# WHO Prequalification of In Vitro Diagnostics
# PUBLIC REPORT

## Product: Genscreen ULTRA HIV Ag-Ab
## WHO reference number: PQDx 0096-031-00

Genscreen ULTRA HIV Ag-Ab with product codes 72386 and 72388, manufactured by Bio-Rad, CE-marked regulatory version, was accepted for the WHO list of prequalified diagnostics and was listed on 08 April 2013.

## Summary of prequalification status for Genscreen ULTRA HIV Ag-Ab

| | Date | Outcome |
|---|---|---|
| **Prequalification listing** | 08-Apr-2013 | listed |
| **Dossier assessment** | 28-Mar-2013 | MR |
| **Site inspection(s) of quality management system** | 02-Apr-013 | MR |
| **Product performance evaluation** | 21-Dec-2012 | MR |

MR: Meets Requirements

**Report amendments and/or product changes**

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

| Version | Summary of amendment | Date of report amendment |
|---|---|---|
| 2.0 | Improved product manufacturing in order to enhance the detection of unusual variants. | 07-Oct-2021 |

**Intended use**

According to the claim of intended use from Bio-Rad, "*the Genscreen ULTRA HIV Ag-Ab is a semi-quantitative enzyme immunoassay kit for the detection of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum or plasma. This kit can be used for both HIV Ag and HIV Ab screening of blood donations and as an aid in the diagnosis of HIV infection.*"

**Assay description**

According to the claim of assay description from Bio-Rad, "*the Genscreen ULTRA HIV Ag-Ab is a semi-quantitative enzyme immunoassay based on the principle of the sandwich technique for the detection of HIV-1 antigen and the various antibodies associated with HIV-1 and/or HIV-2 virus in human serum or plasma.*
*The solid phase is coated with:*

- *Monoclonal antibodies against p24 HIV-1 antigen*
- *Purified antigens: gp160 recombinant protein, a synthetic peptide mimicking a totally artificial (i.e. encoded by no existing virus) HIV-1 group O-specific epitope and a peptide mimicking the immunodominant epitope of the HIV-2 envelope protein.*

*The conjugates are based upon the use of:*

- *Biotinylated polyclonal antibodies against HIV-1 antigen (conjugate 1)*
- *Streptavidin and HIV antigens - peroxidase conjugate (gp41 and gp36 antigens mimicking the immunodominant epitopes of the HIV-1 and HIV-2 envelope glycoproteins, and one synthetic peptide mimicking a totally artificial HIV-1 group O-specific epitope) (conjugate 2).*

*The assay procedure includes the following reaction steps:*

1. *Conjugate 1 (biotinylated polyclonal antibodies to HIV-1 p24 antigen) is added into the microplate wells.*
2. *Specimens to be assayed and controls are pipetted into the wells.*
    - *If present, HIV antigens bind with the monoclonal antibody bound to the solid phase and the conjugate 1.*
    - *HIV-1 and/or HIV-2 antibodies, if any, bind to the antigens immobilised on the solid phase.*
    - *Deposition of conjugate 1 and specimen is validated through a colour change, from yellow-green to blue.*
3. *After incubation at 37°C then washing, conjugate 2 is added:*
    - *Streptavidin reacts with biotinylated Ab-Ag-Ab complexes.*
    - *Peroxidase labelled, HIV-1 and HIV-2 antigens bind to the IgG, IgM or IgA antibodies captured on the solid phase.*

4. *After incubation at 18-30°C the unbound conjugate 2 fraction is removed by washing. Then substrate is added. After incubation at room temperature (18-30°C) the presence of the complexed conjugate is shown by a change of colour.*
5. *The reaction is stopped and Optical Density is read using a spectrophotometer at 450/620-700 nm. The Optical Density measured on a specimen determines the presence or absence of HIV Ag or HIV-1 and/or HIV-2 antibodies."*

**Test kit contents**

| Component | | 96 tests (product code 72386) | 480 tests (product code 72388) |
|---|---|---|---|
| **Identification on label** | **Description** | | |
| **R1** | **Microplate**<br>12 strips of 8 wells coated with monoclonal antibodies to HIV-1 p24 antigen (mouse) and purified HIV-1 and HIV-2 antigens<br>Specific ID number = 53 | 1 plate | 5 plates |
| **R2** | **Concentrated washing solution (20X)**<br>Tris NaCl buffer pH 7.4<br>Preservative: ProClin 300 - 0.04% | 1 x 70 mL | 1 x 235 mL |
| **R3** | **Negative control**<br>Heat inactivated human plasma negative for HBs antigen, HIV antigen, anti-HIV-1, anti-HIV-2 and anti-HCV antibodies, in synthetic diluent<br>Preservative: Sodium azide < 0.1% | 1 x 2.5 mL | 1 x 2.5 mL |
| **R4** | **HIV Ab positive control**<br>Heat inactivated human plasma positive for anti-HIV antibodies, negative for HBs antigen and anti-HCV antibodies, in synthetic diluent<br>Preservative: ProClin 300 < 0.1%. | 1 x 1 mL | 1 x 1 mL |
| **R5** | H**IV Ag positive control**<br>Purified HIV-1 antigen inactivated with a chaotropic agent, in synthetic diluent Preservative: ProClin 300 < 0.1 %. | 1 x 1 mL | 1 x 1 mL |
| **R6** | **Conjugate 1** | 1 x 10 mL | 2 x 10 mL |

| | | | |
|---|---|---|---|
| | Biotinylated polyclonal antibodies to HIV-1 p24 antigen(sheep) coloured yellow – green<br>Preservative: ProClin 300 - 0.5%. | | |
| **R7a** | **Conjugate 2**<br>Lyophilised peroxidase labelled Streptavidin and purified HIV-1 and HIV-2 antigens<br>Preservative: ProClin 300 < 0.1% | 1 x 12.5 mL *q.s.ad* | 2 x 30 mL *q.s.ad* |
| **R7b** | **Conjugate 2 diluent**<br>Skimmed milk solution coloured red<br>Preservative: ProClin 300 - 0.5% | 1 x 12.5 mL | 2 x 30 mL |
| **R8** | **Substrate buffer**<br>Citric acid and sodium acetate solution pH 4.0, containing H2O2 (0.015%) and dimethyl sulfoxide DMSO (4%) | 1 x 60 mL | 2 x 60 mL |
| **R9** | **Chromogen: TMB solution (11X)**<br>Solution containing 3.3' , 5.5' tetramethylbenzidine (TMB) | 1 x 5 mL | 2 x 5 mL |
| **R10** | **Stopping solution**<br>Sulphuric acid solution (H2SO4 1N) | 1 x 28 mL | 3 x 28 mL |

**Storage:**

The test kit should be stored at 2 - 8 °C.

**Conservation:**

**R1:** After opening the vacuum-sealed bag, store the microwell strips at +2-8°C for up to 30 days, in their original bag with desiccant resealed with tape

**R2:** The diluted washing solution can be stored at +2-30°C for 2 weeks. The concentrated washing solution (R2) can be stored at +2-30°C until the expiration date, even once opened.
**R7a + R7b:** After reconstitution, the reagents can be stored at +2-8°C for 30 days, or frozen until the expiry date of the kit. Once frozen it can be thawed up to 11 times.
**R8 + R9:** After reconstitution, the reagents stored in the dark can be used for 6 hours at room temperature (18-30°C).

**Shelf-life:**
18 months.

**Warnings/limitations:**

Please refer to the IFU.

**Prioritization for prequalification:**

Bio-Rad submitted an application for prequalification of Genscreen ULTRA HIV Ag-Ab. Based on the established prioritization criteria, Genscreen ULTRA HIV Ag-Ab was given priority for prequalification assessment.

## Dossier assessment

Bio-Rad submitted a product dossier for Genscreen ULTRA HIV Ag-Ab 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 Genscreen ULTRA HIV Ag-Ab for prequalification.

**Commitments for prequalification:**

The manufacturer committed to amend and submit additional documentation on the following issues:

1. In-use stability studies. This issue was fulfilled, issue closed.
2. New version of labelling that is complaint with the new European regulation (IVDR 2017/746) will be launched once the certification is obtained.

## Manufacturing site inspection

An inspection (17-19 June 2014) was performed at two of the sites of the legal manufacturer, Bio-Rad, located at Route de Cassel 59114 Steenvoorde (two days) and at 3, bd Raymond Poincare 92430 Marnes La Coquette (one day). The inspection covered four products, including the Genscreen ULTRA HIV Ag-Ab test and was performed as per 'Information for manufacturers on WHO prequalification inspection procedures for the sites of manufacture of diagnostics.' (PQDx_014 v1).

The inspection was based on 'ISO 13485:2003 Medical devices - Quality management systems - Requirements for regulatory purposes' and other internationally recognized standards relevant to the manufacture of in vitro diagnostics. In addition, the claims made in the submitted product dossier were verified and the adequacy of mechanisms for lot release of the product to customers was audited. With consideration that the product should be suitable for use in resource limited settings, particular attention was paid to suitability of product labelling currently in use (including instructions for use and storage requirements), stability testing (in-use, transportation and storage stability), and effective mechanisms for customer training, service and feedback.

The inspection found that the legal manufacturer had an acceptable quality management system and good manufacturing practices that ensured the consistent manufacture of a product of good quality. The manufacturer's final responses to the nonconformities found at the time of the inspection were accepted 12 October 2016.

**Commitments for prequalification:**

1. The manufacturer has committed to addressing nonconformities found at the WHO inspection, including updating real time stability studies. Commitment was fulfilled, issued closed.
2. The manufacturer has committed to an acceptable timeline for updating the risk analysis and risk management and has announced the appointment of a Risk Analysis Specialist to the Bio-Rad team. Commitment was fulfilled, issue closed.
3. The manufacturer has committed to the revision of the Instructions for Use that will consider the WHO remarks regarding suitability for end users in resource limited settings. Commitment was fulfilled, issued closed.

## Product performance evaluation

Genscreen ULTRA HIV Ag-Ab (Bio-Rad) is an enzyme immunoassay for the combined detection of HIV-1/2 antibodies and HIV-1 p24 antigen in human serum and plasma. A volume of 75 µl of specimen is needed to perform the assay. This type of assay requires laboratory equipment and cannot be performed in laboratories with limited facilities. Reading of the results must be performed with a spectrophotometer.

In this limited performance evaluation on a panel of 1120 specimens, we found an initial sensitivity (95% CI) of 100% (99.2% - 100%) and an initial specificity (95% CI) of 99.09% (98.0% - 99.7%) compared to the reference results. The final sensitivity (95% CI) was 100% (99.2% - 100%) and the final specificity (95% CI) was 99.24% (98.2% - 99.8%) compared to the reference results. Lot to lot variation observed was within the acceptance range.

