NEW LAV BLOT II

18 Determinations 72252

CONFIRMATION KIT FOR ANTI-HIV2 ANTIBODIES DETECTION IN SERUM/PLASMA BY IMMUNOBLOTTING

IVD

Manufacturer Quality Control

All the products manufactured and commercialized by the Bio-Rad Company are submitted to a complete quality assurance system starting from receipt of raw materials to commercialization of finished products.

Each lot of finished product is submitted to a quality control and released on the market only when it is in accordance with the acceptance criteria.

Literature related to manufacturing and control of each lot is kept within our company.

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1 - INTENDED USE

The NEW LAV-BLOT II kit is intended to the detection of human anti-HIV2 antibodies in serum or plasma by immunoblotting in order to confirm a positive anti-HIV2 response and specify its antigenic specificity within the scope of AIDS diagnosis.

2 - CLINICAL VALUE

Acquired immunodeficiency syndrome (AIDS) was described and recognised as a well-characterized disease in 1981.

Three retroviruses (LAV, HTLV III, ARV), related to the Lentivirus group and not differentiated by conventional serological tests, were isolated from the lymphocytes of patients stricken with AIDS or AIDS prodromes. The decision to gather these three viruses under the same denomination (HIV) was made in 1986.

In 1986, a new retrovirus (LAV II/HIV2) was isolated from West-African patients suffering from AIDS. This virus is clearly related to HIV1 by its morphology, its tropism and its cytopathogenic effect on the T4 lymphocytes. Genetic analyses showed that this virus was different from HIV1, especially in its envelope, and was affinitive to STLV III. On the other hand, serological studies show that it exists in most cases a simultaneous recognition of the core proteins of the HIV1 and HIV2 viruses by the patient's antibodies. However, some serums are not identified as positive by the HIV1 diagnosis kits. Screening is based on the detection of antibodies in serum or plasma samples, using an immunoenzymatic technique. The quality of the antigens used in these tests does allow the elimination of some non-specific responses. Considering the seriousness of the diagnosis to be made, it is mandatory to confirm or invalidate the response to the screening tests by another technique.

WHO experts recommend the use of immunoblotting (Western Blot) in the case of the HIV1 virus. This technique allows the characterization of the antibodies aimed at each virus protein, hence the confirmation of seropositivity. Within the scope of AIDS diagnosis, it becomes necessary for the characterization of the infection by the HIV1 or HIV2 viruses.

3 - PRINCIPLE OF THE TEST

The test is based on indirect ELISA technique on a nitrocellulose strip containing all the HIV2 constituent proteins and an internal anti-IgG control. The band corresponding to the internal control is localized on the strip end without any number, before the p16 reaction and allows to validate the addition of the sample and reagents as well as the correct progress of the procedure.

Inactivated HIV2 proteins are separated according to their molecular weights by polyacrylamide gel electrophoresis in dissociating and reducing medium and subsequently electrically transferred onto a nitrocellulose membrane sheet.

The procedure comprises the following steps

1. Strip rehydration.
2. Incubation of the samples to be confirmed or the control serums.

   If anti-HIV2 antibodies are present, they bind to the identified viral proteins, present on the strip.
3. After washing, the alkaline phosphatase-labeled anti-human IgG antibodies are incubated. The conjugate binds to anti-HIV2 antibodies captured on the solid phase.
4. After washing and removing the excess conjugate, the color development solution allows demonstrating the enzymatic activity of the complexes bound to nitrocellulose.
5. The appearance of specific colored bands allows demonstrating the presence of anti-HIV2 antibodies in the sample.

4 - CONTENTS OF THE KIT

All the reagents are intended to in vitro diagnostic use only.
Each kit contains reagents sufficient for 18 determinations. The determinations may be performed in multiple independent runs.

