WHO Prequalification of In Vitro Diagnostics Programme
Amended PUBLIC REPORT

Product: SD BIOLINE Malaria Ag P.f/Pan and
SD BIOLINE Malaria Ag P.f/Pan POCT

PQDx Reference Number: PQDx 0030-012-01

Abstract

SD BIOLINE Malaria Ag P.f/Pan with product code 05FK60 manufactured by Standard Diagnostics, Inc., Republic of Korea, CE-mark regulatory version was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 08 July 2013. This public report was amended 22 February 2016 to include SD BIOLINE Malaria Ag P.f/Pan POCT with product code 05FK63. This public report was further amended on 2 May 2016 to reflect a change to the labelling of the cassette.

Intended use:
SD BIOLINE Malaria Ag P.f/Pan (and SD BIOLINE Malaria Ag P.f/Pan POCT) is a one step, rapid, qualitative and differential test for the detection of HRP-II (Histidine-rich protein II) specific to Plasmodium falciparum and pLDH (Plasmodium lactate dehydrogenase) pan specific to Plasmodium species in human blood specimens. The kit is intended for in vitro use and is intended for the detection of Malaria infection in human blood specimens, indicating differential diagnosis between P.f HRP-II (Plasmodium falciparum, histidine-rich protein II) and other Plasmodium species (Pan, pLDH) (P. vivax, P. malariae, P. ovale). The kit is intended for professional use, only for diagnostic purposes and reactive specimens should be confirmed by a supplemental assay such as microscopic examination of a thin blood smear.

Test principle:
SD BIOLINE Malaria Ag P.f/Pan (and SD BIOLINE Malaria Ag P.f/Pan POCT) test cassette contains a membrane strip which is pre-coated with mouse monoclonal antibodies specific to HRP-II of P. falciparum on the test line P.f region and with mouse monoclonal antibodies specific to lactate dehydrogenase of Plasmodium species (P. falciparum, P. vivax, P. malariae and P. ovale) on the test line Pan region respectively. The mixture of mouse monoclonal antibodies specific to HRP-II of P.f and mouse monoclonal antibodies specific to pLDH of pan – colloidal gold conjugate reacts with the malaria antigen in the specimen. They move along the membrane chromatographically to the test region (P.f and Pan) and form a visible line as the antibody-antigen-antibody gold particle complex. All the test lines and the control line in the result window are not visible before applying the specimen. The control line is used for procedural control and should appear when liquid is added to the test device and the test reagents are stable.
Test kit contents:

<table>
<thead>
<tr>
<th>Item</th>
<th>25T/kits (product code 05FK60)</th>
<th>1T/kit x 25 ea (product code 05FK63)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test cassettes</strong></td>
<td>25 test devices</td>
<td>25x 1 test device</td>
</tr>
<tr>
<td>individually packed in foil pouch with a desiccant</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Assay diluent</strong></td>
<td>1 x 5ml/bottle</td>
<td>25x 180µl/vial</td>
</tr>
<tr>
<td>dispensed in plastic bottle</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Specimen transfer devices</strong></td>
<td>25 units of 5µl</td>
<td>25 pouches each containing one specimen transfer device (5µl), one lancet, one alcohol swab</td>
</tr>
<tr>
<td>disposable</td>
<td>25 units</td>
<td></td>
</tr>
<tr>
<td><strong>Lancets (optional)</strong></td>
<td>25 units</td>
<td></td>
</tr>
<tr>
<td>disposable, sterile</td>
<td>25 units</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol swabs (optional)</strong></td>
<td>25 units</td>
<td></td>
</tr>
<tr>
<td>disposable</td>
<td>25 units</td>
<td></td>
</tr>
<tr>
<td><strong>Instructions for use</strong></td>
<td>1 copy</td>
<td>1 copy</td>
</tr>
<tr>
<td><strong>Summarized instructions for use</strong></td>
<td>N/A</td>
<td>25 copies</td>
</tr>
</tbody>
</table>

Storage:
The test kit should be stored at 1 – 40 °C.

Shelf-life:
24 months.

SD BIOLINE Malaria Ag P.f/Pan and SD BIOLINE Malaria Ag P.f/Pan POCT were accepted for the WHO list of prequalified in vitro diagnostics on the basis of data submitted and publicly available information.

