

**WHO Prequalification of Diagnostics Programme
PUBLIC REPORT**

**Product: SD Bioline HIV Ag/Ab Combo
Number: PQDx 0069-012-00**

Abstract

SD Bioline HIV Ag/Ab Combo with product codes 03FK30 and 03FK35, manufactured by Standard Diagnostics, Inc., “rest of the world” regulatory version, was accepted for the WHO list of prequalified diagnostics and was listed on 22 March 2013.

SD BIOLINE HIV Ag/Ab Combo test kit is a rapid, qualitative test for the detection of HIV-1 p24 antigen and antibodies to certain isotypes (IgG, IgM and IgA) specific to HIV-1 including subtype-O and/or HIV-2 simultaneously in human serum, plasma or whole blood.

SD BIOLINE HIV Ag/Ab Combo test kit contains a membrane strip, which is pre-coated with recombinant HIV-1/HIV-2 antigen on test line “1” region and immobilized avidin on test line “2” region respectively. The mixture (mouse monoclonal anti-HIV-1 p24 in conjugate pad + HIV-1 p24 antigen in specimen and/or recombinant HIV-1/HIV-2 antigen in conjugate pad + antibodies to HIV-1/HIV-2 in specimen) moves upward on the membrane chromatographically by capillary action. For a reactive result, the recombinant HIV-1/HIV-2 antigen gold conjugate + antibodies to HIV-1/HIV-2 - coloured complexes will form in the test band 1 region and/or mouse monoclonal anti-HIV-1 p24 gold conjugate + HIV-1 p24 antigen + biotinylated anti-p24 antibody – coloured complexes will form in the test band 2 region of result window. The test lines and control line in the result window have been clearly labelled: "1" for Test line of antibodies to HIV-1/HIV-2, "2" for Test line of HIV-1 p24 antigen and "C" for Control line. All the test lines and control line in the result window should not be visible before applying any sample. The control line is used as a procedural control for the addition of reagents and may still appear if no specimen is added to the test device.

SD BIOLINE HIV Ag/Ab Combo test kit is intended as an aid in the diagnosis of infection with HIV-1/2.

The test kit is marketed the following different configurations:

SD BIOLINE HIV Ag/Ab Combo [25 Tests/kit] product code 03FK35:

- 25 test devices individually foil pouched with a desiccant
- Assay diluent (1 x 2ml/vial)
- 25x capillary pipettes, 25x lancets, 25x alcohol swab (optional)
- Instructions for use

SD BIOLINE HIV Ag/Ab Combo [30 Tests/kit] product code 03FK30

- 30 test devices individually foil pouched with a desiccant
- Assay diluent (1x 2ml/vial)
- Instructions for use

Storage:

The test kit should be stored at 1 - 30 °C.

Shelf-life:

18 months.

Summary of prequalification status for SD Bioline HIV Ag/Ab Combo

	Initial acceptance	
	Date	Outcome
Status on PQ list	22 March 2013	listed
Dossier assessment	13 December 2011	MR
Inspection status	19 February 2013	MR
Laboratory evaluation	27 February 2013	MR

MR: Meets Requirements

NA: Not Applicable

SD Bioline HIV Ag/Ab Combo was accepted for the WHO list of prequalified diagnostics on the basis of data submitted and publicly available information.

Background information

Standard Diagnostics, Inc. submitted an application for prequalification of SD Bioline HIV Ag/Ab Combo. Based on the established prioritization criteria, SD Bioline HIV Ag/Ab Combo was given priority for prequalification.

Product dossier assessment

Standard Diagnostics, Inc. submitted a product dossier for SD Bioline HIV Ag/Ab Combo 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 SD Bioline HIV Ag/Ab Combo for prequalification.

Commitments for prequalification:

The information submitted in the product dossier met the minimal requirements for acceptance. The manufacturer committed to amend and submit additional documentation on the following issues:

1. Analytical performance studies
2. Clinical performance studies
3. Stability studies
4. A new version of the labels and instructions for use.

