

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 packaged in 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 µL Microtubes 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 dual 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 specificity¹ (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

Geenius™ HIV 1/2 Confirmatory Assay

Σ 20 REF 72460

20 x 1 Device

1 x 5 ml Buffer

1 x 20 Microtube 15 µl

IVD CE 0459 +2°C +30°C 883601 - 2013/01

LOT 6A0023 1S6A0023171130

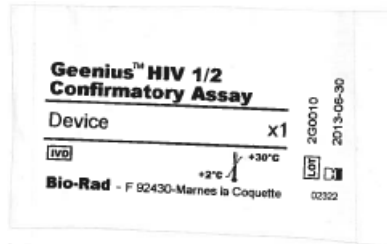
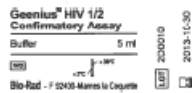
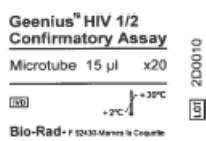
2017-11-30

Device	6A0023	Microtube 15 µl	5M0023
	2017-11-30		
Buffer	6B0024		
	2018-02-28		

(01)03610520014042
(17)171130
(10)6A0023

1324

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

Geenius™ HIV 1/2 Confirmatory Controls

REF 72329

1 x 120 µl Positive Control*

1 x 120 µl Negative Control*



**ProClin™ 300 (0.25%), NaN₃ (< 0.1%)*


883109 **IVD** **CE** 0459 +2°C +8°C 883600 - 2012/10 **0487**


H317
P280
P333 + P313
P302 + P352
P501


* PI reference XXXXXX YYYY/MM is a variable mention


Geenius™ HIV 1/2 Confirmatory Controls REF 72329

LOT 2B0010		(01)03610520013830
 2013-02-15		(17)130215
		(10)2B0010

Positive Control: LOT: 2B0010  2013-02-15


PC12B0010130215

Negative Control: LOT: 2B0010  2013-02-15




NC12B0010130215 0113



II - REAGENT LABELS


Positive Control

Geenius™ HIV 1/2 Confirmatory Controls

Positive Control 120 µl

862207  **LOT** 2B0010  +8°C



 2013-02-15  +2°C



Bio-Rad 0002 


Negative Control

Geenius™ HIV 1/2 Confirmatory Controls

Negative Control 120 µl

862207  **LOT** 2B0010  +8°C

 2013-02-15  +2°C

Bio-Rad 0002 

Geenius™ HIV 1/2 Confirmatory Assay

72460 - ▽ 20

REF 72460

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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



883601 - 2013/01



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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 worldwide, 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 colloidal 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

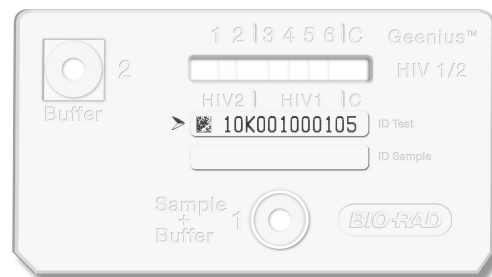
All components for the Geenius™ HIV 1/2 Confirmatory Assay are ready-to-use as supplied.

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

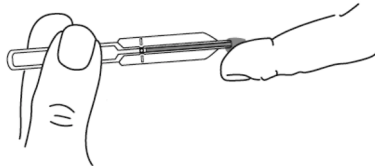
See specimen preparation on § 6.1 Specimen types.

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.



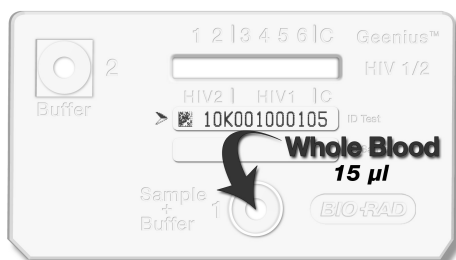
Step 2:

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.



