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Certification
Médical-Santé
Notified Body N° 0459

ATTESTATION/ *CERTIFICATE* **N° 24927 rev. 6**
Délivrée à Paris le 19 juin 2018
Issued in Paris on June 19th, 2018

ATTESTATION CE / *EC CERTIFICATE*

Examen CE de la Conception (du produit) */ EC Design Examination (of the product)*
ANNEXE IV point 4 Directive 98/79/CE relative aux dispositifs médicaux de diagnostic in vitro
ANNEX IV section 4 DIRECTIVE 98/79/EC concerning in vitro diagnostic medical devices

Fabricant */ Manufacturer*

BIO-RAD
3 boulevard Raymond Poincaré
92430 MARNES LA COQUETTE FRANCE

Digitally signed by Botca Petru
Date: 2022.10.29 14:01:03 EEST
Reason: MoldSign Signature
Location: Moldova

Catégorie du(des) dispositif(s) */ Device(s) category*

Dispositif médical de diagnostic in vitro
pour la confirmation de marqueurs de l'infection VIH (VIH 1 et 2)

In vitro Diagnostic Medical Device
for the confirmation of markers of HIV infection (HIV 1 and 2)

Identification du(des) dispositif(s) */ Identification of device(s)*

Geenius HIV 1/2 Confirmatory Assay (Ref. 72460)
(GMDN 48454)

Le LNE/G-MED atteste qu'à l'examen des résultats figurant dans le rapport référencé P178772, le(s) produit(s) énuméré(s) ci-dessus est (sont) conforme(s) aux exigences de l'annexe I de la directive 98/79/CE.

LNE/G-MED certifies that, on the basis of the results contained in the file referenced P178772, the product(s) complie(s) with the requirements of the directive 98/79/EC, annex 1.

Début de validité */ Effective date* **:June 19th, 2018 (included)**
Valable jusqu'au */ Expiry date* **: February 3rd, 2023 (included)**

Laboratoire national de métrologie et d'essais LNE

On behalf of the G-MED Certification Director
Béatrice LYS
G-MED Certification Technical Director

GMED_cApA-V2-01-2013

LNE - 24927 rev. 6
Modifie le certificat 24927-5

EU DECLARATION OF CONFORMITY

MANUFACTURER: Bio-Rad
ADDRESS: 3 boulevard Raymond Poincaré, 92430 Marnes-la Coquette, France

EUROPEAN AUTHORIZED REPRESENTATIVE: Bio-Rad
ADDRESS: 3 Boulevard Raymond Poincaré, 92430 Marnes-la-Coquette, France

PRODUCT(S) NAME(S) and CATALOG NUMBER(S): Geenius™ HIV 1/ 2 Confirmatory Assay – Code 72460

GENERIC DEVICE GROUP CODE (GMDN nomenclature):
48454

GENERIC DEVICE GROUP TERM (GMDN Nomenclature):
HIV1 / HIV2 antibody, IVD kit immunochromatographic test (ITC) rapid

We hereby declare that the above mentioned product(s) meet(s) the provisions of the following Directives

- Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* Diagnostic medical devices

CLASSIFICATION:

- ☒ ANNEX II-A
- ☐ ANNEX II-B
- ☐ DEVICE FOR SELF TESTING
- ☐ OTHER DEVICE

CONFORMITY ROUTE

- ☐ ANNEX III
- ☒ ANNEX IV.3 Full Quality System
- ☒ ANNEX IV.4 Product Design Examination

EC CERTIFICATE No.:24927
Name of Notified Body :LNE/G-MED
Notified Body Identification No.: 0459
Expiration Date : 3rd February 2023

- ☐ ANNEX V Type Examination

EC CERTIFICATE No.:
Name of Notified Body :
Notified Body Identification No.:
Expiration Date :

- ☐ ANNEX VII Production Quality System

NEW PRODUCT(S) (Notification according to article 10 point 4) ☐ YES ☒ NO

Date of the first issuance of the EU Declaration of Conformity: April 4th, 2013

Signature	Marnes-la-Coquette	February,07th 2018
	Issued in	Date
Fernez Sylvie	Regulatory Affairs Manager	
Name	Function	

WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls
WHO reference number: PQDx 0181-031-00

Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls with product codes **72460, 72329**, manufactured by **Bio-Rad**, **CE-marked version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 17 March 2017.

Intended use:
Geenius™ HIV 1/2 Confirmatory Assay is a single-use immunochromatographic test for the confirmation and differentiation of individual antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV-1 and HIV-2) in fingerstick whole blood, venous whole blood, serum or plasma samples. Geenius™ HIV 1/2 Confirmatory Assay is intended for use as an additional test to confirm the presence of antibodies to HIV-1 and HIV-2 for specimens found to be repeatedly reactive by screening assays.

Assay description:
Geenius™ HIV 1/2 Confirmatory Assay employs antibody binding protein A, which is conjugated to colloidal gold dye particles as conjugate and HIV-1 (p31, gp160, p24, gp41) and HIV-2 antigens (gp36, gp140), which are bound to the membrane solid phase. The patient specimen is applied to the SAMPLE + BUFFER well. The buffer causes the specimen to flow laterally and facilitates the binding of patient antibodies to the antigens immobilized on the solid phase. After the sample and buffer have migrated onto the test strip, additional buffer is added to the BUFFER well. The buffer enables the migration of colloidal gold Protein A and promotes its binding to the patient antibodies.

In a reactive sample, the anti-HIV antibodies are captured by the antigens immobilized in the TEST area (bands 1 to 6): the colloidal gold protein A present in the buffer binds to the captured antibodies, producing pink/purple lines in the TEST area.

In the absence of HIV antibodies, there are no pink/purple lines in the TEST area. In both cases the specimen continues to migrate along the membrane and Immunoglobulin G from patient specimen binds to Protein A which is immobilized in CONTROL (C) area; the colloidal gold Protein A binds to the captured IgG, producing a pink/purple line in CONTROL (C) area.. This Control line serves to demonstrate that specimen and reagents have been properly applied and have migrated through the device.

Test kit contents:

Geenius™ HIV 1/2 Confirmatory Assay components	**20 tests (product code 72460)**
Device: White plastic cassette encasing a nitrocellulose membrane containing HIV-1 and HIV-2 antigens in TEST area, protein A in CONTROL area and colloidal gold protein A in BUFFER well area, individually packagedin sealed pouch containing desiccant	20 x 1
Buffer: Buffer dropper with preservative (sodium azide < 0.1%, gentamicin sulphate 0.125%, streptomycin sulphate 0.125%)	1 x 5 ml
Microtubes: 15 µLMicrotubes capillarity plastic pipettes (no anti-coagulant, for fingerstick protocol)	20
Instructions for use	1

Geenius™ HIV 1/2 Confirmatory Controls components	**20 tests (product code 72329)**
Positive Control: Human plasma negative for HBs Ag and HCV Ab and containing Anti HIV-1 and HIV-2 Ab Preservative: ProClin™ 300 (0.25%), NaN3 (< 0.1%)	1 x 120 µl
Negative Control: Human plasma negative for HBs Ag, HCV Ab, Anti HIV-1 and HIV-2 Ab Preservative: ProClin™ 300 (0.25%), NaN3 (< 0.1%)	1 x 120 µl
Positive Control Labels Card: Barcode labels of Positive Control	20
Negative Control Labels Card: Barcode labels of Negative Control	20
Instructions for use	1

Items required but not provided:

Item
Consumables: Disposable gloves Biohazard disposal containers
Durables: Clock, watch or other timing device Precision pipette capable of delivering 5 µl (serum/plasma) and 15 µl (venous blood) of specimen
Equipment: Geenius™ Reader with dedicated software

Storage:

Geenius™ HIV 1/2 Confirmatory Assay (product code 72460) should be stored at 2 to 30 °C.
Geenius™ HIV 1/2 Confirmatory Controls (product code 72329) should be stored at 2 to 8°C.

Shelf-life upon manufacture:
Geenius™ HIV 1/2 Confirmatory Assay (product code 72460): 24 months.
Geenius™ HIV 1/2 Confirmatory Controls (product code 72329): 12 months.

Warnings/limitations:

1. WHO reviewed the current version of the instructions for use (version 2013/01), and BioRad has agreed to implement a number of revisions into the next version of the instructions for use.

   WHO notes that the instructions for visual interpretation of the control line may be subjective for end-users. Specifically, the current instructions state that a faint control line should be interpreted as an invalid test result.

   Furthermore, a statement is made that all visible bands, even a faint band should be considered as reactive. This obviously is contradictory to the statement above regarding the control line intensity.

2. The performance characteristics stated in the instructions for use excludes specimens with indeterminate results in the calculation of diagnostic specificity, diagnostic sensitivity, analytical specificity, and analytical sensitivity. When indeterminate results that should be recorded as false negative and false positive results are excluded from the calculation of performance characteristics, the reported sensitivity and specificity appear artificially high.

3. HIV-1 and HIV-2 are viruses with similar morphology and lymphotropism. The HIV-1 and HIV-2 genomes exhibit about 60% homology in conserved genes such as *gag* and pol, and 39-45% homology in the *env* genes. Serological studies have also shown that the core proteins of HIV-1 and HIV-2 display frequent cross-reactivity whereas the envelope proteins are more type-specific.

   The user should be aware that there is evidence that this product has good discriminatory value when the individual has been infected with HIV-1. However, considerable cross-reaction between the two viruses can be observed in individual with HIV-2. Given the higher incidence of HIV-1 infection, it should not be assumed that all cross-reactions are attributable to infection with HIV-2 or to duel infection. This is an inherent limitation of many serological assays.

4. This assay should only be used in accordance with the intended use stated by the manufacturer, i.e. as a confirmatory assay to confirm the HIV antibody status of specimens that are anti-HIV-1/2 reactive on screening (first-line) assays, only.

5. The Geenius™ Reader was included in the WHO performance evaluation only, and it will be further reviewed at the next re-inspection.

Summary of WHO prequalification assessment for Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls

	Date	Outcome
PQ listing	17 March 2017	listed
Dossier review	27 August 2015	MR
Site inspection(s) of quality management system	17 to 19 June 2014	MR
Laboratory evaluation of performance and operational characteristics	2 March 2016	MR

MR: Meets requirements
N/A: Not applicable

Prioritization for prequalification
Based on the established criteria, Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV1/2 Confirmatory Controls was given priority for WHO prequalification.

Product dossier assessment
Bio-Rad submitted a product dossier for Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls as per the "Instructions for compilation of a product dossier" (PQDx_018 v1). The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

The manufacturer's responses to the nonconformities found during dossier screening and assessment findings were accepted on 27 August 2015.

Based on the product dossier screening and assessment findings, the product dossier for Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls meets WHO prequalification requirements.

Manufacturing site inspection
A comprehensive inspection was performed at the sites of manufacture (3, bd Raymond Poincaré, 92430, Marnes-La-Coquette, France and Route de Cassel, 59114, Steenvoorde, France) of Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls in 17 to 19 June 2014 as per the "Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics" (PQDx_014 v1). The inspection found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality.

The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on 12 October 2016.

Commitments for prequalification:

1. Review of evidence for Geenius™ Reader.

Based on the site inspection and corrective action plan review, the quality management system for Geenius™ HIV 1/2 Confirmatory Assay with Geenius™ HIV 1/2 Confirmatory Controls meets WHO prequalification requirements.

Laboratory evaluation

Geenius™ HIV 1/2 Confirmatory Assay was evaluated by WHO in the 3rd and 4th quarter of 2015 using serum/plasma specimens. From this evaluation, we drew the following conclusions:

Geenius™ HIV 1/2 Confirmatory Assay is a single-use immunochromatographic assay for the confirmation and differentiation of individual antibodies to HIV-1 and HIV-2 in human serum/plasma and whole blood specimens. A volume of 5 µL of serum/plasma or 15 µl of whole blood is needed to perform the assay. This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory settings. Reading of the results can be done visually (i.e. subjectively read), but the interpretation can be complex. Reading and interpretation can also be done by the software of the automated Geenius™ Reader. During the performance evaluation, the performance of the assay was calculated for visual reading alone as well as for use of the assay with the Geenius™ Reader (see comment above in Warning section).

In this limited evaluation on a panel of 1117 clinically-derived specimens, we found an initial sensitivity (95% CI) of 100% (99.2% - 100%) and an initial specificity[1] (95% CI) of 95.6% (93.7% - 97.0%) compared to the reference assays, for both visual interpretation and interpretation with the Geenius™ Reader. The final sensitivity (95% CI) was 100% (99.2% - 100%) and the final specificity (95% CI) was 97.3% (95.7% - 98.4%) for visual interpretation compared to the reference assays and 97.4% (95.9% - 98.5%) for interpretation with the Geenius™ Reader. On initial testing, the ability of the Geenius™ HIV 1/2 Confirmatory Assay to correctly identify HIV-2 was limited, it was 33% when interpretation was done visually and 81% when interpretation was done with the Geenius™ Reader. Lot to lot variation was acceptable except for one dilution series (WHO3-0778) when interpreted visually and two dilution series (WHO3-0789 and WHO3-0778) when interpreted with the Geenius™ Reader.

For eight seroconversion panels, Geenius™ HIV 1/2 Confirmatory Assay (both with visual and Geenius™ Reader interpretation) detected on average 0.875 specimens later than the benchmark assay; Enzygnost Anti-HIV 1/2 Plus (Siemens Healthcare Diagnostics), a screening (first line) enzyme immunoassay for detection of antibody. Geenius™ HIV 1/2 Confirmatory

[1] The intended use of this assay is to confirm HIV seropositivity in a specimen that has previously been found to be reactive by a screening assay. Therefore, the performance of the Geenius™ HIV 1/2 Confirmatory Assay should be interpreted with caution.

Assay was also compared to Vironostika HIV Ag/Ab, a screening (first-line) enzyme immunoassay for detection of antigen and antibody, and detected on average 1.5 specimens later than this assay. Geenius™ HIV 1/2 Confirmatory Assay was also compared to another confirmatory assay, INNO-LIA HIV I/II Score, and detected 0.25 specimens later.

For the mixed titer panel, Geenius™ HIV 1/2 Confirmatory Assay detected all specimens. For two specimens Geenius™ HIV 1/2 Confirmatory Assay was more sensitive than the reference confirmatory assay (INNO-LIA HIV I/II Score). There was one discordant result between visual interpretation and interpretation by the Geenius™ Reader. One specimen was indeterminate for HIV-1 when interpreted visually, with reactivity on the gp41 band. Interpretation by the Geenius™ Reader concluded this specimen as HIV-negative.

For the 1st International Reference Panel for anti-HIV [NIBSC code 02/210], Geenius™ HIV 1/2 Confirmatory Assay detected all specimens.

In this study, 2.2% and 2.3% of the results were recorded as indeterminate when interpreted, visually and by the Geenius™ Reader respectively. Results were interpreted independently by three technicians and additionally by the Geenius™ Reader. The inter-reader variability was 4.2% when interpreted visually. The variability between visual interpretation and interpretation by the software was 7.7% for test bands that were reactive with visual interpretation and non-reactive with interpretation by the software and 0.7% for test bands that were non-reactive with visual interpretation and reactive with interpretation by the software.

Performance characteristics in comparison with an agreed reference standard		
	Initial (95% CI)	**Final (95% CI)**
Sensitivity % (Visual interpretation)	100% (99.2% - 100%)	100% (99.2% - 100%)
Sensitivity % (Interpretation with the Geenius™ reader)	100% (99.2% - 100%)	100% (99.2% - 100%)
Specificity % (Visual interpretation)	95.6% (93.7% - 97.0%)	97.3% (95.7% - 98.4%)
Specificity % (Interpretation with the Geenius™ reader)	95.6% (93.7% - 97.0%)	97.4% (95.9% - 98.5%)
Invalid rate %	0	N/A
Indeterminate rate %	2.3	N/A
Inter-reader variability % (Visual interpretation)	4.2	N/A

On initial testing, the ability of the Geenius™ HIV 1/2 Confirmatory Assay to correctly identify HIV-2 was limited, it was 33% when interpretation was done visually and 81% when interpretation was done with the Geenius™ Reader.

Additional performance characteristics	
Sensitivity during seroconversion on 8 seroconversion panels in comparison with a benchmark assay; (Enzygnost Anti-HIV 1/2 Plus (Siemens Healthcare Diagnostics)	Seroconversion sensitivity index of +0.875, therefore detection is 0.875 days later than the benchmark assay
Analytical sensitivity on a mixed titer panel in comparison with an agreed reference standard	25 of 25 specimens were correctly classified.
Lot to lot variation on a dilution panel in comparison with an agreed reference standard	Acceptable, except for 1 dilution series when interpreted visually and 2 dilution series when interpreted with the Geenius™ reader.

Key operational characteristics	
Validated specimen types	Serum, plasma (citrate, heparin or EDTA), venous whole blood, capillary whole blood
Number of steps	3 with precision required
Time to result	27 minutes
Endpoint stability	20-30 minutes
Internal QC	Yes. The control line acts as both a procedural control and as a control for addition of specimen when adequate volume is added.
In-use stability	Cassette: 60 minutes after opening pouch Buffer: until date of expiration

Labelling

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

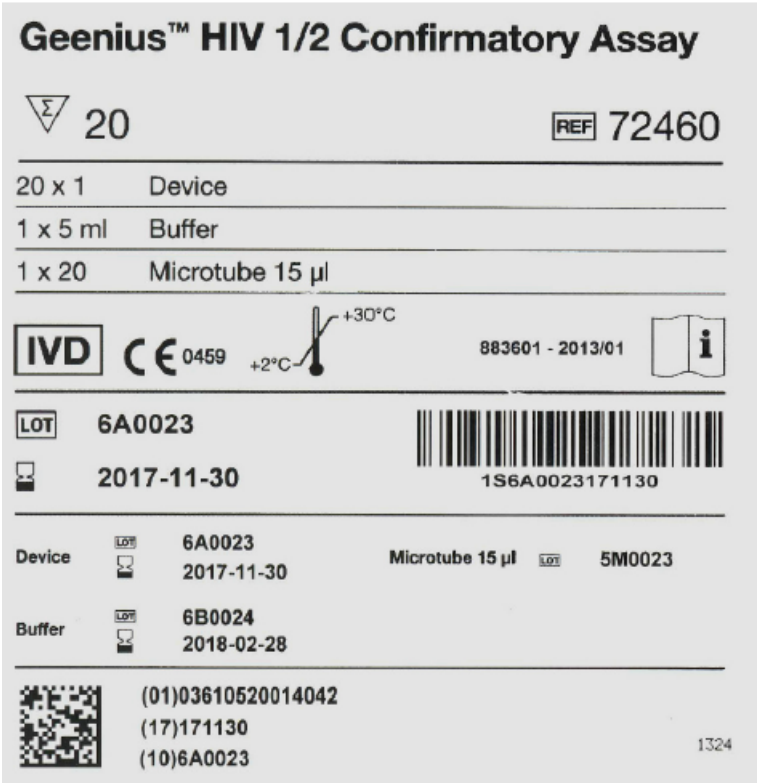
LABELS

I - BOX LABELS

1- Text printed on the box

Bio-Rad
3, Boulevard Raymond Poincaré
92430 Marnes-la-Coquette - France
Tél. : 33 (0) 1 47 95 60 00
Fax : 33 (0) 1 47 41 91 33
www.bio-rad.com

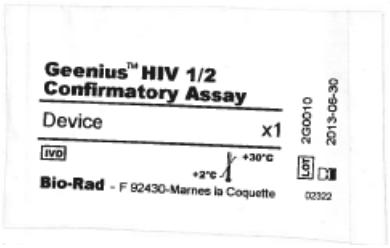
2- Box labels



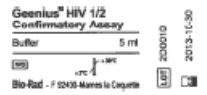
PI reference XXXXXX YYYY/MM is a variable mention

II - REAGENT LABELS

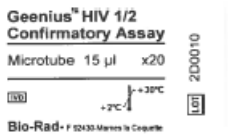
Device



Buffer



Microtubes 15 µl



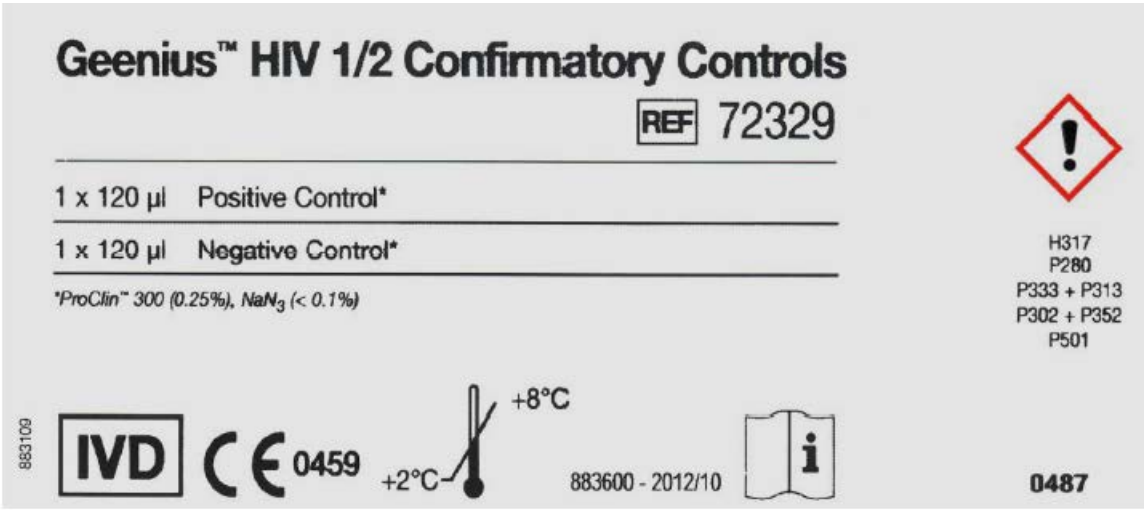
LABELS

I - BOX LABELS

1- Text printed on the box

Bio-Rad
3, Boulevard Raymond Poincaré
92430 Marnes-la-Coquette - France
Tél. : 33 (0) 1 47 95 60 00
Fax : 33 (0) 1 47 41 91 33
www.bio-rad.com

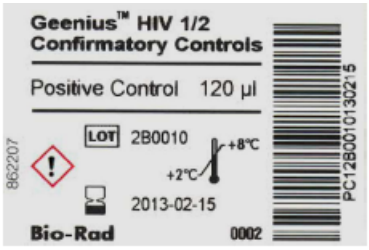
2- Box labels



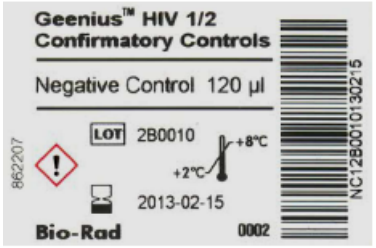
* ***PI reference XXXXXX YYYY/MM is a variable mention***

II - REAGENT LABELS

Positive Control



Negative Control



Geenius™ HIV 1/2 Confirmatory Assay

72460 - ▽ 20

REF 72460

(BG) • Други езици можете да получите от представителя на Bio-Rad. Задължително използвайте варианта на листовката, описан върху опаковката (📖).

(CZ) • Ostatní požadované jazyky jsou k dispozici u vašeho místního prodejce Bio-Rad. Používejte pouze verzi příbalového letáku uvedenou na obalu (📖).

(DE) • Andere Sprachen sind auf Anfrage von Ihrer Bio-Rad-Vertretung vor Ort erhältlich. Es ist zwingend die auf der Schachtel genannte Version der Packungsbeilage zu verwenden (📖).

(DK) • Hvis der ønskes andre sprog, kan de fås hos den lokale Bio-Rad-repræsentant. Indlægssedlen, som er angivet på kassen, skal altid anvendes (📖).

(EE) • Teistes keeltes juhendi saate soovi korral kohalikult Bio-Rad esindajalt. Kohustuslik on kasutada karbil mainitud pakendi infolehe versiooni (📖).

(EN) • Other requested languages can be obtained from your local Bio-Rad agent. Imperatively use the package insert version mentioned on the box (📖).

(ES) • Puede solicitar otros idiomas a su agente local Bio-Rad. Utilice obligatoriamente el paquete adjunto, versión indicada en la caja (📖).

(FI) • Muita kieliä on saatavilla omalta Bio-Rad -edustajaltanne. Käytä ehdottomasti laatikossa mainittua tuoteselosteversiota (📖).

(FR) • Pour obtenir d'autres langues, contacter votre agent Bio-Rad. Utiliser obligatoirement la version de la notice mentionnée sur la boîte (📖).

(GR) • Τις άλλες απαιτούμενες γλώσσες μπορείτε να τις πάρετε από τον τοπικό πράκτορά σας Bio-Rad. Χρησιμοποιήστε οπωσδήποτε την παραλλαγή ένθετου συσκευασίας που αναγράφεται στο κουτί (📖).

(HU) • Egyéb nyelveken a helyi Bio-Rad képviselettől szerezhető be. A dobozon szereplő verziószámú tájékoztatót kell kötelező érvénnyel használni (📖).

(IT) • E' possibile avere i Manuali di Istruzioni in altre lingue richiedendoli al collaboratore Bio-Rad di zona. Utilizzare tassativamente il manuale di istruzioni della versione citata sulla confezione (📖).

(LT) • Informaciją gimtąja kalba galima gauti iš vietinio „Bio-Rad“ atstovo. Privaloma naudoti įdėtinę paketo versiją, nurodytą ant dėžutės (📖).

(LV) • Citas pieprasītās valodas varat iegūt no Jūsu vietējā Bio-Rad pārstāvja. Noteikti izmantojiet preparāta lietošanas norādījumus, kas norādīti uz iepakojuma (📖).

(MT) • Lingwi oħrajn mitlubin jistgħu jinkisbu mingħand l-aġent ta' Bio-Rad lokali tiegħek. Huwa mistenni li tuża l-verżjoni tal-fuljett ta' tagħrif imsemmija fuq il-kaxxa (📖).

(NL) • Andere gevraagde talen kunnen worden verkregen bij uw plaatselijke Bio-Rad agent. Gebruik uitsluitend de op de doos vermelde versie van de bijsluiter (📖).

(NO) • Andre etterspurte språk kan fås fra din lokale Bio-Rad representant. Om nødvendig bruk pakningsvedlegget som følger med (📖).

(PL) • Informację w innych językach można otrzymać u miejscowego przedstawiciela firmy Bio-Rad. Należy bezwzględnie zapoznać się z ulotką dołączoną do produktu wskazaną na opakowaniu (📖).

(PT) • É possível obter outros idiomas solicitados junto da sua agência Bio-Rad local. Consulte obrigatoriamente a versão do folheto informativo referida na embalagem (📖).

(RO) • Alte limbi solicitate pot fi obținute de la agentul dumneavoastră local Bio-Rad. Este imperativ să utilizați versiunea prospectului menționată pe cutie (📖).

(SE) • Andra språk kan fås av din lokala Bio-Rad-återförsäljare. Använd alltid den version av bipacksedeln som anges på förpackningen (📖).

(SI) • Druge želene jezike lahko dobite pri krajevnem zastopniku Bio-Rad. Obvezno uporabite različico navodil za uporabo, navedeno na škatli (📖).

(SK) • Ďalšie jazyky si môžete vyžiadať u svojho miestneho zástupcu Bio-Rad. Bezpodmienečne používajte verziu príbalového letáku uvedenú na škatuli (📖).