LABEL	REAGENT COMPOSITION	PRESENTATION
R1	**HIV2 Nitrocellulose Strip** Activated by transfer of HIV2 viral proteins and internal anti-IgG control Strips are placed in disposable trays	18 strips in 3 trays (6 cells each)
R2	**Buffer solution/Diluent (X 5)** concentrated (5x) Contains 0.5% chloroform	1 vial 100 ml
R3	**Negative Control** Human serum negative for HBsAg, anti-HIV1 and anti-HIV2 and anti-HCV antibodies Preservative : < 0.1 % sodium azide	1 vial 0.2 ml
R4	**Anti-HIV2 Positive Control** Human serum positive for anti-HIV2 antibodies, negative for anti-HCV antibodies and HBsAg, heat-inactivated Preservative : < 0.1 % sodium azide	1 vial 0.2 ml
R5	**Conjugate** Goat alkaline phosphatase-labeled anti-human IgG antibodies Preservative : < 0.1 % sodium azide	1 vial 40 ml
R6	**Color Development Solution (BCIP/NBT)** 5 Bromo-4 Chloro-3 Indolyl Phosphate (BCIP) and NitroBlue Tetrazolium (NBT) as developing buffer.	1 vial 40 ml

5 - PRECAUTIONS

The reliability of results depends on correct observance of the following Good Laboratory Practices :

- Do not use expired reagents.
- Do not mix reagents from different lots within a given test run.

Note : It is possible to use other buffer solution (Label identification : R2 in blue) and color development solution (R6) lots with the restriction that the very same lot is used within a given test run.

- Before use, it is required to wait 30 minutes to allow the reagents stabilizing at room temperature (18-30°C).
- Carefully reconstitute reagents avoiding any contamination.
- Use glassware thoroughly washed and rinsed with distilled water or preferably, disposable material.
- Use a new dispensing tip for each sample.
- Never use the same container to dispense conjugate and color development solution.
- Check pipettes for accuracy and precision and if the instruments being used are correctly working.
- Do not change the assay procedure.
- Control sera should be tested in parallel with patient samples for each test run.
- Do not allow strips to dry more than 10 minutes during the test.
- If suspended particles are present in the development solution, allow to settle in the vial before pipetting. (These particles do not interfere with the test.)

6 - HEALTH AND SAFETY INSTRUCTIONS

All the kit reagents are intended to *"in vitro"* diagnostic use.

- Never handle the strips with bare hands : Use plastic tweezers.
- Wear disposable gloves when handling reagents.
- Do not pipette by mouth.
- Human source material used in the preparation of the negative control (R3) was tested and found non reactive for hepatitis B surface antigen (HBsAg), and anti-HIV1, anti-HIV2, and anti-HCV antibodies.
- Human source material used in the preparation of the positive control (R4), was tested and found non-reactive for hepatitis B surface antigen (HBsAg), and anti-HCV. It was heat-inactivated.

- Because no known test method can offer complete assurance that the HIV, Hepatitis B or C virus or other infectious agents are absent, consider these reagents, as well as patient samples, as potentially infectious and handle them carefully.
- Any equipment directly in contact with samples and human source reagents as well as buffer solutions should be considered as contaminated products and treated accordingly.
- Avoid spilling samples or solutions containing samples.
- Contaminated surfaces should be cleaned 10% diluted bleach. If the contaminating fluid is an acid, the contaminated surfaces should be first neutralized with sodium bicarbonate, then cleaned with bleach, and dried with absorbent paper. The material used for cleaning should be discarded into a biohazardous waste container.
- Samples, human source reagents, as well as contaminated material and products should be discarded after decontamination:

  - either by soaking into bleach at a final concentration of 5% sodium hypochlorite (1 volume of bleach per 10 volumes of contaminated fluid or water) for 30 minutes
  - or by autoclaving at 121°C for 2 hours minimum. Autoclaving is the best method to inactivate HIV and HBV.

  CAUTION : DO NOT PLACE SOLUTIONS CONTAINING SODIUM HYPOCHLORITE IN THE AUTOCLAVE
- Do not forget to neutralize and/or autoclave the wash waste solutions or any fluid containing biological samples before discarding them into the sink.
- Chemicals should be handled and discarded in accordance with Good Laboratory Practices.
- Some reagents contain sodium azide as a preservative. Sodium azide may form copper or lead azides in laboratory plumbing. Such azides are explosive. To prevent azide built-up, flush the pipes with a large amount of water if solutions containing azide are discarded into the sink after inactivation.