For eight seroconversion panels, Genscreen ULTRA HIV Ag-Ab detected on average 1.375 specimens earlier than the benchmark assay (Enzygnost Anti-HIV 1/2 Plus [Siemens

Healthcare Diagnostics] EIA) and on average 0.750 specimens earlier than Vironostika HIV Ag/Ab (bioMérieux) EIA.

For the mixed titer panel, Genscreen ULTRA HIV Ag-Ab classified one specimen as false positive, all other specimens were correctly identified. For the HIV-1 p24 antigen panel, Genscreen ULTRA HIV Ag-Ab correctly classified all specimens. For the HIV culture supernatant panel, Genscreen ULTRA HIV Ag-Ab detected all HIV-1 subtypes, the HIV-2 culture isolate was also detected.

For the 1st International Reference Panel for anti-HIV [NIBSC code 02/210], Genscreen ULTRA HIV Ag-Ab detected all subtypes tested (HIV-1 A, HIV-1 B, HIV-C, HIV-1 CRF01_AE, HIV-1 O and HIV-2). For the HIV-1 p24 antigen standard [NIBSC code 90/636], Genscreen ULTRA HIV Ag-Ab detected to 0.78 international units). In contrast, Vironostika HIV Ag/Ab (bioMérieux) detected to 12.5 international units.

In this study, 0.18% of the results were recorded as indeterminate. The invalid rate was 0%.

# Labelling

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

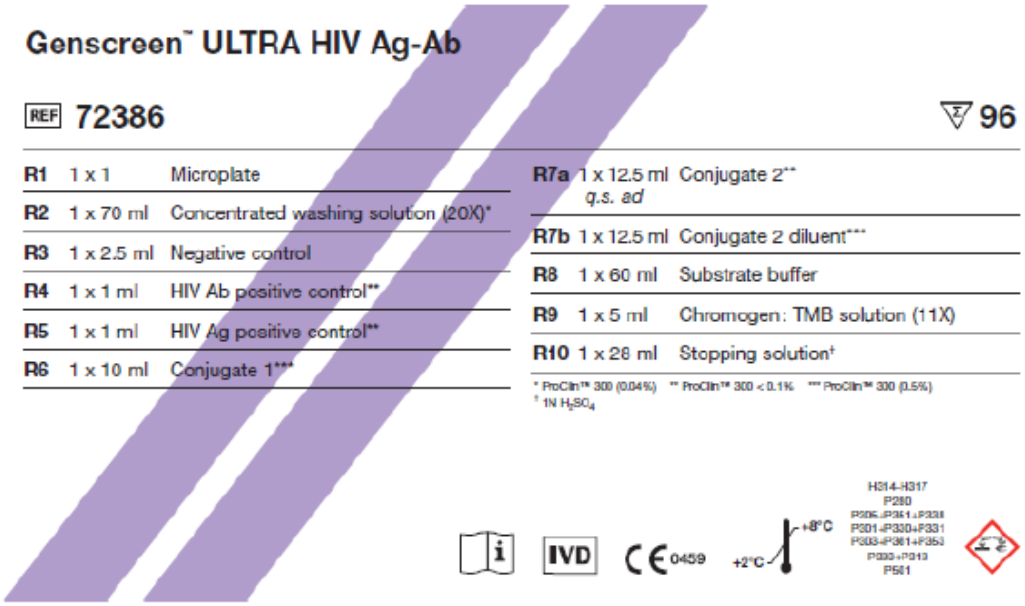
# 1. Labels

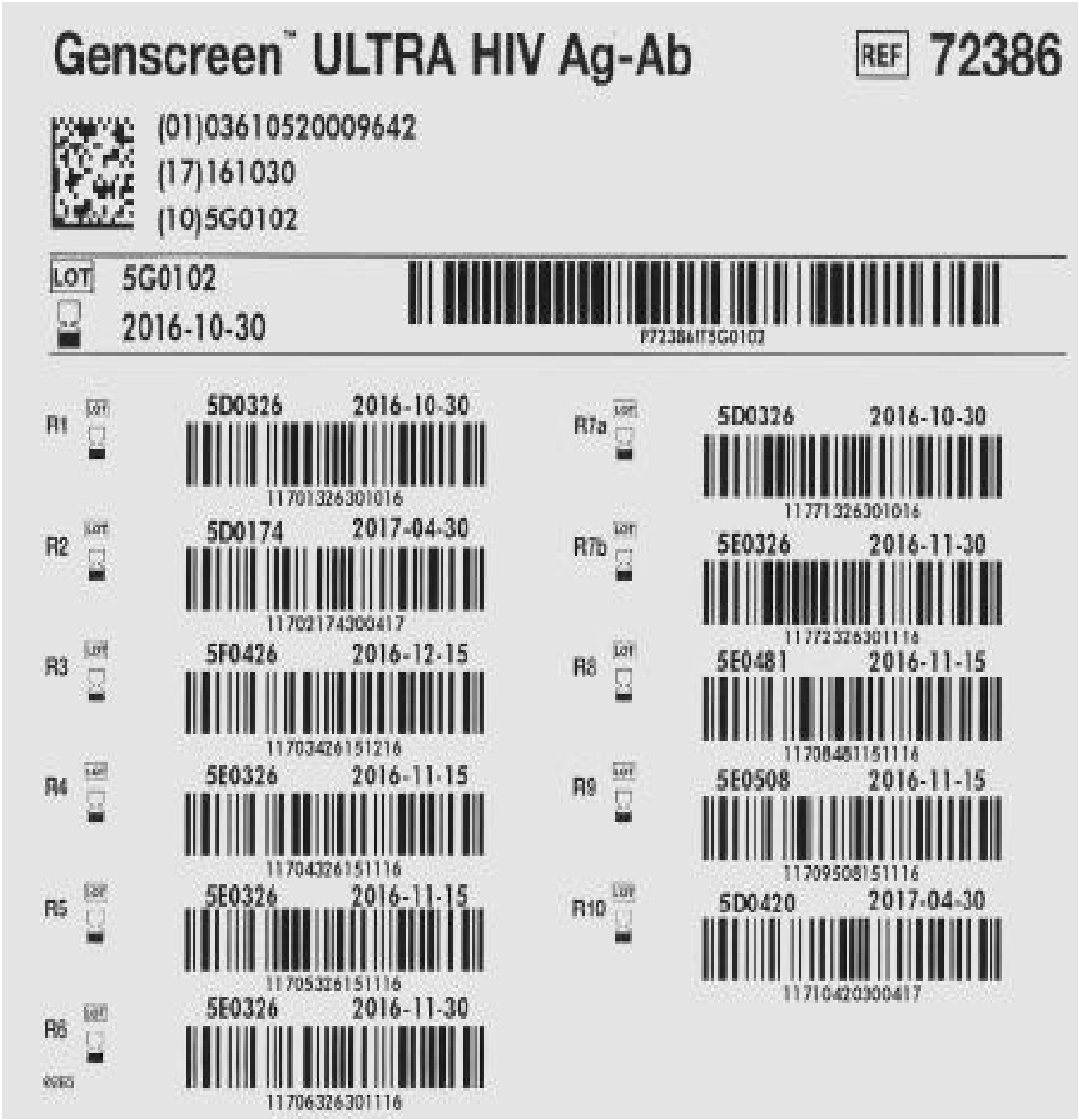
## 1.1. Product code 72386:

## 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




Genscreen™ ULTRA HIV Ag-Ab
REF 72386
(01)03610520009642
(17)161030
(10)5G0102
LOT 5G0102
2016-10-30
F72386IT5G0102
R1 5D0326 2016-10-30
11701326301016
R2 5D0174 2017-04-30
11702174300417
R3 5F0426 2016-12-15
11703426151216
R4 5E0326 2016-11-15
11704326151116
R5 5E0326 2016-11-15
11705326151116
R6 5E0326 2016-11-30
11706326301116
R7a 5D0326 2016-10-30
11771326301016
R7b 5E0326 2016-11-30
11772326301116
R8 5E0481 2016-11-15
11708481151116
R9 5E0508 2016-11-15
11709508151116
R10 5D0420 2017-04-30
11710420300417

**Component labels**



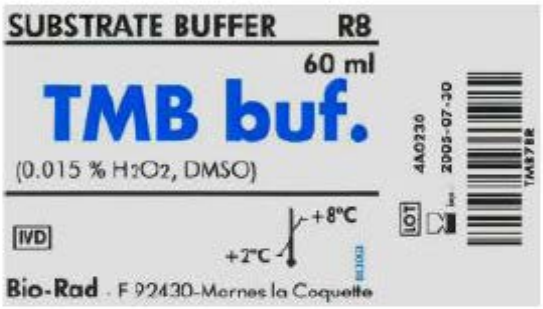


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 1 10 ml
R6
IVD
+8°C
+2°C
LOT
883118
Bio-Rad - F 92430-Marnes la Coquette
4A0277
2015-07-30
11706277300715


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 2 12.5 ml
q.s. ad
R7a
IVD
+8°C
+2°C
LOT
883116
Bio-Rad - F 92430-Marnes la Coquette
4A0277
2015-07-30
11771277300715


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 2 diluent 12.5 ml
R7b
IVD
+8°C
+2°C
LOT
883118
Bio-Rad - F 92430-Marnes la Coquette
4A0277
2015-07-30
11772277300715


CONCENTRATED
WASHING SOLUTION R2
20X
70 ml
(20x)
3C0010
2014-09-30
IVD
+2°C
+30°C
Bio-Rad - F 92430-Marnes la Coquette


SUBSTRATE BUFFER R8
60 ml
TMB buf.
(0.015 % H2O2, DMSO)
4A0230
2005-07-30
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette

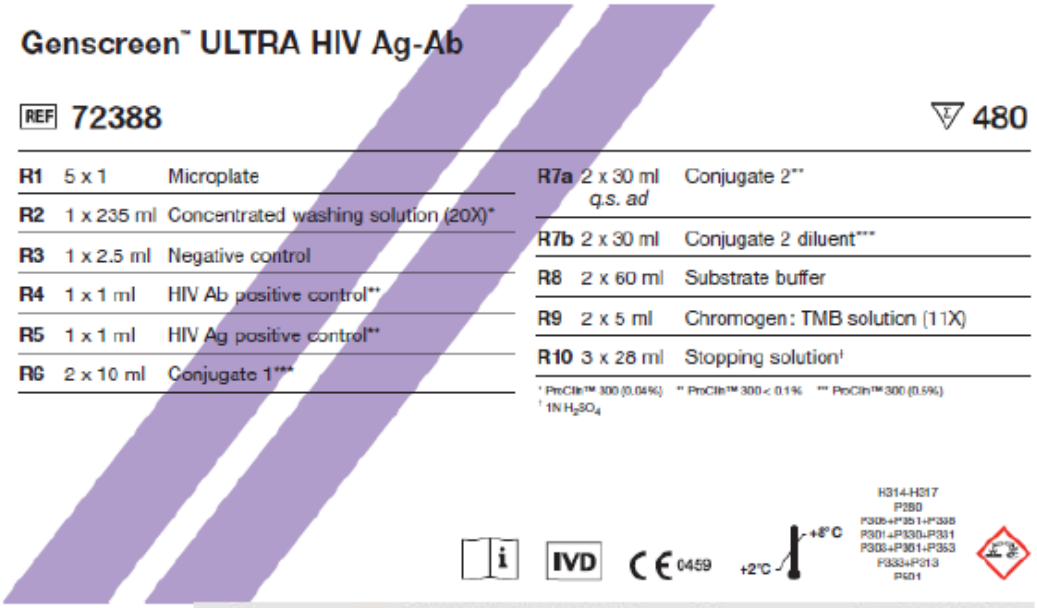

CHROMOGEN : TMB SOLUTION R9
TMB 11X
5 ml
8D0010
2009-10-15
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette


STOPPING SOLUTION R10
1N
(H2SO4 1N)
28 ml
2B0023
2002-09-19
IVD
+2°C
+8°C
Bio-Rad - F 92430-Marnes la Coquette

## 1.2. Product code 72388:

**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



**Genscreen™ ULTRA HIV Ag-Ab**

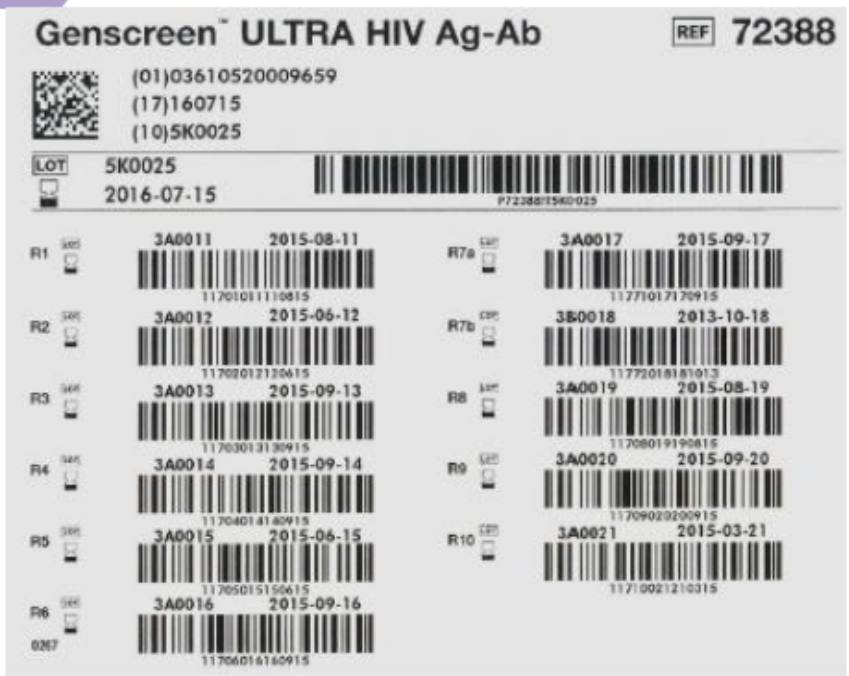
REF **72388** Σ **480**

| | | |
|---|---|---|
| **R1** | 5 x 1 | Microplate |
| **R2** | 1 x 235 ml | Concentrated washing solution (20X)* |
| **R3** | 1 x 2.5 ml | Negative control |
| **R4** | 1 x 1 ml | HIV Ab positive control** |
| **R5** | 1 x 1 ml | HIV Ag positive control** |
| **R6** | 2 x 10 ml | Conjugate 1*** |
| **R7a** | 2 x 30 ml *q.s. ad* | Conjugate 2** |
| **R7b** | 2 x 30 ml | Conjugate 2 diluent*** |
| **R8** | 2 x 60 ml | Substrate buffer |
| **R9** | 2 x 5 ml | Chromogen: TMB solution (11X) |
| **R10** | 3 x 28 ml | Stopping solution† |

* ProClin™ 300 (0.04%) ** ProClin™ 300 < 0.1% *** ProClin™ 300 (0.5%)
† 1N $H_2SO_4$

IVD CE 0459 +2°C +8°C

H314-H317
P280
P305+P351+P338
P301+P330+P331
P308+P361+P353
P333+P313
P501



**Genscreen™ ULTRA HIV Ag-Ab** REF **72388**

(01)03610520009659
(17)160715
(10)5K0025

LOT 5K0025
2016-07-15

| | | | | | |
|---|---|---|---|---|---|
| R1 | 3A0011 | 2015-08-11 | R7a | 3A0017 | 2015-09-17 |
| R2 | 3A0012 | 2015-06-12 | R7b | 3B0018 | 2013-10-18 |
| R3 | 3A0013 | 2015-09-13 | R8 | 3A0019 | 2015-08-19 |
| R4 | 3A0014 | 2015-09-14 | R9 | 3A0020 | 2015-09-20 |
| R5 | 3A0015 | 2015-06-15 | R10 | 3A0021 | 2015-03-21 |
| R6 | 3A0016 | 2015-09-16 | | | |

0267

**Component labels**

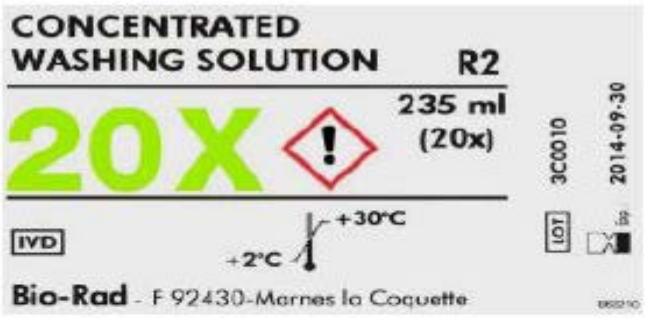


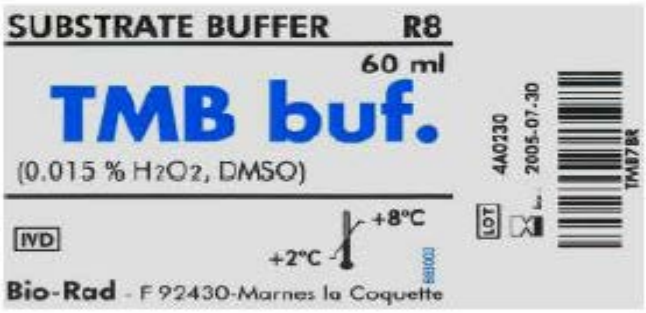

Genscreen™ ULTRA
HIV Ag-Ab
HIV Ag positive control 1 ml
R5
IVD
+2°C
+8°C
LOT
4B0233
2016-02-28
Bio-Rad - F 92430-Marnes la Coquette


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 1 10 ml
R6
IVD
+2°C
+8°C
LOT
4A0277
2015-07-30
Bio-Rad - F 92430-Marnes la Coquette


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 2 30 ml
R7a
IVD
+2°C
+8°C
LOT
4A0277
2015-07-30
Bio-Rad - F 92430-Marnes la Coquette


Genscreen™ ULTRA
HIV Ag-Ab
Conjugate 2 diluent 30 ml
R7b
IVD
+2°C
+8°C
LOT
4A0277
2015-07-30
Bio-Rad - F 92430-Marnes la Coquette


CONCENTRATED
WASHING SOLUTION R2
20X
235 ml
(20x)
3C0010
2014-09-30
IVD
+30°C
+2°C
LOT
Bio-Rad - F 92430-Marnes la Coquette


SUBSTRATE BUFFER R8
60 ml
TMB buf.
(0.015 % H2O2, DMSO)
4A0230
2005-07-30
TMB7BR
IVD
+8°C
+2°C
LOT
Bio-Rad - F 92430-Marnes la Coquette


CHROMOGEN : TMB SOLUTION R9
TMB 11X
5 ml
8D0010
2009-10-15
IVD
+8°C
+2°C
LOT
Bio-Rad - F 92430-Marnes la Coquette
862213


STOPPING SOLUTION R10
1N
28 ml
(H2SO4 1N)
2B0023
2002-09-19
STP1BR
IVD
+8°C
+2°C
LOT
Bio-Rad - F 92430-Marnes la Coquette
862211

## 2. Instructions for use[1]

[1] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

# Genscreen™ ULTRA HIV Ag-Ab

1 plate - Σ 96 REF 72386

5 plates - Σ 480 REF 72388

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SCREENING KIT FOR THE DETECTION OF HIV P24 ANTIGEN
AND ANTIBODIES TO HIV-1 AND HIV-2 IN HUMAN SERUM/PLASMA
BY ENZYME IMMUNOASSAY

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IVD CE 0459

883637 - 2013/10

BIO-RAD

CONTENTS

## 1. INTENDED USE

The Genscreen™ ULTRA HIV Ag-Ab is a qualitative enzyme immunoassay kit for the detection of HIV p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum or plasma. This kit can be used for both HIV Ag and HIV Ab screening of blood donations and for diagnostic use.

## 2. SUMMARY AND EXPLANATION OF THE TEST

The acquired immunodeficiency syndrome (AIDS) is a virus inducing infectious disease characterised by strongly depressed immunity.

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

Knowledge on genetic variability of the HIV virus strains was acquired by sequencing the GAG, POL, and ENV genes of the representative strains of each subtype. The HIV-1 viruses are divided into 2 groups: the M group, including 9 sub-types (A to I) and the O group. The HIV-2 virus includes 5 sub-types. The geographical distribution of the different sub-types is now quite well defined. Some HIV-1 variants have only 70% homology for the GAG and POL genes with the main isolates and only 50% for the ENV gene; these differences can explain the failure of the diagnosis of infection in some patients.

The various HIV-2 isolates share common antigens with the SIV simian virus in all proteins (envelope proteins and core proteins: heterology = 30%), but exhibit less than 40% homology with the HIV-1 envelope proteins.

HIV antigens and antibodies appear and are detectable at different stages of the seroconversion and of the infection. The Genscreen™ ULTRA HIV Ag-Ab allows the simultaneous detection of anti-HIV-1 (M and O groups) and anti-HIV-2 antibodies and antigens (see also limitation of the procedure).

