

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 1/2 was 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 $\leq 4\%$ 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.
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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

BIO-RAD

Genie™ Fast HIV 1/2

REF 72327

1 x 25 Devices

1 x 5 ml Diluent

1 x 50 Pipettes

LOT 7A0023

2018-05-15

257A0023180515

Devices 650114 2018-05-17

Diluent 610031 2018-05-15

Pipettes 161118

IVD **CE** 0459 **+2°C** **+30°C** **www.bio-rad.com** 883676-2016/01

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92430 Marnes-la-Coquette - France
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II- REAGENT LABELS

Device

Genie™ Fast HIV 1/2

Device

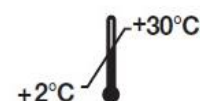
x1

IVD For In Vitro
Diagnostic Use

LOT



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



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

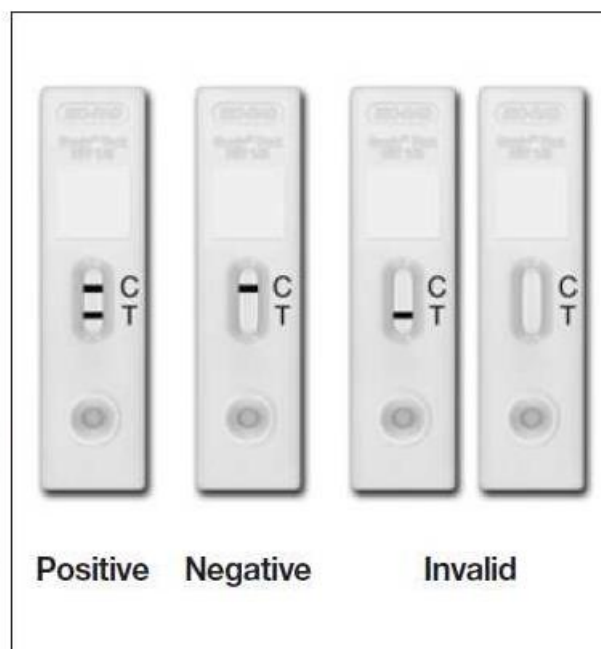
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

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**Genie™ Fast HIV 1/2**

Pipettes

x50For *In Vitro*
Diagnostic Use**LOT** XXXXXX**Bio-Rad**

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PRODUCT CODE 72330 (50 tests)**I - BOX LABELS**

BIO-RAD

Genie™ Fast HIV 1/2

REF 72330

1 x 50 Devices

1 x 5 ml Diluent

1 x 50 Pipettes

LOT 4H0022

2015-10-15

284H0022161015

Devices **140416**

2015-10-15

Diluent **4H0023**

2016-02-28

Pipettes **140416**

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IVD **CE** 0459 **+2°C** **+30°C** **www.bio-rad.com** 883676-2016/01

II - REAGENT LABELSDevice

Genie™ Fast HIV 1/2

Device

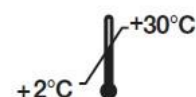
x1

IVD For In Vitro
Diagnostic Use

LOT



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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

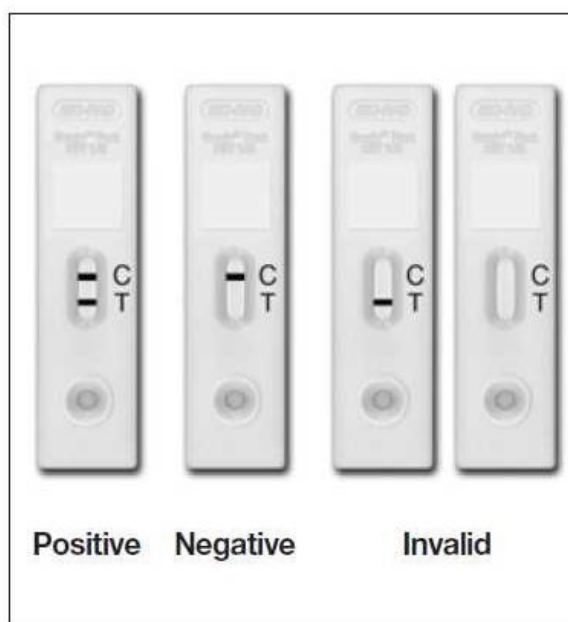
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