7 - EQUIPMENT REQUIRED BUT NOT SUPPLIED

- Distilled or demineralized water.
- 100 ml, 250 ml and 500 ml graduated cylinders.
- 2 ml graduated pipettes.
- Automatic or semi-automatic pipettes, adjustable or fixed, allowing measuring or dispensing 20 µl.
- Disposable gloves.
- Liquid jet vacuum pump with safety bottle.
- Sodium hypochlorite (Bleach).
- Absorbent paper.
- Tweezers.
- 1, 2 or 3 dimensional shaker (shaking to ensure a homogeneous environment and total immersion of the strips during the shaking steps).
- Container for biohazardous waste.
- Protective glasses.

8 - REAGENT RECONSTITUTION AND STORAGE

Each kit contains reagents sufficient for 18 determinations. The determinations may be performed in multiple independent runs.

Ready to use reagents

R1: HIV2 nitrocellulose strips
R3: Negative control
R4: Anti-HIV2 positive control
R5: Conjugate
R6: Color development solution (BCIP/NBT).

Reagents to be reconstituted

R2: Buffer solution/diluent (5X)

PREPARATION : Shake the vial before collection. Dilute the buffer solution/diluent to 1:5 in distilled water (e.g. for a complete tray: 30 ml buffer solution + 120 ml distilled water). Homogenize.

STORAGE : Store the kit at +2-8°C. Once opened, all the kit reagents may be stored at +2-8°C until the expiration date stated on the box (except for specific instructions).
The diluted buffer solution/diluent (R2) is stable for 1 month at +2-8°C.
Avoid any microbial contamination of the reagents.

9 - SAMPLE COLLECTION AND HANDLING

Collect a blood sample according to the current practices.

The tests should be performed with undiluted serum or plasma samples (collected with anticoagulants such as EDTA, heparin, citrate).

Extract the serum or plasma from the clot or red cells as soon as possible in order to avoid hemolysis. Extensive hemolysis may affect test performance. Samples with aggregates should be clarified by centrifugation prior testing. Suspended fibrin particles or aggregates may yield falsely positive results.

The samples can be stored at +2-8°C if the test is performed within 7 days or they may be deep-frozen at -20°C.

Plasma samples should be quickly thawed by heating for a few minutes at 40°C (to limit fibrin precipitation).

Samples that have been frozen and thawed more than 3 times should not be used.

If the samples have to be shipped, they should be packaged in accordance with the regulations effective for the transport of etiological agents.

DO NOT USE CONTAMINATED, HYPERLIPEMIC OR HYPERHEMOLYZED SERUM OR PLASMA SAMPLES.

NOTE : Samples containing up to 90g/l albumin, 100 mg/l bilirubin, lipemic samples containing up to the equivalent of 36 g/l trioleine, and hemolyzed samples containing up to 10 g/l hemoglobin do not affect the test results.

10 - TEST PROCEDURE

1. Before use, it is required to wait 30 minutes to allow reagents stabilizing at room temperature (18-30°C).
   Remove the transparent cover of the tray being used.
   Make sure that the strip side with the reference mark and the number is visible, so that the viral proteins on this side are covered by the various reaction media throughout the test.
   Strips should be carefully handled with plastic tweezers.
   Do not allow the strips to dry more than 10 minutes during the test.