BIO-RAD

Geenius™ HIV 1/2 Confirmatory Assay

72460 - ▽ 20

REF 72460

A QUALITATIVE ASSAY FOR THE CONFIRMATION AND DIFFERENTIATION OF INDIVIDUAL ANTIBODIES TO HIV-1 AND HIV-2 IN WHOLE BLOOD, SERUM, OR PLASMA SPECIMENS

IVD CE 0459

883601 - 2013/01

BIO-RAD

Table of Content

1. INTENDED USE

The Bio-Rad Geenius™ HIV 1/2 Confirmatory Assay is a single-use immunochromatographic test for the confirmation and differentiation of individual antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV-1 and HIV-2) in fingerstick whole blood, venous whole blood, serum or plasma samples.

The Geenius™ HIV 1/2 Confirmatory Assay is intended for use as an additional test to confirm the presence of antibodies to HIV-1 and HIV-2 for specimens found to be repeatedly reactive by screening procedures.

2. SUMMARY AND EXPLANATION OF THE TEST

Discovered in 1983, the Human Immunodeficiency Virus (HIV) is a retrovirus identified as the etiologic agent for Acquired Immunodeficiency Syndrome (AIDS). AIDS is characterized by changes in the population of T-cell lymphocytes that play a key role in the immune defence system. In the infected individual the virus causes a depletion of a subpopulation of T-cells, called T-helper cells, which leaves these patients susceptible to opportunistic infections and certain malignancies. The major routes of transmission are sexual contact, contamination by blood or blood products and mother-to-newborn transmission.
At the end of 2010 there were approximately 34 million people living with HIV/AIDS worldwilde, up 17% from 2001.

There were 2.7 million [2.4 -2.9] new HIV infection in 2010 including an estimated 390 000 [340 000-440 000] among children. This was 15% less than 2001 and 21% below the number of new infections at the peak of the epidemic in 1997.

While the HIV virus consists of a genomic RNA molecule protected by a capsid and an envelope, the HIV envelope is the major target for humoral antibody response. The presence of the virus in patients causes the immune system to elicit the production of antibodies to HIV. The detection of these antibodies can be used as a diagnostic tool.

The Geenius™ HIV 1/2 Confirmatory Assay is a rapid immunochromatographic test, which is simple and easy to use. The Geenius™ HIV 1/2 Confirmatory Assay utilizes immobilized antigens for the detection of antibodies to HIV-1 and HIV-2 in serum, plasma or whole blood specimens.

3. PRINCIPLE OF THE PROCEDURE

The Geenius™ HIV 1/2 Confirmatory Assay employs antibody binding protein A, which is conjugated to colloidal gold dye particles as conjugate and HIV-1 (p31, gp160, p24, gp41) and HIV-2 antigens (gp36, gp140), which are bound to the membrane solid phase. The sample is applied to the SAMPLE + BUFFER well. After the sample and buffer have migrated onto the test strip, additional buffer is added to the BUFFER well. The buffer facilitates the lateral flow of the released products and promotes the binding of antibodies to the antigens.

In a reactive sample, the anti-HIV antibodies are captured by the antigens immobilized in the TEST area (bands 1 to 6): the colloidal gold protein A binds to the captured antibodies, producing pink/purple lines.

In the absence of HIV antibodies, there are no pink/purple lines in the TEST area.

In both cases the sample continues to migrate along the membrane and produces a pink/purple line in the CONTROL (C) where protein A is immobilized.

Immunoglobulin G from sample bound to protein A is immobilized in (C) zone of the membrane solid phase to produce a pink/purple line.

This Control line serves to demonstrate that sample and reagents have been properly applied and have migrated through the device.

The Geenius™ HIV 1/2 Confirmatory Assay cassette contains a Control band (C) and six (6) test lines which are numbered on the cassette corresponding to the following:

Band 1:	gp36 (HIV-2, envelop peptide)	HIV-2 ENV
Band 2:	gp140 (HIV-2, envelop peptides)	HIV-2 ENV
Band 3:	p31 (HIV-1, polymerase peptide)	HIV-1 POL
Band 4:	gp160 (HIV-1, envelop recombinant protein)	HIV-1 ENV
Band 5:	p24 (HIV-1, core recombinant protein)	HIV-1 GAG
Band 6:	gp41 (Group M and O) (HIV-1, envelop peptides)	HIV-1 ENV
CTRL band:	Protein A	

4. REAGENTS

4.1 Description

Identification on label	Description	Presentation
Device	Nitrocellulose membrane containing HIV-1 and HIV-2 antigens in TEST area, protein A in CONTROL area and colloïdal gold protein A in BUFFER well area	20 x 1 Ready for use
Buffer	Buffer dropper with preservative (sodium azide < 0.1%, gentamicin sulphate 0.125%, streptomycin sulphate 0.125%)	1 x 5 ml Ready to use
Microtubes 15 µl	15 µl Microtubes capillarity plastic pipettes (no anti-coagulant, for fingerstick protocol)	1 x 20 Ready to Use

4.2 Storage and handling requirements

The Geenius™ HIV 1/2 Confirmatory Assay (Device and Buffer) should be stored at 2°C to 30°C, until the expiration date stated on the kit.

Do not freeze. Do not open the pouch until performing a test.
The Buffer is stable until expiration date after the first use in routine.

5. WARNING AND PRECAUTIONS

For *in vitro* diagnostic use. For healthcare professional use.

5.1 Health and Safety precautions

- This test kit should be handled only by adequately qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately with the requisite Good Laboratory Practices.

- The test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Therefore, all human blood derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Precautions for as defined by local, regional and 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, with an appropriate chemical disinfectant that is effective for the potential biohazards relative to the samples involved (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.

  NOTE: Do not place solutions containing bleach into the autoclave

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or biohazardous wastes must be handled and discarded in accordance with all local, regional and national regulations.

- For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

5.2 Precautions related to the procedure

5.2.1 Preparing

- Read the Product Insert completely before using this assay. Follow the instructions carefully as not doing so may result in inaccurate test results.
- Use of this test kit with sample types other than those specifically approved for use with this device may result in inaccurate test results.
- This test should be performed at 18°C to 30°C. If stored refrigerated, before use wait at least 30 min for the reagents to stabilize at room temperature.
- DO NOT USE the test device if there is no desiccant packet in the device pouch. Discard the test device and use a new device from a pouch that contains a desiccant.
- DO NOT USE the test device if the device pouch is damaged.
- Each test device is for single use only.
- Do not use the test device or kit reagent beyond their expiration dates. Always check expiration dates prior to testing.
- Do not mix reagents from different lot numbers of kits.
- Adequate lighting is required to read the test results.

- If the test kit is stored at temperatures outside the storage temperature 2°C to 30°C, or used outside the operating temperature 18°C to 30°C, use the Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329, to ensure proper performance of the test.

5.2.2 Processing

- After the closed bag has been opened, the device must be used within 60 min.
- Do not change the assay procedure.

6. SPECIMENS

The Geenius™ HIV 1/2 Confirmatory Assay can be performed on venous or fingerstick whole blood, serum or plasma samples.

6.1 Specimen types

Venous Whole Blood

Draw blood following laboratory procedure for obtaining venous blood. Collect sample in a tube containing citrate, heparin or EDTA. Be sure the tube of blood is well mixed before sampling. Use a laboratory pipette to withdraw 15 µl of the blood. Test immediately, following Test Procedure instructions.

Fingerstick Whole Blood

Clean the finger of the person being tested with an antiseptic wipe. Allow the finger to dry thoroughly or wipe dry with a sterile gauze pad. Using a sterile lancet, puncture the skin just off the center of the finger and wipe away the first drop with sterile gauze and avoid squeezing the fingertip to accelerate bleeding as this may dilute the blood with excess tissue fluid. Collect 15 µl of the sample from the second drop touching the disposable Microtube pipette provided to the drop of blood until the pipette is full, following the procedure below.

Test immediately, following Test Procedure Instructions.

Serum or Plasma

Draw blood following laboratory procedure for obtaining serum or plasma samples. Collect serum samples in clotting agent-containing tubes that do not contain any anticoagulant (serum). Collect plasma samples in tubes containing citrate, heparin, or EDTA anticoagulants. Collect sample in a clean container following standard laboratory procedures. Be sure that the tube of serum or plasma is well mixed before sampling. Use a laboratory pipette to withdraw 5 µl of the sample. Test immediately following Test Procedure instructions.

6.2 Specimen Handling

Fingerstick whole blood should be tested immediately after collection.

Venous whole blood, specimens may be tested immediately or stored at 2°C to 8°C for up to 3 days following collection before being tested.

DO NOT FREEZE WHOLE BLOOD.

Serum and plasma specimens may be tested immediately or stored at 2°C to 8°C for up to 7 days following collection before being tested.

For long-term storage, the serum and plasma specimens should be frozen (at -20°C or colder).

Samples should not be used if they have incurred more than 5 freeze-thaw cycles. Mix samples thoroughly and gently after thawing, and bring to room temperature.

No interference has been shown in samples containing up to 200 mg/l of bilirubin, or in lipemic samples containing up to 33 g/l of triolein, or in hemolyzed samples containing up to 2 g/l of hemoglobin. Abnormally high albuminemia or proteinemia (120 g/l) did not show either any interference.

6.3 Specimen Shipping

If specimens are to be shipped, they should be packed in compliance with regulations covering the transportation of etiologic agents.

Venous whole blood, specimens should be shipped refrigerated with cold packs or wet ice.

Serum and plasma specimens should be shipped frozen in dry ice.

7. PROCEDURE

7.1 Materials required

Materials provided

- Device (20 units), Buffer Dropper (1 x 5 ml) and Microtubes 15 µl (1 x 20) per kit.
- See § 4.1 Description.

Material required provided separately

- Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329.

Materials required but not provided

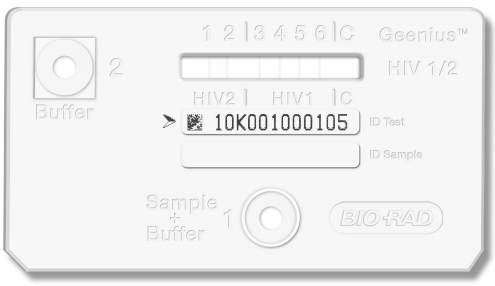
- Clock, watch or other timing device.
- Pipettor capable of delivering 5 µl (serum/plasma) and 15 µl (venous blood) of sample.
- Disposable gloves.
- Biohazard disposal containers.

7.2 Reagent preparation

All components for the Geenius™ HIV 1/2 Confirmatory Assay are ready-to-use as supplied.

7.3 Assay Procedure

Whole Blood PROCEDURE

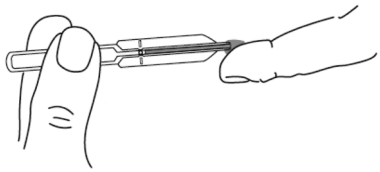
1.	Remove the Geenius™ HIV 1/2 Confirmatory Assay device from its pouch and place it on a flat surface (it is not necessary to remove the desiccant from the pouch). **NOTE**: If desiccant packet is missing from the pouch, DO NOT USE. Discard test device and use a new test device. Label the test device with patient ID or identification number (see Figure 1 below). Note that the Geenius™ HIV 1/2 Confirmatory Assay device has six (6) blue coloured lines in the Test area (no blue line in Control area); If any of the 6 coloured lines are absent, DO NOT USE. Discard the test device and use a new test device.	**Figure 1** 

Venous Whole Blood
See specimen preparation on § 6.1 Specimen types.

Fingerstick Whole Blood
See specimen preparation on § 6.1 Specimen types.

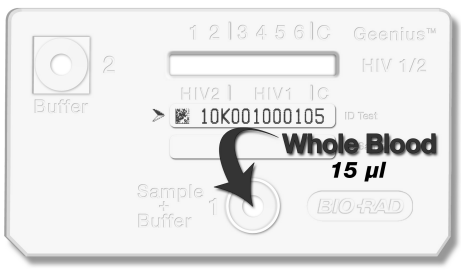
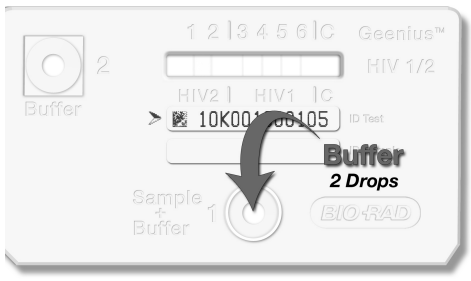
Step 1:

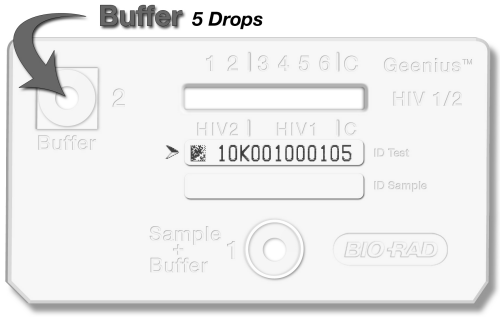
Hold the 15µL Microtube horizontally and touch the blood drop with the tip. Capillary action will automatically draw the sample to the fill line and stop.



Step 2:

To expel the sample, align the tip of the tube with the sample target and squeeze the bulb. If a sample won't expel, hold the tube vertically and slide a finger over the vent hole. Then align the tip with the sample target and squeeze the bulb.

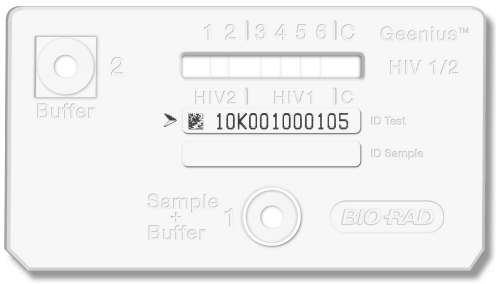
2. Dispense 15 µl of whole blood to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below). For venous whole blood use a laboratory pipette. For Fingerstick whole blood, follow the protocol using the Microtube 15 µl of the kit (see step 1 and 2 above). **Figure 2** 	3 **Immediately** following the addition of the sample, use the Buffer dropper to **add 2 drops** (60 µl) of Buffer, into the SAMPLE + BUFFER Well 1 (see Figure 3 below). **Figure 3** 

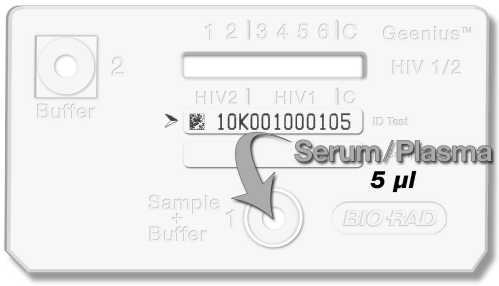
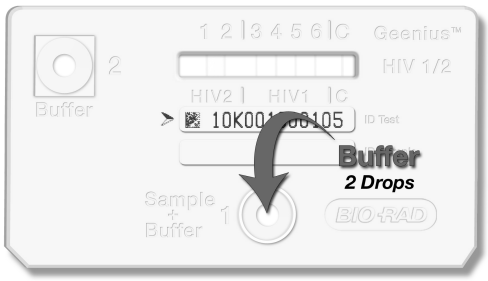
4. **Wait 5-7 minutes** the 6 blue coloured TEST lines should have disappeared from the rectangular TEST area. If not, discard the test device and repeat the procedure with a new test device. NOTE: A slight bluish-greenish colour may remain on the membrane, but none of the actual coloured lines should be seen at this point. Use the Buffer dropper to **add 5 drops** (150 µl) of Buffer into BUFFER Well 2 (see Figure 4 below).	**Figure 4** 

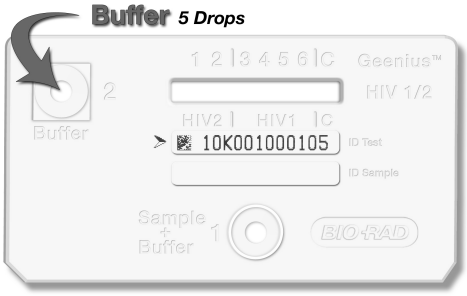
5. Read the test results between 20 to 30 minutes after the addition of the Buffer to BUFFER Well 2 **Do not read results after 30 minutes** Read results in a well-lit area. **NOTE:** Discard the used pipette tips, test device and any other test materials into a biohazard container.	

Serum or Plasma PROCEDURE

See specimen preparation on § 6.1 Specimen types.

1. Remove the Geenius™ HIV 1/2 Confirmatory Assay device from its pouch and place it on a flat surface (it is not necessary to remove the desiccant from the pouch). **NOTE**: If desiccant packet is missing from the pouch, DO NOT USE. Discard test device and use a new test device. Label the test device with patient ID or identification number (see Figure 1 below). Note that the Geenius™ HIV 1/2 Confirmatory Assay device has six (6) blue coloured lines in the Test area (no blue line in Control area); If any of the 6 coloured lines are absent, DO NOT USE. Discard the test device and use a new test device.	**Figure 1** 

2. Using a laboratory pipette, dispense 5 µl of serum/plasma) to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below). **Figure 2**  	3 Immediately following the addition of the sample, use the diluent dropper bottle to **add 2 drops** (60 µl) of Buffer into the SAMPLE + BUFFER Well 1 (see Figure 3 below). **Figure 3** 

4. **Wait 5-7 minutes.** All the 6 blue coloured TEST lines should have disappeared from the rectangular TEST area. If not, discard the test device and repeat the procedure with a new test device. NOTE: A slight bluish-greenish colour may remain on the membrane, but none of the actual coloured lines should be seen at this point. Use the diluent dropper bottle to **add 5 drops** (150 µl) of Buffer into BUFFER Well 2 (see Figure 4 below).	**Figure 4** 

5. Read the test results between 20 to 30 minutes after the addition of the Buffer to BUFFER Well 2

Do not read results after 30 minutes

Read results in a well-lit area.

NOTE: Discard the used pipette tips, test devices and any other test materials into a biohazard container.

7.4 Quality Control

7.4.1 Built-in Control Feature

The control line serves as a built-in internal control and gives confirmation of sample addition and proper test performance. A pink/purple line will appear in the CONTROL (C) area if the test has been performed correctly and the device is working properly (Please see: Interpretation of Test Results).

7.4.2 External Quality Control

Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329 is available separately for use with the Geenius™ HIV 1/2 Confirmatory Assay.

It is recommended to perform the Geenius™ HIV 1/2 Confirmatory Controls under the following circumstances:

- When opening a new test kit lot.
- Whenever a new shipment of test kits is received.
- If the temperature of the test storage area falls outside of 2°C to 30°C.
- If the temperature of the testing area falls outside of 18°C to 30°C.
- At periodic intervals as indicated by the user facility.

7.5 Test Validation criteria

BAND reactivity

All visible bands. Even a faint band must be considered as reactive.

Validation criteria

VALID:
A test is valid only if a pink/purple line appears in the CONTROL (C) area, whether or not a line appears in the TEST line area.
(The Control Band must be strong: a faint band is not acceptable for the Control Band)

INVALID:
If there is no distinct pink/purple line visible (including a faint band) in the CONTROL (C) area, then the test is INVALID.
An INVALID test cannot be interpreted. It is necessary to repeat sample testing with a new device.

7.6 Interpretation of the Results

The following definitions describe the criteria employed by the Geenius™ HIV 1/2 Confirmatory Assay to determine the presence or absence of antibodies to HIV-1 and/or HIV-2.
The user subsequently analyzes the combined type specific band profiles for each assay according to the criteria listed in the Interpretation of Results Table below.

7.6.1 Interpretation criteria

HIV-1 Interpretation criteria

Interpretation	Bio-Rad criteria
POSITIVE	Any 2 bands of the 4 HIV-1 test lines with at least 1 ENV - gp160 (Band 4) or gp41 (Band 6)
NEGATIVE	No Band
INDETERMINATE	1ENV (Band 4 or 6) 1GAG (Band 5) 1POL (Band 3) 1GAG and 1POL (Bands 5 and 3)

HIV-2 Interpretation criteria

Interpretation	Bio-Rad criteria
POSITIVE	2 HIV-2 bands must be present: gp36 and gp140 (Band 1 and 2)
NEGATIVE	No Band

INDETERMINATE	1 ENV: gp36 (Band 1) or gp140 (Band 2) gp36 (Band 1) alone gp140 (Band 2) alone

GLOBAL HIV-1/HIV-2 Interpretation criteria

The following Interpretation of Results table describes the criteria employed by the Geenius™ HIV 1/2 Confirmatory Assay to interpret the combined type specific band patterns observed for each assay.

HIV-2 RESULT	HIV-1 RESULT	GLOBAL ASSAY INTERPRETATION
Negative	Negative	**HIV NEGATIVE**
Indeterminate	Negative	**HIV-2 INDETERMINATE**
Negative	Indeterminate	**HIV-1 INDETERMINATE**
Indeterminate	Indeterminate	**HIV INDETERMINATE**
Negative	Positive	**HIV-1 POSITIVE**
Indeterminate	Positive	**HIV-1 POSITIVE**
Positive	Negative	**HIV-2 POSITIVE**
Positive	Indeterminate	**HIV-2 POSITIVE**
Positive	Positive **case 1** = 1 ENV HIV-1 (gp 160 or gp41) + GAG or POL **case 2** = 2 ENV HIV-1 (gp 160 and gp41) +/- GAG and/or +/-POL	**HIV-2 POSITIVE** **(with HIV-1 cross-reactivity)** **HIV POSITIVE UNTYPABLE**

8. TEST LIMITATION

8.1 General Limitations

1. Visual reading can introduce some variability in the final conclusion between two different technicians or two different tests: this difference may be linked to the subjectivity of the visual interpretation.
2. For a reactive result, the intensity of the test lines does not necessarily correlate with the titer of antibody in the sample.
3. A person who is confirmed HIV-1 Positive or HIV-2 Positive is presumed to be infected with the virus, except that a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.
4. Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.
5. The variability of HIV-1 (group M and group O) and HIV-2 viruses does not exclude the possibility of false negative reactions. No known test method can offer complete assurance that the HIV virus is absent.
6. A nonreactive result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several months to reach detectable levels. A positive screening test associated with a negative confirmatory test may occur during the first stage of infection; hence, a negative result indicates that the tested sample does not contain anti-HIV antibodies detectable with Geenius™ HIV 1/2 Confirmatory Assay. Such a result does not, however, exclude the possibility of a recent HIV-1/HIV-2 infection. A new sample should be tested later.
7. An indeterminate result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several months to reach detectable levels. A positive screening test associated with an indeterminate confirmatory test may occur during the first stage of infection; hence, an indeterminate result indicates that the tested sample may contain anti-HIV antibodies detectable with Geenius™ HIV 1/2 Confirmatory Assay. Such a result does not, however, exclude the possibility of a recent HIV-1/HIV-2 infection. A new sample should be tested later.
8. The Geenius™ HIV 1/2 Confirmatory Assay is intended as an aid in the diagnosis of infection with HIV-1 and or HIV-2. HIV and AIDS related conditions are clinical syndromes and their diagnosis can only be established clinically.
9. The Geenius™ HIV 1/2 Confirmatory Assay must ONLY be used with capillary blood, whole venous blood, serum or plasma. Using other types of samples or testing of venipuncture whole blood samples collected using a tube containing an anticoagulant other than citrate, heparin or EDTA may not yield accurate results.
10. The Geenius™ HIV 1/2 Confirmatory Assay must be used in accordance with the instructions in this product insert to obtain accurate results.
11. Reading test results earlier than 20 minutes or later than 30 minutes since the addition of Running Buffer to BUFFER Well 2 may yield erroneous results.

8.2 Assay Interpretation limitations

An “indeterminate” profile does not exclude one of the following situations: seroconversion, or a cross-reaction with other retroviruses**.** The homology between HIV-1 and HIV-2 viruses can lead to cross reactivity between both anti-HIV-1 and anti-HIV-2 antibodies against HIV-2 and HIV-1 viruses.

Samples which meet HIV-1 positive criteria show in very rare cases some cross reactivity on one of the HIV-2 Envelop bands. Nevertheless, such rare profile of single HIV-1 infection does not also exclude in very rare cases the possibility of a secondary HIV-2 seroconversion (surinfection).

Samples which meet HIV-2 positive criteria can show cross reactivity on one or more HIV-1 bands. In most of the cases, an HIV-1 indeterminate profile associated to an HIV-2 positive

profile confirms a single HIV-2 infection. However it does not exclude the possibility of a secondary HIV-1 seroconversion (surinfection).

Samples that meet both HIV-1 and HIV-2 positive criteria are generally HIV-2 positive samples which show HIV-1 cross reactivity when they have only one detected envelop band (gp160 or gp41). Such profiles do not exclude the rare possibility of HIV-1-HIV-2 coinfection.

HIV Untypable samples with all 4 envelop bands detected (all of the HIV-1 env and HIV-2 env) are in most of the cases HIV-2 positive samples with HIV2 reactivity that cannot be visually differentiated from HIV-1 reactivity. Such profiles do not exclude the possibility of HIV 1/2 coinfection.

Samples which meet both HIV-1 and HIV-2 positive criteria are in very rare cases HIV-1 positive samples which show HIV-2 cross-reactivity.

9. PERFORMANCES CHARACTERISTICS

9.1 Precision Study

A precision panel (N=6) made of 3 serum and 3 whole blood samples of different HIV status (HIV negative, HIV-1 positive, HIV-2 positive) was tested. For each precision study and panel member, an agreement percentage was determined as the number of responses correctly identified compared to the sample status.

9.1.1 Repeatability

Precision panel was tested in 10 replicates during the same run. Repeatability measurement was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive.

Panel member	Repeatability results for Serum					Repeatability results for Whole blood				
	N	NEG	IND	POS	agreement	N	NEG	IND	POS	agreement
HIV NEG	10	10	0	0	100%	10	10	0	0	100%
HIV-1 POS	10	0	0	10	100%	10	0	0	10	100%
HIV-2 POS	10	0	0	10	100%	10	0	0	10	100%

9.1.2 Intermediate precision

Run and Day precision

Serum precision panel was tested in duplicate per run, with 2 runs per day during 10 days and whole blood precision panel in triplicate per run, with 2 runs per day during 3 days. A run-to-run and day-to-day precision was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive samples.

Panel member	Run and day precision results for Serum					Run and day precision results for Whole blood				
	N	NEG	IND	POS	agreement	N	NEG	IND	POS	agreement
HIV NEG	40	40	0	0	100%	18	18	0	0	100%
HIV-1 POS	40	0	0	40	100%	18	0	0	18	100%
HIV-2 POS	40	0	0	40	100%	18	0	0	18	100%

Lot and Operator precision

Precision panel was tested in duplicate on 2 lots of reagent and by 3 operators with 1 run per day during 3 days. An inter-operator and inter-batch precision was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive samples.

Panel member	Lot and Operator precision results for Serum					Lot and Operator precision results for Whole blood				
	N	NEG	IND	POS	Agreement	N	NEG	IND	POS	Agreement
HIV NEG	36	36	0	0	100%	36	36	0	0	100%
HIV-1 POS	36	0	0	36	100%	36	0	0	36	100%
HIV-2 POS	36	0	0	36*	100%	36	0	0	36	100%

* 2 replicates gave HIV-1 cross reactivity

9.2 Clinical performance

9.2.1 Diagnostic Specificity

Blood donors

A total of 400 specimens (serum, plasma and venous blood) drawn from 300 non selected known and first time donors, were tested on the Geenius™ HIV 1/2 Confirmatory Assay in a blood bank site. 398 specimens tested negative and 2 tested indeterminate. Indeterminate results representing 0.5% (2/400) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 398 specimens was 100.0% (398/398) with a confidence interval at 95% of [99.1; 100.0].