## 3. PRINCIPLES OF THE PROCEDURE

The Genscreen™ ULTRA HIV Ag-Ab is a qualitative enzyme immunoassay based on the principle of the sandwich technique for the detection of HIV antigen and of the various antibodies associated with HIV-1 and/or HIV-2 virus in human serum or plasma.

The solid phase is coated with:

- Monoclonal antibodies against p24 HIV-1 antigen
- Purified antigens: gp160 recombinant protein, a synthetic peptide mimicking a totally artificial (i.e. encoded by no existing virus) HIV-1 group O-specific epitope and a peptide mimicking the immunodominant epitope of the HIV-2 envelope protein.

The conjugates are based upon the use of:

- Biotinylated polyclonal antibodies to HIV Ag (conjugate 1)
- Streptavidin and HIV antigens - peroxidase conjugate (gp41 and gp36 peptides mimicking the immunodominant epitopes of the HIV-1 and HIV-2 envelope glycoproteins, and the same synthetic peptide mimicking a totally artificial HIV-1 group O-specific epitope used for the solid phase) (conjugate 2).

The assay procedure includes the following reaction steps:

1. Conjugate 1 (biotinylated polyclonal antibody to p24 HIV-1 Ag) is added into the microplate wells.
2. Serum samples to be assayed and controls are pipetted into the wells.
   - If present, HIV antigens bind with the monoclonal antibody bound to the solid phase and the conjugate 1.
   - HIV-1 and/or HIV-2 antibodies, if any, bind to the antigens immobilised on the solid phase.
   - Deposition of conjugate 1 and sample is validated through a colour change, from yellow-green to blue.
3. After incubation at 37°C then washing, conjugate 2 is added:
   - Streptavidin reacts with biotinylated Ab-Ag-Ab complexes
   - Peroxidase labelled, purified HIV-1 and HIV-2 antigens bind in turn to the IgG, IgM or IgA antibodies captured on the solid phase.
4. After incubation at 18-30°C the unbound conjugate 2 fraction is removed by washing. After incubation in presence of the substrate at room temperature (18-30°C) the presence of the complexed conjugate is shown by a change of colour.
5. The reaction is stopped and absorbances are read using a spectrophotometer at 450/620-700 nm. The absorbance measured on a sample determines the presence or absence of HIV Ag or HIV-1 and/or HIV-2 antibodies.

## 4. REAGENTS

### 4.1. Description

| Identification on label | | Description | Presentation/Preparation 72386 | 72388 |
|---|---|---|---|---|
| **R1** | **Microplate** | **Microplate**<br>12 strips of 8 wells coated with monoclonal antibodies to p24 HIV-1 (mouse) and purified HIV-1 and HIV-2 antigens<br>*Specific ID number = 53* | 1 plate<br>Ready to use | 5 plates<br>Ready to use |
| **R2** | **Concentrated washing solution (20X)** | **Concentrated washing solution (20X)**<br>Tris NaCl Buffer ph 7.4<br>Preservative: Proclin™ 300 (0.04%) | 1 vial<br>70 ml<br>To be diluted | 1 vial<br>235 ml<br>To be diluted |
| **R3** | **Negative control** | **Negative control**<br>Heat inactivated human plasma negative for HBs antigen, HIV antigen, anti-HIV-1, anti-HIV-2 and anti-HCV antibodies<br>Preservative: Sodium azide < 0.1% | 1 vial<br>2.5 ml<br>Ready to use | 1 vial<br>2.5 ml<br>Ready to use |
| **R4** | **HIV Ab positive control** | **Positive control (human)**<br>Heat inactivated human plasma positive for anti-HIV-1 antibodies, negative for HIV and HBs antigens and anti-HCV antibodies, in synthetic diluent<br>Preservative: ProClin™ 300 < 0.1% | 1 vial<br>1 ml<br>Ready to use | 1 vial<br>1 ml<br>Ready to use |
| **R5** | **HIV Ag positive control** | **HIV Ag positive control**<br>Purified HIV 1 antigen inactivated with a chaotropic agent, in synthetic diluent<br>Preservative: ProClin™ 300 < 0.1 % | 1 vial<br>1 ml<br>Ready to use | 1 vial<br>1 ml<br>Ready to use |
| **R6** | **Conjugate 1** | **Conjugate 1**<br>Biotinylated polyclonal antibodies to p24 HIV 1 (sheep) coloured yellow – green<br>Preservative: ProClin™ 300 (0.5%) | 1 vial<br>10 ml<br>Ready to use | 2 vials<br>2 x 10 ml<br>Ready to use |
| **R7a** | **Conjugate 2** | **Conjugate 2**<br>Lyophilised peroxidase labelled Streptavidin and purified HIV 1 and HIV 2 antigens<br>Preservative: ProClin™ 300 < 0.1 % | 1 vial<br>*q.s. ad*<br>12.5 ml<br>To be reconstituted | 2 vials<br>*q.s. ad*<br>2 x 30 ml<br>To be reconstituted |
| **R7b** | **Conjugate 2 diluent** | **Conjugate 2 diluent**<br>Skimmed milk solution coloured red<br>Preservative: ProClin™ 300 (0.5%) | 1 vial<br>12.5 ml<br>To be reconstituted | 2 vials<br>2 x 30 ml<br>To be reconstituted |
| **R8** | **Substrate buffer** | **Substrate buffer**<br>Citric acid and sodium acetate solution pH 4.0, containing $H_2O_2$ (0.015%) and dimethyl sulfoxide DMSO (4%) | 1 vial<br>60 ml<br>To be reconstituted | 2 vials<br>2 x 60 ml<br>To be reconstituted |
| **R9** | **Chromogen: TMB solution (11X)** | **Chromogen: TMB solution**<br>Solution containing 3.3' , 5.5' tetramethylbenzidine (TMB) | 1 vial<br>5 ml<br>To be reconstituted | 2 vials<br>2 x 5 ml<br>To be reconstituted |
| **R10** | **Stopping solution** | **Stopping solution**<br>Sulphuric acid solution ($H_2SO_4$ 1N) | 1 vial<br>28 ml<br>Ready to use | 3 vials<br>3 x 28 ml<br>Ready to use |

### 4.2. Storage and handling requirements

This kit should be stored at +2-8°C. Each item of the kit preserved at +2-8°C can be used up to the expiry date mentioned on the package (unless otherwise indicated).
After opening and in the absence of contamination, the R2, R3, R4, R6, R7, R8, R9 and R10 reagents preserved at +2-8°C can be used up to the expiry date shown on the label.

| Identification | Preservation |
|---|---|
| R1 | After opening the vacuum-sealed bag, the microwell strips stored at +2-8°C can be used for 1 month in their carefully resealed original bag. |
| R2 | The diluted washing solution can be stored at +2-30°C for 2 weeks. The concentrated washing solution (R2) can be stored at +2-30°C. |
| R7a + R7b | After reconstitution, the reagents can be stored at +2-8°C for 1 month.<br>After the frozen reconstitution, until the expiry date of the kit, it can be frozen then thawed up to 11 times. |
| R8 + R9 | After reconstitution, the reagents stored in the dark can be used for 6 hours at room temperature (18-30°C). |

## 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 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. Human origin material used in the preparation of the negative control (R3) has been tested and found non-reactive for hepatitis B surface antigen (HBs Ag), HIV antigen, antibodies to hepatitis C, and antibodies to human immunodeficiency virus (HIV-1 and HIV-2). Human origin material used in the preparation of HIV 1 antibodies positive control (R4) has been tested and found non-reactive for hepatitis B surface antigen (HBs Ag) and antibodies to hepatitis C. 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 Universal Precautions for blood borne pathogens 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.
- 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 biohazardous waste disposal. Then the area should be decontaminated with one of the chemical disinfectants.

**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**

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

- Do not use expired reagents.
- Do not mix or associate reagents from different lots within a test run.
- Before use wait for 30 minutes for the reagents to stabilize at room temperature (18-30°C).
- The name of the test, as well as a specific identification number for the test, are written on the frame of each microplate. This specific identification number is stated on each strip too.
  **Genscreen™ ULTRA HIV Ag-Ab: Specific ID number = 53**
  Verify the specific identification number before use. If the identification number is missing, or different from the stated number corresponding to the assay to be tested, the strip should not be used.

*REMARK: For washing solution (R2, label identification: 20X coloured green), peroxidase substrate buffer (R8, label identification: TMB buf., coloured blue), chromogen (R9, label identification: TMB 11X coloured purple) and stopping solution (R10, label identification: 1N coloured red), it is possible to use other lots than those contained in the kit, provided the same lot is used within a given test run. These reagents can be used with some other products of our company. Contact our technical service for detailed information.*

- Carefully reconstitute the reagents avoiding any contamination.
- Use glassware thoroughly washed and rinsed with deionized water or preferably, disposable material.
- Do not allow the microplate to dry between the end of the washing operation and the reagent distribution.
- The sample distribution must begin immediately after the conjugate 1 distribution. Waiting time between the dispensing of the conjugate 1 and the samples should not exceed 30 minutes.
- The enzyme reaction is very sensitive to metal ions. Consequently, do not allow any metal element to come into contact with the various conjugate or substrate solutions.
- The development solution (substrate buffer + chromogen) must be coloured pink. The modification of this pink colour within a few minutes of reconstitution indicates that the reagent cannot be used and must be replaced.
  Preparation of the development solution can be made in a clean disposable single use plastic tray or glass container that has first been pre-washed with 1N HCl and rinsed thoroughly with distilled water and dried. This reagent must be stored in the dark.
- Never use the same container to distribute conjugate and development solution.

**5.2.2. Processing**

- Do not change the assay procedure.
- Do not carry out the test in the presence of reactive vapours (acid, alkaline, aldehyde vapours) or dust that could alter the enzymatic activity of the conjugate.
- Use a new distribution tip for each sample.
- Well washing is a critical step in this procedure: respect the recommended number of washing cycles and make sure that all wells are completely filled and then completely emptied. Incorrect washing may lead to inaccurate results.
- Carefully follow the washing procedures described to obtain maximum test performance. With some instrument, it could be necessary to optimize the washing procedure (increase of number of cycle of washing step and/or volume of wash buffer for each cycle) to obtain an acceptable level of OD background for the negative sample.
  Contact our company for the adaptations and special procedures.