   The controls provided should be tested in parallel with patient samples for each test run. The positive control is required to validate the test and correctly interpret the bands.
2. Add 2 ml of the reconstituted buffer solution/diluent into each cell.
   Incubate for 5 ± 1 minutes at room temperature (18-30°C) under shaking.
3. Add 20 µl of each sample or control serum into the corresponding cell.
   Incubate for 2 hours ± 5 minutes at room temperature (18-30°C) under shaking.
4. Completely drain the contents of each cell using a vacuum pump with a trap containing a disinfectant (25 % bleach).
   Be sure that the strip is not moved during aspiration, use the aspiration well dedicated for this purpose. Rinse under the tap the aspiration tip, which is in contact with the samples between each aspiration to avoid sample cross-contamination.
   Wash each strip with 2 ml of the reconstituted buffer solution/diluent and immediately remove it by aspiration, following the same precautions.
   Wash each strip twice, allow the contact for 5 minutes, under shaking, with 2 ml of the reconstituted buffer solution/diluent (i.e. a total of 3 wash steps).
   Remove the solution used for the last washing.
5. Dispense 2 ml of conjugate into each cell, the conjugate solution should be previously stabilized at room temperature.
   Incubate for 1 hour ± 5 minutes at room temperature (18-30°C) under shaking.
6. Washing : proceed as described in step 4.
7. Dispense 2 ml of color development solution into each cell.
   If suspended particles are present in the development solution, allow to settle in the vial before pipetting. (These particles do not interfere with the test).
   Incubate under shaking and monitor the appearance of the coloration. All the bands corresponding to the viral proteins should be observed with the positive control serum. (Development time : 5 minutes at least).
8. Stop the reaction by removing the development solution and rinsing the strips 3 times with distilled water.
9. Dry the strips between 2 sheets of absorbent paper at room temperature (18-30°C).
   Sort the strips, position them perfectly using the reference mark. Validate then interpret.
   CAUTION : Do not stick adhesive plastic band on the strip side corresponding to the viral proteins.

11 - VALIDATION, READING AND INTERPRETATION OF RESULTS

Validation

The internal anti-IgG control band should be present with a strong color. It allows to validate the addition of the sample, reagents as well as the correct progress of the test procedure. The absence or weak intensity of the coloration of the internal anti-IgG control band indicates either that the sample or reagents were not dispensed or that the test procedure was not followed.
Positive control : presence of all band corresponding to the viral proteins and the control band
Negative control : none of the viral protein should be present, the control band is present.

Reading

The presence of anti-HIV 2 constituent protein antibodies in controlled samples is shown by the appearance of specific colored bands (blue-purple). Their position corresponds to the molecular masses of the viral proteins listed in the following table.
Use the positive control to identify the shown antibodies and check that the internal control band is present on each test strip.
Use the positive control (**cf figure page 71**) to locate and identify the shown antibodies and check that the internal control band is present on each test strip.
Each specific and readable band must be interpreted.

NAME	GENOME	NATURE	ASPECT IN WESTERN BLOT
GP 140	ENV	Precursor of GP 105 and GP 36	± Diffuse band
GP 105/GP 125	ENV	Envelope glycoprotein	Diffuse band
P68	POL	Reverse transcriptase	Clear band
P56	GAG	Precursor of core proteins	Clear band
GP36	ENV	Transmembrane glycoprotein	Diffuse band
P34	POL	Endonuclease	Clear band*
P26	GAG	Core protein	Clear band
P16	GAG	Core protein	Clear band

*The p34 band is a well defined band in the same position as the diffuse GP 36 Band.

Interpretation

INTERPRETATION	PROFILE
Positive	ENV + GAG + POL
Indeterminate	ENV + GAG
	ENV + POL
	GAG +POL
	GAG
	POL
	ENV
Negative	Non-classified bands No band

NOTE

- Positive or indeterminate profiles may be obtained by contamination with a positive serum.
- Using other interpretation criteria is also possible. It is recommended in Germany by the German association against viral disease (DVV) [Positive : presence at least of a Env protein and a Gag or Pol protein – Indeterminate: corresponds to any profile that does not meet the above criteria – Negative : no band present. In this scope, gp105/125/140 are considered as the same protein.]

12 - PERFORMANCES

The NEW LAV BLOT II (NLBII) test specificity was studied with samples from blood donors (196) and hospitalized patients (201). Specificity was also studied with patient samples, HIV antibodies non reactive (EIA tests) but with other disorders such as rubella, toxoplasmosis, pneumonia, hepatitis A, B and C as well as samples from pregnant females, samples reactive for rheumatoid factor and 39 samples considered as false positive with an EIA test and not confirmed have also been included. Therefore 119 difficult samples were tested.

All results were interpreted using package insert criteria, stated in the interpretation table.

Over all none of the 516 samples were found positive with the NLB II assay.

