WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: STANDARD Q HIV/Syphilis Combo Test
WHO reference number: PQDx 0382-117-00

STANDARD Q HIV/Syphilis Combo Test with product code 09HIV20D, manufactured by SD Biosensor, Inc, Rest-of-World regulatory version, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 26 May 2020.

Summary of WHO prequalification assessment for STANDARD Q HIV/Syphilis Combo Test

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prequalification listing</td>
<td>26-May-2020</td>
<td>listed</td>
</tr>
<tr>
<td>Dossier assessment</td>
<td>1-May-2020</td>
<td>MR</td>
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<tr>
<td>Site inspection(s) of quality management system</td>
<td>17-19-Apr-2019</td>
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<td>Product performance evaluation</td>
<td>Quarter 4-2019</td>
<td>MR</td>
</tr>
</tbody>
</table>

MR: Meets Requirements

Intended use

According to the claim of intended use from SD Biosensor Inc, “STANDARD Q HIV/Syphilis Combo Test is a rapid chromatographic immunoassay for the qualitative detection of antibodies specific to HIV-1 including subtype O, HIV 2 and Syphilis (Treponema pallidum) in human serum, plasma or whole blood. The test is for in vitro diagnostic use and intended as an aid to early diagnosis of HIV and Syphilis infection for HIV or Syphilis infected patients, patients with signs and symptoms for HIV and Syphilis and persons at risk. It provides only an initial screening test result. More specific alternative diagnosis methods should be performed in order to obtain the confirmation of HIV Virus and Syphilis infection."

Assay description

According to the claim of assay description from SD Biosensor Inc, “STANDARD Q HIV/Syphilis Combo Test has “H1”, “H2”, “SYP” and “C” line region pre-coated with recombinant HIV-1 GP41 protein / recombinant HIV-1 subtype O GP41, recombinant HIV-2 GP36 protein, recombinant p17 Treponema pallidum protein (recombinant TPP 17 protein) and monoclonal anti-HIV-1 / monoclonal anti-syphilis respectively. The anti-HIV-1/anti-HIV-1 subtype O in patient sample interacts with the recombinant HIV-1 GP41-gold / recombinant HIV-1 subtype O GP41-gold and the anti-HIV-2 in patient sample interacts with the recombinant HIV-2 GP36-gold in the conjugation pad. The anti-syphilis in patient
sample interacts with the recombinant TPP 17 protein-gold. The complex moves along the membrane chromatographically with assay diluent and is captured by the recombinant HIV-1 and HIV-2 antigens and/or recombinant TPP 17 antigen on the each test line (H1, H2, SYP). If the antibodies against HIV 1/2 and/or syphilis are in the patient sample, visible lines are formed in the each test line. The control line should always appear if the test procedure is performed properly.”

Test kit contents

<table>
<thead>
<tr>
<th>Component</th>
<th>25 tests (product code 09HIV20D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test device (individually in a foil pouch with desiccant)</td>
<td>25</td>
</tr>
<tr>
<td>Buffer Bottle</td>
<td>1 x 4 mL</td>
</tr>
<tr>
<td>Capillary tube (20μl)</td>
<td>Pack of 25</td>
</tr>
<tr>
<td>Instructions for use</td>
<td>1</td>
</tr>
<tr>
<td>Sterile lancet</td>
<td>25</td>
</tr>
<tr>
<td>Alcohol swabs</td>
<td>25</td>
</tr>
</tbody>
</table>

Items required but not provided

- Micropipette and tip
- Blood collection tube
- PPE (Personal Protective Equipment)
- Biohazard container
- Timing device

Storage

The test kit should be stored at 2-40°C.

Shelf-life upon manufacture

24 months.

Warnings/limitations

Please refer to the instructions for use attached to this public report.
Prioritization for prequalification
Based on the established eligibility criteria, STANDARD Q HIV/Syphilis Combo Test was given priority for WHO prequalification assessment.

Dossier assessment

SD Biosensor Inc submitted a product dossier for STANDARD Q HIV/Syphilis Combo Test as per the “Instructions for compilation of a product dossier” (PQDx_018 version 3). The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

The manufacturer's responses to the nonconformities found during dossier review were accepted on 1 May 2020.

