assessed by testing these 13 samples on 1 lot, in duplicate, in 2 different runs per day (am and pm), by two operators for a period of 20 days.

The inter lot precision was assessed by testing these 13 samples in 5 replicates with 4 different lots using 4 different calibrator lots.

The results are shown in the following tables:

Intra-assay Precision:

N=30		Mean (ratio signal / cut-off)	% C.V.
Negative samples		0.28	10.6
Low 1 samples	**HIV-1**	2.19	4.1
	HIV-2	2.20	4.7
	HIV-1-O	1.91	2.6
	HIV-1-Ag	2.40	5.0
Low 2 samples	**HIV-1**	0.96	5.9
	HIV-2	0.95	4.4
	HIV-1-O	1.16	4.6
	HIV-1-Ag	1.20	4.6
Medium 1 samples	**HIV-1**	2.86	5.8
	HIV-2	3.81	3.4
	HIV-1-O	3.34	4.2
	HIV-1-Ag	3.30	3.7

Inter-assay Precision:

N=80		Mean (ratio signal / cut-off)	% C.V.
Negative samples		0.30	10.1
Low 1 samples	**HIV-1**	2.35	5.6
	HIV-2	2.37	5.1
	HIV-1-O	1.88	4.6
	HIV-1-Ag	2.35	7.6
Low 2 samples	**HIV-1**	1.02	5.6
	HIV-2	1.03	5.6
	HIV-1-O	1.15	4.9
	HIV-1-Ag	1.17	4.9
Medium 1 samples	**HIV-1**	3.04	5.1
	HIV-2	3.99	4.9
	HIV-1-O	3.23	4.6
	HIV-1-Ag	3.12	4.7

Inter-lot Precision:

N=20		Inter Cal % C.V.	Inter RP % C.V.	Total % C.V.
Negative samples		12.1	12.3	15.0
Low 1 samples	**HIV-1**	11.0	7.4	11.4
	HIV-2	9.8	9.0	12.4
	HIV-1-O	10.2	6.5	10.8
	HIV-1-Ag	8.3	7.0	9.5
Low 2 samples	**HIV-1**	10.3	6.2	10.7
	HIV-2	10.3	7.2	11.3
	HIV-1-O	10.2	5.5	10.3
	HIV-1-Ag	10.4	14.8	16.9
Medium 1 samples	**HIV-1**	9.8	5.7	10.4
	HIV-2	10.2	11.0	13.9
	HIV-1-O	8.5	10.4	12.1
	HIV-1-Ag	11.0	13.0	15.5

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HIV combo Calibrators
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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) using the Access Immunoassay Systems.

IVD **For *In Vitro* Diagnostic Use**

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Each lot is submitted to a quality control and is only released on the market when conforming to the acceptance criteria.
The records relating to production and control of each single lot are kept within our company.

Summary and Explanations

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.

Traceability

The measurand (analyte) in the Access HIV combo Calibrators is traceable to the manufacturer's working calibrators. Traceability process is based on EN ISO 17511.

Product Information

Access HIV combo Calibrators
Cat. No. A59429: C0-C1, 1.7 mL/vial

- Provided ready to use.
- 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.
- Signs of possible deterioration are control values out of range.

C0:	Negative (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.
C1:	Positive (reactive) human serum for anti-HIV-1 antibodies with 0.1% sodium azide and 0.25% ProClin*300.
Calibration Card:	1

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Human source material used in the preparation of the calibrators has been tested and found nonreactive for Hepatitis B surface antigen (HBsAg), antibodies to Hepatitis C virus (HCV), antibodies to Human Immunodeficiency virus (HIV-1 and HIV-2) and HIV-1 antigen, except Calibrator C1, that is positive for HIV-1 antibodies. Because no known test method can offer complete assurance that infectious agents are absent, handle reagents and patient samples as if capable of transmitting infectious disease[37].
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal flush with a large volume of water to prevent azide build-up[38].
  ProClin*300 is a potential skin sensitizer. Avoid spilling or splashing this reagent on skin or clothing. In case of contact with the reagent, flush thoroughly with soap and water.

  Xn. Harmful: 0.1% Sodium Azide and 0.25% ProClin*300.

  

  R 22: Harmful if swallowed.

  R 43: May cause sensitization by skin contact.

  S 23: Do not breathe gas/fumes/vapour/spray

  S 24: Avoid contact with skin.

  S 37: Wear suitable gloves.

  S 60: This material and its container must be disposed of as hazardous waste.
- The Material Safety Data Sheet (MSDS) is available upon request.

Procedure

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

Calibration Details

The Access HIV combo Calibrators are provided as negative (C0) and positive (C1). The Access HIV combo assay requires a calibration (determination of the cut-off value) in order to have an active “calibration”. Calibration data are valid up to 56 days.

Each calibration requires 220 µL of the C0 calibrator (duplicate determinations) and 330 µL of the C1 calibrator (triplicate determinations) in addition to the sample container and system dead volume. One drop is equal to approximately 40 µL.

Limitations of the Procedure

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

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HIVcombo QC
REF A59430

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The Access HIV combo QC is intended for monitoring system performance of the Access HIV combo assay.

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The records relating to production and control of each single lot are kept within our company.

Summary and Explanations

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[40, 43-49]. 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.

Traceability

The measurand (analyte) in the Access HIV combo QC is traceable to the manufacturer's working calibrators. Traceability process is based on EN ISO 17511.

Product Information

Access HIV combo QC
Cat. No. A59430: 4.4 mL/vial, 2 vials each level

- Provided ready to use.
- 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.
- Signs of possible deterioration are control values out of range.
- Refer to the QC value card for mean values and standard deviations (SD).

QC 1:	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.
QC 2:	Human serum positive (reactive) for anti-HIV-1 antibodies with 0.1% sodium azide and 0.25% ProClin*300.
QC 3:	Purified HIV-1 antigen heat inactivated with a chaotropic agent in Tris Buffer with 0.1% ProClin*300
QC Card:	1

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Human source material used in the preparation of the control has been tested and found non-reactive for Hepatitis B surface antigen (HBsAg), antibodies to Hepatitis C virus (HCV). Because no known test method can offer complete assurance that infectious agents are absent, handle reagents and patient samples as if capable of transmitting infectious disease[37].
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal flush with a large volume of water to prevent azide build-up[38].

  ProClin*300 is a potential skin sensitizer. Avoid spilling or splashing this reagent on skin or clothing. In case of contact with the reagent, flush thoroughly with soap and water.

  Xn. Harmful: 0.1% Sodium Azide and 0.25% ProClin*300.

  

  R 22: Harmful if swallowed.

  R 43: May cause sensitization by skin contact.

  S 23: Do not breathe gas/fumes/vapour/spray

  S 24: Avoid contact with skin.

  S 37: Wear suitable gloves.

  S 60: This material and its container must be disposed of as hazardous waste.
- The Material Safety Data Sheet (MSDS) is available upon request.

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[40]. 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, quality control sample test request entry, and reviewing quality control data.

Limitations of the Procedure

1. The use of the Access HIV combo QC has not been established with assays other than the Access HIV combo assay.
2. 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[40]. Include any commercially available controls and/or additional controls obtained from other sources for the laboratory’s quality control system.
3. 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.
4. If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

Expected Values

The expected means (×) and SDs (σ) for the Access HIV combo QC1, QC2 and QC3 are provided on the QC value card contained in the kit for initial quality control system configuration. 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 after sufficient data have been collected.

Given that specific levels of reactivity may vary among various manufacturer’s assays, different procedures, different lot numbers and different laboratories, 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.

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