Specificity on blood Donors	Total number specimens	Negative	Indeterminate	Positive	Specificity (%)	95 CI (%)
Serum (SSTII Gel sep)	100	98	2 (**)	0	100.0 (98/98)	[96.3 - 100.0]
Plasma (*) (EDTA-K2)	100	100	0	0	100.0 (100/100)	[96.4 - 100.0]
Whole venous blood (EDTA-K2)	200	100	0	0	100.0 (200/200)	[98.2 - 100.0]
TOTAL 300 donors	400	398	2 (**)	0	100.0 (398/398)	[99.1 - 100.0]

(*) specimens of plasma paired to whole venous blood samples obtained from the same 100 donors
(**) Indeterminate results have not been considered as false positive / further investigation is needed

Hospitalized patients and pregnant women

A total of 508 specimens from 326 hospitalized patients were tested on the Geenius™ HIV 1/2 Confirmatory Assay at 2 different sites. Among these patients, 99 had serum sampling alone, 100 had whole blood sampling alone, 72 had both serum and whole blood sampling, 30 patients had both serum, plasma and whole blood sampling, and 25 had serum, plasma and capillary blood sampling.
30 serum from pregnant women from 2 sites were also tested.
Whole venous blood and plasma samples were collected on EDTA-K2 tubes and serum on SSTII with gel separator tubes. No anticoagulant was used for capillary blood collection.

529 specimens tested negative and 9 tested indeterminate. Indeterminate results representing 1.7% (9/538) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 529 specimens was 100.0% (529/529) with a confidence interval at 95% of [99.3; 100.0].

Site	Patients	Fresh Serum /SSTII Gel	Fresh Plasma /EDTA-K2	Fresh venous blood /EDTA-K2	Fresh Capillary blood	Total specimens	Pregnant women (frozen serum)	GrandTotal specimens
Site 1	99	99	/	/	/	99	10	109
Site 2	227	/ 72 30 25	/ / 30 25	100 72 30 /	/ / / 25	100 144 90 75	/ / / /	100 144 90 75
Site 5		/	/	/	/		20	20
Total	**326**	**226**	**55**	**202**	**25**	**508**	**30**	**538**
Negative **Indeterminate** **Positive**	/	221 5(*)(***) **0**	54 1(*)(***) **0**	201 1(*)(***) **0**	25 0 **0**	501 7 (***) **0**	28 2 (***) **0**	529 9 (***) **0**
Specificity (%)	/	**100.0 (221/221)**	**100.0 (54/54)**	**100.0 (201/201)**	**100.0 (25/25)**	**100.0 (501/501)**	**100.0 (28/28)**	**100.0 (529/529)**
95 CI (%)	/	[98.3 - 100.0]	[93.4 - 100.0]	[98.2 -100.0]	N/A(**)	[99.3 - 100.0]	N/A(**)	[99.3 - 100.0]

(*) 1 patient had 1 indeterminate result for both serum, venous blood and plasma
(**) not applicable with N<30 population
(***) Indeterminate results have not been considered as false positive / further investigation is needed

Blood donors giving false positive results at screening

A total of 275 serum specimens drawn from blood donors giving false positive results with HIV ELISA screening assays, were tested on the Geenius™ HIV 1/2 Confirmatory Assay at two clinical sites.
258 specimens tested negative and 17 tested indeterminate. Indeterminate results representing 6.2% (17/275) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 258 specimens was 100.0% (258/258) with a confidence interval at 95% of [98.6; 100.0].

Specificity on blood Donors	Total number specimens	Negative	Indeterminate	Positive	Specificity (%)	95 CI (%)
TOTAL 275 donors	275	258	17 (*)	0	100.0 (258/258)	[98.6 - 100.0]

(*) Indeterminate results have not been considered as false positive / further investigation is needed

9.2.2 Diagnostic Sensitivity

HIV-1 infected patients

A total of 599 specimens from 263 patients confirmed as HIV-1 infected from 2 sites (155 patients at site 1 and 108 patients at site 2) were tested on the Geenius™ HIV 1/2 Confirmatory Assay
On 1 site,, 108 fresh serum and paired plasma , 5 fresh serum and 50 genotyped HIV-1 strains (2 CRF01, 5 CRF02, 1 CRF05, 1 CRF06, 2 CRF09, 1 CRF11, 1 CRF12, 1 CRF13, 1 CRF14, 1 CRF15, 1 CRF18, 1 CRF19, 1 CRF22, 1 CRF27, 1 CRF30, 1 CRF36, 1 CRF42, 4 subtype A, 5 subtype B, 2 subtype C, 2 subtype D, 2 subtype F, 2 subtype G, 2 subtype H, 2 subtype J, 1 subtype K, 5 group O) samples were tested.
On the second site, among the 108 patients, 82 had whole blood, serum and plasma samplings, 20 had both whole blood, capillary whole blood, serum and plasma samplings, and 6 had capillary whole blood, serum and plasma sampling.

Whole venous blood and plasma samples were collected on EDTA-K2 tubes and serum samples on SSTII with gel separator tubes.
All the 599 specimens tested HIV-1 positive, leading to an overall sensitivity of 100.0% (599/599) with a confidence interval at 95% of [99.4 - 100.0].
HIV-1 sensitivity on patients was 100% (263/263).
On the total of 599 specimens, 3 specimens were found HIV untypable instead of HIV-1 positive, therefore HIV-1 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 99.5% (596/599) with a confidence interval at 95% of [98.5 - 99.9].

Site	Patients	Fresh Serum (SSTII Gel)	Genotyped serum	Fresh Plasma (EDTA-K2)	Fresh venous blood (EDTA-K2)	Fresh Capillary blood	Total specimens
Site 1 **N= 155**	100 5 50	/ 5 /	/ / 50	100 / /	100 / /	/ / /	200 5 50
Site 2 **N= 108**	82 20 6	82 20 6	/ / /	82 20 6	82 20 /	/ 20 6	246 80 18
Total	**263**	**113**	**50**	**208**	**202**	**26**	**599**
HIV-1 Positive		113	49	207	201	26	
HIV untypable		0	1	1(*)	1(*)	0	
Sensitivity (%)		**100.0 (113/113)**	**100.0 (50/50)**	**100.0 (208/208)**	**100.0 (202/202)**	**100.0 (26/26)**	**100.0 (599/599)**
95 CI (%)		[97.8 - 100.0]		[98.2 - 100.0]	[98.2 -100.0]	N/A(**)	[99.4 - 100.0]

(*) specimens of plasma paired to venous blood sample obtained from the same HIV-1 infected patient
(**) not applicable with N<30 population

HIV-2 infected patients

A total of 283 specimens from 172 patients confirmed as HIV-2 infected (serum, plasma, venous blood and capillary blood with some paired samples drawn from the same patients) were tested on the Geenius™ HIV 1/2 Confirmatory Assay at three clinical sites. 66 serum specimens were obtained from two clinical sites samples collections. All others specimens were freshly obtained from patients.
Whole venous blood and plasma samples were collected on EDTA-K2 or EDTA-K3 tubes and serum collected samples on SSTII with gel separator or dry tubes.

281 specimens tested HIV positive and 2 tested HIV-2 indeterminate. The two HIV-2 indeterminate results (gp140 not detected) were obtained on serum and whole blood drawn from the same patient found gp105 negative with a CE-marked HIV I/II confirmation assay. Indeterminate results representing 0.7% (2/283) of total specimens have not been considered as false negative. Overall sensitivity (true positive/ true positive + false negative) on the 281 specimens was 100.0% (281/281) with a confidence interval at 95% of [98.7; 100.0].

172 specimens over 283 were correctly found HIV-2 positive (with or without cross HIV-1 reactivity) or HIV-2 indeterminate and 111 HIV untypable, therefore HIV-2 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 60.8% (172/283) with a confidence interval at 95% of [54.8 - 66.5].

Sites	Patients	Fresh Serum (SSTII Gel)	Frozen serum	Fresh Plasma (EDTA-K2)	Fresh venous blood (EDTA-K2 or K3)	Fresh Capillary blood	Total specimens
Site 1	5 16	5 /	/ 16	5 /	2 /	3 /	15 16
Site 2	50	/	50	/	/	/	50
Site 3	101	101	/	/	101	/	202
Total	**172**	**106**	**66**	**5**	**103**	**3**	**283**
HIV-2 Positive	/	33	15	3	28	3	82
HIV-2 positive with HIV-1 reactivity		33	19	1	35	0	88
HIV untypable		39	32	1	39	0	111
Indeterminate		1(*)(***)	0	0	1(*)(***)	0	2 (***)
Sensitivity (%)		**100.0 (171/171)**		**100.0 (5/5)**	**100.0 (102/102)**	**100.0 (3/3)**	**100.0 (281/281)**
95 CI (%)		**[97.9 - 100.0]**		**N/A****	**[96.5 - 100.0]**	**N/A****	**[98.7 – 100.0]**

(*) specimens of serum paired to venous blood sample obtained from the same HIV-2 infected patient
(**) not applicable with N<30 population
(***) Indeterminate results have not been considered as false negative / further investigation is needed

HIV-1/HIV-2 co-infected patients

A total of 22 specimens from 15 patients confirmed as HIV-1/ HIV-2 coinfected (13 serum, 2 plasma and 7 paired whole venous blood drawn from same 7 patients) were tested on the Geenius™ HIV 1/2 Confirmatory Assay at two clinical sites. Six serum and 2 plasma specimens were obtained from one clinical samples collection site and the seven paired serum-whole venous blood were freshly obtained from another clinical site patients.
Overall sensitivity was 100% (22/22) (serum and whole venous blood) without indeterminate results.
At the first intent, all specimens were correctly found HIV untypable (HIV-1 positive with two envelops detection and HIV-2 positive), except one whole blood and one serum specimens. Whole blood was improperly found HIV-2 positive due to recent surinfection. After recall few weeks later, this patient was correctly found HIV untypable. Serum was improperly found HIV-2 positive with HIV-1 reactivity instead of HIV untypable but was also improperly found HIV-2 positive (without HIV-1 reactivity) on several CE-marked HIV differentiation assays. 21 over 22 specimens were correctly found HIV untypable after one patient recall. Therefore, HIV-1+2 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 95.5% (21/22).

HIV-1 seroconversion samples

Sensitivity of Geenius™ HIV1/2 Confirmatory Assay has been estimated with 32 seroconverter panels (154 samples). 41.6% (64/154) were positive with Geenius™ HIV1/2 Confirmatory Assay, meanwhile 12.3% (19/154) were positive with a CE-marked Western Blot assay. The detection of the first positive bleed point was in average earlier of 1.4 (44/32) time-points per panel with Geenius™ HIV 1/2 Confirmatory Assay.

When testing 83 early-seroconversion samples (negative or indeterminate by Western Blot), 10.8% (9/83) were positive with Geenius™HIV1/2 Confirmatory Assay.

Based on 10 seroconversion samples tested in a clinical site and comparison to the same reference Western blot assay, Geenius™ HIV1/2 Confirmatory Assay was more sensitive for the detection of antibodies to gp41 and had a similar sensitivity for the detection of antibodies to gp160.

Geenius™ HIV1/2 Confirmatory Assay complies with the state of art in term of sensitivity estimated with HIV seroconversion panels.

9.3 Analytical Specificity

9.3.1 Cross Reactivity

251 potentially cross-reacting samples representing 29 different diseases/ states testing positive for the following markers were tested on the Geenius™ HIV 1/2 Confirmatory Assay in different clinical sites.

HTLV I/ II (20), Hepatitis C (10 HCV), Hepatitis B (10 anti-HBS) and Hepatitis A (10 HAV IgG); Cytomegalovirus (10 CMV IgG), Epstein-Barr (10 EBV IgG),Herpes Simplex (10 HSV), Rubella IgG (10), Toxoplasmosis IgG (5), Syphilis IgG (10), Candida (10), Malaria (26), Dengue (2), Leishmaniosis (2), Vaccinia (10),, Influenza vaccine (5 Flu), Dialysis (10), HAMA (10), Rheumatoid factor (10), Multi-transfusion (10), Myeloma (5) Hemophiliac (10), Autoimmune as Systemic Lupus Erythemateous (12 SLE), Scleroderma (2), Sjogrens (2), Mixed connective tissue (2 MCTD), anti-nuclear antibody (3 ANA), Cancer (5), Cirrhosis (5) and Multipareous women (5).

Over the total 251 difficult samples, 245 specimens tested negative and 6 specimens tested indeterminate (they were indeterminate with HIV-1 Western-Blot and positive for Malaria). Indeterminate results representing 2.4% (6/251) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) was 100.0% (245/245) with a confidence interval at 95% of [98.5 - 100.00].

9.4 Hook effect

Possible hook effect was studied by testing 2 HIV-1 and 2 HIV-2 high titer specimens, neat and diluted. Neither negative or lower intensity results were observed with the neat high titer HIV-1 and HIV-2 positive specimens, when compared to their more diluted forms (1:10 to 1:100000). The equivalence of results between non diluted and diluted samples shows the absence of hook effect.

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Geenius™ HIV 1/2 Confirmatory Controls

REF 72329

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THE GEENIUS™ HIV 1/2 CONFIRMATORY CONTROLS ARE INTENDED FOR MONITORING SYSTEM PERFORMANCE OF THE GEENIUS™ HIV 1/2 CONFIRMATORY ASSAY

IVD

For more details see Ref: 72460 Insert.

1. REAGENTS

Description

Identification	Contents	Description
Positive Control	Human plasma negative for HBs Ag and HCV Ab and containing Anti HIV-1 and HIV-2 Ab Preservative: ProClin™ 300 (0.25%), NaN_3 (< 0.1%)	1 x 120 µl Ready to use
Negative Control	Human plasma negative for HBs Ag, HCV Ab, Anti HIV-1 and HIV-2 Ab Preservative: ProClin™ 300 (0.25%), NaN_3 (< 0.1%)	1 x 120 µl Ready to use
Positive Control Labels Card	Barcode labels of Positive Control	x20
Negative Control Labels Card	Barcode labels of Negative Control	x20

Storage and Handling Requirements

This kit should be stored at +2-8°C.
Reagents can be used until the expiry date mentioned on the package.
After opening the reagents can be used until the expiration date.

2. WARNING AND PRECAUTIONS

For in vitro diagnostic use. For healthcare professional use.

Health and Safety precautions

- This test kit should be handled only 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 with the requisite Good Laboratory Practices.
- The test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Therefore, all human blood derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Precautions as defined by local, regional and 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, with an appropriate chemical disinfectant that is effective for the potential biohazards relative to the samples involved (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.

NOTE: Do not place solutions containing bleach into the autoclave.

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

Precautions Related to the Procedure

Preparing and Processing

- Before use wait for 30 minutes for the reagents to stabilize at room temperature.
- Do not use expired reagents.
- Gently invert each vial to insure that all the volume is inside the vial and not in the cap in case of inverting during the shipment.

3. PROCEDURE

- The Geenius HIV 1/2 Controls must be treated in the same way as patient specimens and run in accordance with the instructions of package insert Ref: 72460.

• Test Validation Criteria

	Validation Criteria	Additional Criteria
Positive Control	All 6 Test Bands must be reactive and the Control Band must be present	See package insert Ref: 72460 for the validation criteria
Negative Control	No Test Bands reactive and the Control Band must be present	See package insert Ref: 72460 for the validation criteria

4. PERFORMANCES

4.1 Intermediate (inter batch) precision protocol

For controls inter-batch reproducibility, 3 lots of Positive and Negative Controls were tested in triplicate (x3) and for 3 days (1 run per day).

3 replicates x 3 days			Geenius™ HIV 1/2 Confirmatory Assay Results		
Geenius™ HIV 1/2 Confirmatory Controls		N	Negative	Positive	Agreement
Lot 1	Negative Control	9	9	-	100%
	Positive Control	9	-	9	100%
Lot 2	Negative Control	9	9	-	100%
	Positive Control	9	-	9	100%
Lot 3	Negative Control	9	9	-	100%
	Positive Control	9	-	9	100%

The inter-batch precision demonstrates 100% response agreement for both Negative and Positive Controls when testing 3 lots in replicates during 3 days on the Geenius™ HIV 1/2 Confirmatory Assay.

H317

P280 - P333+P313 - P302+P352 - P501

(BG)
внимание
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Kan forårsage allergisk hudreaktion.
Bær beskyttelseshandsker / beskyttelsestøj / øjenbeskyttelse / ansigtsbeskyttelse • Ved hudirritation eller udslet: Søg lægehjælp • VED KONTAKT MED HUDEN: Vask med rigeligt sæbe og vand • Bortskaffelse af indholdet / beholderen i henhold til de lokale / regionale / nationale / internationale forskrifter.

(EE)
Hoiatus
Võib põhjustada allergilist nahareaktsiooni.
Kanda kaitsekindaid / kaitserõivastust / kaitseprille / kaitsemaski • Nahaärrituse või _obe korral: pöörduda arsti poole • NAHALE SATTUMISE KORRAL: pesta rohke vee ja seebiga • Sisu / konteineri käitlus vastavuses kohalike / regionaalsete / rahvuslike / rahvusvaheliste nõuetega.

(EN)
Warning
May cause an allergic skin reaction.
Wear protective gloves / protective clothing / eye protection / face protection • If skin irritation or rash occurs: Get medical advice / attention • IF ON SKIN: Wash with plenty of soap and water • Dispose of contents / container in accordance with local / regional / national / international regulations.

(ES)
Atención
Puede provocar una reacción alérgica en la piel.
Llevar guantes que aíslen del frío / gafas / máscara • En caso de irritación o erupción cutánea: Consultar a un médico • EN CASO DE CONTACTO CON LA PIEL: Lavar con agua y jabón abundantes • Eliminar el contenido o el recipiente conforme a la reglamentación local / regional / nacional / internacional.

(FI)
Varoitus
Voi aiheuttaa allergisen ihoreaktion.
Vältä pölyn / savun / kaasun / sumun / höyryn / suihkeen hengittämistä • Käytä suojakäsineitä / suojavaatetusta / silmiensuojainta / kasvonsuojainta • Jos ilmenee ihoärsytystä tai ihottumaa: Hakeudu lääkäriin • JOS KEMIKAALIA JOUTUU IHOLLE: Pese runsaalla vedellä ja saippualla • Säilytä säiliö(t) noudattaen paikallisia / alueellisia / kansallisia / kansainvälisiä määräyksiä.

(FR)
Attention
Peut provoquer une allergie cutanée.
Porter des gants de protection / des vêtements de protection / un équipement de protection des yeux / du visage • En cas d'irritation ou d'éruption cutanée: consulter un médecin • EN CAS DE CONTACT AVEC LA PEAU : laver abondamment à l'eau et au savon • Éliminer le contenu / récipient conformément à la réglementation locale / régionale / nationale / internationale.

(GR)
Προσοχή
Μπορεί να προκαλέσει αλλεργική δερματική αντίδραση.
Να φοράτε προστατευτικά γάντια / προστατευτικά ενδύματα / μέσα ατομικής προστασίας για ταμάτια / πρόσωπο • Εάν παρατηρηθεί ερεθισμός του δέρματος ή εμφανιστεί εξάνθημα: Συμβουλευθείτε / Επισκεφθείτεγιατρό • ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΟ ΔΕΡΜΑ: Πλύνετε με άφθονο νερό και σαπούνι • Απορρίψτε τα περιεχόμενα / δοχείο σύμφωνα με τους τοπικούς / εθνικούς / διεθνείς κανονισμούς.

(HU)
Figyelem
Allergiás bőrreakciót válthat ki.
Védőkesztyű / védőruha / szemvédő / arcvédő használata kötelező • Bőrirritáció vagy kiütések megjelenése esetén: orvosi ellátást kell kérni • HA BŐRRE KERÜL: Lemosás bő szappanos vízzel • Az edény tartalmát / a tartályt a helyi / regionális / nemzeti / nemzetközi szabályozásoknak megfelelően kell hulladékként elhelyezni.

(IT)
Attenzione
Può provocare una reazione allergica cutanea.
Indossare guanti / indumenti protettivi / Proteggere gli occhi / il viso • In caso di irritazione o eruzione della pelle: consultare un medico • IN CASO DI CONTATTO CON LA PELLE: lavare abbondantemente con acqua e sapone • Smaltire il prodotto / recipiente in conformità con le disposizioni locali / regionali / nazionali / internazionali.

(LT)
Atsargiai
Gali sukelti alerginę odos reakciją.
Mūvėti apsaugines pirštines / dėvėti apsauginius drabužius / naudoti akių (veido) apsaugos priemones • Jeigu sudirginama oda arba ją išberia: kreiptis į gydytoją • PATEKUS ANT ODOS: Nuplauti dideliu kiekiu muilo ir vandens • Turinį / talpą išpilti (išmesti) - šalinti pagal vietines / regionines / nacionalines / tarptautines taisykles.

(LV)
Uzmanību / Brīdinājums
Var izraisīt alerģisku ādas reakciju.
Izmantot aizsargcimdus / aizsargdrēbes / acu aizsargus / sejas aizsargus • Ja rodas ādas iekaisums vai izsitumi: lūdziet medi̦ķu palīdzību • SASKARĒ AR ĀDU: nomazgāt ar lielu ziepju un ūdens daudzumu • Izmest saturu / iepakojumu saskaņā ar vietējiem / reģionālajiem / nacionālajiem / starptautiskajiem noteikumiem.

(MT)
Twissija
Jista' jikkawża reazzjoni allerġika tal-ġilda.
Ilbes ingwanti protettivi / ilbies protettiv / protezzjoni għall-għajnejn / protezzjoni għall-wiċċ • Jekk ikun hemm irritazzjoni jew raxx tal-ġilda: Ikkonsulta tabib • JEKK FUQ IL-ĠILDA: Aħsel b'ħafna sapun u ilma • Lupuskan kandungan / bekas menurut peraturan tempatan / wilayah / kebangsaan / antarabangsa.

(NL)
Waarschuwing
Kan een allergische huidreactie veroorzaken.
Beschermende handschoenen / beschermende kleding / oogbescherming / gelaatsbescherming dragen • Bij huidirritatie of uitslag: een arts raadplegen • BIJ CONTACT MET DE HUID: met veel water en zeep wassen • De inhoud en de verpakking verwerken volgens de plaatselijke / regionale / nationale / internationale voorschriften.

(NO)
Advarsel
Kan forårsake allergiske hudreaksjoner.
Bruk vernehansker / verneklær / vernebriller / ansiktsskjerm • Ved hudirritasjon eller -utslett: Kontakt / tilkall lege • VED HUDKONTAKT: Vask med store mengder vann og såpe • Innholdet / emballasjen skal avhendes i henhold til de lokale / regionale / nasjonale / internasjonale forskrifter.

(PL)
Uwaga
Może powodować reakcję alergiczną skóry.
Stosować rękawice ochronne / odzież ochronną / ochronę oczu / ochronę twarzy • W przypadku wystąpienia podrażnienia skóry lub wysypki: Zasięgnąć porady / zgłosić się pod opiekę lekarza • W PRZYPADKU KONTAKTU ZE SKÓRĄ: Umyć dużą ilością wody z mydłem • Zawartość / pojemnik usuwać zgodnie z przepisami miejscowymi / regionalnymi / narodowymi / międzynarodowymi.

(PT)
Atenção
Pode provocar uma reacção alérgica cutânea.
Usar luvas de protecção / vestuário de protecção / protecção ocular / protecção facial • Em caso de irritação ou erupção cutânea: consulte um médico • SE ENTRAR EM CONTACTO COM A PELE: lavar com sabonete e água abundantes • Eliminar o conteúdo / recipiente de acordo com a legislação local / regional / nacional / internacional.

(RO)
Atenție
Poate provoca o reacție alergică a pielii.
Purtați mănuși de protecție / îmbrăcăminte de protecție / echipament de protecție a ochilor / chipament de protecție a feței • În caz de iritare a pielii sau de erupție cutanată: consultați medicul • ÎN CAZ DE CONTACT CU PIELEA: spălați cu multă apă și săpun • Aruncați conținutul / containerul în acord cu regulamentele locale / regionale / naționale / internaționale.

(SE)
Varning
Kan orsaka allergisk hudreaktion.
Använd skyddshandskar / skyddskläder / ögonskydd / ansiktsskydd • Vid hudirritation eller utslag: Sök läkarhjälp • VID HUDKONTAKT: Tvätta med mycket tvål och vatten • Innehållet / behållaren avfallshanteras enligt lokala / regionala / nationella / internationella föreskrifter.

(SI)
Pozor
Lahko povzroči alergijski odziv kože.
Nositi zaščitne rokavice / zaščitno obleko / zaščito za oči / zaščito za obraz • Če nastopi draženje kože ali se pojavi izpuščaj: poiščite zdravniško pomoč / oskrbo • PRI STIKU S KOŽO: umiti z veliko mila in vode • Vsebino / vsebnik odstranite v skladu z lokalnimi / regionalnimi / narodnimi / mednarodnimi predpisi.

(SK)
Pozor
Môže vyvolať alergickú kožnú reakciu.
Noste ochranné rukavice / ochranný odev / ochranné okuliare / ochranu tváre • Ak sa prejaví podráždenie pokožky alebo sa vytvoria vyrážky: vyhľadajte lekársku pomoc / starostlivosť • PRI KONTAKTE S POKOŽKOU: Umyte veľkým množstvom vody a mydla • Zneškodnenie obsahu / obalu v súlade s miestnymi / oblastnými / národnými / medzinárodnými nariadeniami.

(BG) • Този продукт съдържа човешки или животински компоненти. Бъдете внимателни при работа с него.
(CZ) • Tento výrobek obsahuje lidské nebo zvířecí komponenty. Zacházejte s ním opatrně.
(DE) • Dieses Produkt enthält Bestandteile menschlichen oder tierischen Ursprungs. Vorsichtig handhaben.
(DK) • Dette produkt indeholder humane og animalske komponenter. Skal behandles med forsigtighed.
(EE) • Käesolev toode sisaldab inim-või loomseid komponente. Käsitseda ettevaatlikult.
(EN) • This product contains human or animal components. Handle with care.
(ES) • Este producto contiene componentes humanos o animales. Manejar con cuidado.
(FI) • Tässä tuotteessa on ihmisestä tai eläimistä peräisin olevia osia. Käsittele varovasti.
(FR) • Ce produit contient des composants d'origine humaine ou animale. Manipuler avec précaution.
(GR) • Αυτό το προϊόν περιέχει ανθρώπινα ή ζωικά στοιχεία. Χειριστείτε το με προσοχή.
(HU) • A készítmény emberi vagy állati eredetű összetevőket tartalmaz. Óvatosan kezelendő.
(IT) • Questo prodotto contiene componenti umane o animali. Maneggiare con cura.
(LT) • Šiame produkte yra žmogiškosios arba gyvūninės kilmės sudėtinių dalių. Elgtis atsargiai.
(LV) • Šis produkts satur cilvēkiem vai dzīvniekiem paredzētas sastāvdaļas. Apieties uzmanīgi.
(MT) • Dan il-prodott fih komponenti umani jew tal-annimali. Uża b'attenzjoni.
(NL) • Dit product bevat menselijke of dierlijke bestanddelen. Breekbaar.
(NO) • Dette produktet inneholder humane eller animalske komponenter. Håndteres med forsiktighet.
(PL) • Niniejszy produkt zawiera składniki pochodzenia ludzkiego lub zwierzęcego. Należy obchodzić się z nim ostrożnie.
(PT) • Este medicamento contém componentes de origem humana ou animal. Manuseie com cuidado.
(RO) • Acest produs conține materiale de origine umană sau animală. Manevrați-l cu grijă.
(SE) • Denna produkt innehåller beståndsdelar från människa eller djur. Hantera produkten varsamt.
(SI) • Izdelek vsebuje človeške ali živalske sestavine. Rokujte previdno.
(SK) • Tento výrobok obsahuje ľudské alebo zvieracie zložky. Narábajte s ním opatrne.