Commitment for prequalification

SD Biosensor, Inc committed to provide the interim study report and raw data for device stability studies on 24 November 2020 and the final report and raw data on the 23 March 2022.

Based on the product dossier screening and assessment findings, the product dossier for STANDARD Q HIV/Syphilis Combo Test meets WHO prequalification requirements.

Manufacturing site inspection

An inspection of SD Biosensor Inc. located at 74, Osongsaengmyeong 4-ro, Osong-eup, Heungdeok-gu, Cheongju-si, Chungcheongbuk-do, 28161, Republic of Korea was conducted from the 17th to the 19th of April 2019. At the time of considering the product application for Prequalification, the Manufacturer of the product had a well-established quality management system and manufacturing practices in place that would support the manufacture of a product of consistent quality. Routine inspections of the Manufacturing site will be conducted with copies of the WHO Public Inspection Report (WHOPIR) published on the WHO Prequalification web page as per Resolution WHA57.14 of the World Health Assembly. Note that a WHOPIR reflects the information on the most current inspection performed at a manufacturing site for in vitro diagnostic products and gives a summary of the inspection findings.

Information on the most current inspection can be found at:
https://www.who.int/diagnostics_laboratory/evaluations/PQDxSiteInspection/en/
All published WHOPIRs are with the agreement of the manufacturer.
The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on 16th of December 2019.

Based on the site inspection and corrective action plan review, the quality management system for STANDARD Q HIV/Syphilis Combo Test meets WHO prequalification requirements.

**Product performance evaluation**

STANDARD Q HIV/Syphilis Combo Test was evaluated at the Institute of Tropical Medicine, Belgium on behalf of WHO in the 4th quarter of 2019, according to protocol PQDx_150, version 4.1.

**Clinical performance evaluation**

In this limited laboratory-based evaluation of clinical performance characteristics, a panel of 400 serum/plasma specimens was used. The specimens were characterized using the following reference algorithms. For HIV: Vironostika HIV Ag/Ab (bioMérieux) and Enzygnost Anti-HIV 1/2 Plus (Siemens Healthcare Diagnostics) or Genscreen HIV-1/2 Version 2 (Bio-Rad) in parallel; followed by INNO-LIA HIV I/II Score (Fujirebio Inc.) on initially reactive specimens. For Treponema pallidum: Vitros Syphilis TPA Assay (Ortho Clinical Diagnostics), followed by SERODIA-TP.PA (Fujirebio Inc.).

<table>
<thead>
<tr>
<th>Clinical performance characteristics</th>
<th>HIV-1/2</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (N=200)</td>
<td>Initial (N=200)</td>
<td></td>
</tr>
<tr>
<td>Sensitivity %</td>
<td>100 (98.2-100)</td>
<td>95.0 (91.0-97.6)</td>
</tr>
<tr>
<td>Specificity %</td>
<td>99.0 (96.4-99.9)</td>
<td>99.5 (97.2-100)</td>
</tr>
<tr>
<td>Invalid rate %</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Inter-reader variability % (N=400)</td>
<td>3.25%*</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

*All 13 disagreements on HIV-1/2 results were on the HIV-2 line in HIV-1 positive specimens.*

Out of 200 HIV-1 positive specimens, STANDARD Q HIV/Syphilis Combo Test showed the presence of the HIV-2 line in 30 (15 %) specimens, although in most cases (n=28), the HIV-2
line was weaker than the HIV-1 line, which is interpreted as HIV-1 positive result according to the IFU of the assay.