## 6. SPECIMENS

Collect a blood sample according to the current practices. The test should be performed on undiluted serum or plasma (collected on EDTA, heparin, citrate, ACD-based anticoagulants). Separate the serum or plasma from the clot or red cells as soon as possible to avoid any haemolysis. Extensive haemolysis may affect test performance. Specimens with observable particulate matter should be clarified by centrifugation prior testing. Suspended fibrin particles or aggregates may yield falsely positive results.
The specimens can be stored at +2-8°C if screening is performed within 7 days or they may be deep-frozen at -20°C for several months. The plasma must be quickly thawed by warming for a few minutes in a water bath at 40°C (To avoid fibrin precipitation). Do not repeat more than 3 freeze/thaw cycles.

Samples containing up to 90 g/l albumin, 200 mg/l bilirubin, 50 µg/l biotin, lipemic samples containing up to the equivalent of 36 g/l triglyceride, and haemolysed samples containing up to 10 g/l haemoglobin do not affect the results. However, it is not recommended to use hyperlipaemic or hyperhaemolysed sera or plasma samples. It is not recommended to heat the samples.
If the specimens are to be shipped, they must be packaged in accordance with the regulations in force regarding the transport of etiological agents and preferably transport frozen.

## 7. PROCEDURE

### 7.1. Materials required but not provided

- Distilled water.
- Sodium hypochlorite (household bleach) and sodium bicarbonate.
- Absorbent paper.
- Disposable gloves.
- Adhesive film.
- Safety glasses.
- Disposable tubes.
- Automatic or semiautomatic, adjustable or preset pipettes or multipipettes to measure and dispense 25 µl, 75 µl, 80 µl and 100 µl.
- Graduated cylinders of 25 ml; 100 ml; 1000 ml capacity. Vortex mixer.
- Automatic, semi-automatic or manual microplate washing system (*).
- Water-bath, or equivalent microplate incubator, thermostatically set at 37°C ± 1°C (*).
- Container for biohazardous waste.
- Microplate reader equipped with 450 nm, 490 nm and 620-700 nm filters (*).

*(*) Consult us for detailed information about the equipment recommended by our technical department.*

### 7.2. Reagents preparation

#### 7.2.1. Ready for use reagents

**Reagent 1 (R1): Microplate**
Each frame support containing 12 strips is wrapped in a sealed foil bag. Cut the bag using scissors or a scalpel 0.5 to 1 cm above the sealing. Open the bag and take out the frame. Put the unused strips back into the bag. Close the bag carefully and put it back into storage at +2-8°C.
**Reagent 3 (R3): Negative control**
**Reagent 4 (R4): HIV-1 Ab positive control**
**Reagent 5 (R5): HIV Ag positive control**
**Reagent 6 (R6): Conjugate 1**
**Reagent 10 (R10): Stopping solution**

### 7.2.2. Reagents to reconstitute

**Reagent 2 (R2): Concentrated washing solution (20X)**
Dilute 1:20 in distilled water to obtain the ready-for-use washing solution. Prepare 800 ml for one plate of 12 strips.
**Reagent 7a (R7a) + Reagent 7b (R7b): Conjugate 2 working solution**
Gently tap the vial of the lyophilized conjugate 2 (R7a) on the workbench to remove any substance from the rubber cap. Carefully remove the cap and pour the contents of Conjugate Diluent vial (R7b) into the Lyophilized Conjugate vial (R7a). Replace the cap and let stand for 10 minutes, whilst gently shaking and inverting from time to time to ease dissolution.
**Reagent 8 (R8) + Reagent 9 (R9): Enzyme development solution**
Dilute 1:11 the chromogen (R9) in the Substrate Buffer (R8) (e.g. 1 ml reagent R9 +10 ml of R8 reagent) given that 10 ml are necessary and sufficient to treat 12 strips. Homogenize.

### 7.3. Assay Procedure
Strictly follow the proposed procedure.
Use the negative (R3), HIV-1 Ab positive (R4) and HIV Ag positive (R5) controls for each series of determinations in order to validate the test quality.

Follow the following Good Laboratory Practice:
1. Carefully establish the sample distribution and identification plan.
2. Prepare the diluted washing solution R2 and the conjugate 2 working solution (R7a + R7b) (refer to 7.2).
3. Take out from the protective packing the support frame and the necessary number of strips (R1). Put the unused strips back in their packing. Close the packing and replace it at +2-8°C.
4. Distribute in the well in the following order, without prior washing of the plate (advisable plate distribution):
   - 25 µl of conjugate 1 (R6) in each well
   - 75 µl of HIV Ag positive control (R5) in well A1
   - 75 µl of HIV Ab positive control (R4) in well B1,
   - 75 µl of negative control (R3) in well C1, D1 and E1
   - 75 µl of specimen 1 in well F1
   - 75 µl of specimen 2 in well G1, etc.

   Homogenize the mixture by a minimum of 3 aspirations with 75 µl pipette or with a microplate shaker for 5 seconds. The sample distribution must begin immediately after the conjugate 1 distribution. If the sample distribution takes over 30 min, it is recommended to distribute the negative and positive controls after the samples that are to be tested.
   Depending on the used system, it's possible to modify the position of controls or the order of distribution.

   *REMARK: After the samples distribution, the well containing conjugate 1 turns yellow-green to blue. It is possible to verify the presence of the (sample + conjugate 1) in the wells by spectrophotometric reading at 620 nm (refer to §7.7).*
5. When possible, cover the microplate with adhesive film. Press firmly all over the plate to ensure a tight seal.
6. Incubate the microplate in a thermostat-controlled water-bath or microplate incubator at 37°C ± 1°C for 1 hour ± 4 minutes.
7. If necessary, remove the adhesive film. Aspirate the contents of all wells into a container for biohazardous waste (containing sodium hypochlorite). Add into each well a minimum of 0.370 ml of washing solution. Allow a soak time of at least 30 seconds. Aspirate again. Repeat this procedure a minimum of two times (i.e. in total of a minimum of three washes). The residual volume must be lower than 10 µl (if necessary dry the plate by turning it upside down on absorbent paper). If an automatic washer is used, follow the same procedure
8. Quickly dispense 100 µl of conjugate 2 (R7a + R7b) into each well within the plate. The conjugate must be shaken gently before use. Cover, if it's possible, with a new adhesive film and incubate for 30 minutes (± 4 min) at room temperature (18-30°C).

*REMARK: The conjugate 2 is coloured red. It is possible to verify the presence of conjugate 2 in the wells by spectrophotometric reading at 620 nm (refer to §7.7).*

9. If necessary, remove the adhesive film, empty all the wells by aspiration and wash a minimum of 5 times as described above.
10 Prepare the enzymatic development solution (reagent R8 + R9).
11 Quickly distribute 80 µl of prepared enzymatic development solution (R8 + R9) in all the wells. Allow the reaction to develop in the dark for 30 minutes (± 4 min) at room temperature (18 - 30°C). Do not use adhesive film during this incubation.

*REMARK: The distribution of the development solution, which is coloured pink, can be visually controlled at this step of the manipulation. There is a clear difference of colouration between empty well and a well containing the pink substrate solution. (refer to §7.7).*

12 Add 100 µl of the stopping solution (R10) using the same sequence and rate of distribution as for the development solution.

*REMARK: Distribution of the colourless stopping solution can be visually controlled at this handling stage.*
*The substrate colour, pink (for negative samples) or blue (for positive samples), fades from the wells, which become colourless (for negative samples) or yellow (for positive samples) after adding stopping solution.*

13 Carefully wipe each plate bottom. Wait at least 4 minutes after stopping solution addition and within 30 minutes of stopping the reaction, read the optical density at 450/620-700 nm using a plate reader.
14 Check for agreement between the spectrophotometric and visual readings and against the plate and sample distribution and identification plan.

**7.4. Quality control**
Use positive and negative controls in each run of series to validate the assay. (Refer to §7.5).

**7.5. Test Validation criteria**
This test is validated if the conditions below are respected:

**1. For the negative control R3**
The absorbance of each negative control (R3) should be less than 0.170:
$OD\ R3 < 0.170$
The mean of the absorbance of the negative controls (R3) should be less than 0.150:
$\overline{OD\ R3} < 0.150$
If one of the negative controls R3 does not respect this norm, disregard the value and recalculate the mean using the two remaining values.

**2. For the HIV antibodies positive control R4**
The absorbance of the HIV Ab positive control (R4) should be greater than 0.9: $OD\ R4 > 0.9$

**3. For the HIV antigens positive control R5**
The absorbance of the HIV Ag positive control (R5) should be greater than 0.9: $OD\ R5 > 0.9$

**7.6. Calculation/Interpretation of results**
The cut-off is determined with the R3 negative control:
Calculate the mean measured absorbance value for the negative control R3.

$$OD\ R3 = \frac{OD\ (C1) + OD\ (D1) + OD\ (E1)}{3}$$

Calculate the cut-off value:
CO = OD R3 + 0.200

The presence or absence of detectable HIV Antigen or antibodies to HIV-1 and/or HIV-2 is determined by comparing the absorbance measured for each sample to the calculated cut-off value.
The following ratio is calculated for each sample:
Ratio = OD of the sample / CO Value

Samples with an optical density lower than the cut-off value are considered to be negative (ratio < 1) by the Genscreen™ ULTRA HIV Ag-Ab.

Results just below the cut-off value (CO-10 % < O.D. < CO) should however, be interpreted with caution. It is advisable to retest in duplicate the corresponding samples when the systems and laboratory procedures permit.

Samples with an optical density greater or equal to the cut-off (ratio ≥ 1) are considered to be initially positive by the Genscreen™ ULTRA HIV Ag-Ab. They should be retested in duplicate before final interpretation.

If after retesting the ratio value of at least one of the 2 duplicates is equal to or greater than 1, the initial result is repeatable and the sample is declared to be positive with the Genscreen™ ULTRA HIV Ag-Ab. The ratio value of the 2 duplicates are less than 1, the initial results is non-repeatable and the sample is declared to be negative.

Non repeatable reactions are often caused by:
- Inadequate microplate washing,
- Contamination of negative samples by serum or plasma with a high antibody titre,
- Contamination of the substrate solution by oxidizing agents (bleach, metal ions, etc…),
- Contamination of the stopping solution.

The samples which have been retested twice and found negative with Genscreen™ ULTRA HIV Ab-Ag, but with one value near the cut-off value (ratio between 0.9 and 1) should be considered with care. It is advised to retest the patient with another method or another sample.
In case of very low optical density for tested samples (negative O.D.) and when the presence of samples as well as of reagent is controlled, the results can be interpreted as negative.

It is recommended to confirm the positive samples following the current national recommendations and algorithms.