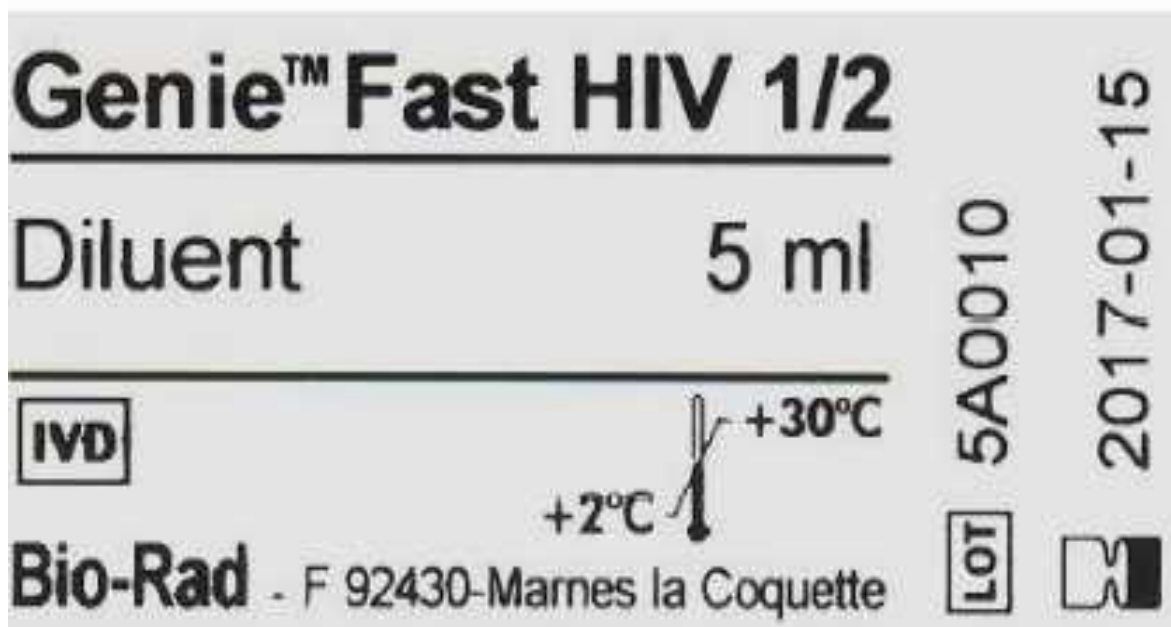
Finger stick protocol

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****Genie™ Fast HIV 1/2**

Pipettes

x50

IVD For *In Vitro*
Diagnostic Use

LOT XXXXXX

Bio-Rad

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

PRODUCT CODE 72347 (25 tests)**I - BOX LABELS****Genie™ Fast HIV 1/2**

▽ 25

REF 72347

 (01) 03610520037195
 (17) xxxxxx
 (10) xxxxxx

1 x 25	Devices	1 x 25	Microsafe 80 µl
1 x 5 ml	Diluent	1 x 25	Lancets
1 x 50	Pipettes	1 x 25	Alcohol swab