Manufacturing site inspection

A comprehensive second re-inspection was performed at the site of the legal manufacturer at Kyonggi-do 446-930, Republic of Korea of the **SD BIOLINE Ag/Ab HIV Combo** test in November 2012, as per 'Information for manufacturers on 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, 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), effective mechanisms for customer training, service and feedback, and the adequacy of mechanisms for lot release of the product to customers.

The inspection found that the legal manufacturer Standard Diagnostics Inc. had an acceptable quality management system and manufacturing that should ensure the consistent manufacture of the SD BIOLINE Ag/Ab HIV Combo test of good quality. The manufacturer's responses to the nonconformities found at the time of the inspection and the provision of an internal audit report of the laboratory lot release procedures dated 15 February 2013 were accepted 19 February 2013.

Note: A full audit of the SD BIOLINE Ag/Ab HIV Combo test was not possible as the product was not in production at the time of the inspection. The SD BIOLINE Ag/Ab HIV Combo test had had few lots produced to date with the most recent in May 2012. Hence review will be required when the company scales up production and data for quality control of lot release and long term stability studies become available.

Commitments for prequalification:

1. The manufacturer has committed to continuing improvements in the quality management system particularly in the areas of clear lines of authority, identification and traceability, warehousing and clarity of work instructions and batch manufacturing records.

2. The manufacturer has committed to continuing close supervision of the lot release procedures together with ongoing communication over time to finalize any outstanding issues noted in the WHO responses to the inspection findings.
3. The manufacturer has committed to carefully monitoring when the anticipated scale up of the SD BIOLINE Ag/Ab HIV Combo test occurs, to ensure the effectiveness of the quality management system and the release of tests of consistently good quality.

Laboratory evaluation

SD BIOLINE HIV Ag/Ab Combo (Standard Diagnostics, Inc.) was evaluated by WHO in the fourth quarter of 2011 using serum/plasma specimens. From this evaluation, we drew the following conclusions:

SD BIOLINE HIV Ag/Ab Combo (Standard Diagnostics, Inc.) is an immunochromatographic assay for the detection of HIV-1/2 antibodies and HIV-1 p24 antigen in human serum/plasma and capillary/venous whole blood. A volume of 50 µL of specimen is required to perform the assay. This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory testing settings. Reading of the results is performed visually i.e. subjectively read.

In this limited evaluation on a panel of 1081 clinically-derived specimens, we found an initial sensitivity (95% CI) of 100% (99.1% - 100%) and an initial specificity (95% CI) of 98.6% (97.4% - 99.4%) compared to the reference assays. The final sensitivity (95% CI) was 100% (99.1% - 100%) and the final specificity (95% CI) was 99.1% (98.0% - 99.7%) compared to the reference assays. Lot to lot variation observed was within the acceptance range.

For eight seroconversion panels, SD BIOLINE HIV Ag/Ab Combo detected on average 0.75 earlier than the benchmark assay (Enzygnost Anti-HIV 1/2 Plus [Siemens Healthcare Diagnostics]) and on average 0.125 specimens earlier than Vironostika HIV Ag/Ab (bioMérieux) EIA.

For the mixed titer panel, SD BIOLINE HIV Ag/Ab correctly classified all specimens. For the HIV-1 p24 antigen panel, SD BIOLINE HIV Ag/Ab correctly classified all but one specimen. For the HIV culture supernatant panel, SD BIOLINE HIV Ag/Ab correctly classified all HIV-1 subtypes, the HIV-2 culture isolate was not detected.

For the 1st International Reference Panel for anti-HIV [NIBSC code 02/210], SD BIOLINE HIV Ag/Ab Combo 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], SD BIOLINE HIV Ag/Ab Combo detected to 3.125 international units. In contrast, Vironostika HIV Ag/Ab (bioMérieux) EIA detected to 12.5 international units.