From 204 samples, reactive for HIV antibodies using EIA and characterized as HIV2 with HIV1/2 differentiation tests (EIA, Immunoblot), 202 has been confirmed NLB II Positive and 2 has shown an indeterminate profile. 41 samples reactive for HIV1 and HIV 2 antibodies have been confirmed positive with NLB II.

With a panel of 131 specimens anti-HIV 1 Positive, 110 samples were Indeterminate and 21 were positive with NEW LAV BLOT II

Reproducibility tests, within-run and inter-run, did not show difference in results.

13 - LIMITATIONS OF THE TEST

- It is required to follow the procedure in order to ensure optimal performance.
- The positive control should be tested in parallel with patient samples for each test run. It is required to validate the test and correctly interpret the bands.
- A positive screening test associated with a negative confirmatory test may occur during the first stage of the infection; hence, a negative result indicates that the tested sample does not contain anti-HIV antibodies detectable with NEW LAV BLOT II. However, such a result does not allow to exclude the possibility of exposure to an HIV1/HIV2 infection. A new later sample collection is recommended.
- The variability of HIV1 and HIV2 does not allow to exclude the possibility of false negative reactions. No known test method can offer complete assurance that the HIV virus is absent.
- Using interpretation criteria less restrictive may induce a different classification of the samples. Actually some samples classified as indeterminate according to the pack insert interpretation criteria should be reported as reactive according to these criteria.
- An "indeterminate" profile should not exclude one of the following situations : seroconversion, HIV1, or cross-reaction due to other retroviruses.

14 - REFERENCES

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CAUTION : precise bands may differ in reality. Don't use this picture for final interpretation. Use the positive control strip to identify the patient antibodies and check that the internal control band is present on each strip.

ATTENTION : les bandes obtenues en réalité peuvent être différentes de celles figurant sur cette image. Ne pas utiliser cette image pour l'interprétation finale. L'interprétation finale doit être effectuée avec l'aide de la bandelette du contrôle positif pour identifier les anticorps du patient. La bande du contrôle interne doit être présente sur chaque bandelette.

ATENCIÓN : las bandas obtenidas realmente pueden ser diferentes de las que figuran en este imagen. No utilice esta imagen para la interpretación final. Utilice las tiras de control positivo para identificar los anticuerpos del paciente. La banda de control interno debe estar presente en cada tira.

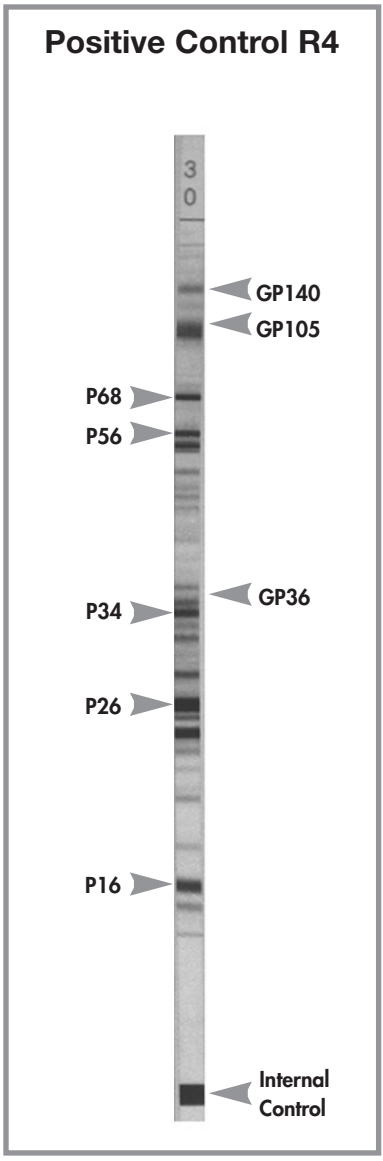
ACHTUNG : Die Banden können sich in Wirklichkeit von denjenigen auf dem oben stehenden Bild unterscheiden: Das Bild sollte nicht für die Schlussauswertung verwendet werden. Die Schlussauswertung muss anhand des positiven Kontrollstreifens erfolgen um die Antikörper des Patienten identifizieren zu können. Die interne Kontrollbande muss auf jedem Streifen sichtbar sein.