Summary of prequalification status for the SD BIOLINE Malaria Ag P.f/Pan and SD BIOLINE Malaria Ag P.f/Pan POCT

<table>
<thead>
<tr>
<th>Initial acceptance</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PQ amended</strong></td>
<td></td>
</tr>
<tr>
<td>22 February 2016 and 2 May 2016</td>
<td>listed</td>
</tr>
<tr>
<td><strong>Status on PQ list</strong></td>
<td></td>
</tr>
<tr>
<td>08 July 2013</td>
<td>listed</td>
</tr>
<tr>
<td><strong>Dossier assessment</strong></td>
<td></td>
</tr>
<tr>
<td>01 March 2011</td>
<td>MR</td>
</tr>
<tr>
<td><strong>Inspection status</strong></td>
<td></td>
</tr>
<tr>
<td>24 July 2015</td>
<td>MR</td>
</tr>
<tr>
<td><strong>Laboratory evaluation</strong></td>
<td></td>
</tr>
<tr>
<td>Round 3 (2011) and Round 5(2014)</td>
<td>MR</td>
</tr>
</tbody>
</table>

MR: Meets Requirements
Background information

Standard Diagnostics, Inc. submitted an application for prequalification of SD BIOLINE Malaria Ag P.f/Pan. Based on the WHO product testing results from Round 5, SD BIOLINE Malaria Ag P.f/Pan was given priority for prequalification.

Product dossier assessment

Standard Diagnostics, Inc. submitted a product dossier for SD BIOLINE Malaria Ag P.f/Pan 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 Malaria Ag P.f/Pan 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 which will be reviewed at the next re-inspection:

1. the risk analysis and control summary reflecting use in resource-limited settings
2. analytical and stability studies
3. revised labels and instructions for use.

Manufacturing site inspection

A comprehensive third re-inspection\(^1\) was performed at the sites of the legal manufacture (Production: 65, Borahagal-ro, Giheung-gu, Yongin-si, Gyeonggi-do, Republic of Korea 446-930 and Warehouse: 19-22, Dongtansandan 3-gil, Dongtan-myeon, Hwaseong-si, Gyeonggi-do, Republic of Korea) in May 2015 as per Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics. (PQDx_014 v1).

The inspections were 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.

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\(^1\) Previous site inspections were carried out in September 2010, March 2012, and November 2012.
The inspections found that the manufacturer had an acceptable quality management system and manufacturing that should ensure the consistent manufacture of the above mentioned products of good quality. For the most recent inspection, the manufacturer's responses to the nonconformities found at the time of the inspection were accepted 24 July 2015.

Commitments for prequalification: N/A.

**Laboratory evaluation**

SD BIOLINE Malaria Ag P.f/Pan was submitted to Round 3 and Round 5 of WHO Product Testing Programme in 2011 and 2014\(^2\). The product was evaluated against a *Plasmodium falciparum* cultured line panel, *P. falciparum* wild type parasite panel, *P. vivax* wild type parasite panel and a mixed panel of *P. falciparum* and non- *P. falciparum* to determine specificity. Thermal stability was assessed after 2 months of storage at elevated temperature and humidity, and a descriptive ease of use assessment was recorded.

In Round 3, the following results were observed: *P. falciparum* panel detection score (92.9% at 200 parasites/µl), *P. vivax* panel detection score (97.1% at 200 parasites/µl), false-positive rates (3.5% for clean negatives, 0.5% for *P. falciparum* at 200 parasites/µl, 0% for *P. vivax* at 200 parasites/µl, 0.5% for *P. falciparum* at 2000 or 5000 parasites/µl, 0% for *P. vivax* at 2000 or 5000 parasites/µl) and invalid rate (0.3%).

In Round 5, the following results were observed: *P. falciparum* panel detection score (94.0% at 200 parasites/µl), *P. vivax* panel detection score (91.4% at 200 parasites/µl), false-positive rates (0.0% for clean negatives, 0.8% for *P. falciparum* at 200 parasites/µl, 0.7% for *P. vivax* at 200 parasites/µl, 0.5% for *P. falciparum* at 2000 or 5000 parasites/µl, 1.4% for *P. vivax* at 2000 or 5000 parasites/µl) and invalid rate (0.0%), SD BIOLINE Malaria Ag P.f/Pan meets the current laboratory evaluation requirements for prequalification.

<table>
<thead>
<tr>
<th>Summary performance characteristics</th>
<th>Panel detection score</th>
<th>False positive rate (%)</th>
<th>Invalid rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>200 parasites/µl</td>
<td>200 parasites/µl</td>
<td></td>
</tr>
<tr>
<td><strong>Pf</strong></td>
<td>92.9%</td>
<td>0.5</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Pv</strong></td>
<td>97.1%</td>
<td>0.0</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Clean negatives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pf</strong></td>
<td>0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pv</strong></td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Invalid rate (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pf</strong></td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pv</strong></td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD BIOLINE Malaria Ag P.f/Pan POCT was not evaluated.

**Change notification**

In 2015 and 2016, Standard Diagnostics, Inc., submitted two change notification related to:

1. Re-introduction of a single-use buffer vial under the product name SD BIOLINE Malaria Ag P.f/Pan. POCT.

\(^2\) The same product was also submitted to Round 3 Product Testing.
2. Changes to the labelling of the cassette (for product codes 05FK60, 05FK63).