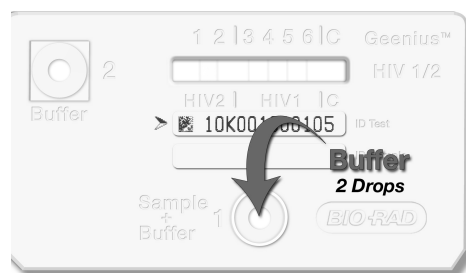
2. Dispense 15 µl of whole blood to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below). For venous whole blood use a laboratory pipette. For Fingerstick whole blood, follow the protocol using the Microtube 15 µl of the kit (see step 1 and 2 above).

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).

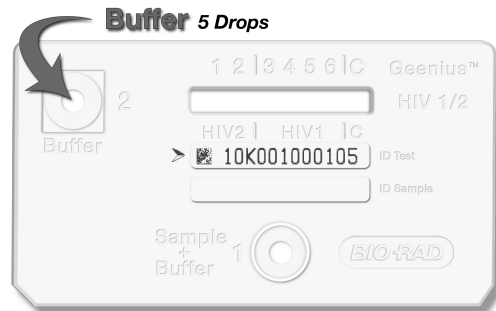
Figure 3



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.

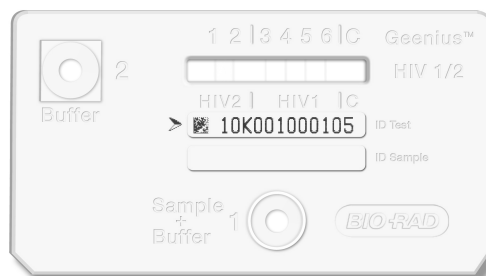
Serum or Plasma PROCEDURE

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.

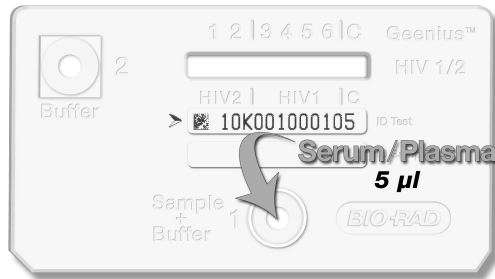
Label the test device with patient ID or identification number (see Figure 1 below). Note that the Geenius™ HIV 1/2 Confirmatory Assay device has six (6) blue coloured lines in the Test area (no blue line in Control area); If any of the 6 coloured lines are absent, DO NOT USE. Discard the test device and use a new test device.

Figure 1



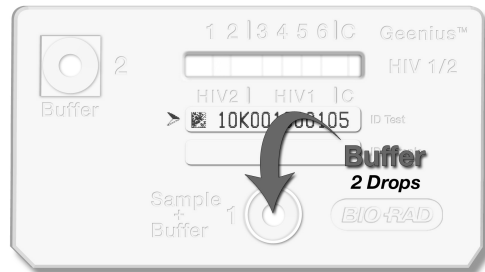
2. Using a laboratory pipette, dispense 5 µl of serum/plasma to the centre of the SAMPLE + BUFFER Well 1 of the device (see Figure 2 below).

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).

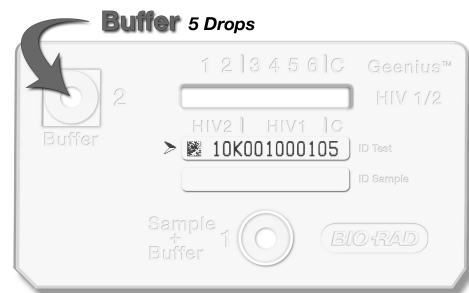
Figure 3



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
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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	/	/	100	/	100	/	100
		72	/	72	/	144	/	144
		30	30	30	/	90	/	90
		25	25	/	25	75	/	75
Site 5		/	/	/	/		20	20
Total	326	226	55	202	25	508	30	538
Negative		221	54	201	25	501	28	529
Indeterminate	/	5(*) (***)	1(*) (***)	1(*) (***)	0	7 (***)	2 (***)	9 (***)
Positive		0	0	0	0	0	0	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	/	/	100	100	/	200
	5	5	/	/	/	/	5
	50	/	50	/	/	/	50
Site 2 N= 108	82	82	/	82	82	/	246
	20	20	/	20	20	20	80
	6	6	/	6	/	6	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	5	/	5	2	3	15
	16	/	16	/	/	/	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 coinfecting (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 envelopes 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 Multiparous 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.