Bio-Rad
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CE 0459
2012/10
883600

WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Genie™ Fast HIV 1/2
Number: PQDx 0153-031-00

Abstract

Genie™ Fast HIV 1/2 with product codes **72327, 72347** and **72330**, manufactured by **Bio-Rad**, **CE-marked** regulatory version, was accepted for the WHO list of in vitro prequalified diagnostics and was listed on 22 December 2017.

Intended use

Genie™ Fast HIV 1/2 Assay is a rapid immunochromatographic assay intended for the detection of antibodies to HIV-1 and HIV-2 in capillary whole blood, venous whole blood, serum or plasma human specimens. It is a qualitative assay used as an aid to diagnose HIV infection.

The test is suitable for use in multi-test algorithms designed for the validation of rapid HIV test results. When multiple rapid HIV tests are available, this test can be used in appropriate multi-test algorithms.

Test Principle

HIV-1 gp120, gp41 and HIV-2 gp36 recombinant antigens, conjugated to colloidal gold, are adsorbed at the base of a strip of nitrocellulose membrane.

HIV-1 and HIV-2 antigens are immobilized in the test zone (T). Anti-HIV antibodies are immobilized in the control zone (C). When the specimen is dispensed at the bottom of the strip, it starts migrating by capillary diffusion, rehydrating the antigen-conjugated gold. In the presence of anti-HIV-1 and/or HIV-2 antibodies, these will bind to the conjugated antigens to form a particular complex which will be carried by the specimen migration. This particular complex will continue to migrate as far as zone (T) and will be captured by the HIV-1 and HIV-2 antigens immobilized in this zone, to produce a visible red line in zone (T). The excess antigen-conjugated gold will continue to migrate as far as zone (C), where it will be captured and aggregated by the anti-HIV antibodies to produce a red line in zone (C), indicating the validity of the test (proof of specimen migration).

In the absence of anti-HIV-1 or anti-HIV-2 antibodies in the specimen, there will be no red line in zone (T), but the antigen-conjugated gold will continue to migrate alone as far as zone (C), where it will be captured to produce a red line indicating the validity of the test (proof of specimen migration).

Any sample found to be reproducibly positive must be confirmed using an appropriate validated testing algorithm in accordance with WHO guidance to prove the presence of anti-HIV antibodies.

Test kit contents:

Component	**25 tests (product code 72327)**	**25 tests (product code 72347)**	**50 tests (product code 72330)**
Test cassettes	25	25	50
Diluent, contains sodium azide (<0.1%)	5ml x 1 bottle	5ml x 1 bottle	5ml x 1 bottle
Disposable transfer pipettes, plastic	50	50	50
Microsafes, 80µl	N/A	25	N/A
Lancets	N/A	25	N/A
Alcoopads	N/A	25	N/A

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

Shelf-life:
18 months.

Warning/Limitations:

1. Refer to current version of manufacturer's instructions for use.
2. A new instructions for use will be issued within the next six months, the number of drops of specimen and of diluent must be strictly observed.

Summary of prequalification status for Genie™ Fast HIV 1/2

	Initial acceptance	
	Date	**Outcome**
Status on PQ list	22 December 2017	listed
Dossier assessment	15 September 2017	MR
Inspection status	17-19 June 2014	MR
Laboratory evaluation	20 March 2014	MR

MR: Meets Requirements
NA: Not Applicable

Genie™ Fast HIV 1/2was accepted for the WHO list of prequalified *in vitro* diagnostics on the basis of data submitted and publicly available information.

Background information

Bio-Rad submitted an application for prequalification of Genie™ Fast HIV 1/2. Based on the established prioritization criteria, Genie™ Fast HIV 1/2 was given priority for prequalification.

Product dossier assessment
Bio-Rad submitted a product dossier for Genie™ Fast HIV 1/2 as per the Instructions for compilation of a product dossier (PQDx_018 v1). The information submitted in the product dossier was reviewed by WHO staff and external experts (assessors) appointed by WHO in accordance with the internal report on the screening and assessment of a product dossier (PQDx_009 v2). Based on the product dossier screening and assessment findings, a recommendation was made to accept the product dossier for Genie™ Fast HIV 1/2 for prequalification.

Commitments for prequalification:
1. Revised instructions for use to be supplied with next lot manufactured.

Manufacturing site inspection
A comprehensive inspection was performed at the site of manufacture (3, bd Raymond Poincare 92430 Marne La Coquette and Route de Cassel 59114 Steenvoorde, France) of Genie™ Fast HIV 1/2 in 17-19 June 2014 as per the Information for manufacturers on prequalification inspection procedures for the sites of manufacture of *in vitro* diagnostics (PQDx_014 v1). The inspection found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality. The manufacturer's responses to the

nonconformities found at the time of the inspection were accepted on 12 October 2016 with an exception that had been successfully addressed with additional information on 6 December 2016. A review of the corrective action implementation will be reviewed at next inspection.

Bio-Rad will implement acceptance criteria of rate $\leqslant$ 4% for invalid rates, including high background as of December 2017. A review of effective implementation will be made at the next inspection.

Laboratory evaluation

Genie™ Fast HIV 1/2 was evaluated by WHO in the last quarter of 2013 using characterized serum/plasma specimens. From this evaluation, the following conclusions were drawn:

Genie™ Fast HIV 1/2 is a lateral flow immunochromatographic assay for the detection of HIV-1/2 antibodies in human serum/plasma and venous/capillary whole blood. A volume of 80 µL of serum/plasma is needed to perform the assay. The assay does not require sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory settings. Reading of the results can be done visually i.e. subjectively reading. In this limited evaluation using a panel of 1118 clinically-derived specimens, the performance is summarized in the tables below:

Performance characteristics in comparison with an agreed reference standard		
	Initial (95% CI)	**Final (95% CI)**
Sensitivity %	100% (99.2% - 100%)	100% (99.2% - 100%)
Specificity %	98.3% (97.0% - 99.2%)	98.5% (97.2% - 99.3%)
Invalid rate %	0.1%	
Inter-reader variability %	0.7%	

Additional performance characteristics	
Sensitivity during seroconversion on eight seroconversion panels in comparison with a benchmark assay; Enzygnost Anti-HIV 1/2 Plus (Siemens Healthcare Diagnostics)	Seroconversion sensitivity index of 0.125 specimens later than the benchmark assay.
Analytical sensitivity on a mixed titer panel in comparison with an agreed reference standard	All anti-HIV positive and anti-HIV negative specimens of the HIV mixed titer panel in comparison with the expected results. One anti-HIV negative/HIV-1 p24 antigen positive specimen was not detected

Lot to lot variation on a dilution panel in comparison with an agreed reference standard	Acceptable.

Key operational characteristics	
Validated specimen types	Serum, plasma (EDTA, heparin or sodium citrate), venous whole blood, capillary whole blood.
Number of steps	2 with precision required.
Time to result	11 minutes.
Endpoint stability	20 minutes.
Internal QC	Yes, the control band appears when only buffer is added to the device (without specimen) and is therefore a reagent addition control.
In-use stability of reagents	The diluent bottle can be stored at 2 °C to 30 °C until the expiration date of the kit, even after its first use.

Labelling

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

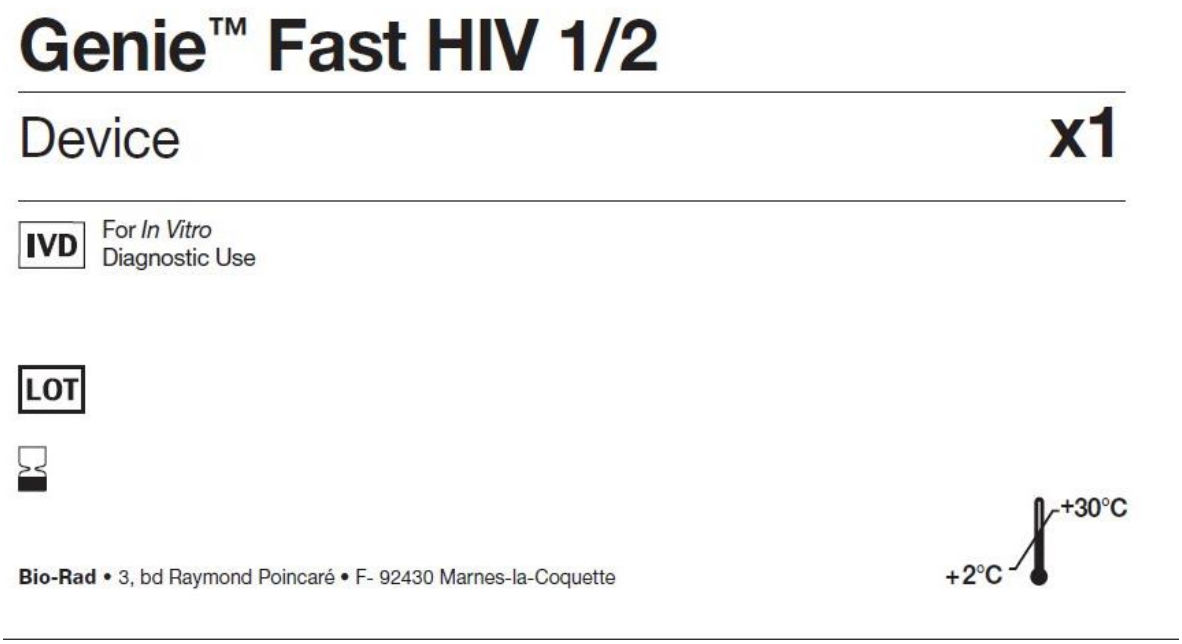
1. Labels

PRODUCT CODE 72327 (25 tests)

I - BOX LABELS

II- REAGENT LABELS

Device



Allow the test cassette to reach room temperature (minimum 30 minutes).
Open the pouch.

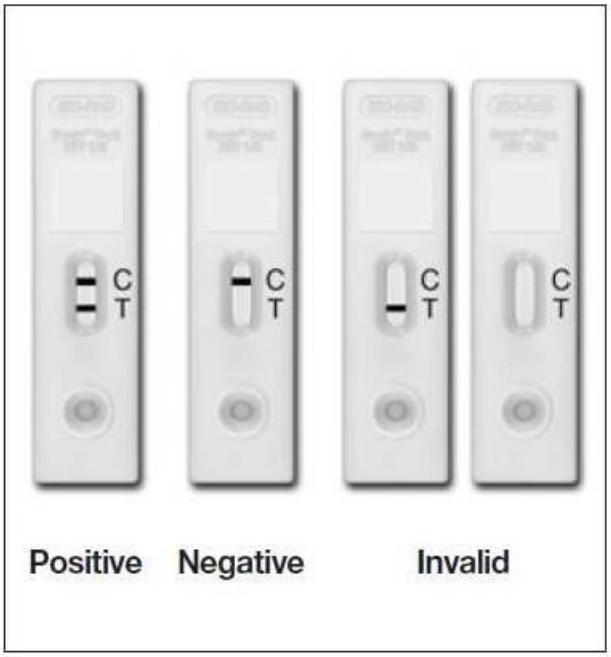
Serum/plasma protocol
Add 80 µl of serum/plasma or 3 drops using the plastic pipette of the kit.

Whole Blood protocol
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

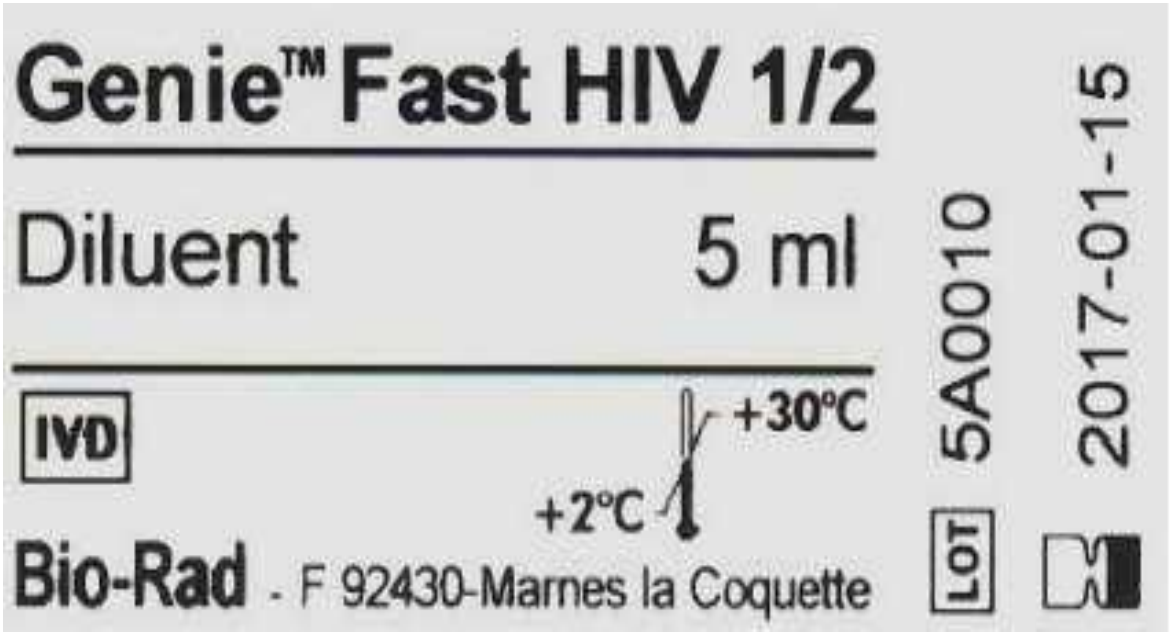
Finger stick protocol
Add 80 µl of blood using an appropriate pipette, then add immediately 2 drops of diluent buffer (80 µl).

Place the cassette on flat surface and read the results within 30 minutes.

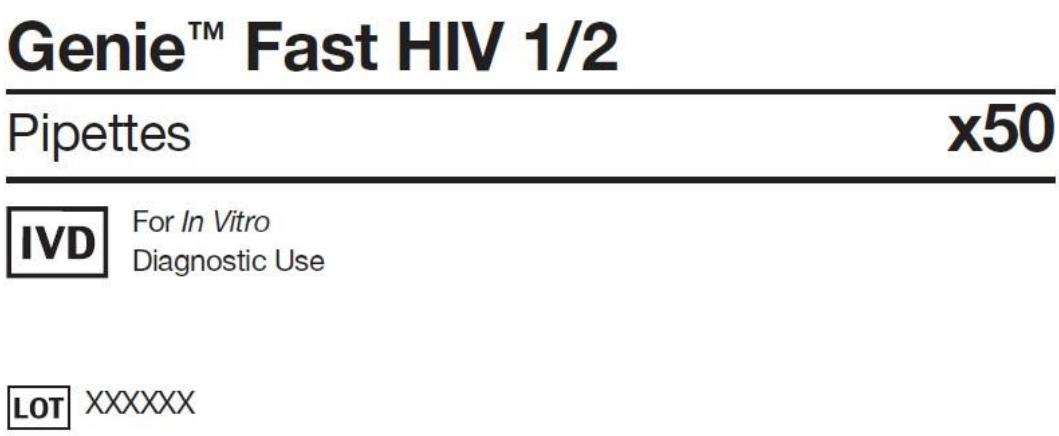
Never read the results after 30 minutes.



Diluent



Pipettes



PRODUCT CODE 72330 (50 tests)

I - BOX LABELS

II - REAGENT LABELS

Device

Genie™ Fast HIV 1/2

Device x1

IVD For *In Vitro* Diagnostic Use

LOT

Bio-Rad • 3, bd Raymond Poincaré • F- 92430 Marnes-la-Coquette

+2°C +30°C

Allow the test cassette to reach room temperature (minimum 30 minutes).
Open the pouch.

Serum/plasma protocol
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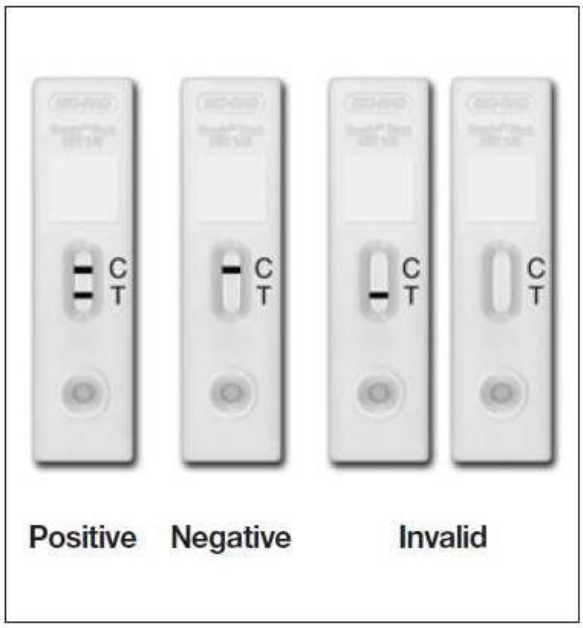
Whole Blood protocol
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

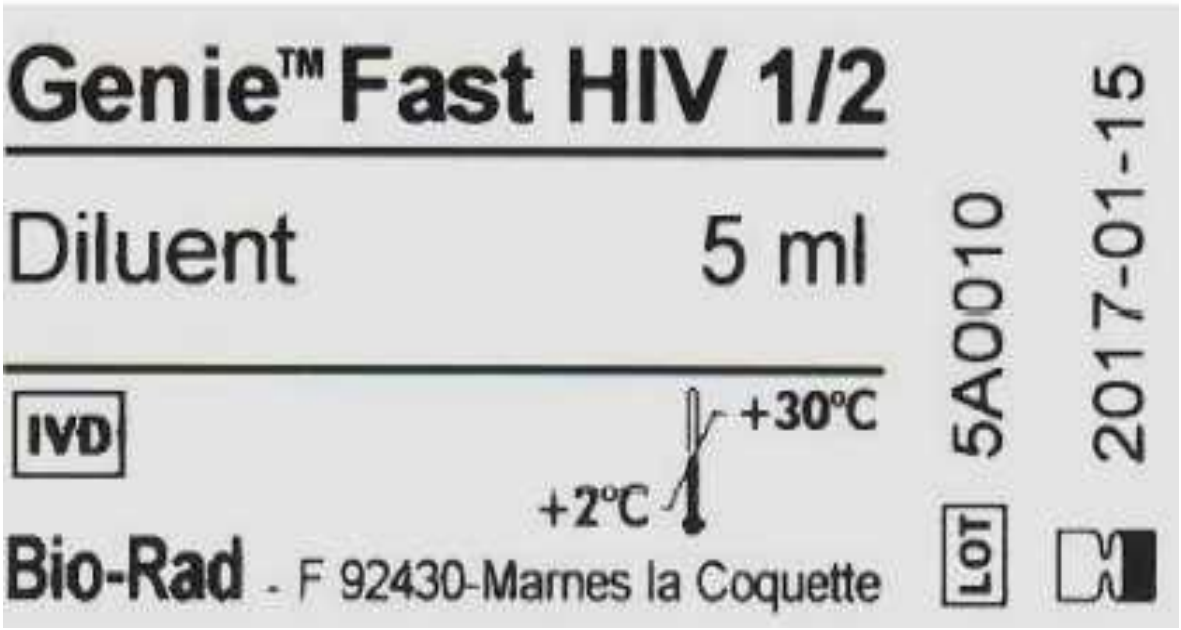
Finger stick protocol
Add 80 µl of blood using an appropriate pipette, then add immediately 2 drops of diluent buffer (80 µl).

Place the cassette on flat surface and read the results within 30 minutes.

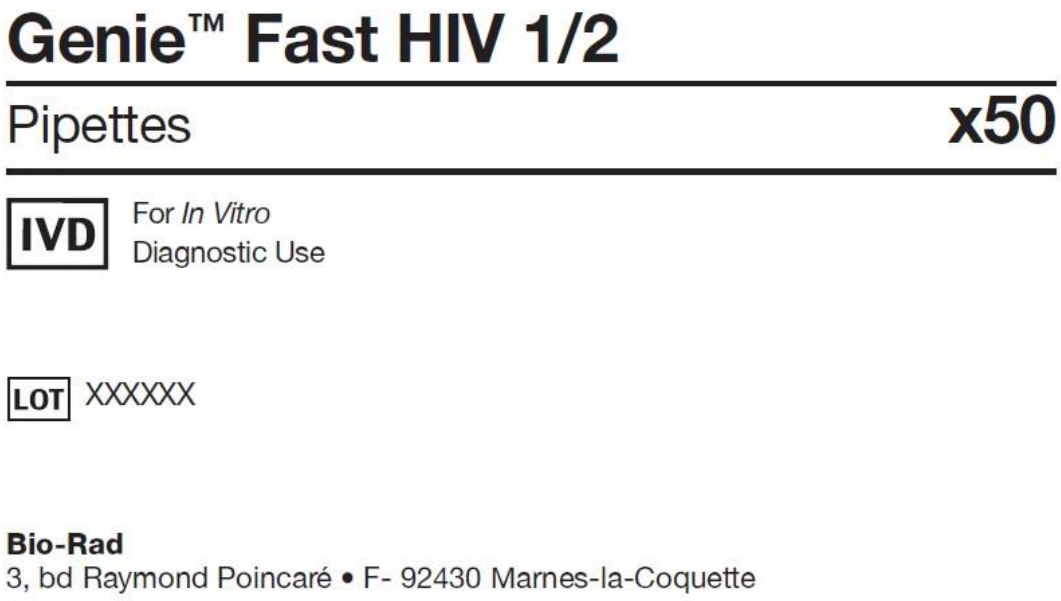
Never read the results after 30 minutes.



Diluent

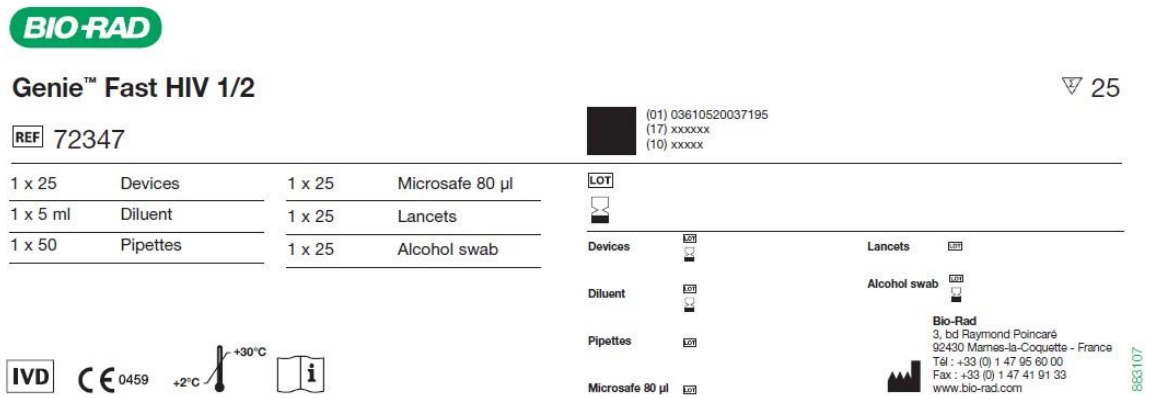


Pipettes



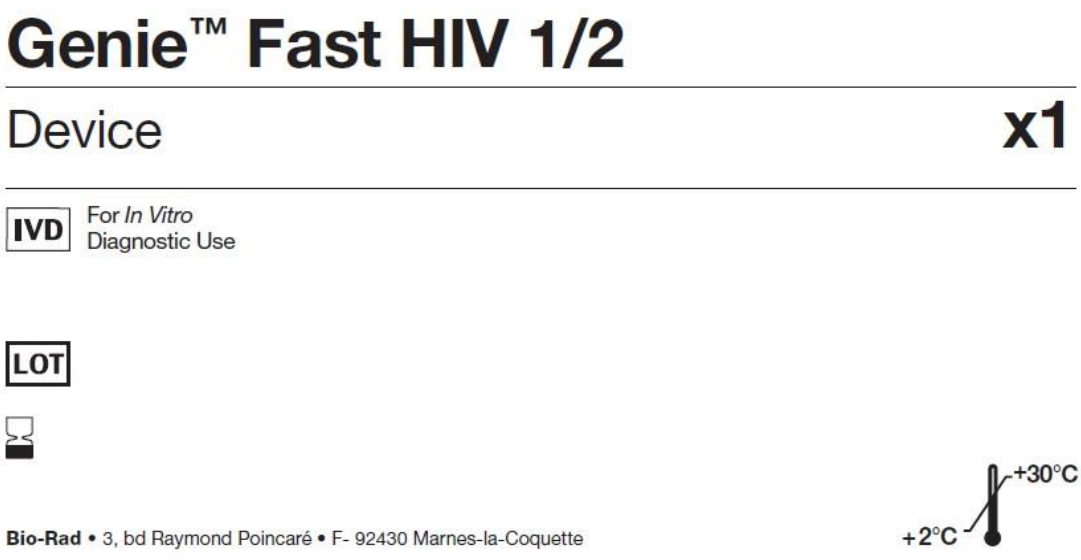
PRODUCT CODE 72347 (25 tests)

I - BOX LABELS



II - REAGENT LABELS

Device



Allow the test cassette to reach room temperature (minimum 30 minutes).
Open the pouch.

Serum/plasma protocol
Add 80 µl of serum/plasma or 3 drops using the plastic pipette of the kit.