**7.7. Spectrophotometric verification of sample and conjugate pipetting (optional)**
**Sample and Conjugate 1 (R6) pipetting verification**
It is possible to verify the simultaneous presence of the conjugate 1 (R6) and the samples into the well can be verified by automatic reading at 620 nm.
Each well containing sample and conjugate 1 (R6) must have and O.D. greater than 0.600.

**Conjugate 2 working solution pipetting verification**
The presence of conjugate 2 (R7a + R7b) can be verified by automatic reading at 450 / 620 nm. The O.D. value of each well must be greater than 0.100 (a lower OD indicates a poor dispensing of the conjugate 2).

**Development solution pipetting verification**
It is possible to verify the presence of pink development solution into the well by automatic reading at 490 nm.
A well with development solution must have an optical density greater than 0.100 (a lower OD indicates a poor dispensing of the development solution).

## 8. TEST LIMITATIONS

Very low titres of HIV antigen or antibodies may not be detected during the first stage of the infection; consequently a negative result indicates that the tested sample does not contain detectable HIV antigen or anti-HIV antibodies with Genscreen™ ULTRA HIV Ag-Ab.
However, such a result does not preclude the possibility of exposure to an HIV-1/HIV-2 infection. The variability of HIV-1 (group M and group O) and HIV-2 allows the possibility of false negative reactions. No known test method can offer complete assurance that the HIV virus is absent.
Highly sensitive ELISA techniques may produce false positive results. To verify the specificity of the reaction, every positive result (in accordance with the interpretation criteria of Genscreen™ ULTRA HIV Ag-Ab test) should be confirmed with an appropriate method (with a specific HIV Ag test such as the Genscreen System HIV Ag EIA, then neutralization to prove the presence of HIV Ag - or Western-Blot to prove the presence of anti-HIV antibodies). Heating of samples may affect the quality of the results.

The spectrophotometric method for verifying the sample, conjugate development solution deposition does not allow to verify the accuracy of the dispensed volume of samples and conjugate. This method shows only the presence of sample and conjugate. The error rate with this method is closely linked to the accuracy of the utilized system (a cumulated coefficient of variation of over 10% for dispensing and reading will significantly decrease the quality of this step).
Some icteric hyperlipemic or hyperhemolysed samples may affect the spectrophotometric method for verifying the conjugate 1 deposition.

Only the presence of sample can be verified in this case. In case of very poor washing efficiency after the conjugate incubation, the automatic verification of the development solution pipetting (by reading OD of wells at 490 nm) may provide wrong results with OD above 0.100 in the absence of development solution. However this phenomenon has not been observed during evaluation on 939 tested samples.

## 9. PERFORMANCES CHARACTERISTICS

### 9.1. Precision Measurement

The precision measurement of Genscreen™ ULTRA HIV Ag-Ab test has been determined, by the analysis of 10 samples: 1 negative sample, 3 HIV-1 Antibody positive, 3 HIV-2 Antibody positive and 3 HIV-1 Antigen positive. The intra assay repeatability has been evaluated by testing these 10 samples 30 times in the same run. The intermediate precision has been evaluated by testing these 10 samples in duplicate during 20 days on 2 independent runs each day. The ratio means, standard deviations (SD) and coefficients of variation (CV) were calculated.

#### 9.1.1. Repeatability

| Samples Panel | | N | Mean Ratio | SD | CV% |
|---|---|---|---|---|---|
| Negative | | 30 | 0.28 | 0.02 | 5.37 |
| HIV-1 Ab | Low positive | 30 | 1.62 | 0.07 | 4.32 |
| | Medium positive | 30 | 2.98 | 0.13 | 4.33 |
| | High positive | 30 | 5.37 | 0.18 | 3.32 |
| HIV-2 Ab | Low positive | 30 | 2.5 | 0.18 | 7.20 |
| | Medium positive | 30 | 5.35 | 0.45 | 8.48 |
| | High positive | 30 | 11.19 | 0.58 | 5.21 |
| HIV Ag | Low positive | 30 | 1.58 | 0.06 | 3.64 |
| | Medium positive | 30 | 4.19 | 0.17 | 4.13 |
| | High positive | 30 | 9.21 | 0.34 | 3.65 |

### 9.1.2. Intermediate Precision

| | | | | Within run | | Between run | | Between day/operator | | Total Precision | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Samples Panel | | N | Mean Ratio | SD | CV | SD | CV | SD | CV | SD | CV |
| Negative | | 72 | 0.26 | 0.016 | 6.2% | 0.014 | 5.5% | 0.014 | 5.5% | 0.025 | 9.9% |
| HIV-1 Ab | Low positive | 72 | 1.04 | 0.029 | 2.8% | 0.044 | 4.3% | 0.056 | 5.4% | 0.078 | 7.5% |
| | Medium positive | 72 | 2.67 | 0.076 | 2.8% | 0.097 | 3.6% | 0.170 | 6.4% | 0.210 | 7.9% |
| | High positive | 72 | 4.91 | 0.114 | 2.3% | 0.166 | 3.4% | 0.328 | 6.7% | 0.385 | 7.8% |
| HIV-2 Ab | Low positive | 72 | 1.73 | 0.114 | 6.6% | 0.121 | 7.0% | 0.263 | 15.2% | 0.311 | 17.9% |
| | Medium positive | 72 | 4.40 | 0.477 | 10.8% | 0.000 | N/A | 0.484 | 11.0% | 0.680 | 15.4% |
| | High positive | 72 | 10.94 | 0.427 | 3.9% | 0.319 | 2.9% | 0.366 | 3.4% | 0.647 | 5.9% |
| HIV Ag | Low positive | 72 | 1.29 | 0.052 | 4.0% | 0.038 | 3.0% | 0.053 | 4.1% | 0.084 | 6.5% |
| | Medium positive | 72 | 3.47 | 0.085 | 2.5% | 0.134 | 3.9% | 0.068 | 2.0% | 0.173 | 5.0% |
| | High positive | 72 | 8.89 | 1.272 | 14.3% | 0.000 | N/A | 0.000 | N/A | 1.272 | 14.3% |

### 9.2. Diagnostic performance

The performances of Genscreen™ ULTRA HIV Ag-Ab have been determined by testing samples from random blood donors, from patients with HIV infection and commercial seroconversion panels. Moreover the HIV Ag sensitivity limit has been tested using the French ANSM Standard and the WHO international Standard (90/636).
Patients with diseases unrelated to HIV infection have been tested too.

### 9.2.1 Diagnostic Specificity

Specificity determined on a total of 6038 random blood donors from 3 different sites was found at 99.95% with a confidence interval at 95% of [ 99.85 – 99.99%]. (6035 negative samples / 6038 tested samples).
The 3 repeated reactive samples were confirmed negative for HIV by Western Blot and HIV p24 Ag testing.

409 samples from 2 hospital clinical laboratories were also tested with the Genscreen™ ULTRA HIV Ag-Ab assay; 14 samples were found initial reactive and 12 of them were repeatedly reactive (positive in a second testing): 11 were confirmed by HIV Western-Blot, 1 was not confirmed and considered as false positive. Specificity on this population was (397/398) 99.75%, CI 95% [98.61 – 99.99%].

### 9.2.2 Diagnostic Sensitivity

Sensitivity was evaluated by testing confirmed HIV Ab positive samples, specimens from acute infected patients and from commercial seroconversion panels and HIV Ag samples (neat or diluted).

**1) Confirmed HIV Ab positive samples**

763 positive samples from follow-up of HIV-1 and HIV-2 infected patients have been tested. This study was showing a sensitivity of 100%.

| | Types | Number of samples | Number of reactive samples | Sensitivity |
|---|---|---|---|---|
| HIV-1 | A, B, C (CDC classification) | 200 | 200 | 100% |
| | HIV-1 WB with complete profiles or with light anti-gag Ab bands | 200 | 200 | 100% |
| | HIV 1 group M (18A, 71B, 23C, 9D, 12E, 4F) | 137 | 137 | 100% |
| | Group O | 22 | 22 | 100% |
| | Group N | 1 | 1 | 100% |
| | BBI PRZ 204 panel | 7 | 7 | 100% |
| HIV-2 | HIV-2 WB with complete profiles | 196 | 196 | 100% |

25 additional fresh positive samples (within 1 day after blood collection) were tested and found positive.

**2) Specimens from acute infected patients and from commercial seroconversion panels**

- 81 specimens sourced from acute or recently HIV-1 infected patients (35 samples from 28 patients with a Western-Blot seroconversion profile and 46 samples from recent seroconversion) were found positive with Genscreen™ ULTRA HIV Ag-Ab.
- 20 per-seroconversion samples (very early seroconversion samples with negative Western-Blot profile or with very light band for p24 and/ or gp160 on HIV Western-blot): 19 of them were found positive.
- A total of 90 well documented commercial HIV seroconversion panels were also studied and compared to commercially available EIA assays. From which results were compared on 85 panels to a CE marked Ag-Ab test: Genscreen™ PLUS HIV Ag-Ab.

| Genscreen™ ULTRA HIV Ag-Ab Results compared to Genscreen™ PLUS HIV Ag-Ab | Earlier detection (at least one bleed) | Equivalent detection (Same sample recognized as positive) | Later detection |
|---|---|---|---|
| Number of seroconversions | 44 | 41 | 0 |

At least 170 early seroconversion samples were tested with Genscreen™ ULTRA HIV Ag-Ab.

### 9.3. Analytical sensitivity

**HIV Ag Standards**

The analytical sensitivity has been estimated by testing the 1st International WHO HIV P24 Antigen standard (90/636) and found at 0.85 IU/ml CI 95% [0.73 - 1.01 IU/ml] .
The limit of the test was also determined on the ANSM HIV P24 Antigen standard by interpolation of the curve obtained by dilutions testing (initial concentration 100 pg/ml) and found to be < 25 pg/ml.
During the external evaluations, the limit of detection was established at 13.6 pg/ml by regression of the standard range of the “Ag HIV SFTS 1998” panel (HIV Ag panel from the French Society of Blood Transfusion).

**Sensitivity on HIV Ag positive samples:** 56 samples were tested: 53 samples containing at least 25 pg/ml of HIV Ag were positive and 3 samples with respectively 13, 16 and 19 pg/ml of HIV Ag had ratios (Optical Density / Cut-off) between 0.9 and 1.00

**Sensitivity on culture cells supernatants:** 83 supernatants from the following genotypes were tested: 76 HIV-1 group M samples (16 A, 16 B, 11 C, 7D, 13 E, 4 F, 4 G, 3 H, 2 J), 4 HIV-1 group O, 1 HIV-1 group N and 2 HIV 2 samples. All of the HIV-1 samples were reactive except one group O sample with a concentration of 29 pg/ml of HIV Ag which was found with a ratio (Optical density / Cut off) of 0.60.