These change notifications were assessed and the product was found to meet WHO prequalification requirements.
Labelling

1. Labels
2. Instructions for use
1. Labels

1.1 Package box for 05FK60

1.2 Foil pouch for test cassettes of 05FK60
Immunochromatographic Assay

SD Rapid Test
For in vitro diagnostic use only.
Store at 1-40°C (34°F-104°F) sealed.

Manufactured by STANDARD DIAGNOSTICS, INC.

Malaria Ag P.f/Pan
05ED15030A
Mfg : 2015.06.08
2017.06.07
FKC-F-0
1.3 Package box for 05FK63 [POCT]
1.4 Outer pouch for 05FK63 [POCT]
1.5 1-test foil pouch for test cassettes of 05FK63 [POCT]
2. Instructions for use

2.1 IFU for 05FK60
2.2 IFU for 05FK63 [POCT]
2.3 Summarized IFU for 05FK63 [POCT]
**SD 0030-012–01**

**Malaria Ag Pf/Pan (SD030)**

**ENGLISH**

**Intended Use**

The SD 0030 Malaria Ag Pf/Pan test is a one step, rapid, qualitative immunochromatographic test for detection of P. falciparum and P. vivax specific antigen in human whole blood.

**Materials provided**

- Buffer system
- Control line (C)
- Test line (T)
- Specimen cap
- Specimen dilution
- Specimen dilution (SD) solution

**Kit storage and stability**

1. The kit should be stored at a temperature between 15°C and 40°C. Do not freeze the kit unopened.
2. When stored at refrigerator, all kit components must be stored in their original package and may be stored up to 2 years from date of manufacture.
3. Do not open the kit or use the contents before the expiration date.
4. The test device is sensitive to both heat and humidity. 
5. Check the buffer solution for any visible discoloration. If visible discoloration is detected, do not use the kit.
6. Do not use the test if the cap is damaged or the test device is contaminated.
7. When transporting or storing the kit, avoid exposure to high temperature above 4°C for periods longer than 2 weeks.

**Specimen collection using a lancet**

1. The patient's hand or finger should be cleaned with alcohol.
2. Squeeze the lancet end and allow a drop of blood with a small lancet to appear.
3. With a lanced finger, carefully roll the exposure needle into the blood sample.
4. With the plunger retracted, allow the specimen to flow into the control system.

**Test procedure**

Please refer to the test manual.

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**FRANÇAIS**

**Utilisation prévue**

La test SD 0030 Malaria Ag Pf/Pan test is a one step, rapid, qualitative immunochromatographic test for detection of P. falciparum and P. vivax specific antigens in human whole blood.

**Matériel fourni**

- Réactif de test
- Tuyau de prélèvement
- Capuchon de test
- Solution de dilution de test

**Stockage et stabilité du kit**

1. Le kit doit être conservé à une température entre 15°C et 40°C.
2. Il peut rester à température ambiante jusqu'à expiration du produit à l'emballage ou dans le réfrigérateur ou au congélateur.
3. Ne pas retirer le capuchon du test avant utilisation.
4. Ne pas utiliser le kit s'il est endommagé ou si la solution de dilution est décolorée.

**Précautions**

1. Ne pas utiliser le kit s'il est endommagé ou s'il est décoloré.
2. Ne pas retirer le capuchon du test avant utilisation.
3. Ne pas retirer le capuchon du test avant utilisation.
4. Ne pas utiliser le kit s'il est endommagé ou si la solution de dilution est décolorée.

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**WHO PQx PR**

May 2016, version 3.0
Specimen collection / Prélèvement des échantillons

1. Open the sample tube and dispose of the cap in a sharps container.
2. Hold the tube horizontally and collect a drop of blood on the device.
3. Close the sample tube cap.

Test procedure / Procédure de test

1. Dispense 5 μl of dropwise blood onto the sample pad of the device.
2. Wait for 5 minutes to allow for detection of results.
3. Interpret the results according to the table below.

Interpretation / Interprétation

- **Aussi sanguin positif** (Also positive blood)
- **Aussi sanguin negatif** (Also negative blood)
- **Presence de parasites** (Presence of parasites)
- **Non infecté** (Non-infected)
- **Non infecté** (Non-infected)

Table below:

<table>
<thead>
<tr>
<th>Result</th>
<th>C Pan PF</th>
<th>C Pan PF</th>
<th>C Pan PF</th>
<th>C Pan PF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive/Potentiel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative/Négatif</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Visible</td>
<td>C Pan PF</td>
<td>C Pan PF</td>
<td>C Pan PF</td>
<td>C Pan PF</td>
</tr>
</tbody>
</table>

Note: Results must be read within 5 minutes of dispensing blood.