Whole Blood protocol
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

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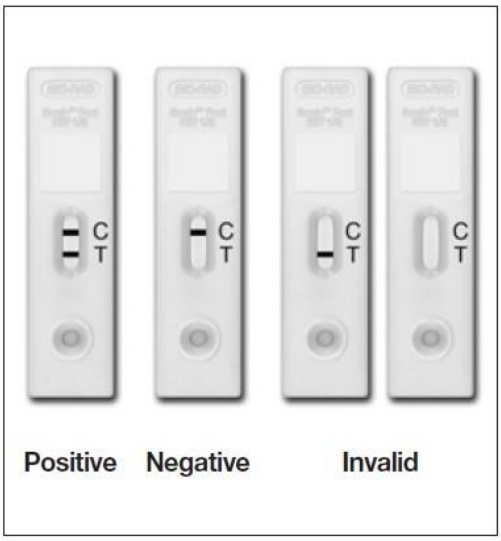
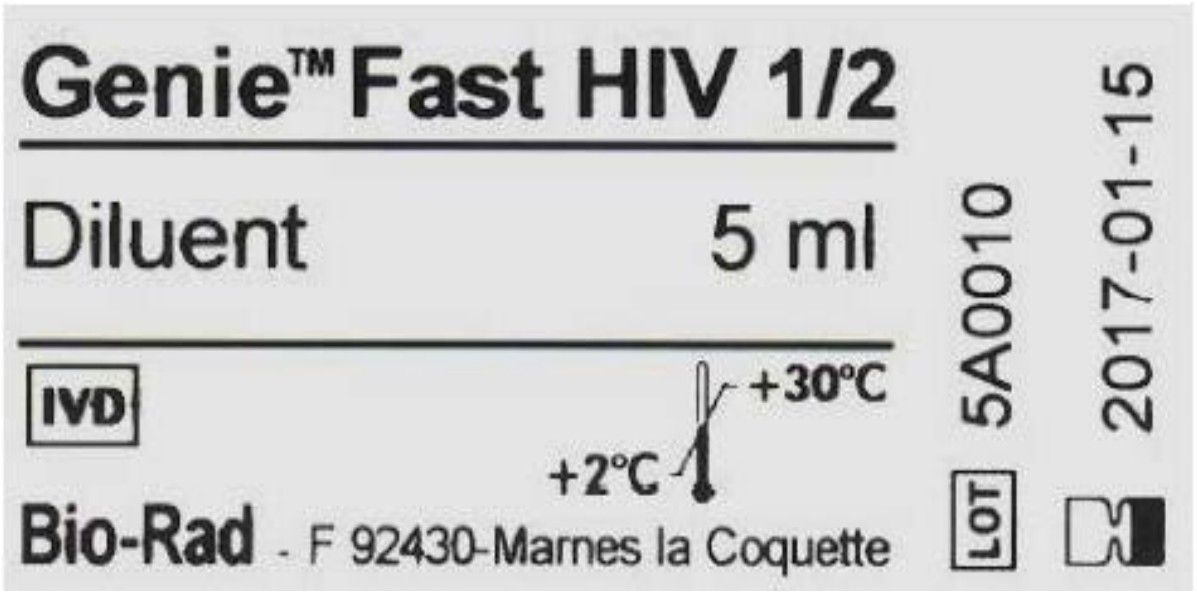
Place the cassette on flat surface and read the results within 30 minutes.

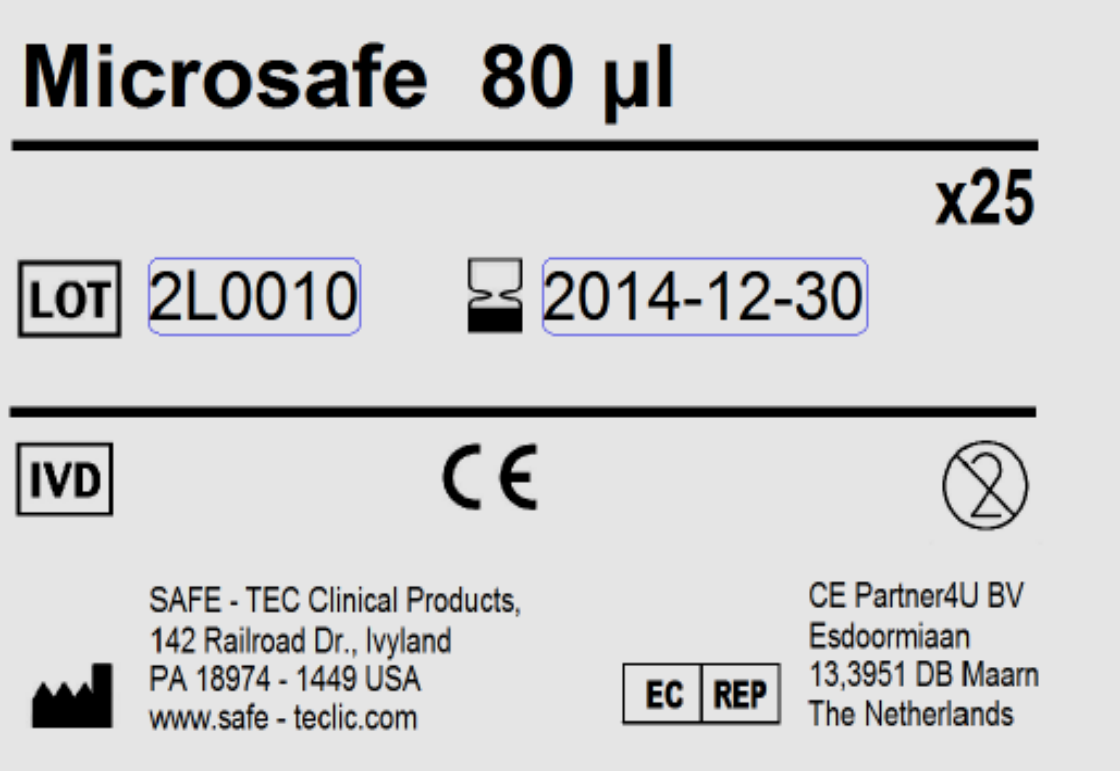
Never read the results after 30 minutes.



Diluent



Microsafe 80 µl



Genie™ Fast HIV 1/2

Σ 50	REF 72330
Σ 25	REF 72327
Σ 25	REF 72347

RAPID IMMUNOCHROMATOGRAPHIC ASSAY FOR QUALITATIVE DETECTION OF ANTI-HIV-1 AND ANTI-HIV-2 ANTIBODIES IN VENOUS WHOLE BLOOD, CAPILLARY WHOLE BLOOD, SERUM, OR PLASMA HUMAN SPECIMENS

IVD CE 0459

16004652 – 2017-10

BIO-RAD

TABLE OF CONTENTS

1 - INTENDED USE

The Bio-Rad Genie™ Fast HIV 1/2 Assay is rapid immunochromatographic assay intended for the detection of antibodies to HIV-1 and HIV-2 in capillary whole blood, venous whole blood, serum or plasma, all of human origin. It is a qualitative assay used as an aid to diagnose HIV infection.

The test is suitable for use in multi-test algorithms designed for the statistical validation of rapid HIV test results. When multiple rapid HIV tests are available, this test can be used in appropriate multi-test algorithms.

Note: National regulations may preclude the use of rapid tests for blood screening and/or routine diagnostic analysis.

2 - SUMMARY AND EXPLANATION OF THE TEST

Acquired immunodeficiency syndrome (AIDS) is caused by viruses transmitted by sexual contact, exposure to blood (including sharing contaminated needles and syringes) or certain blood products, or transmitted from an infected mother to her fetus or child during the perinatal period. Additionally, transmission of these viruses can occur through tissue transplantation. Human Immunodeficiency Virus Type 1 (HIV-1) has been isolated from patients with AIDS and AIDS-related complex (ARC). HIV-1 was thought to be the sole causative agent of these syndromes until 1986, when a second type of Human Immunodeficiency Virus (HIV-2) was isolated and also reported to cause AIDS. Since the initial discovery, hundreds of cases of HIV-2 infection have been documented worldwide, including cases of AIDS related to HIV-2.

The Bio-Rad Genie™ Fast HIV 1/2 Assay is a rapid immunochromatographic assay which utilizes antigens specific to HIV-1 and HIV-2 viruses to detect antibodies to HIV-1 and HIV-2.

3 - PRINCIPLES OF THE PROCEDURE

HIV-1 gp120, gp41 and HIV-2 gp36 recombinant antigens, conjugated to colloidal gold, are adsorbed at the base of a strip of nitrocellulose membrane.
HIV-1 and HIV-2 antigens are immobilized in the test zone (T).
Anti-HIV antibodies are immobilized in the control zone (C).
When the specimen is dispensed at the bottom of the strip, it starts migrating by capillary diffusion, rehydrating the antigen-conjugated gold.
In the presence of anti-HIV-1 and/or HIV-2 antibodies, these will bind to the conjugated antigens to form a particular complex which will be carried by the specimen migration. This particular complex will continue to migrate as far as zone (T) and will be captured by the HIV-1 and HIV-2 antigens immobilized in this zone, to produce a visible red line in zone (T). The excess antigen-conjugated gold will continue to migrate as far as zone (C), where it will be captured and aggregated by the anti- HIV antibodies to produce a red line in zone (C), indicating the validity of the test (proof of specimen migration).
In the absence of anti-HIV-1 or anti-HIV-2 antibodies in the specimen, there will be no red line in zone (T), but the antigen-conjugated gold will continue to migrate alone as far as zone (C), where it will be captured to produce a red line indicating the validity of the test (proof of specimen migration).
Refer to chapter 7.6 Interpretation of results.

4 - REAGENTS

4.1 Description

Identification on label	Description	Product code 72330 (50 tests)	Product code 72327 (25 tests)	Product code 72347 (25 tests)
Device	Nitrocellulose strip, the base of which contains recombinant HIV-1 and HIV-2 antigens conjugated to gold, HIV-1 and HIV-2 antigens in zone T and anti-HIV antibodies in zone C.	50	25	25
Diluent	Diluent (for the whole blood protocol) Preservative : Sodium azide (< 0.1 %)	1 dropper bottle 5 ml	1 dropper bottle 5 ml	1 dropper bottle 5 ml
Pipettes	Plastic pipette for dispensing serum, plasma and venous blood	50	50	50
Microsafe 80 µl	Capillary plastic pipettes (without anti-coagulant) for Fingerstick protocol	0	0	25
Lancets	Safety sterile lancets with needle for Fingerstick protocol	0	0	25
Alcoopad	Alcohol swab for skin disinfection	0	0	25

4.2 Storage and handling requirements

This kit should be stored between 2°C and 30°C.
Every item in the Genie™ Fast HIV 1/2 kit stored between 2°C and 30°C can be used until the expiry date noted on the box.
After opening the pouch, the cassette must be used within 20 minutes of this opening.
The bottle of diluent can be stored between 2°C and 30°C, until the expiration date of the kit, even after its first use.

5 - WARNING AND PRECAUTIONS

Medical device for *in vitro* diagnostic for use by professional user.

5.1. Health and Safety precautions:

- This test kit should be handled only 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 with the requisite Good Laboratory Practices.
- 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, with an appropriate chemical disinfectant that is effective for the potential biohazards relative to the specimens involved.
- 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 bio hazardous waste disposal. Then the area should be decontaminated with one of the chemical disinfectants.

- The specimens, reagents of human origin and the equipment and contaminated products will be disposed of after decontamination:
  - either by soaking in bleach at a final concentration of 10% sodium hypochlorite (1 volume of bleach per 10 volumes of contaminated liquid or water) for 30 minutes.
  - or by autoclaving at 121°C for at least 2 hours.

NOTE : Do not place solutions containing bleach into the autoclave !

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or bio hazardous wastes must be handled and discarded in accordance with all local, regional and national regulations.
- Do not forget to neutralize and/or autoclave the solutions or washing wastes or any fluid containing biological specimens before discarding them into the sink.
- For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

5.2. Precautions related to the procedure

5.2.1. Preparation

- Do not mix or use reagents from different lots within a test run.
- Do not use the test device if the device pouch is damaged.
- If reagents are stored at 2°C to 8°C, before use stabilize during 30 minutes the reagents at the laboratory temperature (18°C to 30°C).
- Do not use expired reagents.
- Use the reagents in such a way as to prevent contamination.
- The quality of results depends on the extent to which the following good laboratory practices are respected.
- Do not use the test device if there is no desiccant packet in the device pouch. Discard the test device and use a new device from a pouch that contains a desiccant.
- Once the pouch is open, do not leave the cassette in the open air for more than 20 minutes before dispensing the specimen.

5.2.2. Processing

- Use a new pipette tip or a new disposable pipette, provided in the kit, for each specimen.
- Do not change the assay procedure.
- Perform the test at the laboratory temperature (18°C to 30°C).
- Wait at least 10 minutes and no more than 30 minutes after adding the last deposit (specimen or diluent) before reading the assay. Wait the full 30 minutes before declaring a negative result (see section 7.3 Assay procedure).
- Interpret the results under good light conditions to avoid misreading of the test results.

6 - SPECIMENS

Take a blood specimen according to the usual method. The test must be performed on undiluted specimens of serum, plasma, venous or fingerstick capillary blood. Plasma and venous blood are collected with the following anticoagulants: EDTA-K2, Lithium Heparinate, ACD (Citrate-Dextrose). Fibrin particles or aggregates in suspension may lead to false positive results.

Chemical treatments, heating or dilution of the blood may alter the results and give inappropriate results.

If the specimens have to be transported, pack them according to current regulations for transporting etiological agents.

Fresh specimens can be stored at 2-8°C up to 7 days for serum and plasma and up to 3 days for whole venous blood, without interference on the negative or positive results. Whole blood tested more than 24 hours after collection may produce a high invalid rate.

Fresh serum and plasma can also be frozen and thawed up to 3 times, without interference on the negative or positive results.

Comment: DO NOT USE HYPERHEMOLYZED WHOLE BLOOD, SERUM OR PLASMA - very pronounced hemolysis may affect test performance.

No interference has been shown in specimens containing up to 100 mg/l of bilirubin or in lipemic specimens containing up to 30 g/l of triolein and in hemolyzed specimens containing up to 5 g/l of

haemoglobin. Abnormally high albuminemia (100 g/l) can give false positive results.

7 - PROCEDURE

7.1 Materials required but not provided

Automatic or semi-automatic pipettes or multi-pipettes, adjustable or fixed, to measure and dispense the specimen.

7.2 Reagents preparation

Cassette:
Each cassette is packaged in a sealed aluminum pouch (see 5.2.1).

Diluent for the venous whole blood or fingerstick capillary blood protocol:
This diluent is supplied in a dropper bottle for kits product codes 72330, 72327 and 72347.

Consumables:
Lancets, alcohol swab and capillary plastic pipettes dedicated for the fingerstick capillary blood protocol are provided in the kit product code 72347. These consumables are for a single use.

7.3 Assay procedure

The procedure will be respected as follows:

7.3.1 Open the pouch and remove the cassette (the specimen must be dispensed on the cassette within 20 minutes of opening the pouch).

7.3.2 Place the cassette on a flat horizontal surface with the circular deposit zone facing the operator.

7.3.3 Dispense the specimen

a) Plasma/Serum protocol: dispense 80 µl of the specimen in the circular deposit zone, using an automatic pipette, or 3 drops using the plastic pipette provided in the kit.

b) Venous Blood protocol: dispense 80 µl of blood in the circular deposit zone, using an automatic pipette or 2 drops using the plastic pipette provided in the kit, then add 2 drops of diluent using the dropper bottle provided with kits product codes 72327, 72330 and 72347.

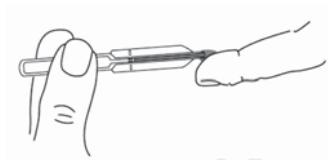
c) **Fingerstick capillary blood protocol:** According to the laboratory practice, use a fingerstick sterile lancet (Lancet) and the appropriate capillary plastic pipette (Microsafe 80 µl) both consumables provided in the kit product code 72347 to collect capillary whole blood by capillary action.

Follow the procedure below.

Step 1:
Clean the finger of the person being tested with an antiseptic wipe (Alcoopad) provided in kit product code 72347). Allow the finger to dry thoroughly, or wipe dry with a sterile gauze pad. Using the sterile lancet, puncture the skin just off the center of the finger and wipe away the first drop with sterile gauze and avoid squeezing the fingertip to accelerate bleeding as this may dilute the blood with excess tissue fluid.

Collect 80 µl of the specimen from the second drop, by holding the 80 µl capillary plastic pipette (Microsafe 80 µl) horizontally and touching the blood drop with the tip. Capillary action will automatically draw the specimen to the fill line and stop.

Caution: If the capillary pipette is not full repeat the puncture of another finger.



Step 2:
Fingerstick capillary blood must be tested immediately after collection.

Dispense 80 µl of fingerstick capillary blood : align the tip of the capillary pipette in the circular deposit zone of the device by touching slightly the pad, and squeeze the bulb. Check the complete deposit of the capillary pipette volume.
If a specimen doesn't expel, hold the capillary pipette vertically and slide a finger over the vent hole. Then align the tip with the circular deposit zone and squeeze the bulb.
Caution : Avoid any excess specimen or diluent flowing outside the circular deposit zone.

Then add 2 drops (~ 80 µl) of diluent using the dropper bottle provided with the kit without touching the pad.

Summary of the **Fingerstick capillary blood protocol** :

- Using capillary pipette (provided in the kit product code 72347), draw 80 µl of specimen to the calibrated fill line (black mark) and stop
- Dispense 80 µl of the capillary pipette
- Immediately add 2 drops of diluent
- Read results between 10 and 30 minutes

7.3.4 Reading

Visual reading takes place between 10 min. and 30 min. after the last deposit (specimen or diluent). Reading results before 10 minutes or after 30 minutes may not give accurate results. Check the control line (C) is present before interpreting the result.

Caution: Interpret the results under good light conditions to avoid misreading of the test results. In addition, wait the full 30 minutes after the last deposit before declaring a negative result.

7.4 Quality control

7.4.1 Built-in Control Feature

The control line serves as a built-in internal control and gives confirmation of proper test performance. A red line will appear in the CONTROL (C) area if the test has been performed correctly and the device is working properly (See Test Validation criteria).

7.4.2 External Quality Control

Under the following circumstances, it is recommended to perform an external Quality Control :

- When opening a new test kit lot.
- Whenever a new shipment of test kits is received.
- If the temperature of the test storage area falls outside of 2°C to 30°C.
- If the temperature of the testing area falls outside of 18°C to 30°C.
- At periodic intervals as indicated by the user facility.

7.5 Test Validation criteria

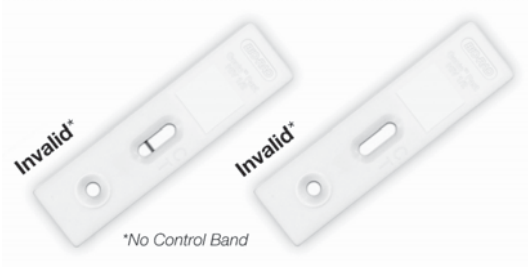
The test validity can be read in the Control zone (C) :

Serum/Plasma protocol: to validate the test, a red Control line (C) must be present.

Venous and fingerstick capillary blood protocol: to validate the test, both a red Control line (C) and red color in the circular deposit zone, due to the blood cells trapped, must be present.
If the validity conditions are nonconforming, the test is considered to be invalid, the cassette must be disposed of and the test repeated with a new cassette.

Invalid result Interpretation:

a) INVALID (No Control Line):
If there is no pink/red Control line in the Control zone (C), even if a pink/red line appears in the Test zone (T), the result is INVALID and the test should be repeated.
If the problem persists, contact Bio-Rad Technical Support.



b) INVALID (smear or background):

If red cells migrate into the Test zone (T), or if the cassette contains background in the band area that may interfere with test interpretation of negative or slightly positive specimens, the cassette should not be read and the test must be repeated.

7.6 Interpretation of the results

7.6.1 Positive Result interpretation

The appearance of a red line (even of very low intensity) in the Test zone (T) after 10 to 30 minutes indicates the presence of anti-HIV-1 or HIV-2 antibodies.
You are recommended to wait for 10 minutes before reading the results (even if red line appear quickly in the test zone), in order to confirm that the coloring is maintained, before declaring a positive result).
No positive result must be declared beyond 30 minutes.
Comment: Any red line even observed faintly in the Test zone (T) must be considered and interpreted as a positive result.

7.6.2 Negative Result Interpretation

The absence of a red line in the Test zone (T) after 30 minutes means that anti-HIV-1 or HIV-2 antibodies have not been detected. However, this does not exclude the possibility of an early stage of HIV infection.
Comments: Never interpret beyond 30 minutes after the last deposit.
No negative result must be declared below 30 minutes after the last deposit.

8 - TEST LIMITATIONS

It is recommended to retest any specimen initially found to be positive, in accordance with the criteria described in chapter 7.
To prove the presence of anti-HIV antibodies, any specimen found to be reproducibly positive must be confirmed using appropriate methods according to national validated testing algorithms and WHO guidance on testing strategies.
A negative result means that the specimen tested does not contain anti-HIV antibodies detectable by the Genie™ Fast HIV 1/2 test.
Such a result does not exclude the possibility of HIV-1 or HIV-2 infection. Indeed low levels of antibodies may not be detected if the infection was recent.
The variability of HIV-1 (group M, group O) and HIV-2 means that false negative reactions cannot be excluded.
No known method can guarantee that the HIV virus is absent. See also the limits linked to specimens, refer to chapter 6.

9 - PERFORMANCES CHARACTERISTICS

9.1. Precision Measurement

The performance of Genie™ Fast HIV 1/2 has been evaluated on five different clinical sites by testing specimens taken from blood donors, HIV positive patients and seroconversion panels.

9.1.1. Reproducibility studies

a) Inter-assay reproducibility

- The inter-assay reproducibility study was performed with 7 different specimens of serum (1 HIV-negative, 3 weak, moderate and strong HIV-1, 3 weak, moderate and strong HIV-2, and 5 different specimens of whole venous blood (1 HIV-negative, 2 weak and strong HIV-1, 2 weak and strong HIV-2. The analysis of specimens using Genie™ Fast HIV 1/2 reagent was performed twice a day for 5 days (10 replicates) for the serum or once a day in triplicate for 3 days (9 replicates) for whole venous blood. For all the specimens tested, both negative and positive, no discordance was found between replicates.

b) Inter-operator reproducibility

- The study of inter-operator reproducibility was performed with 5 specimens of whole venous blood (1 HIV-negative, 2 weak and moderate HIV-1, 2 weak and moderate HIV-2) tested in triplicate by three different operators on two batches of reagent.
  For all the specimens tested, both negative and positive, no discordance was found between the three operators.

c) Inter-batch reproducibility

- The inter-batch reproducibility study was performed on three batches, with 5 specimens of whole venous blood (1 HIV-negative, 2 weak and moderate HIV-1, 2 weak and moderate HIV-2) and 7 plasma specimens (1 HIV-negative, 2 weak and moderate HIV-1, 4 weak, moderate and strong HIV-2) tested in triplicate on each of the three batches.
  For all the specimens tested, both negative and positive, no discordance was found between the three batches.

9.2. Diagnostic performance

9.2.1. Diagnostic Specificity studies

a) Blood donor population

- 2517 specimens from blood bank donors (1108 of serum, 708 of plasma and 701 of whole venous blood) were tested with Genie™ Fast HIV 1/2 reagent. Specificity was 99.5% (2505/2517) with a confidence interval (CI) of 95% from [99.2 to 99.7].

Donor specificity	Total number of specimens	Repeatable positives (RR)	Specificity RR (%)	CI 95 (%)
Serum (Gel, Act)	1108	5	**99.5** (1103/1108)	[98.9; 99.9]
Plasma (EK2, HeLi, ACD)	708	5	**99.3** (703/708)	[98.4; 99.8]
Whole venous blood (EK2, Heli)	701	2	**99.7** (699/701)	[99.0; 100.0]
Total	**2517**	**12**	**99.5** (2505/2517)	**[99.2; 99.7]**

Acronyms: Gel means gel type of serum; Act means coagulation activator; EK2 means EDTA-K2; HeLi means Lithium heparin and ACD means citrate-dextrose.

b) Population of hospitalised patients

- 1010 specimens from patients not infected with HIV and taken from hospital complexes (428 of serum, 227 of plasma, 327 of whole venous blood and 28 of fingerstick capillary blood paired with venous blood) were tested with Genie™ Fast HIV 1/2 reagent. Overall specificity was 99.5% (1005/1010), CI 95% [98.9 - 99.8%] with 99.3% (425/428) and 99.1% (225/227) for serum and plasma respectively, 100% for whole venous blood (327/327) and capillary blood (28/28). *Comment: The whole venous blood and capillary blood from the same 28 patients gave equivalent results.*

Specificity for hospitalized patients	Total number of specimens	Repeatable positives (RR)	Specifity RR (%)	CI 95 (%)
Serum (Gel)	428	3	**99.3** (425/428)	[98.0; 99.9]
Plasma (EK2, HeLi)	227	2	**99.1** (225/227)	[96.9; 99.9]
Whole venous blood (EK2, HeLi)	327	**0**	**100** (327/327)	[98.9; 100]
Capillary blood	28 (*)	0	**100** (28/28)	[87.7; 100.0]
Total	**1010**	**5**	**99.5** (1005/1010)	**[98.9; 99.8]**

(*) specimens of capillary blood paired with whole venous blood from 28 patients.

9.2.2. Diagnostic Sensitivity studies

a) Specimens of HIV-1 positive patients

- 1050 specimens from patients known to be infected with HIV-1 (385 of serum, 301 of plasma, 338 of whole venous blood and 26 of capillary blood paired with venous blood) were tested with Genie™ Fast HIV 1/2 reagent.
  Sensitivity was **100%** (1050/1050), CI 95 [99.7 - 100%] for the four types of specimens (serum, plasma, whole venous blood and capillary blood).
  Comment: The whole venous blood and capillary blood from the same 26 patients gave equivalent results.

Sensitivity for HIV-1 patients	Total number of specimens	Number of reactive specimens	Sensitivity (%)	CI 95 (%)
Serum (gel)	385	385	100 (385/385)	[99.1; 100]
Plasma (EK2, Heli)	301	301	100 (301/301)	[99.8; 100]
Whole venous blood (EK2, Heli)	338	338	100 (338/338)	[99.9; 100]
Capillary blood	26 (*)	26	100 (26/26)	[86.3; 100]
Total	**1050**	**1050**	**100 (1050/1050)**	**[99.7; 100]**

(*) specimens of capillary blood paired with whole venous blood from 26 patients.

b) Specimens from HIV-2 positive patients

• 101 serums and 8 fresh plasma, from patients treated or not for their HIV-2 infection, tested with the Genie™ Fast HIV 1/2 reagent were all found to be positive.
Sensitivity was **100%** (109/109) with a confidence interval of 95% [96.7; 100].

Sensitivity for HIV-2 patients	Total number of specimens	Number of reactive specimens	Sensitivity (%)	CI 95 (%)
Serum	**109**	**109**	**100** (109/109)	**[96.7; 100]**

c) Specimens from genotyped HIV-1 positive patients

• 154 serums from patients infected by an HIV-1 strain of known genotype (see table below), tested with Genie™ Fast HIV 1/2 reagent were all found to be positive, giving a sensitivity of 100% (154/154) with a confidence interval of 95% [97.6-100].

Genotype	Total number of specimens	Number of reactive specimens
CRF01	9	9
CRF02	20	20
CRF05	1	1
CRF06	7	7
CRF08	1	1
CRF09	5	5
CRF10	1	1
CRF11	6	6
CRF12	1	1
CRF13	2	2
CRF14	6	6
CRF15	3	3
CRF19	3	3
CRF27	1	1
Subtype A	12	12
Subtype B	21	21
Subtype C	9	9
Subtype D	9	9
Subtype F	9	9
Subtype G	12	12
Subtype H	6	6
Subtype J	4	4
Subtype K	1	1
Group O	5	5
Total	**154**	**154**
Sensitivity : 100%		

d) Fresh specimens from HIV-1 and HIV-2 positive patients

• 113 fresh serum (SST2 gel tubes), 216 fresh plasma (EDTA-K2/Lithium Heparinate), 243 fresh whole venous blood (EDTA-K2/Lithium Heparinate) and 26 fresh capillary blood specimens, (taken from ≤ 1 day) from patients known to be infected with HIV-1 and 8 fresh plasma (EDTA-K2) from patients known to be infected with HIV-2 were tested with Genie™ Fast HIV 1/2 reagent. All the specimens were found to be positive, giving a sensitivity of **100%** no matter what the type of specimen.