**Analytical performance evaluation**

<table>
<thead>
<tr>
<th>Analytical performance characteristics</th>
<th>HIV-1/2</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity during seroconversion in comparison with a benchmark assay (Enzygnost Anti-HIV 1/2 Plus)</td>
<td>Of a total of 52 specimens in 8 panel, 23 were detected by the assay under evaluation; versus 21 specimens detected by the benchmark assay (Enzygnost Anti-HIV 1/2 Plus). Seroconversion sensitivity index of -0.25, therefore detection is 0.25 specimens earlier than the benchmark assay.</td>
<td>Of a total of 9 specimens in 1 panel, 5 were detected by the assay under evaluation; versus 2 specimens detected by the benchmark assay (Vitro Syphilis TPA Assay).</td>
</tr>
<tr>
<td>Analytical sensitivity on a mixed titer panels</td>
<td>All 25 specimens of panel PRB-205 (SeraCare) were correctly classified.</td>
<td>All 17 specimens of panel PSS-202 (SeraCare) were correctly classified.</td>
</tr>
<tr>
<td>Analytical sensitivity on WHO reference preparation panels</td>
<td>All 6 HIV subtypes/groups in the 1st International Reference Panel for anti-HIV (NIBSC code 02/210) were detected.</td>
<td>The 1st International Standard for human syphilitic plasma IgG (NIBSC code 05/122) was detected.</td>
</tr>
<tr>
<td>Lot to lot variation on a dilution panel</td>
<td>Lot to lot variation was within +/- 1 two-fold dilutions for all 10 dilution series.</td>
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</tr>
</tbody>
</table>

**Operational characteristics and ease of use**

This assay does not require laboratory equipment and can be performed in laboratories with limited facilities or in non-laboratory settings.
The assay was found easy to use by the operators performing the evaluation.

<table>
<thead>
<tr>
<th><strong>Key operational characteristics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of steps</strong>*</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Time to result</strong></td>
</tr>
<tr>
<td><strong>Endpoint stability (interval)</strong></td>
</tr>
<tr>
<td><strong>Internal QC</strong></td>
</tr>
</tbody>
</table>

*Definition: each action required to obtain a result (excluding specimen collection, device preparation – opening the pouch), e.g. for RDTs: add specimen, add buffer (2 steps).

Based on these results, the performance evaluation for STANDARD Q HIV/Syphilis Combo Test meets the WHO prequalification requirements.
Labelling

1. Labels
2. Instructions for use
1. Labels

1.1 Device Package
CONTENTS
1) Test device x 25
2) Capillary tube (20µl) x 25
3) Buffer bottle x 1
4) Sterile Lancet x 25
5) Alcohol swab x 25
6) Instructions for use x 1
1.2 Foil pouch
STANDARD Q HIV/Syphilis Combo

QHSC01B / CAT No.: 09HIV20D

XXXXXXXXXX
YYYY.MM.DD.
YEEE.MM.DD.
#Buffer Lot: XXXXXXXXXX
1.3 Buffer label

1.4 Inverted cup (5 μl) label
1.5 Sterile Lancet label

Disposable Sterile Lancets

LOT No.: 
MFG Date: 
EXP Date: 

INTENDED USE
To obtain a capillary blood specimen from the fingertip.

INSTRUCTIONS FOR USE
To use, twist-off the protective cap.

CAUTION
The lancet is guaranteed sterile while protective cap is sealed to the base.
Do not use if the seal has been damaged or broken.

Manufactured by
Beijing Ruicheng Medical Supplies Co., Ltd.
No. 558 Zhangzikou, Yangsong Town,
Huairou District, 101400 Beijing, China

Authorized Representative
Lotus NL B.V.
Koningin Julianaplein 10, 1e Verd,
Tel: +31645171879, +31626669008

CE 0197  STERILE R 2  i  25
1.6 Alcohol swab label

![Alcohol swab label](image-url)

Front

Back
2. Instructions for use

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.
[Kit Contents]
- Test device (individually in a foil pouch with desiccant)
- Capillary tube (20μl)
- Buffer bottle
- Sterile Lancet
- Alcohol swab
- Instructions for use

[Preparation]
1. Carefully read the instruction for using the STANDARD Q HIV/Syphilis Combo Test.
2. Check the expiry date at the back of the foil pouch. Use another lot, if expiry date has passed.
3. Open the foil pouch, and check the test device and the color indicator desiccant pack in foil pouch.

[Test Procedure]
1. Collecting of Sample
   1.1. For serum/plasma/venous whole blood specimen
       Collect the 10μl of serum/plasma or 20μl of venous whole blood specimen using a micropipette.
       ① Clean a fingertip by wiping with an alcohol swab.
       ② Dry and pierce the wiped fingertip with a sterile lancet to bleed.
       ③ Collect the 20μl of capillary whole blood to the black line of the capillary tube (20μl).