In this study, 0% of the results were recorded as indeterminate. Results were interpreted independently by three technicians; the overall inter-reader variability was 0.8%. The

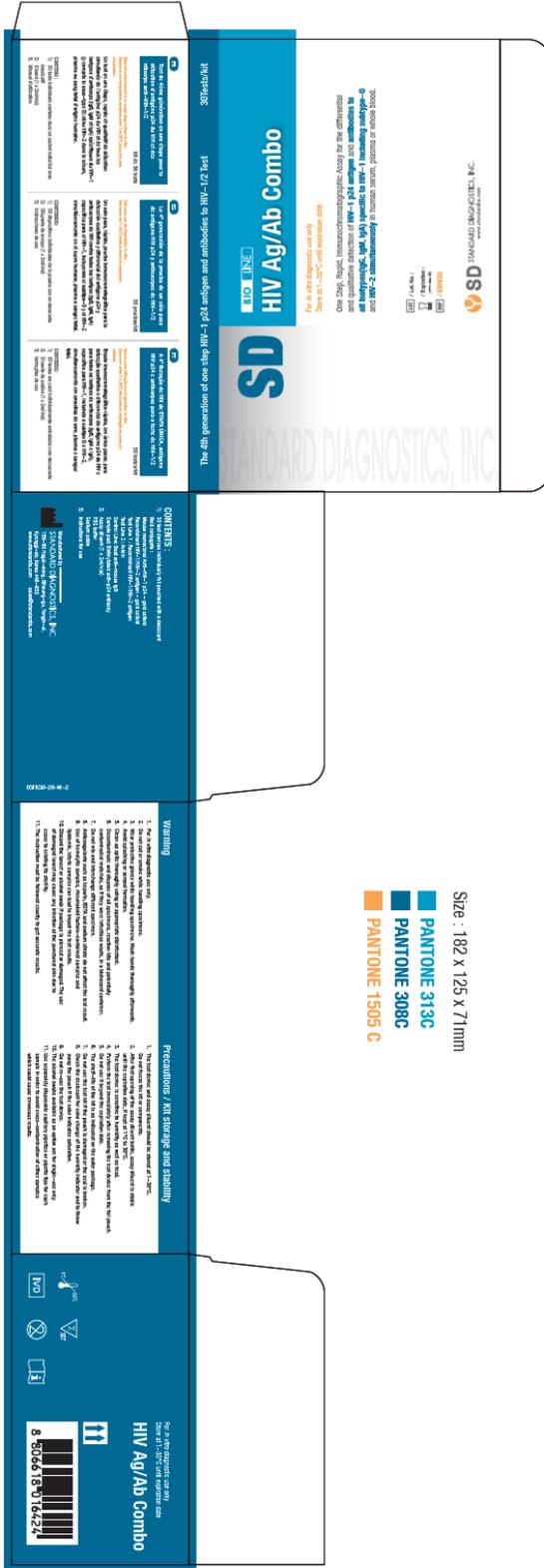
inter-reader variability for the HIV-1/2 antibody band was 0.3% %, the inter-reader variability for the HIV-1 p24 antigen band was 0.5%. The invalid rate was 0.1%

Labelling

4. Labels

5. Instructions for use

4. Labels



SD **BIO LINE**

HIV Ag/Ab Combo

For in vitro diagnostic use only. Store at 1-8°C, and use expiration date.

One step, rapid, sensitive and quantitative immunoassay for the simultaneous detection of HIV-1 p24 antigen and HIV-1 IgG antibody to HIV-1 p24 antigen and HIV-2 antibody to HIV-2 antigen in human serum, plasma or whole blood.