### 9.4. Analytical Specificity/Cross reactivity study

**9.4.1. Cross reactivity Study**

404 patients showing different pathologies or status not linked to the HIV (pregnant women, rheumatoid factor,autoimmune (SLE), cirrhotic, chronic renal failure, dialysis, anti-mouse Ig or other viral or bacterial infections (Hepatitis A, B, C, rubella, Toxoplasmosis, Mumps, Measles, CMV, HSV, EBV, VZV, HTLVI, Malaria, Flu vaccinated patients) were tested with Genscreen™ ULTRA HIV Ag-Ab. 4 samples were found false Repeat Reactive (1 measle IgG, 1 HSV IgG, 1 rubella, 1 SLE). Specificity was 99.0% CI95% [97.5- 99.7%] (400/404).

**9.5. Hook Effect**

HIV Ag positive sample: 19 dilutions were realized from non-diluted 1000ng/mL to 3.125 pg/mL p24 HIV antigen in negative serum matrix.

No negative results on non-diluted samples were observed when compare to diluted samples.

HIV Ab positive sample: Five (5) very high anti HIV Ab positive samples were tested from pure to 1/512e dilution. No negative results on non-diluted samples were observed when compare to diluted samples.

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

H314 - H317

P280 - P305+P351+P338 - P301+P330+P331 - P303+P361+P353 - P333+P313 - P501

(BG)
**опасно**
Причинява тежки изгаряния на кожата и сериозно увреждане на очите. Може да причини алергична кожна реакция.
Използвайте предпазни ръкавици/предпазно облекло/предпазни очила/предпазна маска за лице. ПРИ КОНТАКТ С ОЧИТЕ: Промивайте внимателно с вода в продължение на няколко минути. Свалете контактните лещи, ако има такива и доколкото това е възможно. Продължавайте да промивате. ПРИ ПОГЛЪЩАНЕ: изплакнете устата. НЕ предизвиквайте повръщане. ПРИ КОНТАКТ С КОЖАТА (или косата): Незабавно свалете цялото замърсено облекло. Облейте кожата с вода/вземете душ При поява на кожно дразнене или обрив на кожата: Потърсете медицински съвет/помощ. Изхвърлете съдържанието/контейнера в съответствие с местните/регионалните/националните/ международните разпоредби.

(CZ)
**Nebezpečí**
Způsobuje těžké poleptání kůže a poškození očí. Může vyvolat alergickou kožní reakci.
Používejte ochranné rukavice/ochranný oděv/ochranné brýle/obličejový štít. PŘI ZASAŽENÍ OČÍ: Několik minut opatrně vyplachujte vodou. Vyjměte kontaktní čočky, jsou-li nasazeny a pokud je lze vyjmout snadno. Pokračujte ve vyplachování. PŘI POŽITÍ: Vypláchněte ústa. NEVYVOLÁVEJTE zvracení. PŘI STYKU S KŮŽÍ (nebo s vlasy): Veškeré kontaminované části oděvu okamžitě svlékněte. Opláchněte kůži vodou/osprchujte. Při podráždění kůže nebo vyrážce: Vyhledejte lékařskou pomoc/ošetření. Obsah/nádobu likvidujte v souladu s místními/regionálními/národními/mezinárodními předpisy.

(DE)
**Gefahr**
Verursacht schwere Verätzungen der Haut und schwere Augenschäden. Kann allergische Hautreaktionen verursachen. Schutzhandschuhe/Schutzkleidung/Augenschutz/Gesichtsschutz tragen. BEI KONTAKT MIT DEN AUGEN: Einige Minuten lang behutsam mit Wasser spülen. Vorhandene Kontaktlinsen nach Möglichkeit entfernen. Weiter spülen. BEI VERSCHLUCKEN: Mund ausspülen. KEIN Erbrechen herbeiführen. BEI KONTAKT MIT DER HAUT (oder dem Haar): Alle beschmutzten, getränkten Kleidungsstücke sofort ausziehen. Haut mit Wasser abwaschen/duschen. Bei Hautreizung oder -ausschlag: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen. Entsorgung des Inhalts / des Behälters gemäß den örtlichen / regionalen / nationalen/ internationalen Vorschriften.

(DK)
**Fare**
Forårsager svære forbrændinger af huden og øjenskader. Kan forårsage allergisk hudreaktion.
Bær beskyttelseshandsker/beskyttelsestøj/øjenbeskyttelse/ ansigtsbeskyttelse VED KONTAKT MED ØJNENE: Skyl forsigtigt med vand i flere minutter. Fjern eventuelle kontaktlinser, hvis dette kan gøres let. Fortsæt skylning. I TILFÆLDE AF INDTAGELSE: Skyl munden. Fremkald IKKE opkastning. VED KONTAKT MED HUDEN (eller håret): Tilsmudset tøj tages straks af/fjernes. Skyl/brus huden med vand. Ved hudirritation eller udslet: Søg lægehjælp. Bortskaffelse af indholdet/beholderen i henhold til de lokale/regionale/nationale/internationale forskrifter.

(EE)
**Ettevaatust**
Põhjustab rasket nahasöövitust ja silmakahjustusi. Võib põhjustada allergilist nahareaktsiooni.
Kanda kaitsekindaid/kaitserõivastust/kaitseprille/kaitsemaski. SILMA SATTUMISE KORRAL: loputada mitme minuti jooksul ettevaatlikult veega. Eemaldada kontaktläätsed, kui neid kasutatakse ja kui neid on kerge eemaldada. Loputada veel kord. ALLANEELAMISE KORRAL: loputada suud. MITTE kutsuda esile oksendamist. NAHALE (või juustele) SATTUMISE KORRAL: võtta viivitamata kõik saastunud rõivad seljast. Loputada nahka veega/loputada duši all. Nahaärrituse või _obe korral: pöörduda arsti poole. Sisu/konteineri käitlus vastavuses kohalike/regionaalsete/rahvuslike/rahvusvaheliste nõuetega.

(EN)
**Danger**
Causes severe skin burns and eye damage. May cause an allergic skin reaction.
Wear protective gloves/protective clothing/eye protection/face protection. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. IF SWALLOWED: rinse mouth. Do NOT induce vomiting. IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower. If skin irritation or rash occurs: Get medical advice/attention. Dispose of contents/container in accordance with local/regional/national/international regulations.

(ES)
**Peligro**
Provoca quemaduras graves en la piel y lesiones oculares graves. Puede provocar una reacción alérgica en la piel.
Llevar guantes que aíslen del frío/gafas/máscara. EN CASO DE CONTACTO CON LOS OJOS: Aclarar cuidadosamente con agua durante varios minutos. Quitar las lentes de contacto, si lleva y resulta fácil. Seguir aclarando. EN CASO DE INGESTIÓN: Enjuagarse la boca. NO provocar el vómito. EN CASO DE CONTACTO CON LA PIEL (o el pelo): Quitarse inmediatamente las prendas contaminadas. Aclararse la piel con agua o ducharse. En caso de irritación o erupción cutánea: Consultar a un médico. Eliminar el contenido o el recipiente conforme a la reglamentación local/regional/nacional/ internacional.

(FI)
**Vaara**
Voimakkaasti ihoa syövyttävää ja silmiä vaurioittavaa. Voi aiheuttaa allergisen ihoreaktion.
Käytä suojakäsineitä/suojavaatetusta/silmiensuojainta/ kasvonsuojainta. JOS KEMIKAALIA JOUTUU SILMIIN: Huuhdo huolellisesti vedellä usean minuutin ajan. Poista piilolinssit, _edical voi tehdä helposti. Jatka huuhtomista. JOS KEMIKAALIA ON NIELTY: Huuhdo suu. Ei saa oksennuttaa. JOS KEMIKAALIA JOUTUU IHOLLE (tai hiuksiin): Riisu saastunut vaatetus välittömästi. Huuhdo/suihkuta iho vedellä. Jos ilmenee ihoärsytystä tai ihottumaa: Hakeudu lääkäriin. Säilytä säiliö(t) noudattaen paikallisia/alueellisia/kansallisia/ kansainvälisiä määräyksiä.

(FR)
**Danger**
Provoque des brûlures de la peau et des lésions oculaires graves. Peut provoquer une allergie cutanée.
Porter des gants de protection/des vêtements de protection/un équipement de protection des yeux/du visage. EN CAS DE CONTACT AVEC LES YEUX: rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer. EN CAS D'INGESTION: rincer la bouche. NE PAS faire vomir. EN CAS DE CONTACT AVEC LA PEAU (ou les cheveux): enlever immédiatement les vêtements contaminés. Rincer la peau à l'eau/se doucher. En cas d'irritation ou d'éruption cutanée: consulter un médecin. Éliminer le contenu/récipient conformément à la réglementation locale/régionale/nationale/internationale.

(GR)
**Κίνδυνος**
Προκαλεί σοβαρά δερματικά εγκαύματα και οφθαλμικές βλάβες. Μπορεί να προκαλέσει αλλεργική δερματική αντίδραση.
Να φοράτε προστατευτικά γάντια/προστατευτικά ενδύματα/μέσα ατομικής προστασίας για ταμάτια/πρόσωπο. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΑ ΜΑΤΙΑ: Ξεπλύνετε προσεκτικά με νερό για αρκετά λεπτά. Εάν υπάρχουν φακοί επαφής, αφαιρέστε τους, εφόσον είναι εύκολο. Συνεχίστε να ξεπλένετε. ΣΕ ΠΕΡΙΠΤΩΣΗ ΚΑΤΑΠΟΣΗΣ: Ξεπλύνετε το στόμα. ΜΗΝ προκαλέσετε εμετό. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΟ ΔΕΡΜΑ (ή με τα μαλλιά): Αφαιρέστε αμέσως όλα τα μολυσμένα ενδύματα. Ξεπλύνετε το δέρμα με νερό/στο ντους. Εάν παρατηρηθεί ερεθισμός του δέρματος ή εμφανιστεί εξάνθημα: Συμβουλευθείτε/Επισκεφθείτεγιατρό. Απορρίψτε τα περιεχόμενα/δοχείο σύμφωνα με τους τοπικούς/εθνικούς/διεθνείς κανονισμούς.