Sensitivity for Fresh HIV-1 and HIV-2 positive specimens (≤ 1 day)	**Total number of specimens**	**Number of reactive specimens**	**Sensitivity (%)**
Serum HIV-1 (SST2 Gel)	113	113	**100** (113/113)
Plasma HIV-1 (EK2, HeLi) and HIV-2 (EK2)	216 8	224	**100** (224/224)
Whole venous blood HIV-1 (EK2, HeLi)	243	243	**100** (243/243)
Capillary blood HIV-1	26	26	**100** (26/26)
Total	606	606	**100** (606/606)

e) Sensitivity in seroconversion panels

• 31 commercial seroconversion panels, of which 30 included 65 early seroconversion points (*), and furthermore 40 specimens representing a per-seroconversion stage (***) were tested with Genie™ Fast HIV 1/2 reagent and a CE marked comparative rapid test.

Panels tested	**Total number of specimens**	**Number of positive specimens with CE marked reference rapid test**	**Number of positive specimens with Genie™ Fast HIV 1/2**
Seroconversion (31 panels)	118	80	83 (**)
Early seroconversion (30 panels)	65	30	33 (**)
Per-seroconversion	40	37	37

(*) As defined in the EU Common Technical Specifications (CTS: 27 nov 2009 C(2009) 9464 EU document).

(**) In 3 seroconversion panels, the first positive point was detected at least one point earlier on Genie™ Fast HIV 1/2 and in 1 seroconversion panel, the first positive point was detected one point later than with the reference rapid test.

(***) Perseroconversion stage defined as ELISA 4th generation positive with few bands on the Western-Blot HIV-1 assay.

9.3. Analytical specificity

9.3.1. Cross reactivity Study

- Specificity was also evaluated on specimens from 200 pregnant women and 107 patients suffering from pathologies not linked to HIV infection (7 dengue, 3 filariasis; 5 bilharzia; 4 leishmaniosis; 11 lupus erythematous; 10 malaria; 10 rheumatoid factors; 9 influenza; 8 ANA (anti-nuclear factors); 10 hepatitis A; 10 hepatitis B; 10 hepatitis C; 10 HTLV). Specificity was found to be 100%, CI95% [98.2 – 100] for the pregnant women (200/200) and 97.2%, CI95% [92.0 – 99.4] for the other pathologies (104/107) with three repeatable positive results (2 cases of malaria and 1 case of hepatitis B).

Samples	Total number specimens	Initial Reactive (IR)	Repeat Reactive (RR)
Pregnant women	200	3	0
Dengue	7	0	0
Filariosis	3	0	0
Bilharziasis	5	0	0
Leishmaniasis	4	0	0
Lupus erythematosus	11	0	0
Malaria	10	2	**2**
Rheumatoïd factor	10	0	0
Flu	9	0	0
ANA (Antinuclear Ab)	8	0	0
Hepatitis A	10	0	0
Hepatitis B	10	1	**1**
Hepatitis C	10	3	0
HTLV	10	0	0
Total	107	6	3

9.4. Hook effect

- No hook effect was observed with the Genie™ Fast HIV 1/2 reagent with a series of dilutions of specimens strongly positive in HIV-1 and HIV-2 antibodies: four commercial HIV-1 positive serum specimens and two HIV-2 positive serum specimens were tested without dilution and after serial dilution (1/2; 1/5; 1/10; 1/20; 1/50; 1/100; 1/200; 1/500) in HIV-negative serum.

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CE 0459

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Geenius™ HIV 1/2 Confirmatory Assay

72460 - ▽ 20

REF 72460

A QUALITATIVE ASSAY FOR THE CONFIRMATION AND DIFFERENTIATION OF INDIVIDUAL ANTIBODIES TO HIV-1 AND HIV-2 IN WHOLE BLOOD, SERUM, OR PLASMA SPECIMENS

IVD CE 0459

883601 - 2013/01

BIO-RAD

Table of Content

1. INTENDED USE

The Bio-Rad Geenius™ HIV 1/2 Confirmatory Assay is a single-use immunochromatographic test for the confirmation and differentiation of individual antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV-1 and HIV-2) in fingerstick whole blood, venous whole blood, serum or plasma samples.

The Geenius™ HIV 1/2 Confirmatory Assay is intended for use as an additional test to confirm the presence of antibodies to HIV-1 and HIV-2 for specimens found to be repeatedly reactive by screening procedures.

2. SUMMARY AND EXPLANATION OF THE TEST

Discovered in 1983, the Human Immunodeficiency Virus (HIV) is a retrovirus identified as the etiologic agent for Acquired Immunodeficiency Syndrome (AIDS). AIDS is characterized by changes in the population of T-cell lymphocytes that play a key role in the immune defence system. In the infected individual the virus causes a depletion of a subpopulation of T-cells, called T-helper cells, which leaves these patients susceptible to opportunistic infections and certain malignancies. The major routes of transmission are sexual contact, contamination by blood or blood products and mother-to-newborn transmission.
At the end of 2010 there were approximately 34 million people living with HIV/AIDS worldwilde, up 17% from 2001.

There were 2.7 million [2.4 -2.9] new HIV infection in 2010 including an estimated 390 000 [340 000-440 000] among children. This was 15% less than 2001 and 21% below the number of new infections at the peak of the epidemic in 1997.

While the HIV virus consists of a genomic RNA molecule protected by a capsid and an envelope, the HIV envelope is the major target for humoral antibody response. The presence of the virus in patients causes the immune system to elicit the production of antibodies to HIV. The detection of these antibodies can be used as a diagnostic tool.

The Geenius™ HIV 1/2 Confirmatory Assay is a rapid immunochromatographic test, which is simple and easy to use. The Geenius™ HIV 1/2 Confirmatory Assay utilizes immobilized antigens for the detection of antibodies to HIV-1 and HIV-2 in serum, plasma or whole blood specimens.

3. PRINCIPLE OF THE PROCEDURE

The Geenius™ HIV 1/2 Confirmatory Assay employs antibody binding protein A, which is conjugated to colloidal gold dye particles as conjugate and HIV-1 (p31, gp160, p24, gp41) and HIV-2 antigens (gp36, gp140), which are bound to the membrane solid phase. The sample is applied to the SAMPLE + BUFFER well. After the sample and buffer have migrated onto the test strip, additional buffer is added to the BUFFER well. The buffer facilitates the lateral flow of the released products and promotes the binding of antibodies to the antigens.

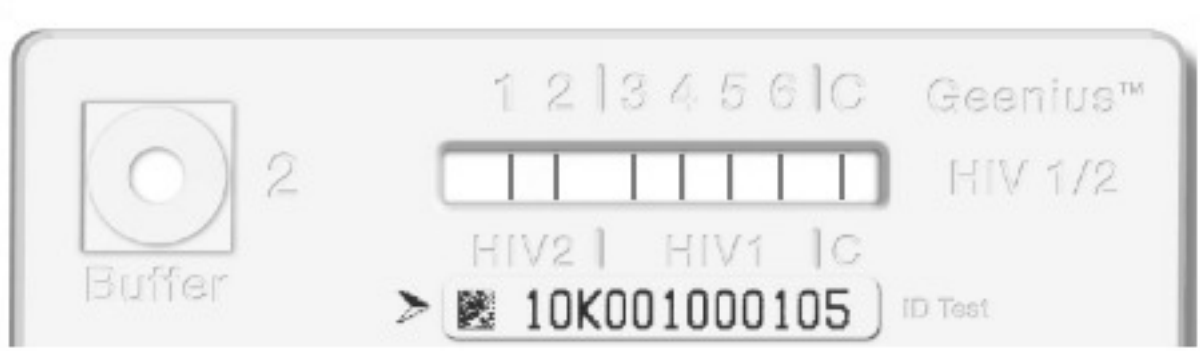
In a reactive sample, the anti-HIV antibodies are captured by the antigens immobilized in the TEST area (bands 1 to 6): the colloidal gold protein A binds to the captured antibodies, producing pink/purple lines.

In the absence of HIV antibodies, there are no pink/purple lines in the TEST area.

In both cases the sample continues to migrate along the membrane and produces a pink/purple line in the CONTROL (C) where protein A is immobilized.

Immunoglobulin G from sample bound to protein A is immobilized in (C) zone of the membrane solid phase to produce a pink/purple line.

This Control line serves to demonstrate that sample and reagents have been properly applied and have migrated through the device.



The Geenius™ HIV 1/2 Confirmatory Assay cassette contains a Control band (C) and six (6) test lines which are numbered on the cassette corresponding to the following:

Band 1:	gp36 (HIV-2, envelop peptide)	HIV-2 ENV
Band 2:	gp140 (HIV-2, envelop peptides)	HIV-2 ENV
Band 3:	p31 (HIV-1, polymerase peptide)	HIV-1 POL
Band 4:	gp160 (HIV-1, envelop recombinant protein)	HIV-1 ENV
Band 5:	p24 (HIV-1, core recombinant protein)	HIV-1 GAG
Band 6:	gp41 (Group M and O) (HIV-1, envelop peptides)	HIV-1 ENV
CTRL band:	Protein A	

4. REAGENTS

4.1 Description

Identification on label	Description	Presentation
Device	Nitrocellulose membrane containing HIV-1 and HIV-2 antigens in TEST area, protein A in CONTROL area and colloïdal gold protein A in BUFFER well area	20 x 1 Ready for use
Buffer	Buffer dropper with preservative (sodium azide < 0.1%, gentamicin sulphate 0.125%, streptomycin sulphate 0.125%)	1 x 5 ml Ready to use
Microtubes 15 µl	15 µl Microtubes capillarity plastic pipettes (no anti-coagulant, for fingerstick protocol)	1 x 20 Ready to Use

4.2 Storage and handling requirements

The Geenius™ HIV 1/2 Confirmatory Assay (Device and Buffer) should be stored at 2°C to 30°C, until the expiration date stated on the kit.

Do not freeze. Do not open the pouch until performing a test.
The Buffer is stable until expiration date after the first use in routine.

5. WARNING AND PRECAUTIONS

For *in vitro* diagnostic use. For healthcare professional use.

5.1 Health and Safety precautions

- This test kit should be handled only by adequately qualified personnel trained in laboratory procedures and familiar with their potential hazards. Wear appropriate protective clothing, gloves and eye/face protection and handle appropriately with the requisite Good Laboratory Practices.

- The test kit contains human blood components. No known test method can offer complete assurance that infectious agents are absent. Therefore, all human blood derivatives, reagents and human specimens should be handled as if capable of transmitting infectious disease, following recommended Precautions for as defined by local, regional and 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, with an appropriate chemical disinfectant that is effective for the potential biohazards relative to the samples involved (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.

  NOTE: Do not place solutions containing bleach into the autoclave

- Dispose of all specimens and material used to perform the test as though they contain an infectious agent. Laboratory, chemical or biohazardous wastes must be handled and discarded in accordance with all local, regional and national regulations.

- For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

5.2 Precautions related to the procedure

5.2.1 Preparing

- Read the Product Insert completely before using this assay. Follow the instructions carefully as not doing so may result in inaccurate test results.
- Use of this test kit with sample types other than those specifically approved for use with this device may result in inaccurate test results.
- This test should be performed at 18°C to 30°C. If stored refrigerated, before use wait at least 30 min for the reagents to stabilize at room temperature.
- DO NOT USE the test device if there is no desiccant packet in the device pouch. Discard the test device and use a new device from a pouch that contains a desiccant.
- DO NOT USE the test device if the device pouch is damaged.
- Each test device is for single use only.
- Do not use the test device or kit reagent beyond their expiration dates. Always check expiration dates prior to testing.
- Do not mix reagents from different lot numbers of kits.
- Adequate lighting is required to read the test results.

- If the test kit is stored at temperatures outside the storage temperature 2°C to 30°C, or used outside the operating temperature 18°C to 30°C, use the Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329, to ensure proper performance of the test.

5.2.2 Processing

- After the closed bag has been opened, the device must be used within 60 min.
- Do not change the assay procedure.

6. SPECIMENS

The Geenius™ HIV 1/2 Confirmatory Assay can be performed on venous or fingerstick whole blood, serum or plasma samples.

6.1 Specimen types

Venous Whole Blood

Draw blood following laboratory procedure for obtaining venous blood. Collect sample in a tube containing citrate, heparin or EDTA. Be sure the tube of blood is well mixed before sampling. Use a laboratory pipette to withdraw 15 µl of the blood. Test immediately, following Test Procedure instructions.

Fingerstick Whole Blood

Clean the finger of the person being tested with an antiseptic wipe. Allow the finger to dry thoroughly or wipe dry with a sterile gauze pad. Using a sterile lancet, puncture the skin just off the center of the finger and wipe away the first drop with sterile gauze and avoid squeezing the fingertip to accelerate bleeding as this may dilute the blood with excess tissue fluid. Collect 15 µl of the sample from the second drop touching the disposable Microtube pipette provided to the drop of blood until the pipette is full, following the procedure below.

Test immediately, following Test Procedure Instructions.

Serum or Plasma

Draw blood following laboratory procedure for obtaining serum or plasma samples. Collect serum samples in clotting agent-containing tubes that do not contain any anticoagulant (serum). Collect plasma samples in tubes containing citrate, heparin, or EDTA anticoagulants. Collect sample in a clean container following standard laboratory procedures. Be sure that the tube of serum or plasma is well mixed before sampling. Use a laboratory pipette to withdraw 5 µl of the sample. Test immediately following Test Procedure instructions.

6.2 Specimen Handling

Fingerstick whole blood should be tested immediately after collection.

Venous whole blood, specimens may be tested immediately or stored at 2°C to 8°C for up to 3 days following collection before being tested.

DO NOT FREEZE WHOLE BLOOD.

Serum and plasma specimens may be tested immediately or stored at 2°C to 8°C for up to 7 days following collection before being tested.

For long-term storage, the serum and plasma specimens should be frozen (at -20°C or colder).

Samples should not be used if they have incurred more than 5 freeze-thaw cycles. Mix samples thoroughly and gently after thawing, and bring to room temperature.

No interference has been shown in samples containing up to 200 mg/l of bilirubin, or in lipemic samples containing up to 33 g/l of triolein, or in hemolyzed samples containing up to 2 g/l of hemoglobin. Abnormally high albuminemia or proteinemia (120 g/l) did not show either any interference.

6.3 Specimen Shipping

If specimens are to be shipped, they should be packed in compliance with regulations covering the transportation of etiologic agents.

Venous whole blood, specimens should be shipped refrigerated with cold packs or wet ice.

Serum and plasma specimens should be shipped frozen in dry ice.

7. PROCEDURE

7.1 Materials required

Materials provided

- Device (20 units), Buffer Dropper (1 x 5 ml) and Microtubes 15 µl (1 x 20) per kit.
- See § 4.1 Description.

Material required provided separately

- Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329.

Materials required but not provided

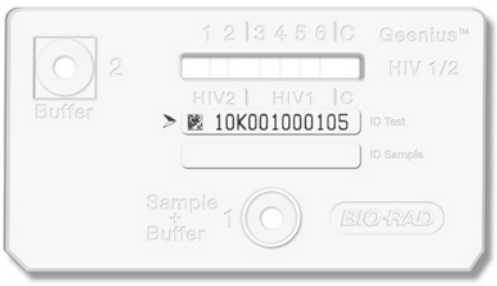
- Clock, watch or other timing device.
- Pipettor capable of delivering 5 µl (serum/plasma) and 15 µl (venous blood) of sample.
- Disposable gloves.
- Biohazard disposal containers.

7.2 Reagent preparation

All components for the Geenius™ HIV 1/2 Confirmatory Assay are ready-to-use as supplied.

7.3 Assay Procedure

Whole Blood PROCEDURE

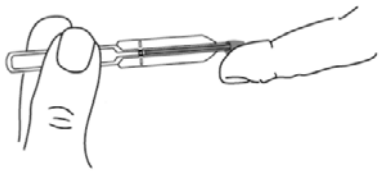
1.	Remove the Geenius™ HIV 1/2 Confirmatory Assay device from its pouch and place it on a flat surface (it is not necessary to remove the desiccant from the pouch). **NOTE**: If desiccant packet is missing from the pouch, DO NOT USE. Discard test device and use a new test device. Label the test device with patient ID or identification number (see Figure 1 below). Note that the Geenius™ HIV 1/2 Confirmatory Assay device has six (6) blue coloured lines in the Test area (no blue line in Control area); If any of the 6 coloured lines are absent, DO NOT USE. Discard the test device and use a new test device.	**Figure 1** 

Venous Whole Blood
See specimen preparation on § 6.1 Specimen types.

Fingerstick Whole Blood
See specimen preparation on § 6.1 Specimen types.

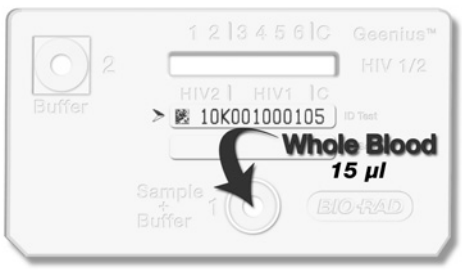
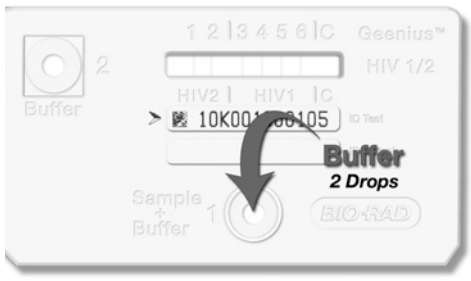
Step 1:

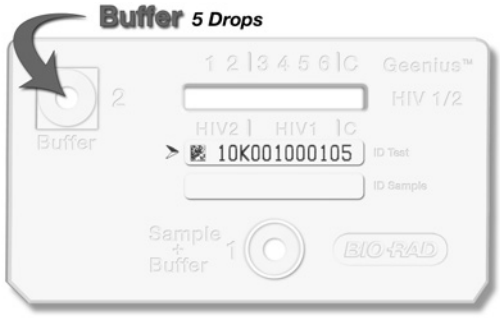
Hold the 15µL Microtube horizontally and touch the blood drop with the tip. Capillary action will automatically draw the sample to the fill line and stop.



Step 2:

To expel the sample, align the tip of the tube with the sample target and squeeze the bulb. If a sample won't expel, hold the tube vertically and slide a finger over the vent hole. Then align the tip with the sample target and squeeze the bulb.

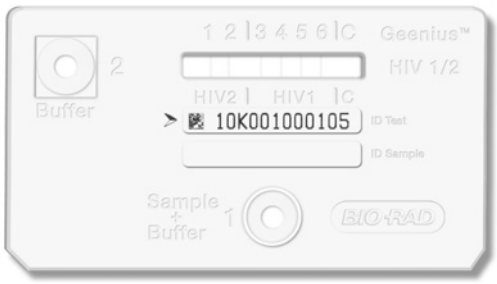
2. Dispense 15 µl of whole blood to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below). For venous whole blood use a laboratory pipette. For Fingerstick whole blood, follow the protocol using the Microtube 15 µl of the kit (see step 1 and 2 above). **Figure 2** 	3 **Immediately** following the addition of the sample, use the Buffer dropper to **add 2 drops** (60 µl) of Buffer, into the SAMPLE + BUFFER Well 1 (see Figure 3 below). **Figure 3** 

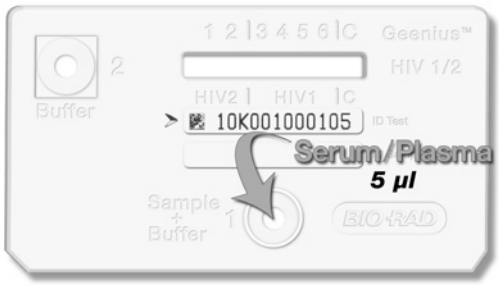
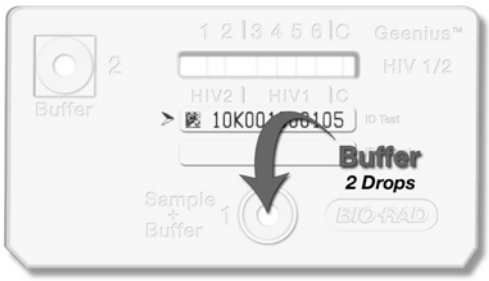
4. **Wait 5-7 minutes** the 6 blue coloured TEST lines should have disappeared from the rectangular TEST area. If not, discard the test device and repeat the procedure with a new test device. NOTE: A slight bluish-greenish colour may remain on the membrane, but none of the actual coloured lines should be seen at this point. Use the Buffer dropper to **add 5 drops** (150 µl) of Buffer into BUFFER Well 2 (see Figure 4 below).	**Figure 4** 

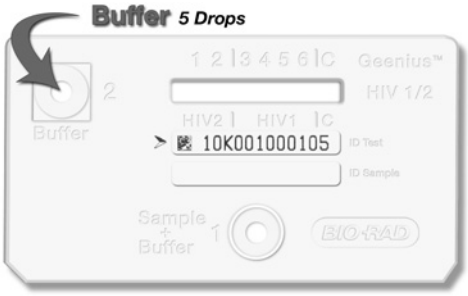
5. Read the test results between 20 to 30 minutes after the addition of the Buffer to BUFFER Well 2 **Do not read results after 30 minutes** Read results in a well-lit area. **NOTE:** Discard the used pipette tips, test device and any other test materials into a biohazard container.	

Serum or Plasma PROCEDURE

See specimen preparation on § 6.1 Specimen types.

1. Remove the Geenius™ HIV 1/2 Confirmatory Assay device from its pouch and place it on a flat surface (it is not necessary to remove the desiccant from the pouch). **NOTE**: If desiccant packet is missing from the pouch, DO NOT USE. Discard test device and use a new test device. Label the test device with patient ID or identification number (see Figure 1 below). Note that the Geenius™ HIV 1/2 Confirmatory Assay device has six (6) blue coloured lines in the Test area (no blue line in Control area); If any of the 6 coloured lines are absent, DO NOT USE. Discard the test device and use a new test device.	**Figure 1** 

2. Using a laboratory pipette, dispense 5 µl of serum/plasma) to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below). **Figure 2**  	3 Immediately following the addition of the sample, use the diluent dropper bottle to **add 2 drops** (60 µl) of Buffer into the SAMPLE + BUFFER Well 1 (see Figure 3 below). **Figure 3** 

4. **Wait 5-7 minutes.** All the 6 blue coloured TEST lines should have disappeared from the rectangular TEST area. If not, discard the test device and repeat the procedure with a new test device. NOTE: A slight bluish-greenish colour may remain on the membrane, but none of the actual coloured lines should be seen at this point. Use the diluent dropper bottle to **add 5 drops** (150 µl) of Buffer into BUFFER Well 2 (see Figure 4 below).	**Figure 4** 

5.	Read the test results between 20 to 30 minutes after the addition of the Buffer to BUFFER Well 2 **Do not read results after 30 minutes** Read results in a well-lit area. **NOTE:** Discard the used pipette tips, test devices and any other test materials into a biohazard container.

7.4 Quality Control

7.4.1 Built-in Control Feature

The control line serves as a built-in internal control and gives confirmation of sample addition and proper test performance. A pink/purple line will appear in the CONTROL (C) area if the test has been performed correctly and the device is working properly (Please see: Interpretation of Test Results).

7.4.2 External Quality Control

Geenius™ HIV 1/2 Confirmatory Controls, Ref: 72329 is available separately for use with the Geenius™ HIV 1/2 Confirmatory Assay.

It is recommended to perform the Geenius™ HIV 1/2 Confirmatory Controls under the following circumstances:

- When opening a new test kit lot.
- Whenever a new shipment of test kits is received.
- If the temperature of the test storage area falls outside of 2°C to 30°C.
- If the temperature of the testing area falls outside of 18°C to 30°C.
- At periodic intervals as indicated by the user facility.

7.5 Test Validation criteria

BAND reactivity

All visible bands. Even a faint band must be considered as reactive.

Validation criteria

VALID:
A test is valid only if a pink/purple line appears in the CONTROL (C) area, whether or not a line appears in the TEST line area.
(The Control Band must be strong: a faint band is not acceptable for the Control Band)

INVALID:
If there is no distinct pink/purple line visible (including a faint band) in the CONTROL (C) area, then the test is INVALID.
An INVALID test cannot be interpreted. It is necessary to repeat sample testing with a new device.

7.6 Interpretation of the Results

The following definitions describe the criteria employed by the Geenius™ HIV 1/2 Confirmatory Assay to determine the presence or absence of antibodies to HIV-1 and/or HIV-2.
The user subsequently analyzes the combined type specific band profiles for each assay according to the criteria listed in the Interpretation of Results Table below.

7.6.1 Interpretation criteria

HIV-1 Interpretation criteria

Interpretation	Bio-Rad criteria
POSITIVE	Any 2 bands of the 4 HIV-1 test lines with at least 1 ENV - gp160 (Band 4) or gp41 (Band 6)
NEGATIVE	No Band
INDETERMINATE	1ENV (Band 4 or 6) 1GAG (Band 5) 1POL (Band 3) 1GAG and 1POL (Bands 5 and 3)

HIV-2 Interpretation criteria

Interpretation	Bio-Rad criteria
POSITIVE	2 HIV-2 bands must be present: gp36 and gp140 (Band 1 and 2)
NEGATIVE	No Band

INDETERMINATE	1 ENV: gp36 (Band 1) or gp140 (Band 2) gp36 (Band 1) alone gp140 (Band 2) alone

GLOBAL HIV-1/HIV-2 Interpretation criteria

The following Interpretation of Results table describes the criteria employed by the Geenius™ HIV 1/2 Confirmatory Assay to interpret the combined type specific band patterns observed for each assay.