2. Adding of Sample
   2.1. For serum/plasma/venous whole blood specimen
       Add the collected specimen to the sample well of the test device.
   2.2. For capillary whole blood specimen
       Add the collected specimen to the sample well of the test device.

3. Dropping of Buffer
   Hold the buffer bottle at 90° angle to the test device without touching the specimen well to avoid contamination of the buffer.
   Add 3 drops of the buffer into the specimen well of the test device.

4. Reading Time
   Read the test results between 15 to 20 minutes after adding Buffer.

[Interpretation of Test Result]
- Negative
- HIV-1 Positive
- HIV-2 Positive
- Syphilis Positive
- HIV-1 & Syphilis Positive
- HIV-2 & Syphilis Positive
- Invalid
**SPECIMEN COLLECTION AND PREPARATION**

**[Serum]**
1. Collect whole blood by venipuncture into commercially available tubes without ANTICOAGULANT and, leave it to settle for 30 minutes for blood coagulation and then centrifuge blood to get serum specimen of supernatant.
2. If serum in the plain tube is stored at a 2-8°C, the specimen can be used for testing within 4 days after collection. For prolonged storage, it should be at below -40°C.

**Plasma**
1. Collect the venous whole blood into the commercially available anticoagulant tube such as heparin, EDTA or sodium citrate.
2. If plasma in an anti-coagulant tube is stored at a 2-8°C, the specimen can be used for testing within 4 days after collection. For prolonged storage, it should be at below -40°C.

**Whole blood**
1. Capillary whole blood
   - Capillary whole blood should be collected aseptically by fingertip.
   - Select the tip that is free from callus. Gently roll the tip of the finger to stimulate blood circulation.
   - Squeeze the end of the finger and pierce with a sterile lancet.
   - Collect the capillary whole blood into the capillary tube of the test device.
   - Place the test device on the flat surface after applying the specimen.
   - It should be room temperature prior to use.

   **CAUTION**
   - Do not use hemolyzed blood specimen.
   - Do not use hemolyzed blood specimen.

**INTERPRETATION OF TEST RESULTS**

**Negative Result**
- The presence of only **C** line indicates a negative result.

**Positive Result**
- The presence of two lines as **C** and **H1** line indicates a positive result for HIV-1.
- The presence of two lines as **C**, **H2** and **H1** line indicates a positive result for HIV-2.
- The presence of three lines as **C**, **H1** and **H2** line indicates a positive result for HIV-1 and HIV-2.
- The presence of two lines as **C** and **H2** line indicates a positive result for Syphilis.

**Invalid Result**
- The presence of three lines as **C**, **H1** and **SYP** line indicates a positive result for HIV-1 and Syphilis.

**In Case of a Positive HIV Result**
- A colored line appearing in the control line is an internal reagent and procedural control. It will appear if the test has been performed correctly and the reagent is reactive.
- Do not release the test kit to the customer. The customer's healthcare provider should be contacted and notified of the positive result.

**In Case of a Positive Syphilis Result**
- A positive result indicates that the test kit is capable of detecting the treponemal antigen or its antibodies. A positive result is confirmed by a supplemental test.
- It is recommended that patients with a positive result undergo a supplemental confirmatory test.

**LIMITATION OF TEST**

**HIV-1 & Syphilis Positive Result**
- The presence of three lines as **C**, **H1** and **H2** line indicates a positive result for HIV-1 and Syphilis.

**STANDARD Q HIV/Syphilis Combo Test**
- The STANDARD Q HIV/Syphilis Combo Test has “H1”, “H2”, “SYP” and “C” line region pre-coated with recombinant HIV-1 GP41 protein, HIV-2 recombinant GP41 protein, recombinant TPR 17 protein and monoclonal anti-HIV-1 / monoclonal anti-HIV-2 respectively. The anti-HIV-1/anti-Tp Ab detection is performed using a competition between the recombinant HIV-1 / HIV-2 and the anti-HIV-2 in patient specimen interacts with the recombinant HIV-2 GP41/gp160 in the conjugated at the anti- syphi
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