(HR)
**Ppasnost**
Uzrokuje teške opekline kože i ozljede oka. Može izazvati alergijsku reakciju na koži.
Nositi zaštitne rukavice/zaštitnu odijelo/zaštitu za oči/zaštitu za lice. U SLUČAJU DODIRA S OČIMA: oprezno ispirati vodom nekoliko minuta. Ukloniti kontaktne leće ukoliko ih nosite i ako se one lako uklanjaju. Nastaviti ispiranje. AKO SE PROGUTA: isprati usta. NE izazivati povraćanje. U SLUČAJU DODIRA S KOŽOM (ili kosom): odmah ukloniti/skinuti svu zaganenu odjeću. Isprati kožu vodom/tuširanjem. U slučaju nadražaja ili osipa na koži: zatražiti savjet/pomoć liječnika. Odložite sadržaje /spremnike u skladu s lokalnim/regionalnim/nacionalni/međunarodnim odredbama.

(HU)
**Veszély**
Smarkiai nudegina odą ir pažeidžia akis. Allergiás bőrreakciót válthat ki.
Védőkesztyű/védőruha/szemvédő/arcvédő használata kötelező. SZEMBE KERÜLÉS esetén: Több percig tartó óvatos öblítés vízzel. Adott esetben a kontaktlencsék eltávolítása, ha könnyen megoldható. Az öblítés folytatása. LENYELÉS ESETÉN: a szájat ki kell öblíteni. TILOS hánytatni. HA BŐRRE (vagy hajra) KERÜL: Az összes szennyezett ruhadarabot azonnal el kell távolítani/le kell vetni. A bőrt le kell öblíteni vízzel/zuhanyozás. Bőrirritáció vagy kiütések megjelenése esetén: orvosi ellátást kell kérni. Az edény tartalmát / a tartályt a helyi/regionális/nemzeti/nemzetközi szabályozásoknak megfelelően kell hulladékként elhelyezni.

(IT)
**Pericolo**
Provoca gravi ustioni cutanee e gravi lesioni oculari. Può provocare una reazione allergica cutanea.
Indossare guanti/indumenti protettivi/Proteggere gli occhi/il viso. IN CASO DI CONTATTO CON GLI OCCHI: sciacquare accuratamente per parecchi minuti. Togliere le eventuali lenti a contatto se è agevole farlo. Continuare a sciacquare. IN CASO DI INGESTIONE: sciacquare la bocca. NON provocare il vomito. IN CASO DI CONTATTO CON LA PELLE (o con i capelli): togliersi di dosso immediatamente tutti gli indumenti contaminati. Sciacquare la pelle/fare una doccia. In caso di irritazione o eruzione della pelle: consultare un medico. Smaltire il prodotto/recipiente in conformità con le disposizioni locali / regionali / nazionali / internazionali.

(LT)
**Pavojinga**
Smarkiai nudegina odą ir pažeidžia akis. Gali sukelti alerginę odos reakciją.
Mūvėti apsaugines pirštines/dėvėti apsauginius drabužius/naudoti akių (veido) apsaugos priemones. PATEKUS Į AKIS: Kelias minutes atsargiai plauti vandeniu. Išimti kontaktinius lęšius, jeigu jie yra ir jeigu lengvai galima tai padaryti. Toliau plauti akis. PRARIJUS: išskalauti burną. NESKATINTI vėmimo. PATEKUS ANT ODOS (arba plaukų): Nedelsiant nuvilkti/pašalinti visus užterštus drabužius. Odą nuplauti vandeniu/čiurkšle. Jeigu sudirginama oda arba ją išberia: kreiptis į gydytoją. Turinį/talpą išpilti (išmesti) - šalinti pagal vietines / regionines / nacionalines / tarptautines taisykles.

(NL)
**Gevaar**
Veroorzaakt ernstige brandwonden en oogletsel. Kan een allergische huidreactie veroorzaken.
Beschermende handschoenen/beschermende kleding/oogbescherming/gelaatsbescherming dragen. BIJ CONTACT MET DE OGEN: voorzichtig afspoelen met water gedurende een aantal minuten; contactlenzen verwijderen, indien mogelijk; blijven spoelen. NA INSLIKKEN: de mond spoelen — GEEN braken opwekken. BIJ CONTACT MET DE HUID (of het haar): verontreinigde kleding onmiddellijk uittrekken — huid met water afspoelen/afdouchen. Bij huidirritatie of uitslag: een arts raadplegen. De inhoud en de verpakking verwerken volgens de plaatselijke/regionale/nationale/internationale voorschriften.

(NO)
**Fare**
Forårsaker alvorlige hudforbrenninger og øyeskader. Kan forårsake allergiske hudreaksjoner.
Bruk vernehansker/verneklær/vernebriller/ansiktsskjerm. VED KONTAKT MED ØYNENE: Skyll forsiktig med vann i opptil flere minutter. Fjern evt. kontaktlinser såfremt dette er lett mulig. Fortsett skyllingen. VED SVELGING: Skyll munnen. IKKE fremkall brekninger. VED HUDKONTAKT (eller kontakt med hår): Alle tilsølte klær må fjernes straks. Vask/dusj huden med vann. Ved hudirritasjon eller -utslett: Kontakt / tilkall lege. Innholdet / emballasjen skal avhendes i henhold til de lokale / regionale / nasjonale / internasjonale forskrifter.

(PL)
**Niebezpieczeństwo**
Powoduje poważne oparzenia skóry oraz uszkodzenia oczu . Może powodować reakcję alergiczną skóry.
Stosować rękawice ochronne/odzież ochronną/ochronę oczu/ochronę twarzy. W PRZYPADKU DOSTANIA SIĘ DO OCZU: Ostrożnie płukać wodą przez kilka minut. Wyjąć soczewki kontaktowe, jeżeli są i można je łatwo usunąć. Nadal płukać. W PRZYPADKU POŁKNIĘCIA: wypłukać usta. NIE wywoływać wymiotów. W PRZYPADKU KONTATKU ZE SKÓRĄ (lub z włosami): Natychmiast usunąć/zdjąć całą zanieczyszczoną odzież. Spłukać skórę pod strumieniem wody/prysznicem. W przypadku wystąpienia podrażnienia skóry lub wysypki: Zasięgnąć porady/zgłosić się pod opiekę lekarza. Zawartość / pojemnik usuwać zgodnie z przepisami miejscowymi / regionalnymi / narodowymi / międzynarodowymi.

(PT)
**Perigo**
Provoca queimaduras na pele e lesões oculares graves. Pode provocar uma reacção alérgica cutânea.
Usar luvas de protecção/vestuário de protecção/protecção ocular/protecção facial. SE ENTRAR EM CONTACTO COM OS OLHOS: enxaguar cuidadosamente com água durante vários minutos. Se usar lentes de contacto, retire-as, se tal lhe for possível. Continuar a enxaguar. EM CASO DE INGESTÃO: enxaguar a boca. NÃO provocar o vómito. SE ENTRAR EM CONTACTO COM A PELE (ou o cabelo): despir/retirar imediatamente toda a roupa contaminada. Enxaguar a pele com água/tomar um duche. Em caso de irritação ou erupção cutânea: consulte um médico. Eliminar o conteúdo/recipiente de acordo com a legislação local/regional/nacional/ internacional.

(RO)
**Pericol**
Provoacă arsuri grave ale pielii şi lezarea ochilor. Poate provoca o reacţie alergică a pielii.
Purtaţi mănuşi de protecţie/îmbrăcăminte de protecţie/echipament de protecţie a ochilor/ chipament de protecţie a feţei. ÎN CAZ DE CONTACT CU OCHII: clătiţi cu atenţie cu apă timp de mai multe minute. Scoateţi lentilele de contact, dacă este cazul şi dacă acest lucru se poate face cu uşurinţă. Continuaţi să clătiţi. ÎN CAZ DE ÎNGHIŢIRE: clătiţi gura. NU provocaţi voma. ÎN CAZ DE CONTACT CU PIELEA (sau părul): scoateţi imediat toată îmbrăcămintea contaminată. Clătiţi pielea cu apă/faceţi duş. În caz de iritare a pielii sau de erupţie cutanată: consultaţi medicul. Aruncaţi conţinutul/containerul în acord cu regulamentele locale/regionale/naţionale/internaţionale.

(SE)
**Fara**
Orsakar allvarliga frätskador på hud och ögon. Kan orsaka allergisk hudreaktion.
Använd skyddshandskar/skyddskläder/ögonskydd/ ansiktsskydd. VID KONTAKT MED ÖGONEN: Skölj försiktigt med vatten i flera minuter. Ta ur eventuella kontaktlinser om det går lätt. Fortsätt att skölja. VID FÖRTÄRING: Skölj munnen. Framkalla INTE kräkning. VID HUDKONTAKT (även håret): Ta omedelbart av alla nedstänkta kläder. Skölj huden med vatten/duscha. Vid hudirritation eller utslag: Sök läkarhjälp. Innehållet / behållaren avfallshanteras enligt lokala / regionala / nationella / internationella föreskrifter.

(SI)
**Nevarno**
Povzroča hude opekline kože in poškodbe oči. Lahko povzroči alergijski odziv kože.
Nositi zaščitne rokavice/zaščitno obleko/zaščito za oči/zaščito za obraz. PRI STIKU Z OČMI: previdno izpirajte z vodo nekaj minut. Odstranite kontaktne leče, če jih imate in če to lahko storite brez težav. Nadaljujte z izpiranjem. PRI STIKU Z OČMI: previdno izpirajte z vodo nekaj minut. Odstranite kontaktne leče, če jih imate in če to lahko storite brez težav. Nadaljujte z izpiranjem. PRI STIKU S KOŽO (ali lasmi): takoj odstraniti/sleči vsa kontaminirana oblačila. Izprati kožo z vodo/prho. Če nastopi draženje kože ali se pojavi izpuščaj: poiščite zdravniško pomoč/oskrbo. Vsebino/vsebnik odstranite v skladu z lokalnimi/regionalnimi/narodnimi/mednarodnimi predpisi.

(SK)
**Nebezpečenstvo**
Provoacă arsuri grave ale pielii şi lezarea ochilor. Môže vyvolať alergickú kožnú reakciu.
Noste ochranné rukavice/ochranný odev/ochranné okuliare/ochranu tváre. PO POŽITÍ: vypláchnite ústa. Nevyvolávajte zvracanie. PO POŽITÍ: vypláchnite ústa. Nevyvolávajte zvracanie. PRI KONTAKTE S POKOŽKOU (alebo vlasmi): Odstráňte/vyzlečte všetky kontaminované časti odevu. Pokožku ihneď opláchnite vodou/sprchou. Ak sa prejaví podráždenie pokožky alebo sa vytvoria vyrážky: vyhľadajte lekársku pomoc/starostlivosť. Zneškodnenie obsahu/obalu v súlade s miestnymi/oblastnými/ národnými/medzinárodnými nariadeniami.

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