10. Bibliography references.

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- (SK)** • Tento výrobok obsahuje ľudské alebo zvieracie zložky. Narábajte s ním opatrne.

EUH 208: Contains Gentamycin. May produce an allergic reaction.



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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



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
Може да причини алергична кожна реакция. Използвайте предпазни ръкавици / предпазно облекло / предпазни очила / предпазна маска за лице • При поява на кожно дразнене или обрив на кожата: Потърсете медицински съвет / помощ • ПРИ КОНТАКТ С КОЖАТА: Измийте обилно със сапун и вода • Избягвайте съдържанието / контейнера в съответствие с местните / регионалните / националните / международните разпоредби.

(CZ)

Varování
Může vyvolat alergickou kožní reakci. Používejte ochranné rukavice / ochranný oděv / ochranné brýle / obličejový štít • Při podráždění kůže nebo vyrážce: Vyhledejte lékařskou pomoc / ošetření • PŘI STYKU S KŮŽÍ: Omyjte velkým množstvím vody a mýdla • Obsah / nádobu likvidujte v souladu s místními / regionálními / národními / mezinárodními předpisy.

(DE)

Achtung
Kann allergische Hautreaktionen verursachen. Schutzhandschuhe / Schutzkleidung / Augenschutz / Gesichtsschutz tragen • Bei Hautreizung oder -ausschlag: Ärztlichen Rat einholen / ärztliche Hilfe hinzuziehen • BEI KONTAKT MIT DER HAUT: Mit viel Wasser und Seife waschen • Entsorgung des Inhalts / des Behälters gemäß den örtlichen / regionalen / nationalen / internationalen Vorschriften.

(DK)

Advarsel
Kan forårsage allergisk hudreaktion. Bær beskyttelseshandsker / beskyttelsestøj / øjenbeskyttelse / ansigtsbeskyttelse • Ved hudirritation eller udslæt: 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: pöördu 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 aislen 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 suojäkäsineitä / suojavaateetusta / silmiensuojainta / kasvosuojainta • 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 / Επισκεφθείτε/απορρίψτε / Απορρίψτε τα περιεχόμενα / δοχεία σύμφωνα με τους τοπικούς / εθνικούς / διεθνείς κανονισμούς.

(HU)

Figyelem
Allergiás bőreakciók 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 • Smettere il prodotto / recipiente in conformità con le disposizioni locali / regionali / nazionali / internazionali.

(LT)

Atsargiai
Gali sukelti alerginę odos reakciją. Muvėti apsauginės pirštines / dėvėti apsauginius drabužius / naudoti akių (veido) apsaugos priemonės • 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 medicīnu palīdzību • SASKARĒ AR ĀDU: nomazgāt ar lielu ziepju un ūdens daudzumu • Izvest saturu / iepakojumu saskaņā ar vietējiem / reģionālajiem / nacionālajiem / starptautiskajiem noteikumiem.

(MT)

Twissija
Jista' jikkawża reazzjoni allergjika tal-ġilda. Ilbes ingwanti protettivi / ilbies protettiv / protezzjoni għall-ghajnejn / 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 PELLE: lavar com sabonete e água abundantes • Eliminar o conteúdo / recipiente de acordo com a legislação local / regional / nacional / internacional.

(RO)

Atentie
Poate provoca o reacție alergică a pielii. Purtați mănuși de protecție / îmbrăcămintă 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 • Vsebinsko / 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 vytvorí vyrážka: vyhľadajte lekársku pomoc / starostlivosť • PRI KONTAKTE S POKOŽKOU: Umyte veľkým množstvom vody a mydla • Zneškodnenie obsahu / obalu v súlade s miestnymi / oblasťmi / 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. Käsitseta 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 eläimestä 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 produkto yra žmogiškosios arba gyvūninės kilmės sudėtiniai daliai. 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. Manevrati-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.

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