HIV-2 RESULT	HIV-1 RESULT	GLOBAL ASSAY INTERPRETATION
Negative	Negative	**HIV NEGATIVE**
Indeterminate	Negative	**HIV-2 INDETERMINATE**
Negative	Indeterminate	**HIV-1 INDETERMINATE**
Indeterminate	Indeterminate	**HIV INDETERMINATE**
Negative	Positive	**HIV-1 POSITIVE**
Indeterminate	Positive	**HIV-1 POSITIVE**
Positive	Negative	**HIV-2 POSITIVE**
Positive	Indeterminate	**HIV-2 POSITIVE**
Positive	Positive **case 1** = 1 ENV HIV-1 (gp 160 or gp41) + GAG or POL **case 2** = 2 ENV HIV-1 (gp 160 and gp41) +/- GAG and/or +/-POL	**HIV-2 POSITIVE** **(with HIV-1 cross-reactivity)** **HIV POSITIVE UNTYPABLE**

8. TEST LIMITATION

8.1 General Limitations

1. Visual reading can introduce some variability in the final conclusion between two different technicians or two different tests: this difference may be linked to the subjectivity of the visual interpretation.
2. For a reactive result, the intensity of the test lines does not necessarily correlate with the titer of antibody in the sample.
3. A person who is confirmed HIV-1 Positive or HIV-2 Positive is presumed to be infected with the virus, except that a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.
4. Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.
5. The variability of HIV-1 (group M and group O) and HIV-2 viruses does not exclude the possibility of false negative reactions. No known test method can offer complete assurance that the HIV virus is absent.
6. A nonreactive result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several months to reach detectable levels. A positive screening test associated with a negative confirmatory test may occur during the first stage of infection; hence, a negative result indicates that the tested sample does not contain anti-HIV antibodies detectable with Geenius™ HIV 1/2 Confirmatory Assay. Such a result does not, however, exclude the possibility of a recent HIV-1/HIV-2 infection. A new sample should be tested later.
7. An indeterminate result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several months to reach detectable levels. A positive screening test associated with an indeterminate confirmatory test may occur during the first stage of infection; hence, an indeterminate result indicates that the tested sample may contain anti-HIV antibodies detectable with Geenius™ HIV 1/2 Confirmatory Assay. Such a result does not, however, exclude the possibility of a recent HIV-1/HIV-2 infection. A new sample should be tested later.
8. The Geenius™ HIV 1/2 Confirmatory Assay is intended as an aid in the diagnosis of infection with HIV-1 and or HIV-2. HIV and AIDS related conditions are clinical syndromes and their diagnosis can only be established clinically.
9. The Geenius™ HIV 1/2 Confirmatory Assay must ONLY be used with capillary blood, whole venous blood, serum or plasma. Using other types of samples or testing of venipuncture whole blood samples collected using a tube containing an anticoagulant other than citrate, heparin or EDTA may not yield accurate results.
10. The Geenius™ HIV 1/2 Confirmatory Assay must be used in accordance with the instructions in this product insert to obtain accurate results.
11. Reading test results earlier than 20 minutes or later than 30 minutes since the addition of Running Buffer to BUFFER Well 2 may yield erroneous results.

8.2 Assay Interpretation limitations

An “indeterminate” profile does not exclude one of the following situations: seroconversion, or a cross-reaction with other retroviruses**.** The homology between HIV-1 and HIV-2 viruses can lead to cross reactivity between both anti-HIV-1 and anti-HIV-2 antibodies against HIV-2 and HIV-1 viruses.

Samples which meet HIV-1 positive criteria show in very rare cases some cross reactivity on one of the HIV-2 Envelop bands. Nevertheless, such rare profile of single HIV-1 infection does not also exclude in very rare cases the possibility of a secondary HIV-2 seroconversion (surinfection).

Samples which meet HIV-2 positive criteria can show cross reactivity on one or more HIV-1 bands. In most of the cases, an HIV-1 indeterminate profile associated to an HIV-2 positive

profile confirms a single HIV-2 infection. However it does not exclude the possibility of a secondary HIV-1 seroconversion (surinfection).

Samples that meet both HIV-1 and HIV-2 positive criteria are generally HIV-2 positive samples which show HIV-1 cross reactivity when they have only one detected envelop band (gp160 or gp41). Such profiles do not exclude the rare possibility of HIV-1-HIV-2 coinfection.

HIV Untypable samples with all 4 envelop bands detected (all of the HIV-1 env and HIV-2 env) are in most of the cases HIV-2 positive samples with HIV2 reactivity that cannot be visually differentiated from HIV-1 reactivity. Such profiles do not exclude the possibility of HIV 1/2 coinfection.

Samples which meet both HIV-1 and HIV-2 positive criteria are in very rare cases HIV-1 positive samples which show HIV-2 cross-reactivity.

9. PERFORMANCES CHARACTERISTICS

9.1 Precision Study

A precision panel (N=6) made of 3 serum and 3 whole blood samples of different HIV status (HIV negative, HIV-1 positive, HIV-2 positive) was tested. For each precision study and panel member, an agreement percentage was determined as the number of responses correctly identified compared to the sample status.

9.1.1 Repeatability

Precision panel was tested in 10 replicates during the same run. Repeatability measurement was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive.

Panel member	Repeatability results for Serum					Repeatability results for Whole blood				
	N	NEG	IND	POS	agreement	N	NEG	IND	POS	agreement
HIV NEG	10	10	0	0	100%	10	10	0	0	100%
HIV-1 POS	10	0	0	10	100%	10	0	0	10	100%
HIV-2 POS	10	0	0	10	100%	10	0	0	10	100%

9.1.2 Intermediate precision

Run and Day precision

Serum precision panel was tested in duplicate per run, with 2 runs per day during 10 days and whole blood precision panel in triplicate per run, with 2 runs per day during 3 days. A run-to-run and day-to-day precision was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive samples.

Panel member	Run and day precision results for Serum					Run and day precision results for Whole blood				
	N	NEG	IND	POS	agreement	N	NEG	IND	POS	agreement
HIV NEG	40	40	0	0	100%	18	18	0	0	100%
HIV-1 POS	40	0	0	40	100%	18	0	0	18	100%
HIV-2 POS	40	0	0	40	100%	18	0	0	18	100%

Lot and Operator precision

Precision panel was tested in duplicate on 2 lots of reagent and by 3 operators with 1 run per day during 3 days. An inter-operator and inter-batch precision was found with agreements of 100% for HIV negative, HIV-1 positive and HIV-2 positive samples.

Panel member	Lot and Operator precision results for Serum					Lot and Operator precision results for Whole blood				
	N	NEG	IND	POS	Agreement	N	NEG	IND	POS	Agreement
HIV NEG	36	36	0	0	100%	36	36	0	0	100%
HIV-1 POS	36	0	0	36	100%	36	0	0	36	100%
HIV-2 POS	36	0	0	36*	100%	36	0	0	36	100%

* 2 replicates gave HIV-1 cross reactivity

9.2 Clinical performance

9.2.1 Diagnostic Specificity

Blood donors

A total of 400 specimens (serum, plasma and venous blood) drawn from 300 non selected known and first time donors, were tested on the Geenius™ HIV 1/2 Confirmatory Assay in a blood bank site. 398 specimens tested negative and 2 tested indeterminate. Indeterminate results representing 0.5% (2/400) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 398 specimens was 100.0% (398/398) with a confidence interval at 95% of [99.1; 100.0].

Specificity on blood Donors	Total number specimens	Negative	Indeterminate	Positive	Specificity (%)	95 CI (%)
Serum (SSTII Gel sep)	100	98	2 (**)	0	100.0 (98/98)	[96.3 - 100.0]
Plasma (*) (EDTA-K2)	100	100	0	0	100.0 (100/100)	[96.4 - 100.0]
Whole venous blood (EDTA-K2)	200	100	0	0	100.0 (200/200)	[98.2 - 100.0]
TOTAL 300 donors	400	398	2 (**)	0	100.0 (398/398)	[99.1 - 100.0]

(*) specimens of plasma paired to whole venous blood samples obtained from the same 100 donors
(**) Indeterminate results have not been considered as false positive / further investigation is needed

Hospitalized patients and pregnant women

A total of 508 specimens from 326 hospitalized patients were tested on the Geenius™ HIV 1/2 Confirmatory Assay at 2 different sites. Among these patients, 99 had serum sampling alone, 100 had whole blood sampling alone, 72 had both serum and whole blood sampling, 30 patients had both serum, plasma and whole blood sampling, and 25 had serum, plasma and capillary blood sampling.
30 serum from pregnant women from 2 sites were also tested.
Whole venous blood and plasma samples were collected on EDTA-K2 tubes and serum on SSTII with gel separator tubes. No anticoagulant was used for capillary blood collection.

529 specimens tested negative and 9 tested indeterminate. Indeterminate results representing 1.7% (9/538) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 529 specimens was 100.0% (529/529) with a confidence interval at 95% of [99.3; 100.0].

Site	Patients	Fresh Serum /SSTII Gel	Fresh Plasma /EDTA-K2	Fresh venous blood /EDTA-K2	Fresh Capillary blood	Total specimens	Pregnant women (frozen serum)	GrandTotal specimens
Site 1	99	99	/	/	/	99	10	109
Site 2	227	/ 72 30 25	/ / 30 25	100 72 30 /	/ / / 25	100 144 90 75	/ / / /	100 144 90 75
Site 5		/	/	/	/		20	20
Total	**326**	**226**	**55**	**202**	**25**	**508**	**30**	**538**
Negative **Indeterminate** **Positive**	/	221 5(*)(***) **0**	54 1(*)(***) **0**	201 1(*)(***) **0**	25 0 **0**	501 7 (***) **0**	28 2 (***) **0**	529 9 (***) **0**
Specificity (%)	/	**100.0 (221/221)**	**100.0 (54/54)**	**100.0 (201/201)**	**100.0 (25/25)**	**100.0 (501/501)**	**100.0 (28/28)**	**100.0 (529/529)**
95 CI (%)	/	[98.3 - 100.0]	[93.4 - 100.0]	[98.2 -100.0]	N/A(**)	[99.3 - 100.0]	N/A(**)	[99.3 - 100.0]

(*) 1 patient had 1 indeterminate result for both serum, venous blood and plasma
(**) not applicable with N<30 population
(***) Indeterminate results have not been considered as false positive / further investigation is needed

Blood donors giving false positive results at screening

A total of 275 serum specimens drawn from blood donors giving false positive results with HIV ELISA screening assays, were tested on the Geenius™ HIV 1/2 Confirmatory Assay at two clinical sites.
258 specimens tested negative and 17 tested indeterminate. Indeterminate results representing 6.2% (17/275) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) on the 258 specimens was 100.0% (258/258) with a confidence interval at 95% of [98.6; 100.0].

Specificity on blood Donors	Total number specimens	Negative	Indeterminate	Positive	Specificity (%)	95 CI (%)
TOTAL 275 donors	275	258	17 (*)	0	100.0 (258/258)	[98.6 - 100.0]

(*) Indeterminate results have not been considered as false positive / further investigation is needed

9.2.2 Diagnostic Sensitivity

HIV-1 infected patients

A total of 599 specimens from 263 patients confirmed as HIV-1 infected from 2 sites (155 patients at site 1 and 108 patients at site 2) were tested on the Geenius™ HIV 1/2 Confirmatory Assay
On 1 site,, 108 fresh serum and paired plasma , 5 fresh serum and 50 genotyped HIV-1 strains (2 CRF01, 5 CRF02, 1 CRF05, 1 CRF06, 2 CRF09, 1 CRF11, 1 CRF12, 1 CRF13, 1 CRF14, 1 CRF15, 1 CRF18, 1 CRF19, 1 CRF22, 1 CRF27, 1 CRF30, 1 CRF36, 1 CRF42, 4 subtype A, 5 subtype B, 2 subtype C, 2 subtype D, 2 subtype F, 2 subtype G, 2 subtype H, 2 subtype J, 1 subtype K, 5 group O) samples were tested.
On the second site, among the 108 patients, 82 had whole blood, serum and plasma samplings, 20 had both whole blood, capillary whole blood, serum and plasma samplings, and 6 had capillary whole blood, serum and plasma sampling.

Whole venous blood and plasma samples were collected on EDTA-K2 tubes and serum samples on SSTII with gel separator tubes.
All the 599 specimens tested HIV-1 positive, leading to an overall sensitivity of 100.0% (599/599) with a confidence interval at 95% of [99.4 - 100.0].
HIV-1 sensitivity on patients was 100% (263/263).
On the total of 599 specimens, 3 specimens were found HIV untypable instead of HIV-1 positive, therefore HIV-1 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 99.5% (596/599) with a confidence interval at 95% of [98.5 - 99.9].

Site	Patients	Fresh Serum (SSTII Gel)	Genotyped serum	Fresh Plasma (EDTA-K2)	Fresh venous blood (EDTA-K2)	Fresh Capillary blood	Total specimens
Site 1 N= 155	100 5 50	/ 5 /	/ / 50	100 / /	100 / /	/ / /	200 5 50
Site 2 N= 108	82 20 6	82 20 6	/ / /	82 20 6	82 20 /	/ 20 6	246 80 18
Total	**263**	**113**	**50**	**208**	**202**	**26**	**599**
HIV-1 Positive		113	49	207	201	26	
HIV untypable		0	1	1(*)	1(*)	0	
Sensitivity (%)		**100.0 (113/113)**	**100.0 (50/50)**	**100.0 (208/208)**	**100.0 (202/202)**	**100.0 (26/26)**	**100.0 (599/599)**
95 CI (%)		[97.8 - 100.0]		[98.2 - 100.0]	[98.2 -100.0]	N/A(**)	[99.4 - 100.0]

(*) specimens of plasma paired to venous blood sample obtained from the same HIV-1 infected patient
(**) not applicable with N<30 population

HIV-2 infected patients

A total of 283 specimens from 172 patients confirmed as HIV-2 infected (serum, plasma, venous blood and capillary blood with some paired samples drawn from the same patients) were tested on the Geenius™ HIV 1/2 Confirmatory Assay at three clinical sites. 66 serum specimens were obtained from two clinical sites samples collections. All others specimens were freshly obtained from patients.
Whole venous blood and plasma samples were collected on EDTA-K2 or EDTA-K3 tubes and serum collected samples on SSTII with gel separator or dry tubes.

281 specimens tested HIV positive and 2 tested HIV-2 indeterminate. The two HIV-2 indeterminate results (gp140 not detected) were obtained on serum and whole blood drawn from the same patient found gp105 negative with a CE-marked HIV I/II confirmation assay. Indeterminate results representing 0.7% (2/283) of total specimens have not been considered as false negative. Overall sensitivity (true positive/ true positive + false negative) on the 281 specimens was 100.0% (281/281) with a confidence interval at 95% of [98.7; 100.0].

172 specimens over 283 were correctly found HIV-2 positive (with or without cross HIV-1 reactivity) or HIV-2 indeterminate and 111 HIV untypable, therefore HIV-2 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 60.8% (172/283) with a confidence interval at 95% of [54.8 - 66.5].

Sites	Patients	Fresh Serum (SSTII Gel)	Frozen serum	Fresh Plasma (EDTA-K2)	Fresh venous blood (EDTA-K2 or K3)	Fresh Capillary blood	Total specimens
Site 1	5 16	5 /	/ 16	5 /	2 /	3 /	15 16
Site 2	50	/	50	/	/	/	50
Site 3	101	101	/	/	101	/	202
Total	**172**	**106**	**66**	**5**	**103**	**3**	**283**
HIV-2 Positive	/	33	15	3	28	3	82
HIV-2 positive with HIV-1 reactivity		33	19	1	35	0	88
HIV untypable		39	32	1	39	0	111
Indeterminate		1(*)(***)	0	0	1(*)(***)	0	2 (***)
Sensitivity (%)		**100.0 (171/171)**		**100.0 (5/5)**	**100.0 (102/102)**	**100.0 (3/3)**	**100.0 (281/281)**
95 CI (%)		**[97.9 - 100.0]**		**N/A****	**[96.5 - 100.0]**	**N/A****	**[98.7 – 100.0]**

(*) specimens of serum paired to venous blood sample obtained from the same HIV-2 infected patient
(**) not applicable with N<30 population
(***) Indeterminate results have not been considered as false negative / further investigation is needed

HIV-1/HIV-2 co-infected patients

A total of 22 specimens from 15 patients confirmed as HIV-1/ HIV-2 coinfected (13 serum, 2 plasma and 7 paired whole venous blood drawn from same 7 patients) were tested on the Geenius™ HIV 1/2 Confirmatory Assay at two clinical sites. Six serum and 2 plasma specimens were obtained from one clinical samples collection site and the seven paired serum-whole venous blood were freshly obtained from another clinical site patients.
Overall sensitivity was 100% (22/22) (serum and whole venous blood) without indeterminate results.
At the first intent, all specimens were correctly found HIV untypable (HIV-1 positive with two envelops detection and HIV-2 positive), except one whole blood and one serum specimens. Whole blood was improperly found HIV-2 positive due to recent surinfection. After recall few weeks later, this patient was correctly found HIV untypable. Serum was improperly found HIV-2 positive with HIV-1 reactivity instead of HIV untypable but was also improperly found HIV-2 positive (without HIV-1 reactivity) on several CE-marked HIV differentiation assays. 21 over 22 specimens were correctly found HIV untypable after one patient recall. Therefore, HIV-1+2 differentiation capacity of the Geenius™ HIV 1/2 Confirmatory Assay was 95.5% (21/22).

HIV-1 seroconversion samples

Sensitivity of Geenius™ HIV1/2 Confirmatory Assay has been estimated with 32 seroconverter panels (154 samples). 41.6% (64/154) were positive with Geenius™ HIV1/2 Confirmatory Assay, meanwhile 12.3% (19/154) were positive with a CE-marked Western Blot assay. The detection of the first positive bleed point was in average earlier of 1.4 (44/32) time-points per panel with Geenius™ HIV 1/2 Confirmatory Assay.

When testing 83 early-seroconversion samples (negative or indeterminate by Western Blot), 10.8% (9/83) were positive with Geenius™HIV1/2 Confirmatory Assay.

Based on 10 seroconversion samples tested in a clinical site and comparison to the same reference Western blot assay, Geenius™ HIV1/2 Confirmatory Assay was more sensitive for the detection of antibodies to gp41 and had a similar sensitivity for the detection of antibodies to gp160.

Geenius™ HIV1/2 Confirmatory Assay complies with the state of art in term of sensitivity estimated with HIV seroconversion panels.

9.3 Analytical Specificity

9.3.1 Cross Reactivity

251 potentially cross-reacting samples representing 29 different diseases/ states testing positive for the following markers were tested on the Geenius™ HIV 1/2 Confirmatory Assay in different clinical sites.

HTLV I/ II (20), Hepatitis C (10 HCV), Hepatitis B (10 anti-HBS) and Hepatitis A (10 HAV IgG); Cytomegalovirus (10 CMV IgG), Epstein-Barr (10 EBV IgG),Herpes Simplex (10 HSV), Rubella IgG (10), Toxoplasmosis IgG (5), Syphilis IgG (10), Candida (10), Malaria (26), Dengue (2), Leishmaniosis (2), Vaccinia (10),, Influenza vaccine (5 Flu), Dialysis (10), HAMA (10), Rheumatoid factor (10), Multi-transfusion (10), Myeloma (5) Hemophiliac (10), Autoimmune as Systemic Lupus Erythemateous (12 SLE), Scleroderma (2), Sjogrens (2), Mixed connective tissue (2 MCTD), anti-nuclear antibody (3 ANA), Cancer (5), Cirrhosis (5) and Multipareous women (5).

Over the total 251 difficult samples, 245 specimens tested negative and 6 specimens tested indeterminate (they were indeterminate with HIV-1 Western-Blot and positive for Malaria). Indeterminate results representing 2.4% (6/251) of total specimens have not been considered as false positive. Overall specificity (true negative/ true negative + false positive) was 100.0% (245/245) with a confidence interval at 95% of [98.5 - 100.00].

9.4 Hook effect

Possible hook effect was studied by testing 2 HIV-1 and 2 HIV-2 high titer specimens, neat and diluted. Neither negative or lower intensity results were observed with the neat high titer HIV-1 and HIV-2 positive specimens, when compared to their more diluted forms (1:10 to 1:100000). The equivalence of results between non diluted and diluted samples shows the absence of hook effect.

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CONTENTS

1. INTENDED USE

The fast test device uses the Immunochromatography (ICT or lateral migration) technique to detect anti-HIV-1 and anti-HIV-2 antibodies in human serum, plasma, venous blood and capillary blood.

2. CLINICAL VALUE

Acquired Immunodeficiency Syndrome (AIDS) is an infectious disease of viral origin, reflected in severe cellular immunodeficiency.

Two types of virus related to the lentivirus group have been isolated in lymphocytes of patients suffering from AIDS or its prodromes. The first, named HIV-1, was isolated in France, then the United States. The second, named HIV-2, was isolated in two patients of African origin and found to be responsible for a new AIDS focus in West Africa.

3. PRINCIPLE OF THE Genie™ Fast HIV 1/2

HIV-1 gp120, gp41 and HIV-2 gp36 recombinant antigens, conjugated to colloidal gold, are adsorbed at the base of a strip of nitrocellulose membrane.

HIV-1 and HIV-2 antigens are immobilised in the test zone (T).

Anti-HIV antibodies are immobilised in the control zone (C).

When the sample is deposited at the bottom of the strip, it starts migrating by capillary diffusion, rehydrating the antigen-conjugated gold.

In the presence of anti-HIV-1 and/or HIV-2 antibodies, these will bind to the conjugated antigens to form a particular complex which will be carried by the sample migration. This particular complex will continue to migrate as far as zone (T) and will be captured by the HIV-1 and HIV-2 antigens immobilised in this zone, to produce a visible red strip in zone (T). The excess antigen-conjugated gold will continue to migrate as far as zone (C), where it will be captured and aggregated by the anti-HIV antibodies to produce a red strip in zone (C), indicating the validity of the test (proof of sample migration).

In the absence of anti-HIV-1 or anti-HIV-2 antibodies in the sample, there will be no red strip in zone (T), but the antigen-conjugated gold will continue to migrate alone as far as zone (C), where it will be captured to produce a red strip indicating the validity of the test (proof of sample migration).

See Chapter 12: Results interpretation.

4. COMPOSITION OF THE KIT

LABELLING	TYPE OF REAGENTS	PRESENTATION 72327
Device	Nitrocellulose strip, the base of which contains recombinant HIV-1 and HIV-2 antigens conjugated to gold, HIV-1 and HIV-2 antigens in zone T and anti-HIV antibodies in zone C.	25 cassettes
Diluent	Diluent (for the whole blood protocol) Preservative: Sodium azide (<0.1%)	1 vial (5 ml)
Pipettes	Plastic pipettes for depositing serum, plasma and venous blood	50 pipettes

5. PRECAUTIONS

The quality of results depends on the extent to which the following good laboratory practices are respected:

- Before use, you must wait for 30 minutes for the reagents to stabilise at the laboratory temperature, if this is different from the storage temperature.
- Use the reagents in such a way as to prevent contamination.
- Use disposable equipment by preference.
- Once the pouch is open, do not leave the cassette in the open air for more than 20 minutes before depositing the sample.
- The waiting time between the last deposit (sample or diluent) and the reading, must not exceed 30 minutes.
- Use a new distribution cone or a new disposable pipette, provided in the kit, for each sample.
- Do not change the procedure.

6. HEALTH AND SAFETY INSTRUCTIONS

All the reagents in the kit are for use in "*in vitro*" diagnosis.
Wear disposable gloves when handling reagents.
Do not pipette with your mouth.
Because no method can absolutely guarantee the absence of HIV, Hepatitis B or C virus or other infectious agents, assume that these reagents, as well as the patient samples, are potentially infectious and handle them with the usual precautions.
Consider the equipment in direct contact with the samples and reagents to be contaminated also and treat it as such.
Avoid splashing samples or the solution containing them.
Soiled surfaces will be cleaned with 10% dilute bleach.
The equipment used for cleaning must be thrown into a special contaminated waste container.

The samples, reagents of human origin and the equipment and contaminated products will be disposed of after decontamination:
- either by soaking in bleach at a final concentration of 10% sodium hypochlorite (1 volume of bleach per 10 volumes of contaminated liquid or water) for 30 minutes.
- or by autoclaving at 121°C for at least 2 hours.

Autoclaving at 121°C, for at least one hour, is the best method for deactivating HIV viruses and the hepatitis B virus.
- WARNING : DO NOT PUT SOLUTIONS CONTAINING SODIUM HYPOCHLORITE (BLEACH) INTO THE AUTOCLAVE.

Don't forget to neutralise and/or autoclave effluent solutions or any liquid containing biological samples before placing them in the sink.
Furthermore, chemicals must be handled and disposed of according to good laboratory practices.
Do not use expired reagents.
The safety data sheet is available on request.

7. MATERIAL NOT PROVIDED

Automatic or semi-automatic pipettes or multipipettes, adjustable or fixed, to measure and deposit the sample.
Lancet and pipette required for taking capillary samples.

8. REAGENTS

8.1 Cassette:

Each cassette is packaged in a sealed aluminium pouch.

8.2 Diluent for the venous or capillary blood protocol:

This diluent buffer is supplied in a dropper bottle.

8.3 Consumables:

Plastic pipettes (serum, plasma and venous blood).

9. STORAGE CONDITIONS - SHELF LIFE

The kit must be stored at +2-30°C. Every item in the Genie™ Fast HIV 1/2 kit stored at +2-30°C can be used until the expiry date noted on the box.
After opening the pouch, the cassette must be used within 20 minutes of this opening.
The bottle of diluent can be stored at +2-30°C, until the expiration date of the kit, even after its first use.

10. SAMPLE

Take a blood sample according to the usual method. The test must be performed on undiluted samples of serum, plasma, venous or capillary blood. Plasma and venous blood are collected with the following anticoagulants: EDTA-K2, Lithium Heparinate, ACD (Citrate-Dextrose).
Fibrin particles or aggregates in suspension may lead to false positive results.
Chemical treatments, heating or dilution of the blood may alter the results and give inappropriate results.
If the samples have to travel, pack them according to current regulations for transporting etiological agents.
Fresh samples can be stored at 2-8°C up to 7 days for serum and plasma and up to 3 days for whole venous blood, without interference on the negative or positive results.
Fresh serum and plasma can also be frozen and thawed up to 3 times, without interference on the negative or positive results.

Comment: DO NOT USE HYPERHEMOLYZED SERUM OR PLASMA - very pronounced hemolysis may affect test performance.
No interference has been shown in samples containing up to 100 mg/l of bilirubin or in lipemic samples containing up to 30 g/l of triolein and in hemolyzed samples containing up to 5 g/l of haemoglobin. Abnormally high albuminemia (100 g/l) can give false positive results.

11. ASSAY PROCEDURE

The procedure will be respected as follows:

11.1. Open the pouch and remove the cassette (the sample must be deposited within 20 minutes of opening the pouch).

11.2. Place the cassette on a flat, horizontal surface with the circular zone for sample deposit facing the operator.

11.3. Deposit the sample

a. **Plasma/Serum protocol:** Deposit 3 drops(*) of the sample in the circular sample zone, using the plastic pipette provided with the kit, or 80 µl using an automatic pipette.

b. **Venous Blood protocol:** Deposit 2 drops(*) of blood in the circular sample zone, using the plastic pipette provided with the kit or 80 µl of blood using an automatic pipette, then add 2 drops of diluent using the dropper bottle provided with the kit (~ 80 µl).

c. **Capillary Blood protocol:** According to the laboratory practice, use a fingerstick lancet and an appropriate plastic pipet (without anticoagulant) to collect blood by capillary action. Deposit 80 µL of capillary blood in the circular deposit zone on the device, then add 2 drops (~ 80 µL) of diluent using the dropper bottle provided with the kit.

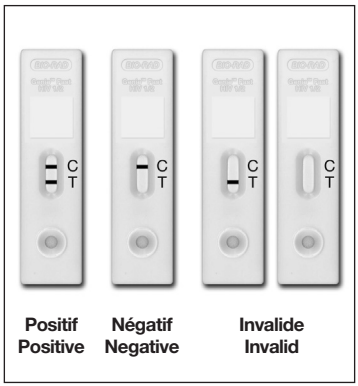
Avoid any excess sample or diluent flowing outside the circular deposit zone.

(*) the number of drops is defined according to the viscosity of the sample.

11.4. Reading

Visual reading takes place between 10 min. and 30 min. after the last deposit (sample or diluent).

12. RESULTS INTERPRETATION AND ANALYSIS



12.1 Test Validity:

The test validity can be read in the Control zone (C).

Serum/Plasma protocol: to validate the test, a red Control strip (C) must be present.