SD STANDARD DIAGNOSTICS, INC.
www.sd-bio.com

25 Tests Kit

The 4th generation of one step HIV-1 p24 antigen and antibodies to HIV-1/2 Test

1. Prerequisite to HIV-2 testing, detection of HIV-2 antibody is required for HIV-2 testing.

2. Prerequisite to HIV-1 testing, detection of HIV-1 p24 antigen is required for HIV-1 testing.

3. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

4. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

5. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

6. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

7. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

8. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

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11. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

12. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

13. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

14. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

15. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

16. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

17. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

18. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

19. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

20. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

21. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

22. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

23. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

24. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

25. Prerequisite to HIV-1/2 testing, detection of HIV-1 p24 antigen and HIV-2 antibody is required for HIV-1/2 testing.

Size : 182 x 125 x 71mm

- PANTONE 313C
- PANTONE 308C
- PANTONE 1505 C

CONTENTS:

- 1. 25 Tests Kit
- 2. 25 Tests Kit
- 3. 25 Tests Kit
- 4. 25 Tests Kit
- 5. 25 Tests Kit
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- 18. 25 Tests Kit
- 19. 25 Tests Kit
- 20. 25 Tests Kit
- 21. 25 Tests Kit
- 22. 25 Tests Kit
- 23. 25 Tests Kit
- 24. 25 Tests Kit
- 25. 25 Tests Kit

Warnings:

1. The kit should be used only for the intended purpose.
2. The kit should be used only for the intended purpose.
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24. The kit should be used only for the intended purpose.
25. The kit should be used only for the intended purpose.

Precautions / Kit storage and stability

1. The kit should be stored at 1-8°C.
2. The kit should be stored at 1-8°C.
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4. The kit should be stored at 1-8°C.
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24. The kit should be stored at 1-8°C.
25. The kit should be stored at 1-8°C.

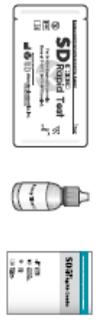
For in vitro diagnostic use only

HIV Ag/Ab Combo

8 5066 18 0164 17

SD HIV Ag/Ab Combo card test, cassette

The 4th Generation of One Step HIV antigen and antibody to HIV-1/2 Test

- 1** Now open the package and look for the following:
1. Test device individually for pouch with a desiccant.
 2. Assay diluent
 3. Instructions for use
- 
- Option**
1. 50µl capillary pipettes
 2. Lances
 3. Alcohol swabs
- 

- 2** Open the foil pouch and look for the following:
1. Seal window
 2. Sample well & Assay diluent well
- 
- 3** First, read carefully the instructions on how to use the SD BOUNE HIV Ag/Ab combo test kit.
- 4** Wash your hands with soap and water.
- 4** [Plasma or Serum specimen]
- 
- Add 50µl of specimen into the sample well (S) using a micropipette.

- 4** [Whole Blood Specimen]
- 
- Add 50µl of specimen into the sample well (S) using a micropipette.
- 5**
- 
- When the specimen is whole blood, add 1 drop of assay diluent into the sample well (S). Exactly, 1 drop should be added.
- 7**
- 
- Dispense 50µl of drawn blood into the sample well (S).
- 8**
- 
- When the specimen is whole blood, add 1 drop of assay diluent into the sample well (S). Exactly, 1 drop should be added.
- 4** I. Blood specimen (with a lance!)
- 5** Force the area to be lanced with an alcohol swab.
- 6** Pierce with a sterile lancet provided.
- 7** Use a 50µl capillary pipette provided, immerse the open end in the blood drop and then reduce the pressure to draw blood into the capillary pipette to black line.
- 8** Wait 1 minute

- II. Blood (by venipuncture), Plasma or Serum specimen**
- 4** Wait 1 minute
- 4** Interpretation
- Interpret test results in 20 minutes after adding assay diluent.
- Caution** : Do not read test results after 30 minutes. Reading too late can give false results.
- 20 min**
- 
- How to interpret test results**
- Negative**
- 
- Positive**
- HIV-1/HIV-2 antibody Positive**
- When 2 lines appear "C" "1" line
- 
- HIV-1 p24 antigen Positive**
- When 2 lines appear "C" "2" line, the infection is suggested at an early stage.
- 
- HIV-1 p24 Ag and HIV-1/HIV-2 Ab Positive**
- When 3 lines appear "C", "1" and "2" line, the infection is suggested at an early stage.
- 
- Invalid**
- No "C" line
- 