ATTENZIONE : in realtà le strisce ottenute possono essere diverse da quelle rappresentate sulla figura. Non utilizzare questa figura per l'interpetazione finale. L'interpetazione finale deve effettuarsi tramite la striscetta di controllo positivo per identificare gli anticorpi del paziente. La striscia di controllo negativo deve essere presente su ogni striscetta.

ATENÇÃO : as bandas reais podem ser diferentes das ilustradas. Não se baseie nesta imagem para uma interpretação final. Utilize a tira do controlo positivo para identificar os anticorpos do doente e verificar se a banda do controlo interno está presente em cada tira.

OBSERVERA : de band som erhålls i verkligheten kan skilja sig från dem som visas på bilden ovan. Använd inte denna bild för den slutliga tolkningen. Använd den positiva kontrollremsan för att identifiera patientens antikroppar och kontrollera att det inre kontrollbandet finns med på varje remsa.

VIGTIGT : De bånd man opnår i virkeligheden kan være anderledes end dem på billedet ovenfor. Brug ikke dette billede til endelig tolkning. Brug den positive kontrolstrimmel til at identificere patientens antistoffer og kontroller, at det interne kontrolbånd er tilstede på hver strimmel.



- CE marking (European directive 98/79/CE on *in vitro* diagnostic medical devices)
- Marquage CE (Directive européenne 98/79/CE relative aux dispositifs médicaux de diagnostic *in vitro*)
- Marcodo CE (Directiva europea 98/79/CE sobre productos sanitarios para diagnóstico *in vitro*)
- EG Markierung (Europäische Richtlinie 98/79/EG über *In vitro*-Diagnostika)
- Marchiatura CE (Direttiva europea 98/79/CE relativa ai dispositivi medico-diagnostici in vitro)
- Marcação CE (Directiva europeia 98/79/CE relativa aos dispositivos médicos de diagnóstico *in vitro*)
- CE-märkning (Europa direktiv 98/79/EG om medicintekniska produkter lör *in vitro*-diagnostik)
- CE-mærkningen (Europa direktiv 98/79/EF om medicinsk udstyr til *in vitro*-diagnostik)

IVD
- For *in vitro* diagnostic use
- Pour diagnostic *in vitro*
- Para diagnóstico *in vitro*
- *In vitro*-Diagnostikum
- Per uso diagnostico *in vitro*
- Para uso em diagnóstico *in vitro*
- *In vitro* diagnostik
- *In vitro* diagnose

REF
- Catalogue number
- Référence catalogue
- Número de catálogo
- Bestellnummer
- Numero di catalogo
- Número de catálogo
- Katalognummer
- Katalognummer

- Manufacturer
- Fabricant
- Fabricante
- Hersteller
- Produttore
- Fabricante
- Tillverkad av
- Fremstillet af

EC REP
- Authorised Representative
- Représentant agréé
- Representante autorizado
- Bevollmächtigter
- Distributore autorizzato
- Representante Autorizado
- Auktoriserad representant
- Autoriseret repræsentant

LOT
- Batch code
- Code du lot
- Código de lote
- Chargen-Bezeichnung
- Codice del lotto
- Código do lote
- Batch nr.
- Batchkoden

- Expiry date YYYY/MM/DD
- Date de péremption AAAA/MM/JJ
- Estable hasta AAAA/MM/DD
- Verwendbar bis JJJJ/MM/TT
- Da utilizzare prima del AAAA/MM/GG
- Data de expiração AAAA/MM/DD
- Utgångsdatum År/Månad/Dag
- Anvendes før ÅÅÅÅ/MM/DD

- Storage temperature limitation
- Limites de températures de stockage
- Temperatura limite
- Lagerungstemperatur
- Limiti di temperatura di conservazione
- Limites de temperatura de armazenamento
- Temperaturbegränsning
- Temperaturbegrænsning

- Consult Instruction for use
- Consulter le mode d'emploi
- Consulte la instrucción para el uso
- Siehe Gebruchsanweisung
- Consultare le istruzioni per uso
- Consulte o folheto Informativo
- Se instruktionsanvisning vid användning
- Se instruktion før brug

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