LOT

Devices

Lancets

Diluent

Alcohol swab

Pipettes

Microsafe 80 µl

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883107



CE 0459

+2°C

**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

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

Whole Blood protocol

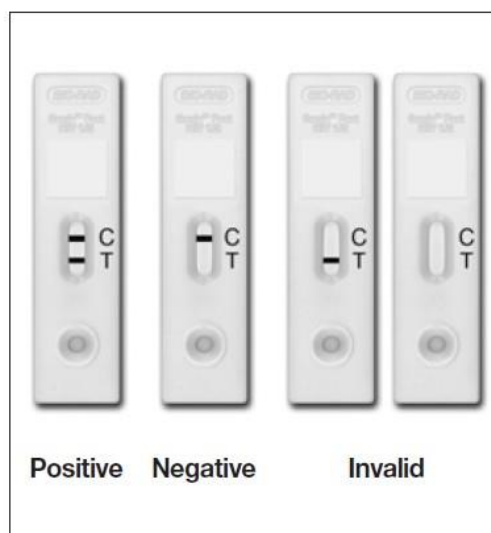
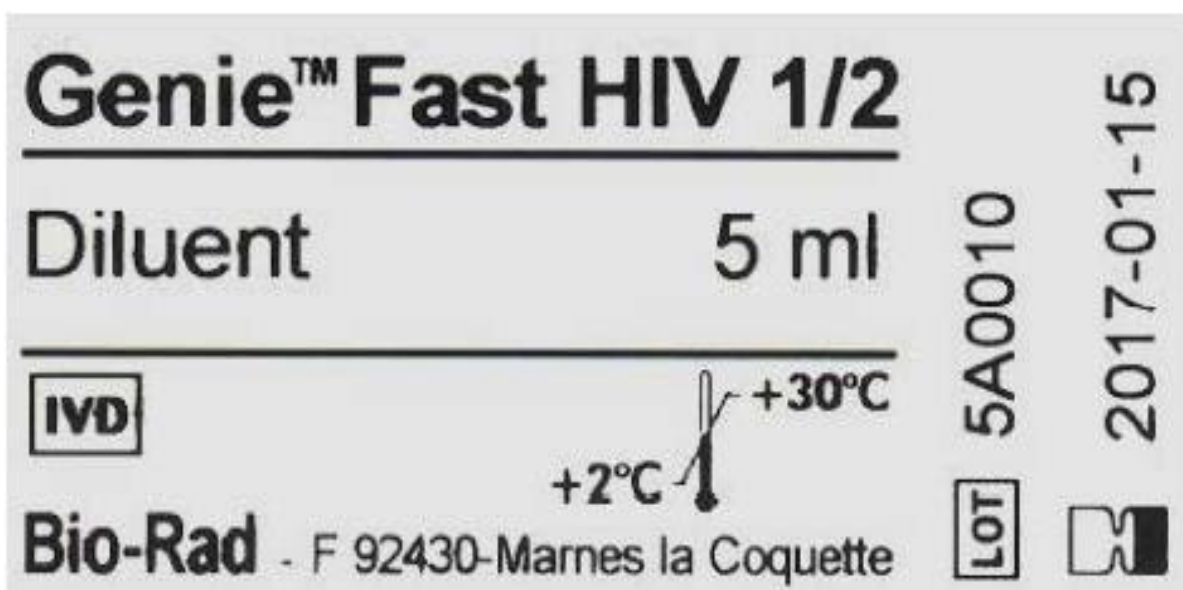
Add 80 µl or 2 drops of whole blood using the plastic pipette of the kit then immediately add 2 drops of diluent buffer (80 µl).

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**

Microsafe 80 µl

Microsafe 80 µl

x25**LOT** 2L0010 2014-12-30**IVD****CE**

SAFE - TEC Clinical Products,
142 Railroad Dr., Ivyland
PA 18974 - 1449 USA
www.safe-teclinc.com

EC **REP**

CE Partner4U BV
Esdoormiaan
13,3951 DB Maarn
The Netherlands

Genie™ Fast HIV 1/2

 50

 72330

 25

 72327

 25

 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



 0459



16004652 – 2017-10

BIO-RAD

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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.

- Dispense 80 µl



- Read results between 10 and 30 minutes



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.

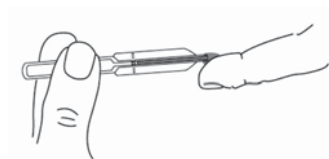
Follow the procedure below.

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.

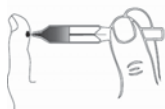
If a specimen doesn't expel, hold the capillary pipette vertically and slide a finger over the vent hole. Then align the tip with the circular deposit zone and squeeze the bulb.

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)	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.

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.

(***) Per-seroconversion 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 erythematosus; 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
Rheumatoid 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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