Venous and capillary blood protocol: to validate the test, a red Control strip (C) and a red circular sample deposit zone must be present.

If the validity conditions are nonconforming, the test is considered to be invalid, the cassette must be disposed of and the test repeated with a new cassette.

If red cells migrate into the Test zone (T), where they could interfere with interpreting negative or slightly positive samples, it is recommended to repeat the test.

12.2 Positive Result:

The appearance of a red strip (even of very low intensity) in the Test zone (T) after 10 to 30 minutes indicates the presence of anti-HIV-1 or HIV-2 antibodies.

You are recommended to wait for 10 minutes before reading the results (even if red strips appear quickly in the test zone), in order to confirm that the colouring is maintained, before declaring a positive result).

No positive result must be declared beyond 30 minutes.

Comment: Any red strip even observed faintly in the Test zone (T) must be considered and interpreted as a positive result.

12.3 Negative Result:

The absence of a red strip in the Test zone (T) after 30 minutes means that anti-HIV-1 or HIV-2 antibodies have not been detected.

However, this does not exclude the possibility of an early stage of HIV infection.

Comment: Never interpret beyond 30 minutes after the last deposit.

13. PERFORMANCE

The performance of Genie™ Fast HIV 1/2 has been evaluated on five different clinical sites by testing samples taken from blood donors, HIV positive patients and seroconversion panels.

13.1 Specificity studies

a) Blood donor population

- 2517 specimens from blood bank donors (1108 of serum, 708 of plasma and 701 of whole venous blood) were tested with Genie™ Fast HIV 1/2 reagent. Specificity was 99.5% (2505/2517) with a confidence interval (CI) of 95% from [99.2 to 99.7].

Donor specificity	Total number of specimens	Repeatable positives (RR)	Specificity RR (%)	CI 95 (%)
Serum (Gel, Act)	1108	5	**99.5** (1103/1108)	[98.9; 99.9]
Plasma (EK2, HeLi, ACD)	708	5	**99.3** (703/708)	[98.4; 99.8]
Whole venous blood (EK2, HeLi)	701	2	**99.7** (699/701)	[99.0; 100.0]
Total	**2517**	**12**	**99.5** (2505/2517)	**[99.2; 99.7]**

b) Population of hospitalised patients

- 1010 samples from patients not infected with HIV and taken from hospital complexes (428 of serum, 227 of plasma, 327 of whole venous blood and 28 of capillary blood paired with venous blood) were tested with Genie™ Fast HIV 1/2 reagent.
  Overall specificity was 99.5% (1005/1010), CI 95% [98.9 - 99.8%] with 99.3% (425/428) and 99.1% (225/227) for serum and plasma respectively, 100% for whole venous blood (327/327) and capillary blood (28/28).

  Comment: The whole venous blood and capillary blood from the same 28 patients gave equivalent results.

Specificity for hospitalised patients	Total number of specimens	Repeatable positives (RR)	Specificity RR (%)	CI 95 (%)
Serum (Gel)	428	3	**99.3** (425/428)	[98.0; 99.9]
Plasma (EK2, HeLi)	227	2	**99.1** (225/227)	[96.9; 99.9]
Whole venous blood (EK2, HeLi)	327	0	**100** (327/327)	[98.9; 100]
Capillary blood	28 (*)	0	**100** (28/28)	[87.7; 100.0]
Total	**1010**	**5**	**99.5** (1005/1010)	**[98.9; 99.8]**

(*) specimens of capillary blood paired with whole venous blood from 28 patients.

c) Cross reactions

- Specificity was also evaluated on samples from 200 pregnant women and 107 patients suffering from pathologies not linked to HIV infection (7 dengue, 3 filariasis; 5 bilharzia; 4 leishmaniosis; 11 lupus erythematous; 10 malaria; 10 rheumatoid factors; 9 influenza; 8 ANA (anti-nuclear factors); 10 hepatitis A; 10 hepatitis B; 10 hepatitis C; 10 HTLV). Specificity was found to be 100%, CI95% [98.2 – 100] for the pregnant women (200/200) and 97.2%, CI95% [92.0 – 100] for the other pathologies (104/107) with three repeatable positive results (2 cases of malaria and 1 case of hepatitis B).

13.2 Sensitivity studies

a) Samples of HIV-1 positive patients

- 1050 samples from patients known to be infected with HIV-1 (385 of serum, 301 of plasma, 338 of whole venous blood and 26 of capillary blood paired with venous blood) were tested with Genie™ Fast HIV 1/2 reagent.
  Sensitivity was **100%** (1050/1050), CI95 [99.7 -100%] for the four types of samples (serum, plasma, whole venous blood and capillary blood).

Comment: The whole venous blood and capillary blood from the same 26 patients gave equivalent results.

Sensitivity for HIV-1 patients	Total number of specimens	Number of reactive samples	Sensitivity (%)	CI 95 (%)
Serum (Gel)	385	385	100 (385/385)	[99.1; 100]
Plasma (EK2, HeLi)	301	301	100 (301/301)	[98.8; 100]
Whole venous blood (EK2, HeLi)	338	338	100 (338/338)	[98.9; 100]
Capillary blood	26 (*)	26	100 (26/26)	[86.3; 100]
Total	**1050**	**1050**	**100** (1050/1050)	**[99.7; 100]**

(*) specimens of capillary blood paired with whole venous blood from 26 patients.

b) Samples from HIV-2 positive patients

- 101 serums and 8 fresh plasma from patients treated or not for their HIV-2 infection, tested with the Genie™ Fast HIV 1/2 reagent were all found to be positive.
  Sensitivity was **100%** (109/109) with a confidence interval of 95% [96.7; 100].

Sensitivity for HIV-2 patients	Total number of specimens	Number of reactive samples	Sensitivity (%)	CI 95 (%)
Serum	109	109	**100** (109/109)	[96.7; 100]

c) Samples from genotyped HIV-1 positive patients

- 154 serums from patients infected by an HIV-1 strain of known genotype (see table below), tested with Genie™ Fast HIV 1/2 reagent were all found to be positive, giving a sensitivity of 100% (154/154) with a confidence interval of 95% [97.6- 100].

Genotype	Total number of specimens	Number of reactive samples
CRF01	9	9
CRF02	20	20
CRF05	1	1
CRF06	7	7
CRF08	1	1
CRF09	5	5
CRF10	1	1
CRF11	6	6
CRF12	1	1
CRF13	2	2
CRF14	6	6
CRF15	3	3
CRF19	3	3
CRF27	1	1
Subtype A	12	12
Subtype B	21	21
Subtype C	9	9
Subtype D	9	9
Subtype F	9	9
Subtype G	12	12
Subtype H	6	6
Subtype J	4	4
Subtype K	1	1
Group O	5	5
Total	**154**	**154**
Sensitivity: 100%		

b) Fresh samples from HIV-1 and HIV-2 positive patients

- 113 fresh serum (SST2 gel tubes), 216 fresh plasma (EDTA-K2/ Lithium Heparinate), 243 fresh whole venous blood (EDTA-K2/ Lithium Heparinate) and 26 fresh capillary blood samples, (taken from ≤ 1 day) from patients known to be infected with HIV-1 and 8 fresh plasma (EDTA-K2) from patients known to be infected with HIV-2 were tested with Genie™ Fast HIV 1/2 reagent. All the samples were found to be positive, giving a sensitivity of **100%** no matter what the type of sample.

Sensitivity for Fresh HIV-1 and HIV-2 positive samples (≤ 1 day)	**Total number of specimens**	**Number of reactive samples**	**Sensitivity (%)**
Serum HIV-1 (SST2 Gel)	113	113	**100** (113/113)
Plasma HIV-1 (EK2, HeLi) and HIV-2 (EK2)	216 8	224	**100** (224/224)
Whole venous blood HIV-1 (EK2, HeLi)	243	243	**100** (243/243)
Capillary blood HIV-1	26	26	**100** (26/26)
Total	606	606	100 **(606/606)**

e) Sensitivity in seroconversion panels

- 31 commercial seroconversion panels, of which 30 included 65 early seroconversion points (*), and further more 40 samples representing a per-seroconversion stage (*) were tested with Genie™ Fast HIV 1/2 reagent and a CE marked comparative rapid test.

Panels tested	**Total number of specimens**	**Number of positive samples with CE marked reference rapid test**	**Number of positive samples with Genie™ Fast HIV 1/2**
Seroconversion (31 panels)	118	80	83 (**)
Early seroconversion (30 panels)	65	30	33 (**)
Per-seroconversion	40	37	37

(*) As defined in the Common Technical Specifications (CTS)
(**) In 3 seroconversion panels, the first positive point was detected at least one point earlier on Genie™ Fast HIV 1/2 and in 1 seroconversion panel, the first positive point was detected one point later than with the reference rapid test.

f) Hook effect

- No hook effect was observed with the Genie™ Fast HIV 1/2 reagent with a series of dilutions of samples strongly positive in HIV-1 and HIV-2 antibodies.

13.3 Reproducibility studies

a) Inter-assay reproducibility

- The inter-assay reproducibility study was performed with 7 different samples of serum (1 HIV-negative, 3 weak, moderate and strong HIV-1, 3 weak, moderate and strong HIV-2, and 5 different samples of whole venous blood (1 HIV-negative, 2 weak and strong HIV-1, 2 weak and strong HIV-2.
  The analysis of samples using Genie™ Fast HIV 1/2 reagent was performed twice a day for 5 days (10 replicates) for the serum or once a day in triplicate for 3 days (9 replicates) for whole venous blood.
  For all the samples tested, both negative and positive, no discordance was found between replicates.

b) Inter-operator reproducibility

- The study of inter-operator reproducibility was performed with 5 samples of whole venous blood (1 HIV-negative, 2 weak and moderate HIV-1, 2 weak and moderate HIV-2) tested in triplicate by three different operators on two batches of reagent.
  For all the samples tested, both negative and positive, no discordance was found between the three operators.

c) Inter-batch reproducibility

- The inter-batch reproducibility study was performed on three batches, with 5 samples of whole venous blood (1 HIV-negative, 2 weak and moderate HIV-1, 2 weak and moderate HIV-2) and 7 plasma samples (1 HIV-negative, 2 weak and moderate HIV-1, 4 weak, moderate and strong HIV-2) tested in triplicate on each of the three batches.
  For all the samples tested, both negative and positive, no discordance was found between the three batches.

14. TEST LIMITS

It is recommended to retest any sample initially found to be positive, in accordance with the criteria described in chapter 12.
Any sample found to be reproducibly positive must be confirmed using an appropriate method (Western-Blot or equivalent) to prove the presence of anti-HIV antibodies.

A negative result means that the sample tested does not contain anti-HIV antibodies detectable by the Genie™ Fast HIV 1/2 test.
Such a result does not exclude the possibility of HIV-1 or HIV-2 infection. Indeed low levels of antibodies may not be detected if the infection was recent.
The variability of HIV-1 (group M, group O) and HIV-2 means that false negative reactions cannot be excluded.
No known method can guarantee that the HIV virus is absent.
See also the limits linked to samples, described in paragraph 10.

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(GB) - CE marking (European directive 98/79/CE on *in vitro* diagnostic medical devices)
(FR) - Marquage CE (Directive européenne 98/79/CE relative aux dispositifs médicaux de diagnostic *in vitro*)
(ES) - Marcado CE (Directiva europea 98/79/CE sobre productos sanitarios para diagnóstico *in vitro*)
(IT) - Marchiatura CE (Direttiva europea 98/79/CE relativa ai dispositivi medico-diagnostici *in vitro*)
(DE) - CE Konformitätskennzeichnung (Europäische Richtlinie 98/79/EG über *In-vitro*-Diagnostika)
(PT) - Marcação CE (Directiva europeia 98/79/CE relativa aos dispositivos médicos de diagnóstico *in vitro*)
(SE) - CE-märkning (Europeiskt direktiv 98/79/EG om medicintekniska produkter för *in vitro*-diagnostik)
(DK) - CE-mærkningen (Europa direktiv 98/79/EF om medicinsk udstyr til *in vitro*-diagnostik)
(GR) - Χαρακτηρισμος CE (ευρωπαικη οδηγια 98/79/CE περι *in vitro* διαγνωστικες ιατρικες συσκευες)
(PL) - CE oznaczenie (Dyrektywa unijna 98/79/CE dotycząca produktów medycznych do badań *in vitro*)
(LT) - CE ženklas (Europos sąjungos direktyva 98/79/CE dėl *in vitro* diagnostikos medicinos prietaisų)
(HU) - CE jelzés (98/79/CE Európai Irányelv az *in vitro* orvosi diagnosztikai eszközökről)
(EE) - CE märgistus (Euroopa direktiiv 98/79/CE *in vitro* diagnostikameditsiiniseadmete kohta)
(SK) - CE označenie o zhode (Európska direktíva 98/79/CE pre *in vitro* diagnostické zdravotnícke postupy)
(CZ) - CE značka (Evropská direktiva 98/79/CE o diagnostických zdravotnických prostředcích *in vitro*)
(NO) - CE-merking (EU-direktiv 98/79/CE om medisinsk utstyr til *in vitro*-diagnostikk)
(RO) - Marca CE (Directiva europeana 98/79/CE pentru dispozitive medicale de diagnostic *in vitro*)
(BG) - CE маркировка (Европейска директива 98/79/CE за *ин витро* диагностичните медицински изделия)

IVD

(GB) - For *in vitro* diagnostic use
(FR) - Pour diagnostic *in vitro*
(ES) - Para diagnóstico *in vitro*
(IT) - Per uso diagnostico *in vitro*
(DE) - *In-vitro*-Diagnostikum
(PT) - Para uso em diagnóstico *in vitro*
(SE) - *In vitro*-diagnostik
(DK) - *In vitro* diagnose
(GR) - Για *in vitro* διαγνωστικη χρηση
(PL) - Do stosowania *in vitro*
(LT) - *in vitro* diagnostikai
(HU) - Csak *in vitro* diagnosztikai alkalmazásra
(EE) - *In vitro* diagnostiliseks kasutamiseks
(SK) - Na diagnostiku *in vitro*
(CZ) - Pro diagnostiku *in vitro*
(NO) - Til *in vitro*-diagnostikk
(RO) - Pentru diagnostic *in vitro*
(BG) - За *ин витро* диагностика

REF

(GB) - Catalogue number
(FR) - Référence catalogue
(ES) - Número de catálogo
(IT) - Numero di catalogo
(DE) - Bestellnummer
(PT) - Número de catálogo
(SE) - Katalognummer
(DK) - Katalognummer
(GR) - Αριθμος καταλογου
(PL) - Numer katalogu
(LT) - Katalogo numeris
(HU) - Cikkszám
(EE) - Katalooginumber
(SK) - Katalógové číslo
(CZ) - Katalogové číslo
(NO) - Katalognummer
(RO) - Număr de catalog
(BG) - Каталожен номер

(GB) - Manufacturer
(FR) - Fabricant
(ES) - Fabricante
(IT) - Produttore
(DE) - Hersteller
(PT) - Fabricante
(SE) - Tillverkad av
(DK) - Fremstillet af
(GR) - Κατασκευαστης
(PL) - Producent
(LT) - Gamintojas
(HU) - Gyártó
(EE) - Tootja
(SK) - Výrobca
(CZ) - Výrobce
(NO) - Produsent
(RO) - Producător
(BG) - Производител

EC REP

(GB) - Authorised Representative
(FR) - Représentant agréé
(ES) - Representante autorizado
(IT) - Distributore autorizzato
(DE) - Bevollmächtigter
(PT) - Representante Autorizado
(SE) - Auktoriserad representant
(DK) - Autoriseret repræsentant
(GR) - Εξουσιοδοτημενος αντιπροσωπος
(PL) - Upoważniony Przedstawiciel
(LT) - Įgaliotasis atstovas
(HU) - Meghatalmazott Képviselő
(EE) - Volitatud esindaja
(SK) - Autorizovaný zástupca
(CZ) - Zplnomocněný zástupce
(NO) - Autorisert representant
(RO) - Reprezentant autorizat
(BG) - Упълномощен представител

LOT

(GB) - Batch code
(FR) - Code du lot
(ES) - Código de lote
(IT) - Codice del lotto
(DE) - Chargen-Bezeichnung
(PT) - Código do lote
(SE) - Batchnr
(DK) - Batchkoden
(GR) - Κωδικας παρτιδας
(PL) - Numer serii
(LT) - Serijos numeris
(HU) - Gyártási szám
(EE) - Partii kood
(SK) - Číslo šarže
(CZ) - Číslo šarže
(NO) - Partikode
(RO) - Număr de lot
(BG) - Партиден номер

(GB) - Expiry date YYYY/MM/DD
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(IT) - Da utilizzare prima del AAAA/MM/GG
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(CZ) - Datum exspirace RRRR/MM/DD
(NO) - Utløpsdato ÅÅÅÅ/MM/DD
(RO) - Data expirarii AAAA/LL/ZZ
(BG) - Срок на годност година/месец/ден

(GB) - Storage temperature limitation
(FR) - Limites de températures de stockage
(ES) - Temperatura límite
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(PT) - Limites de temperatura de armazenamento
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(GR) - Περιορισμος θερμοκρασιας αποθηκευσης
(PL) - Temperatura przechowywania
(LT) - Saugojimo temperatūriniai apribojimai
(HU) - Tárolási hőmérsékleti határok
(EE) - Piirangud säilitustemperatuurile
(SK) - Skladovacia teplota od do
(CZ) - Teplotní rozmezí od do
(NO) - Oppbevaringstemperatur
(RO) - Limitele de temperatură la stocare
(BG) - Температурни граници на съхранение

(GB) - Consult Instruction for use
(FR) - Consulter le mode d'emploi
(ES) - Consulte las instrucciones de uso
(IT) - Consultare le istruzioni per uso
(DE) - Siehe Gebrauchsanweisung
(PT) - Consulte o folheto informativo
(SE) - Se bruksanvisningen
(DK) - Se instruktion før brug
(GR) - Συμβουλευθειτε τις οδηγιες χρησης
(PL) - Sprawdź instrukcję
(LT) - Ieškokite informacijos vartojimo instrukcijoje
(HU) - Olvassa el a használati utasítást
(EE) - Kasutamisel vaata instruktsiooni
(SK) - Katalógové číslo
(CZ) - Viz návod k použití
(NO) - Se bruksanvisninger
(RO) - Consultati prospectul de utilizare
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(FR) • Ce produit contient des composants d'origine biologique humaine ou animale. Manipuler avec précaution.
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(DK) • Dette produkt indeholder humane og animalske komponenter. Skal behandles med forsigtighed.
(GR) • Αυτό το προϊόν περιέχει ανθρώπινα ή ζωικά στοιχεία. Χειριστείτε το με προσοχή.
(PL) • Niniejszy produkt zawiera składniki pochodzenia ludzkiego lub zwierzęcego. Należy obchodzić się z nim ostrożnie.
(LT) • Šiame produkte yra žmogiškosios arba gyvūninės kilmės sudėtinių dalių. Elgtis atsargiai.
(HU) • A készítmény emberi vagy állati eredetű összetevőket tartalmaz. Óvatosan kezelendő.
(EE) • Käesolev toode sisaldab inim-või loomseid komponente. Käsitseda ettevaatlikult.
(SK) • Tento výrobok obsahuje ľudské alebo zvieracie zložky. Narábajte s ním opatrne.
(CZ) • Tento výrobek obsahuje lidské nebo zvířecí komponenty. Zacházejte s ním opatrně.
(RO) • Acest produs conține materiale de origine umană sau animală. Manevrați-l cu grijă.
(BG) • Този продукт съдържа човешки или животински компоненти. Бъдете внимателни при работа с него.
(LV) • Šis produkts satur cilvēkiem vai dzīvniekiem paredzētas sastāvdaļas. Apieties uzmanīgi.
(MT) • Dan il-prodott fih komponenti umani jew tal-annimali. Uża b'attenzjoni.
(NL) • Dit product bevat menselijke of dierlijke bestanddelen. Breekbaar.
(SI) • Izdelek vsebuje človeške ali živalske sestavine. Rokujte previdno.
(FI) • Tässä tuotteessa on ihmisestä tai eläimistä peräisin olevia osia. Käsittele varovasti.

Bio-Rad
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CE 0459

03/2011
Code: 883602

GMED
GROUPE LNE

ATTESTATION / *CERTIFICATE* **N° 9150 rev. 10**
Délivrée à Paris le 15 mars 2019
Issued in Paris on March 15th, 2019

ATTESTATION CE / *EC CERTIFICATE*

Approbation du Système Complet d'Assurance Qualité / *Approval full Quality Assurance System*
Annexe IV excluant les points 4 et 6 Directive 98/79/CE relative aux dispositifs médicaux de diagnostic in vitro
Annex IV excluding sections 4 & 6 Directive 98/79/EC concerning in vitro diagnostic medical devices
Pour les dispositifs de la liste A IVD, un certificat CE de la conception est requis
For list A IVD devices, a EC design certificate is required

Fabricant / *Manufacturer*

BIO-RAD
3 boulevard Raymond Poincaré
92430 MARNES LA COQUETTE FRANCE

Catégorie du(des) dispositif(s) / *Device(s) category*

Dispositifs médicaux de diagnostic in vitro pour la détection,confirmation et quantification de marqueurs de l'infection VIH (VIH 1 et 2) et hépatites B et C.
Dispositifs médicaux de diagnostic in vitro pour la détection des infections humaines à rubéole, toxoplasmose et cytomégalovirus.
In vitro diagnostic medical devices for the detection, confirmation and quantification of markers of HIV infection (HIV 1 and 2) and hepatitis B and C.
In vitro diagnostic medical devices for the detection of human infections : rubella, toxoplasmosis and cytomegalovirus.

Voir détails sur addendum
See attachment for additional information

GMED atteste qu'à l'examen des résultats figurant dans le rapport référencé P182262-1, le système d'assurance qualité - pour la conception, la production et le contrôle final - des dispositifs médicaux énumérés ci-dessus est conforme aux exigences de l'annexe IV excluant les points 4 et 6 de la Directive 98/79/CE.

GMED certifies that, on the basis of the results contained in the file referenced P182262-1, the quality system - for design, manufacturing, and final inspection - of medical devices listed here aboved complies with the requirements of the Directive 98/79/EC, annex IV excluding sections 4 & 6.

La validité du présent certificat est soumise à une vérification périodique ou imprévue
The validity of the certificate is subject to periodic or unexpected verification

Début de validité / *Effective date :* **March 1st, 2019 (Included)**
Valable jusqu'au / *Expiry date :* **December 11th, 2021 (Included)**

GMED SAS GMED SAS GMED GROUPE LNE

On behalf of the President
Béatrice LYS
Technical Director

GMED_04-F-VD-07-2018

GMED 9150 rev. 10
Modifie le certificat 9150-9

Identification des dispositifs / *Identification of devices*

Annexe II liste A :
Dispositifs médicaux de diagnostic *in vitro* pour la détection, confirmation et quantification de marqueurs de l'infection VIH (VIH 1 et 2), et hépatites B et C.
Annexe II liste B :
Dispositifs médicaux de diagnostic *in vitro* pour la détection des infections humaines à rubéole, toxoplasmose et cytomégalovirus.
Annex II list A:
In vitro diagnostic devices for the detection, confirmation and quantification of markers of HIV infection (HIV 1 and 2), and hepatitis B and C.
Annex II list B:
In vitro diagnostic devices for the detection of human infections: rubella, toxoplasmosis and cytomegalovirus.

Réf commerciale du dispositif ou code article	Désignation du dispositif / Accessoires marqués CE	Division	Classe du DM annexe II liste A/B
71120	Genscreen™ HIV-1 Ag Assay	IDD	A
71121	Genscreen™ HIV-1 Ag Confirmatory Assay	IDD	A
72278	Genscreen™ HIV-1/2 Version 2 (96 tests)	IDD	A
72279	Genscreen™ HIV-1/2 Version 2 (480 tests)	IDD	A
72315	Monolisa™ Anti HBc PLUS (96 tests)	IDD	A
72316	Monolisa™ Anti HBc PLUS (480 tests)	IDD	A
72317	Monolisa™ Anti-HCV PLUS Version 2 (96 tests)	IDD	A
72318	Monolisa™ Anti-HCV PLUS Version 2 (480 tests)	IDD	A
72329	Geenius™ HIV 1/2 Confirmatory Controls	IDD	A
72460	Geenius™ HIV 1/2 Confirmatory Assay	IDD	A
72340	Monolisa™ Anti-HCV PLUS Version 3 (96 tests)	IDD	A

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72341	Monolisa™ Anti-HCV PLUS Version 3 (480 tests)	IDD	A
72346	Monolisa™ HBs Ag ULTRA (96 tests)	IDD	A
72348	Monolisa™ HBs Ag ULTRA (480 tests)	IDD	A
72386	Genscreen™ ULTRA HIV Ag-Ab (96 tests)	IDD	A
72388	Genscreen™ ULTRA HIV Ag-Ab (480 tests)	IDD	A
72396	Monolisa™ HBe Ag-Ab PLUS	IDD	A
72408	Monolisa™ HBs Ag ULTRA Confirmatory (25 tests)	IDD	A
72409	Monolisa™ HBs Ag ULTRA Confirmatory (50 tests)	IDD	A
72556	Monolisa™ HCV Ag-Ab ULTRA (96 tests)	IDD	A
72558	Monolisa™ HCV Ag-Ab ULTRA (480 tests)	IDD	A
72561	Monolisa™ HCV Ag-Ab ULTRA V2 (96 tests)	IDD	A
72562	Monolisa™ HCV Ag-Ab ULTRA V2 (480 tests)	IDD	A
72566	Monolisa™ Anti HBs PLUS	IDD	A
92501	Geenius™ HCV Supplemental Assay	IDD	A
92502	Geenius™ HCV Supplemental Controls	IDD	A
72680	PLATELIA™ CMV IgG	IDD	B
72681	PLATELIA™ CMV IgM	IDD	B
72724	PASTOREX™ TOXO	IDD	B
72810	Platelia™ CMV IgG	IDD	B
72811	Platelia™ CMV IgM	IDD	B

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72812	Platelia™ CMV IgG avidity	IDD	B
72840	Platelia™ Toxo IgG	IDD	B
72841	Platelia™ Toxo IgM	IDD	B
72842	Platelia™ Toxo IgG Avidity	IDD	B
72850	Platelia™ Rubella IgG	IDD	B
72851	Platelia™ Rubella IgM	IDD	B
A59428	Access® HIV combo	DVD	A
A59429	Access® HIV combo calibrators	DVD	A
A59430	Access® HIV combo QC	DVD	A
B22822	Access® HIV combo QC4 & QC5	DVD	A
B33458	Access® HCV Ab V3	DVD	A
B33459	Access® HCV Ab V3 Calibrators	DVD	A
B33460	Access® HCV Ab V3 QC	DVD	A

Ce certificat couvre les activités et les sites suivants :
This certificate covers the following activities and sites:

BIO-RAD - 3 Bd Raymond Poincaré - 92430 MARNES LA COQUETTE - FRANCE
Siège social – Responsable de la mise sur le marché - Conception
Headquarters – Legal manufacturer - Design

BIO-RAD - Route de Cassel - 59114 STEENVOORDE - FRANCE
Conception – Production – Contrôle final / *Design - Manufacturing – Final control*

2 sites / *2 locations*

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Technical Director